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Efficacy and Safety of Ultrasound-Guided Pulsed Radiofrequency Therapy of Stellate Ganglion on Refractory Painful Diabetic Peripheral Neuropathy

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Background: The best tool for the management of pain associated with distal symmetric peripheral neuropathy (DSPN) is a matter of debate. Therefore, the study aimed to explore whether ultrasound-guided pulsed radiofrequency (PRF) therapy of the stellate ganglion (SG) in type 2 diabetes mellitus (T2DM) patients with painful DSPN could decrease pain severity and the need for analgesics.

Methods: Fifty-six T2DM patients with refractory painful DSPN were enrolled in this study, who then received bilateral ultrasound-guided PRF therapy of SG. The patients completed visual analog scale (VAS), simplified McGill pain questionnaire (SF-MPQ), Toronto clinical score system (TCSS), sleep duration at night (SDN), pain disability index (PDI), Karnofsky performance status (KPS), and depression screening scale (PHQ-9). After procedures, the degree of perceived pain relief, numbness relief and chills relief of the patients, and side effects were assessed. All patients underwent evaluation after the last procedure at 1, 4, 12 and 24-week follow-up periods.

Results: The postoperative VAS, SF-MPQ, TCSS, PDI and PHQ-9 scores were significantly lower, while the KPS values higher than the preoperative ($P<0.05$). The postoperative SDN was longer than the preoperative ($P<0.05$). The degree of perceived pain relief, chills relief, and numbness relief at 4, 12, and 24 weeks were lower than that at 1 week after the procedures ($P<0.05$). The postoperative rates of administration of analgesic were lower than those of preoperative period ($P<0.05$). The significant effective rates at 1, 4, 12, and 24 weeks after the procedure were 67.86%, 42.86%, 21.43%, and 17.86% and the total effective rates were 89.29%, 71.43%, 46.43%, and 32.14%. No serious complication was observed.

Conclusion: Ultrasound-guided stellate ganglion PRF therapy can effectively relieve pain and improve the quality of life in T2DM patients with refractory painful DSPN.

Keywords: painful diabetic neuropathy, type 2 diabetes mellitus, stellate ganglion, pulsed radiofrequency

Introduction

Peripheral neuropathy is a highly prevalent and morbid condition affecting 2–7% of the population.[1] Distal symmetric peripheral neuropathy (DSPN), the subtype of peripheral neuropathy, is one of the most common complications of T2DM, accounting for approximately 75% of diabetic neuropathy.[2] DSPN most commonly presents as symmetrical pain, chills, or numbness in the distal extremities and chronic sensory loss with stocking and glove distribution.[3] Approximately 20% of patients with diabetes will experience painful DSPN, a progressive, potentially debilitating chronic neuropathic pain condition.[4] Regrettably, DSPN still remains inadequately diagnosed and treated. Available

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therapies for refractory painful DSPN are inadequate, and there is an urgent need to further explore appropriate treatments to relieve symptoms.

The stellate ganglion (SG) is a sympathetic ganglion. The sympathetic nervous system is believed to be an important mediator of pain. Blocking the stellate ganglion (SGB) can effectively improve the blood circulation of the facial and upper limb areas and regulate a disordered endocrine system.[5] SGB has been performed to treat sympathetically mediated pain conditions since the 1940s and Seymour et al reported that a patient with severe angina pectoris associated with recurrent motor aphasia was temporarily relieved of all symptoms within a few minutes after SGB.[6] Ultrasound-guided SGB, with direct visualization of the multiple vulnerable soft tissue structures compacted in a tight vascular space around the sympathetic chain,[7] is also increasingly used in clinical practice. However, due to the short duration of local anesthesia, the number of SGB treatments generally needs to be increased, which increases the chance of secondary injury. The emergence of PRF, on the other hand, compensates for all the above shortcomings.

PRF is a novel therapeutic modality of pain management that delivers short pulses of high-frequency current to nervous tissue without damaging the tissue.[8] Back in 1997, for the first time, PRF was proposed for the treatment of pain and achieved satisfactory therapeutic effect. The exact analgesic mechanism of pulsed radiofrequency is unclear, and it is currently believed that analgesia is mainly produced by neuromodulation.[9,10] Shaaban et al have also reported that SG PRF therapy can be applied to a number of different neuropathic pain syndromes, such as post-mastectomy neuropathic pain syndrome, complex regional pain syndromes, and phantom pain.[2] However, ultrasound-guided pulsed radiofrequency of SG in patients with refractory painful DSPN has not been investigated.

Therefore, this research was conducted to comprehensively explore whether ultrasound-guided pulsed radiofrequency (PRF) therapy of the stellate ganglion (SG) in type 2 diabetes mellitus (T2DM) patients with painful DSPN could decrease pain severity.

Methods

Patients and Design

This clinical study was conducted at our hospital using the medical records of 56 T2DM patients with refractory painful DSPN who underwent a 6-month follow-up period (Figure 1). The patients were enrolled after obtaining institutional review board (IRB) approval. The Institutional Ethics Committee of Shanghai Tenth People's Hospital approved the study with approval number (SHSY-IEC-4.1/21-48/01). The patients provided written informed consent before participating in the study. A previous study found that the rate of 50% pain relief in DPN patients taking medicines was about 40%.[11] It is estimated that the rate of 50% pain relief in DPN patients by our treatment is 65%. Therefore, according to the formula of sample size, 41 subjects should be recruited. Taking the loss to follow-up rate of 25%, 52 subjects must be needed.

$n=\pi_0(1-\pi_0)[(\mu_a+\mu_\beta)/\delta]^2=0.4*(1–0.4)*[(1.96+1.282)/0.25]^2=40.361\approx41$.

The inclusion criteria: clinically diagnosed with T2DM in accordance with the Chinese Diabetes Association guidelines; clinically diagnosed with DSPN by motor, sensory, and reflex functions; symptomatic despite conservative therapy for a minimum of 24 weeks; administered pregabalin or gabapentin with or without other class of analgesic medications at an adequate dose for at least 30 days; older than 18 years and younger than 75 years; capable of subjective evaluation, reading and understanding questionnaires; willing and able to provide informed consent.

Patients were excluded by the following conditions: patients diagnosed with lower limb mononeuropathy or lower limb amputation because of diabetes or had large (≥3 cm) or gangrenous ulcers (or both) of the lower limbs; hemoglobin A1c (HbA1c) more than 10%, or fluctuation of HbA1c by more than 2% during the 24-week follow-up period; body mass index > 45 kg/m^2; with a medical condition or pain in another part of the body, such as primary headache, fibromyalgia, post-herpetic neuralgia, osteoarthritis, peripheral vascular disease, or small vessel disease; a current diagnosis of progressive neurological diseases such as multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, rapidly progressive arachnoiditis, brain or spinal cord tumor, central deafferentation syndrome, complex regional pain syndrome, acute herniating disc, severe spinal stenosis, and brachial plexus injury; significant spinal stenosis or lumbar disc herniation, objective evidence of epidural scarring, and any sign or symptom of myelopathy as

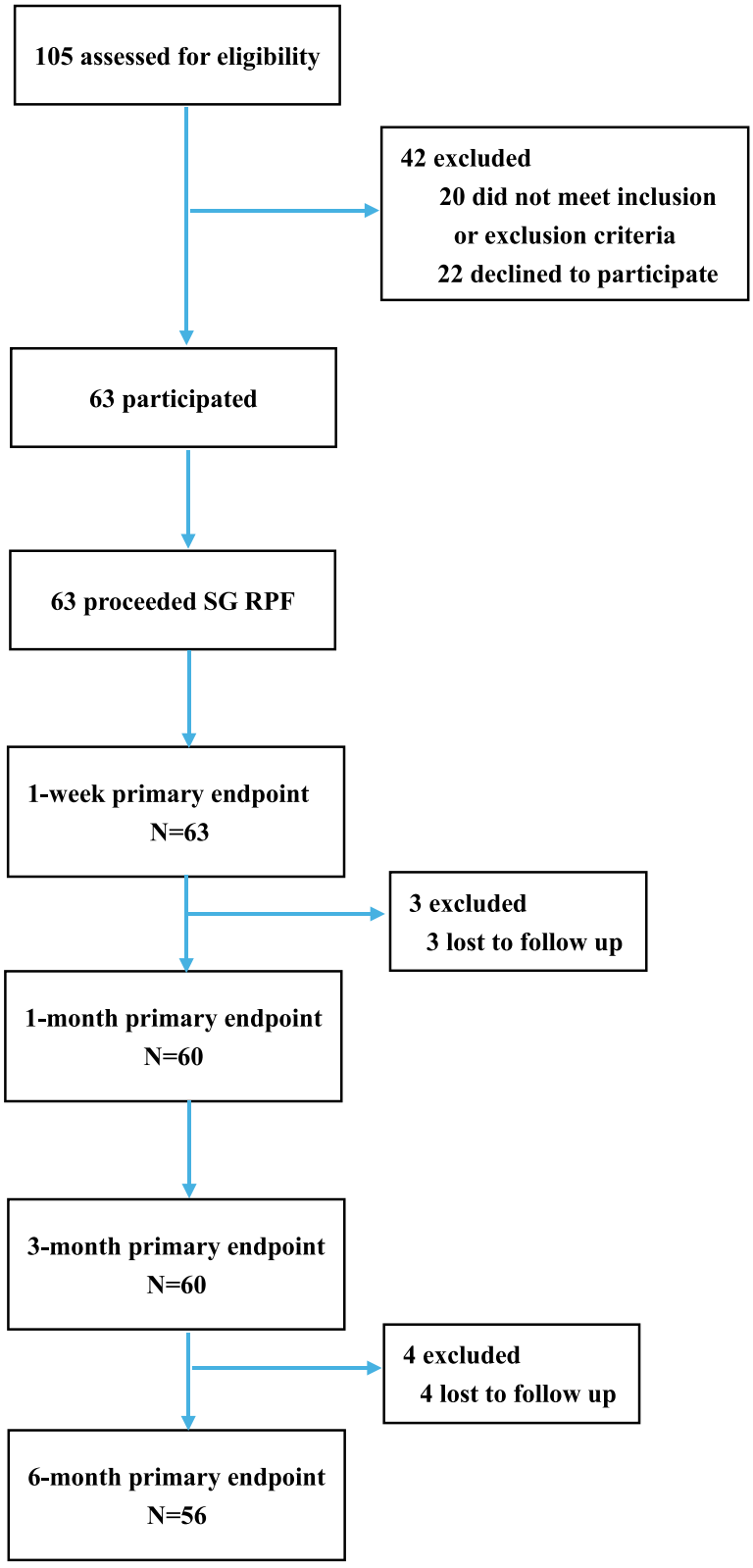

Figure 1 Disposition of all patients screened for study participation.

determined by the investigator based on magnetic resonance imaging conducted within the past 12 months; benefiting from neuroregulatory procedures to treat lower-limb pain (patients should be enrolled for at least 30 days from the last benefit); have either a metastatic malignant neoplasm or untreated local malignant neoplasm; have a local infection at the anticipated surgical entry site or an active systemic infection; participating in another clinical study concurrently; disruptive psychological or psychiatric disorder.

Block Technique

Each patient was placed in the supine position with the neck extended, the head rotated slightly to the opposite side, and the skin was infiltrated with lidocaine. First, we confirmed the anterior tubercle of the transverse process of C6 and the longus colli muscle using a 5 to 12 MHz linear ultrasound transducer (5–12 MHz, EDGE-II; SonoSite, USA) with a short axial view (Figure 2). Next, the ultrasound probe was moved caudally and slowly to trace the longus colli muscle, looking for a structure of continuously strongly echoing lumpinesss on the surface of the longus colli muscle between C7 to T1 segment levels, the image of SG using ultrasound guidance, Figure 3A), A color Doppler image was used to check the vessels through the needle course. After skin infiltration, a 22-gauge 10-cm-long PRF needle with a 5-mm active tip was implanted from the lateral side of the probe. The needle tip was placed in the structure of continuously strongly echoing lumpinesss on the surface of the longus colli muscle, under the prevertebral fascia (Figure 3B); sensory and motor stimulations were applied at 50 and 2 hz, and the patient was checked for paraesthesia to exclude needle misposition. Subsequently, PRF therapy was applied for 900

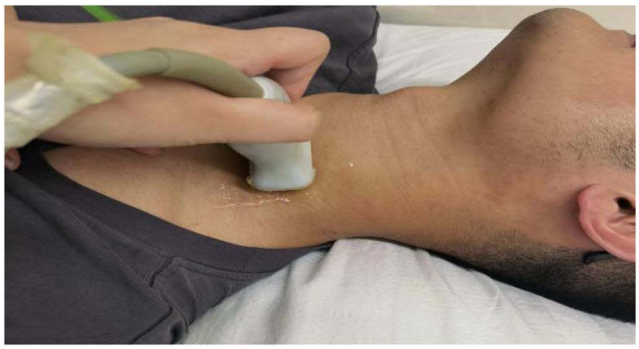

Figure 2 Treatment position of ultrasound-guided pulsed radiofrequency therapy of stellate ganglion.

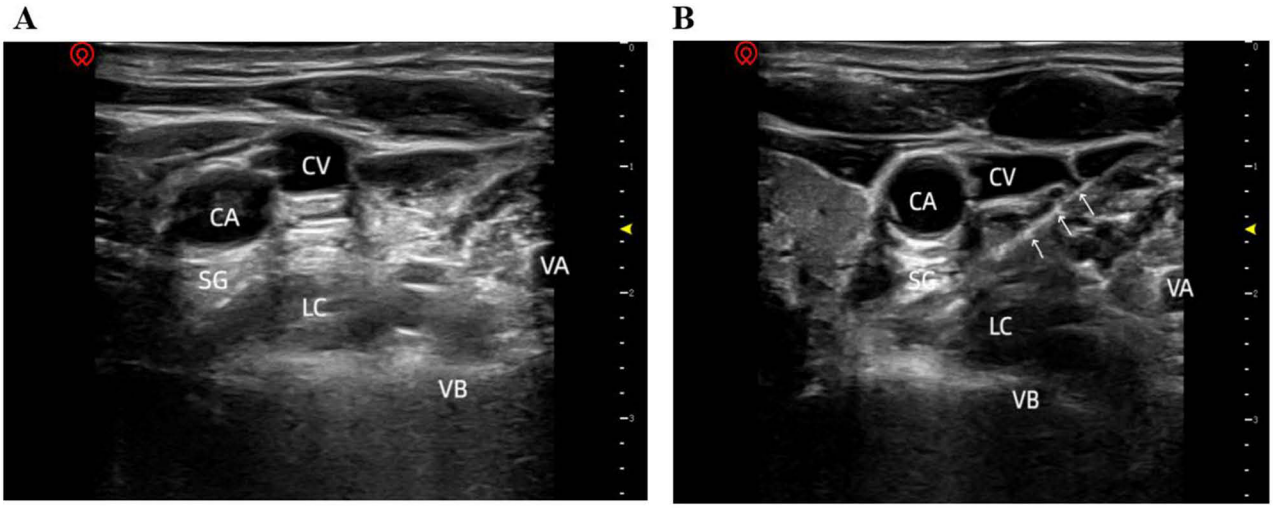

Figure 3 Ultrasound guided image of SG. The structure of continuously strongly echoing lumpiness on the surface of the longus cervicalis muscle between C7 to T1 levels (**A**). Ultrasound image of needle tip insertion site was placed in the structure of continuously strongly echoing lumpiness, on the surface of longus colli muscle, under the prevertebral fascia. White arrow indicates where needle is located (**B**).
Abbreviations: SG, stellate ganglion; VB, vertebral body of C7; CA, carotid artery; CV, carotid vein; LC, longus colli muscle; VA, vertebral artery.

s at 45°C, with a pulse width of 20 m/sec and voltage of 70 v. Lastly, after PRF therapy, 2 mL of 1% lidocaine was injected through the needle, pulled out the radio frequency needle and then terminated the procedure. All measurements were performed by an experienced pain specialist using the same ultrasound instrument. All patients underwent bilateral ultrasound-guided SG PRF therapy on both sides, with one day in between.

Drug Administration

Medications such as pregabalin, gabapentin, or non-steroidal anti-inflammatory drugs (NSAIDs) were administered orally if the pain was severe. The dosage was increased or decreased according to the changes in pain severity.

Questionnaires

Eligible patients completed a series of questionnaires (Table 1) and their sleep conditions at pre-op and again at 1, 4, 12, and 24 weeks after the procedure. The administration of medications (NSAIDs, pregabalin, or gabapentin), subjective sensation (perceived pain relief (%), numbness relief (%), and chills relief (%)) were assessed. Adverse events including hoarseness, dysphagia, and foreign body sensation in the throat, upper limb weakness, hematoma formation, local anesthetic intoxication, general spinal anesthesia, epidural block, pneumothorax, local infection, brachial plexus nerve damage, permanent Horner's disease, and other adverse reactions and complications were assessed at the postoperative follow-up. Effective rates were assessed at 6 months. Significant effective rate (%) = [(number of pain relief ≥50%)/total number] × 100%, and total effective rate (%) = [(number of pain relief ≥25%)/total number] × 100% were used to assess the therapy. The primary outcome was self-reported pain score and DPN-related neurological health-related quality of life, which were separately measured using the visual analog scale (VAS),[12] simplified McGill pain questionnaire (SF-MPQ),[13] Toronto clinical score system (TCSS),[14] pain disability index (PDI),[15] Karnofsky performance status (KPS),[16] the patient health questionnaire (PHQ)-9[17] and generalized anxiety disorder questionnaire (GAD)-7.[18] The secondary outcome was the use of medications.

Data Analysis

One-way ANOVA test was used to compare values of VAS, SF-MPQ, TCSS, SDN, KPS, PDI, PHQ-9, GAD-7, and subjective sensation for all time points among the patients and values were expressed as mean ± standard deviation ($\bar{x} \pm SD$). Categorical variables were presented as proportions and analyzed by using the chi-square test. SPSS version 18.0 (SPSS Inc., Chicago, IL) software was used to statistically analyze all data. $P<0.05$ was considered to be statistically significant.

Results

One hundred and five participants were recruited for this study, among whom, 20 participants did not meet the inclusion criteria, and 22 participants declined to participate in the study. Seven participants failed to follow up (three were lost at

Table 1 A Series of Questionnaires

Outcomes	Variables	Reference
VAS	0–10	[11]
SF-MPQ	0–45	[12]
TCSS	0–19	[13]
PDI	0–70	[14]
KPS	0–100	[15]
PHQ-9	0–27	[16]
GAD-7	0–21	[17]

Abbreviations: VAS, visual analog scale; SF-MPQ, simplified McGill pain questionnaire; TCSS, Toronto clinical score system; PDI, pain disability index; KPS, Karnofsky performance status; (PHQ)-9, patient health questionnaire-9; (GAD)-7, generalized anxiety disorder questionnaire-7.

1-month and four were lost at 6-month follow-up). Therefore, in the final analysis, 56 participants were included (29 men and 27 women; median age, 54±11.7 years; 30–74 years) (Figure 1).

Pain Score Assessment

The VAS values at post-op of 1 (2.00±1.55), 4 (3.41±2.06), 12 (3.93±2.16), and 24 weeks (4.39±2.18) usre lower than the preoperative VAS value (5.28±1.91), (P<0.05) (Table 2). The SF-MPQ scores at post-op of 1 (5.50 ± 5.06), 4 (9.29 ± 6.91), 12 (11.54 ± 8.03), and 24 weeks (12.66 ± 8.99) were lower than the preoperative SF-MPQ score (14.88±8.91), (P<0.05) (Table 2).

DPN-Related Neurological Assessment

The TCSS values at 1 (7.21±4.09), 4 (8.21±4.19), and 12 weeks (9.29±4.64) po-op were lower than the preoperative TCSS values (10.14±4.59) (P<0.05). No significant difference was observed between preoperative and postoperative 24 weeks' TCSS values (9.79±4.89) (P>0.05) (Table 2).

Health-Related Quality of Life Evaluation

As shown in the Table 2, the KPS values at 1 (86.43±8.26), 4 (86.07±7.86), 12 (86.07±7.86), and 24 weeks (85.36±7.93) post-op were significantly higher than the preoperative KPS value (82.07±9.78) (P<0.05). The PDI scores at 1 (11.11 ±9.60), 4 (12.57±9.48), and 12 weeks (14.04±9.95) post-op were lower than the preoperative PDI score (16.69±11.47), (P<0.05), while the postoperative 24weeks' PDI score (15.68±10.13) had no significant difference compared to preoperative PDI value (P>0.05). The SDN at 1 (7.04±1.47), 4 (7.34±2.01), 12 (7.38±1.98), and 24 weeks (7.36±1.68) post-op were longer than the preoperative SDN (6.59±1.72) ((P<0.05). The PHQ-9 scores at 1 (4.61±4.40), 4 (4.54 ±4.57), and 12 weeks (4.57±4.57) were lower than the preoperative PHQ-9 score (5.86±5.53) (P<0.05), while the postoperative 24weeks' PHQ-9 score (4.71±4.29) had no significant difference compared to preoperative PHQ-9 value (P>0.05). No significant difference was observed in the GAD-7 scores between the preoperative and postoperative periods (P>0.05).

Subjective Sensation Assessments

The degrees of perceived pain relief, chills relief, and numbness relief at post-op of 4, 12 and 24 weeks were lower than that at 1 week post-op (P<0.05) (Table 3).

Medication Usage

Rates of oral administration of anticonvulsants at 12 weeks (67.86%) and 24 weeks (75.00%) post-op were significantly lower than the preoperative rate. Additionally, the rates of oral administration of NSAIDs at 1 (46.43%), 4 (78.57%), 12 (67.86%) and 24 weeks (67.86%) post-op were lower than the preoperative rate (Table 4).

Table 2 Changes in Pain Relief, Neurological Assessment and Quality of Life

Time	VAS	SF-MPQ	TCSS	SDN	KPS	PDI	PHQ-9	GAD-7
Pre-op	5.28±1.91	14.88±8.91	10.14±4.59	6.59±1.72	82.07±9.78	16.69±11.47	5.86±5.53	2.72±4.22
1w post-op	2.00±1.55*	5.50±5.06*	7.21±4.09*	7.04±1.47*	86.43±8.26*	11.11±9.60*	4.61±4.40*	1.86±3.35
4w post-op	3.41±2.06*	9.29±6.91*	8.21±4.19*	7.34±2.01*	86.07±7.86*	12.57±9.48*	4.54±4.57*	2.25±3.6
12w postop	3.93±2.16*	11.54±8.03*	9.29±4.64*	7.38±1.98*	86.07±7.86*	14.04±9.95*	4.57±4.57*	2.39±3.61
24w postop	4.39±2.18*	12.66±8.99*	9.79±4.89	7.36±1.68*	85.36±7.93*	15.68±10.13	4.71±4.29	2.68±3.63
F	30.087	19.040	14.299	3.960	6.993	8.736	3.641	2.935
P	<0.001	<0.001	<0.001	0.005	<0.001	<0.001	0.008	0.065

Notes: All data values are means ± SD;* P < 0.05 compared to pre-operation.
Abbreviations: VAS, visual analog scale; SF-MPQ,simplified McGill score; TCSS, Toronto Clinical Score System; PDI,Pain Disability Index; KPS, Karnofsky score; SDN, sleep duration at night; PHQ-9,Patient Health Questionnaire-9; GAD-7,Generalized Anxiety Disorder Questionnaire-7;op, operation.

Table 3 Changes in Subjective Sensation of Patients

Time	Perceived pain relief (%)	Perceived chills relief (%)	Perceived numbness relief (%)
1w post-op	63.57±25.09	59.09±39.12	48.08±30.27
4w post-op	42.86±28.27*	37.27±36.54*	30.00±28.84*
12w post-op	24.11±30.52*	23.18±33.86*	11.54±23.78*
24w post-op	14.82±26.79*	15.91±32.90*	6.15±17.45*
F	58.770	19.305	46.136
P	<0.001	<0.001	<0.001

Notes: All data values are means ± SD; *P < 0.05 compared to 1w post-op.
Abbreviations: op, operation.

Table 4 Changes in Medication Usage

Time	Anticonvulsants	NASIDS
Pre-op	56(100%)	56(100%)
1w post-op	56(100%)	26*(46.43%)
4w post-op	56(100%)	44*(78.57%)
12w post-op	38*(67.86%)	38*(67.86%)
24w post-op	42*(75.00%)	38*(67.86%)
χ^2	21.636	22.690
P	<0.001	<0.001

Notes: Categorical variables were analyzed by chi-square test and expressed as count (percentage); *P < 0.05 compared to pre-op.
Abbreviations: op, operation.

Table 5 Changes in Effective Rate

Time	Significant Effective Rate	Total Effective Rate
1w post-op	38 (67.86%)	50 (89.29%)
4w post-op	24 (42.86%)	40 (71.43%)
12w post-op	12 (21.43%)	26 (46.43%)
24w post-op	10 (17.86%)	18 (32.14%)

Effective Rate

The significant effective and total effective rates showed a decreasing trend at all follow-up periods postoperatively. The significant effective rates were 67.86%, 42.86%, 21.43%, and 17.86%, respectively, at post-op of 1, 4, 12 and 24 weeks. The total efficacy rates were 89.29%, 71.43%, 46.43% and 32.14, respectively, at post-op of 1, 4, 12 and 24 weeks (Table 5).

Adverse Events Assessments

Among the 56 patients included in the final analysis, 20 had hoarseness, and four had transient upper limb numbness. No serious complications, including hematoma formation, local anesthetic intoxication, general spinal anesthesia, epidural block, pneumothorax, infection, nerve damage, or permanent Horner's disease was observed.

Discussion

This was the first study using PRF therapy of SG in T2DM patients with refractory painful DSPN, which showed that the significant and total effective rates at 1-week post-procedure were 67.86% and 89.29%, and as time went on, the significant and total effective rates at 24 weeks post-procedure were 17.86% and 32.14%. These findings suggested that

the clinical effect of ultrasound-guided SG PRF therapy was time dependent. DSPN is associated with marked impairment in quality of life partly due to excruciating neuropathic pain at the ends of the limbs, leading to a huge economic burden for diabetes care.[4,19] Regrettably, the mechanism of diabetic neuropathic pain is complex, and there is a lack of effective treatment. Therefore, it is very important to find more effective treatment methods for DSPN. At present, lifestyle modification and symptomatic treatment of neuropathic pain are often recommended in the treatment guidelines for DSPN,[20] indicating that the treatment is worth promoting.

SGB is a frequently used technique for treating chronic pain,[21] especially for neuropathic pain and reflex sympathetic dystrophy.[22] The treatment of SGB for recalcitrant pain could also be an effective therapy for small fiber neuropathy.[23] The procedure involves injection of local anesthetic in and around the stellate ganglion to temporarily block its function. PRF is a common technique of neuromodulation that has been shown to be effective in regulating neurological function.[9] The RF generator intermittently emits impulse current that is conducted to the needle tip and acts as analgesia near neural tissue through field effects caused by rapid voltage fluctuations. At the same time, the electrode tip temperature was maintained at 42°C without disrupting motor nerve function. The mild thermal energy of PRF therapy did not cause nerve damage and would not produce long-term clinical effects,[24] Moor et al performs SG pulsed radiofrequency to treat cluster headaches (n=2) and shows that 50%, 22%, and 28% have complete, marked/partial, and no improvement, respectively; through 12 months of follow-up, these reduced to 28%, 37%, and 37%, respectively.[25]

The analgesic mechanism of PRF is unclear, and it is currently believed that the analgesia is produced by neuromodulation.[9] Recent studies have shown that PRF results in the induction of *c-Fos* expression and changes in the efficacy of synaptic transmission, as well as reduce neuroinflammation and nerve damage.[26,27] The first case series of the stellate ganglion as an interventional site was conducted in 1991, the authors reported a new technique, PRF, for endoscopic denervation in a mongrel canine model and demonstrates the safety and reliability of PRF.[28] Subsequent case studies involving the anterior ethmoidal nerve,[29] infraorbital nerve,[30] mental nerve,[31] and caudal epidural[32] also suggests satisfactory pain relief that persisted for 6 months. SG pulsed radiofrequency has proved to get long-term pain relief in various neuropathic pain syndromes (post-mastectomy neuropathic pain syndrome, complex regional pain syndromes, and phantom pain),[2] the exact analgesic mechanism is yet to be known, however, the safety and efficacy of SGB treatment have been demonstrated. Yuanyuan Ding et al have reported that SG pulsed radiofrequency treatment of facial and upper limb PHN is safe and effective and improves the quality of life of the patients. They also proved that SG pulsed radiofrequency superior to SGB,[8] it may be due to the gradual metabolism of local anesthetic drugs over time, however. PRF acts primarily through neuromodulation. The effect of neuromodulation is slow, but it can be maintained for an extended period. In this study, the use of SG pulsed radiofrequency in patients with Painful DSPN significantly decreased the VAS scores, SF-MPQ scores, and TCSS indices during the first week after treatment, and the difference was significant compared with preoperative values, and the duration of the clinical maintenance effect (pain relief) exceeds 24 weeks. Although there is no single, standardized scale specifically designed to quantify small fiber neuropathy, these scales could be used to assess painful diabetic peripheral neuropathy.[33]

Patients with DSPN not only have physical pain but also have psychological problems caused by affliction and long-term treatment.[3] Alino et al have found that SG intervention can effectively relieve symptoms in patients with anxiety disorders, psychological conditions improved in PTSD patients after a period of SBG treatment.[34] The results also revealed that relevant indicators of health-related quality of life, including SDN, KPS, PDI, and PHQ-9, improved to varying degrees after the treatment with SG pulsed radiofrequency.

SG neurons are surrounded by peripheral satellite glial cells (SGCs), and SGCs are an important component of the nociceptive signaling pathway.[35,36] Reinauer et al have reported that SGB can improve the neurotrophic status, blocking the vicious cycle of pain.[37] At the same time, it can enhance the defense function and prevent nerve damage.[38] Kim et al performed SG pulsed radiofrequency treatment under ultrasound guidance in patients with CRPS, 91.7% of patients experienced at least moderate improvement (30% self-described degree of benefit), and the mean hand temperature rose by 1.39 ± 0.96°C after the procedure.[39] Therefore, it was hypothesized that SG pulsed radiofrequency therapy could alleviate a series of neuropathy-associated symptoms. In the study, patients' subjective sensations were observed and recorded, including the degree of perceived pain relief (%), numbness relief (%), and chills relief (%). As a result, the degree of perceived pain relief, chills relief, and numbness relief improved after the procedures. It may suggest that

ultrasound-guided SG pulsed radiofrequency therapy can ameliorate pain and other symptoms including chills and numbness.

The study is significant because this is the first time to apply SG pulsed radiofrequency therapy to the treatment of patients with painful DSPN, providing a new treatment for DSPN. However, there are some limitations. First, this experimental study lacks a blank control group, and a simple longitudinal study lacks some reliability, A randomized controlled trial is needed to verify this hypothesis. Second, the sample size is small, more multi-center studies will be required to strengthen the findings of this study. Lastly, further study including more objective measures will be required to validate these observations.

Conclusions

In conclusion, this findings suggest that the SG pulsed radiofrequency method is a safe and effective modality to alleviate painful DSPN. It may be the best available treatment option for T2DM with painful DSPN due to excellent clinical effect and without serious complications.

Institutional Review Board Statement

This study was approved by the Institution Review Board (The Institutional Ethics Committee of Shanghai Tenth People's Hospital, SHSY-IEC-4.1/21-48/01) and registered at the China Clinical Trial Registry Center, registration number ChiCTR2000035544 in accordance with the ethical guidelines of the Declaration of Helsinki.

Informed Consent Statement

Written informed consent was obtained from the patients or relatives of patients. All methods were performed in accordance with the relevant guidelines and regulations.

Abbreviations

DSPN, Distal symmetric peripheral neuropathy; PRF, Pulsed radiofrequency; SG, Stellate ganglion; SGB, Stellate ganglion block; SF-MPQ, Simplified McGill pain questionnaire; T2DM, Type 2 diabetes mellitus; VAS, Visual analog scale; TCSS, Toronto clinical score system; SDN, Sleep duration at night; PDI, Pain disability index; KPS, Karnofsky performance status; IRB, Institutional review board; HbA1c, Hemoglobin A1c; (PHQ)-9, Patient health questionnaire-9; SGCs, Satellite glial cells; op operation.

Data Sharing Statement

The data involved in this study are available from the corresponding author on reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have declared that no conflict of interest exists. This paper has been uploaded to Research Square as a preprint: https://doi.org/10.21203/rs.3.rs-3128530/v1.

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