Pain Ther (2022) 11:1011–1023
https://doi.org/10.1007/s40122-022-00401-0

ORIGINAL RESEARCH

Long-Term Follow-Up Safety and Effectiveness of CT-Guided Radiofrequency Thermocoagulation of Sphenopalatine Ganglion in Refractory Headache Treatment

Bingyue Xin · Keyue Xie · Ge Luo · Ming Yao

Received: April 20, 2022 / Accepted: May 26, 2022 / Published online: July 6, 2022

ABSTRACT

Objective: The purpose of this study was to evaluate the effectiveness and safety of computed tomography (CT)-guided radiofrequency thermocoagulation (RFTA) of the sphenopalatine ganglion (SPG) for patients with refractory headache.

Methods: A total of 14 patients with refractory migraine and 10 patients with cluster headache (CH) who underwent CT-guided SPG RF between May 2019 and August 2021 at the Jiaxing First Hospital, located in Jiaxing City, Zhejiang Province, China, were included and analyzed in this retrospective cohort study. Pain score, sleep quality scores, and treatment effects were observed before operation as well as 1 day and 1, 3, 6, 12, and 24 months after surgery. Also, the incidence of facial numbness at different timepoints after operation was evaluated.

Results: The frequency and duration of attacks decreased after treatment in patients with migraine, and the shortening of the cluster period and the prolongation of the remission period after treatment in patients with CH indicated that the treatment was effective. The numeric rating scale (NRS) ranged from 0 to 10, where 0 meant no pain and 10 meant the worst imaginable pain. The NRS of patients at 1 day and 1, 3, 6, 12, and 24 months after surgery was significantly lower than before operation ($P < 0.05$). The treatment of patients with migraine and CH was effective. The overall incidence of numbness in patients with migraine and the total incidence of numbness in patients with CH was recorded. The total incidence of numbness decreased gradually, but no significant difference was detected in the incidence of numbness between the two groups ($P > 0.05$). No serious adverse reactions, such as orthostatic hypertension, intracranial infection, and visual disturbance, occurred in the patients after operation.

Bingyue Xin and Keyue Xie contributed equally to this work.

B. Xin · M. Yao (✉)
The Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University/The Second School of Medicine, Wenzhou Medical University, No. 109 West Xueyuan Road, Wenzhou City, Zhejiang, China
e-mail: jxyaoming666@163.com

K. Xie
The Second Clinical Medical College, Zhejiang Chinese Medicine University, No. 548 Binwen Road, Hangzhou City, Zhejiang, China

B. Xin · K. Xie · G. Luo · M. Yao
Department of Anesthesiology and Pain Research Center, The First Hospital of Jiaxing or The Affiliated Hospital of Jiaxing University, No. 1882 South Zhonghuan Road, Jiaxing City, Zhejiang, China
B. Xin
e-mail: 15836016192@163.comK. Xie
e-mail: ballbe@163.comG. Luo
e-mail: luoge994849096@163.com

Conclusion: CT-guided RFTA of the SPG significantly relieves headache symptoms in patients with refractory migraine and CH. It has the advantages of rapid onset, long duration, and a safe and reliable treatment process, making it worthy of clinical application.

Keywords: Migraine; Cluster headache; Radiofrequency thermocoagulation; CT guidance; Sphenopalatine ganglion

Key Summary Points

Why carry out this study?

The current treatment strategy is not optimal owing to insufficient efficacy and severe side effects for migraine and CH.

New treatment modalities are essential to fulfill the needs of patients with migraine and CHs, especially those suffering from severe and frequent headaches.

What was learned from the study?

CT-guided RFTA of the SPG significantly relieves headache symptoms in patients with refractory migraine and CH.

It has the advantages of rapid onset, long duration, and a safe and reliable treatment process, making it worthy of clinical application.

INTRODUCTION

Migraine is a primary headache syndrome that affects approximately 12% of the US population each year [1] and is a common chronic disabling neurovascular disorder characterized by severe headaches, autonomic nervous system dysfunction, and, in some patients, aura involving neurological symptoms [2]. Chronic migraine is defined as headaches of at least 15 days per month lasting at least 3 months, with migraine features on at least 8 days per month, with annual prevalence estimates ranging from 1% to 3%, often placing a heavy burden on patients and society. It is rated as one of the most serious disabling diseases by the World Health Organization and is also a common chronic disabling neurovascular disease and may be associated with persistent or progressive brain abnormalities [3]. On the other hand, cluster headache (CH) is a primary disorder characterized by severe headache on one side of the head and cranial autonomic symptoms [4]. If a severe CH episode is left untreated, symptoms may persist for weeks to months and may even trigger suicidal ideation [5]. Thus, significant symptoms caused by CH have become a public health concern and a personal burden for many people [6]. These individuals can be rescued by medication during the acute phase of the attack or by prophylactic medication; however, the current treatment strategy is not optimal owing to insufficient efficacy and severe side effects. Head and facial pain is a common condition but often difficult to cure completely. Since conventional treatment is medication-based, it might fail to provide satisfactory relief to the patients. One study [7] reported placebo response rates (for example, cessation of headache attacks) of 7–43% in previous trials involving patients with migraine and CH. At the same time, additional empirical studies are required to demonstrate the effectiveness and safety of medication compared with a placebo. Therefore, new treatment modalities are essential to fulfill the needs of patients with migraine and CHs, especially those suffering from severe and frequent headaches. Recent neuromodulation techniques provide a novel option. Because of its manageable risk profile, some studies have suggested the application of neuromodulation techniques before initiating anesthesia or invasive permanent surgery.

There is no worldwide consensus on the definition of refractory headache, and criteria vary across the literature. In 2008, the Refractory Headache Special Interest Group (RHSIS) of the American Headache Society (AHS) published a definition of refractory migraine that requires failure of two categories of prophylactic therapy, in addition to the patient needing to fail in three categories of acute therapy [8]. The definition of medication-refractory headache

was proposed by Silberstein et al. in 2010, and in acute headache treatment, headache refractory was defined as ineffective to standard acute therapy, a contraindication to acute therapy, or intolerance to selected treatments. In prophylactic headache treatment, refractory was defined as nonresponse to standard prophylactic therapy or contraindication/intolerance [9]. In the literature, the criteria for determining the duration of treatment required for failure vary. The duration of adequate trials varies from study to study. In 2019, D'Antona et al. [10] proposed that the definition of nonresponse to medication is less than 50% reduction in frequency and/or severity of migraine days per month, the occurrence of intolerable side effects, or contraindications to use.

The sphenopalatine ganglion (SPG) is located in the pterygopalatine fossa (PPF) that harbors three ganglia. The sensory root originates from the maxillary branch of the trigeminal nerve, the parasympathetic root from the facial nerve, and the sympathetic root consists of fibers originating from the internal carotid plexus and the deep petrosal nerve. The fibers emanating from the SPG are the postganglionic fibers of the parasympathetic nerve and the sensory and sympathetic fibers passing from it, forming the branches of the orbital, posterior superior nasal, palatine, and pharyngeal nerves. These branches are distributed in the mucosa of the orbit, lacrimal gland, nasal cavity, pterygoid sinus, maxillary sinus, oral palate, upper gingiva, and pharynx [11]. Several neural structures (parasympathetic, sympathetic, and trigeminal sensory) were compressed in a small area of the PPF. SPG or pterygopalatine ganglion is the core of autonomic fibers (the site of origin of postganglionic parasympathetic fibers) and the transit point for sympathetic fibers crossing afferent nerve pathways from the neck and the head and may play a key role in the development of migraine. SPG has been hypothesized to be associated with facial pain and headache for over a century because of its proximity to several critical neuroanatomical structures in pain perception. Although the mechanism by which SPG produces pain is unclear, studies have shown that SPG radiofrequency (RF) is effective in both migraine and CH [12, 13]. Since the treatment targets, RF parameters, and efficacy evaluation indexes of SPG radiofrequency in different studies are varied, they do not have the same effect on efficacy. Radiofrequency thermocoagulation (RFTA), also known as RF neurotomy, is a method of destroying painful nerves with heat from 70–90 °C. RFTA devices use high frequencies (range 300–500 kHz) to generate charged molecular oscillations through the friction of ions and radio waves. In RFTA, the exposed segment of the RF needle generates an electric field of 5–15 mm, which ultimately increases the temperature of the affected tissue. This temperature can lead to local tissue damage and loss of myelinated fibers. When the needle tip is heated to 80 °C for 60–90 s, it produces an affected area of 8–10 mm [14]. RFTA effectively relieves pain from neuropathy at the corresponding RF target; however, it can cause patients to experience varying degrees of sensory dullness in the in the palate, maxilla, or posterior pharynx or cheek numbness. This phenomenon could be attributed to the sensory roots in the SPG from the pterygopalatine branch of the maxillary nerve, which might be partially and reversibly damaged. However, this pain relief at the cost of numbness is acceptable with respect to patient satisfaction; the numbness would improve gradually.

The present study aimed to evaluate the immediate and long-term clinical effectiveness and safety of computed tomography (CT)-guided RFTA of the SPG in the treatment of refractory migraine and CH.

METHODS

This study was approved by the ethics committee of the First Affiliated Hospital of Jiaxing University, located in Jiaxing City, Zhejiang Province, China (LS2021-XJS-142). The study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments, as well as the International Association for the Study of Pain (IASP) guidelines for pain research in animals and humans. All data were obtained from medical records and the follow-up database established by our

institution, which were anonymized, and therefore informed consent was waived with the approval of the ethics committee. The patients who visited Jiaxing First Hospital for head and facial pain received CT-guided radiofrequency treatment for SPG between May 2019 and August 2021 were reviewed and included for observation and telephone follow-up. Inclusion criteria: (1) All patients met the International Headache Society (IHS) diagnostic criteria for migraine or CH. 2. We refer to the definition of refractory headache by the Refractory Headache Special Interest Group (RHSIS) of the American Headache Society (AHS) [8] and Silberstein et al. [9] to develop a definition of refractory headache: patients are considered refractory if they do not respond to medication after 3 months of conservative treatment (< 50% reduction in migraine days per month and/or severity), or if they cannot tolerate adverse drug reactions or have contraindications to drug use, then it is considered refractory (when the patient has intolerable medication side effects, even if the medication is used for a short period of time or at a suboptimal dose). (3) Underwent CT-guided radiofrequency surgery of the sphenopalatine ganglion. Exclusion criteria: (1) unable to express subjective feelings clearly owing to limited communication; (2) follow-up could not be achieved owing to lack of contact details.

Procedures

The patient was placed in a supine position, monitored for vital signs, and administered oxygen through a nasal cannula. A positioning grid was placed on the affected cheek (Fig. 1), and a half-coronal CT scan was performed. The image was reviewed layer by layer to determine the location of the foramen rotundum (Fig. 2A); the target SPG was located caudally medial to the foramen rotundum (Fig. 2B).

The optimal puncture level was mapped using the CT built-in image processing software, while the puncture depth and angle were measured (Fig. 3A). Then, the puncture level and point were marked on the patient's skin (Fig. 3B).

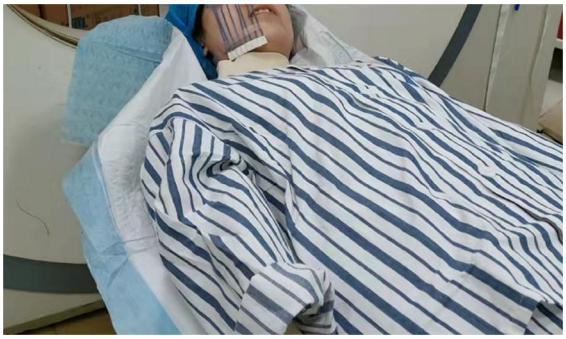

Fig. 1 The patient was positioned supine on the CT-fluoroscopy table. A positioning grid was placed over the cheek of the affected side

After routine disinfection of the towel, the skin and subcutaneous tissue were anesthetized with 2 mL of 1% lidocaine using a 27 G intradermal needle. Under CT guidance, the RF needle (specific model, 10 cm) was inserted and advanced according to predetermined parameters (angle, path, and depth). This process requires repeated correction of the puncture direction and path by CT scan to ensure the optimal puncture path is followed until the SPG target is reached (Fig. 4).

After confirming the lack of evidence of blood, cerebrospinal fluid, or sensory abnormalities, sensory testing was performed via stimulation at 100 Hz and 500 ms pulse width to produce abnormalities at 0.1–0.5 V consistent with the patient's usual original pain site. The motor testing was performed by stimulating the probe at 2 Hz and 0.1–0.5 V to confirm that it was not in close proximity to other adjacent nerves, especially the trigeminal nerve V2 branch, and then 0.5 mL of 1% lidocaine was injected 2 min prior to RF. Subsequently, standard radiofrequency (RF) was performed continuously for 120 s at 90 °C under intravenous propofol anesthesia. Blood pressure, heart rate, electrocardiogram, and oxygen saturation were closely monitored during treatment. At the end of the procedure, the patient was transferred to the postoperative recovery room, and the scores were assessed and recorded. The patient's vital signs were monitored for at least 4 h before discharge. The intra- and postoperative complications were recorded, and

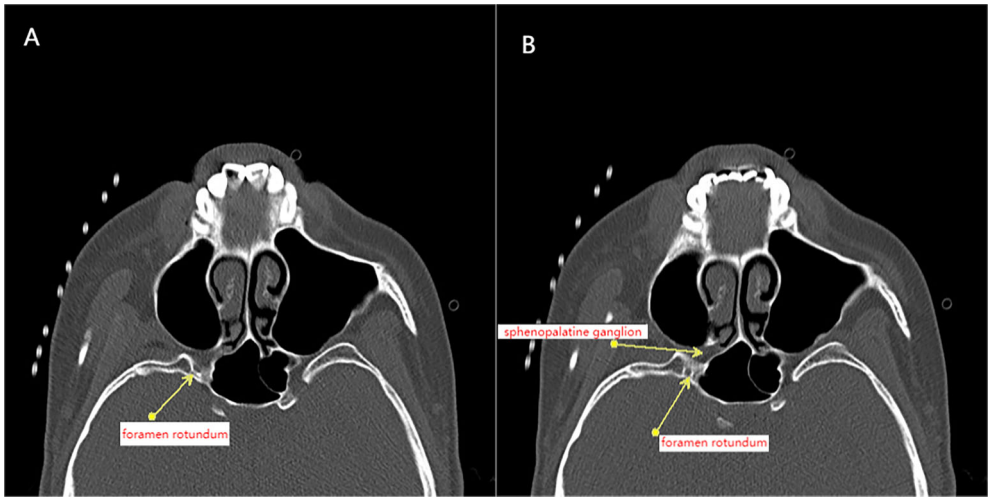

Fig. 2 The location of the foramen rotundum (**a**), with the target nasopalatine ganglion located caudally medial to the FR (**b**)

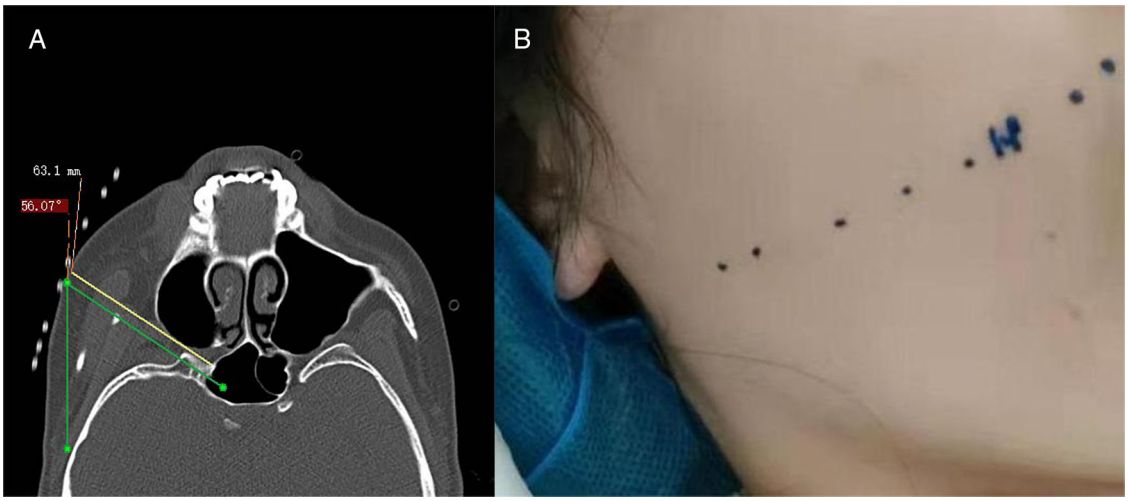

Fig. 3 Design of the RF needle insertion route. The optimal puncture level was mapped using the CT built-in image processing software. Along the lateral wall of the maxillary sinus, a yellow line is drawn from the mid of the foramen rotundum canal to the point of skin entry. Then, the needle insertion depth (distance, 63.1 mm) and the puncture angle (the angle between the yellow line and the sagittal plane ($a = 56.07$) were measured. According to **a**, the puncture level and puncture point corresponding to the optimal puncture route are marked on the patient's skin (**b**)

immediate and long-term outcomes were assessed during follow-up.

Scoring Criteria

We collected general information of patients from the medical record system, including gender, age, course of disease, history of underlying diseases, and preoperative NRS score, and asked patients about the frequency of preoperative and postoperative headache attacks, the duration of each attack, and the occurrence of postoperative complications and adverse reactions. The numeric rating scale (NRS) was used to evaluate the pain level of all patients before surgery as well as 1 day and 1, 3,

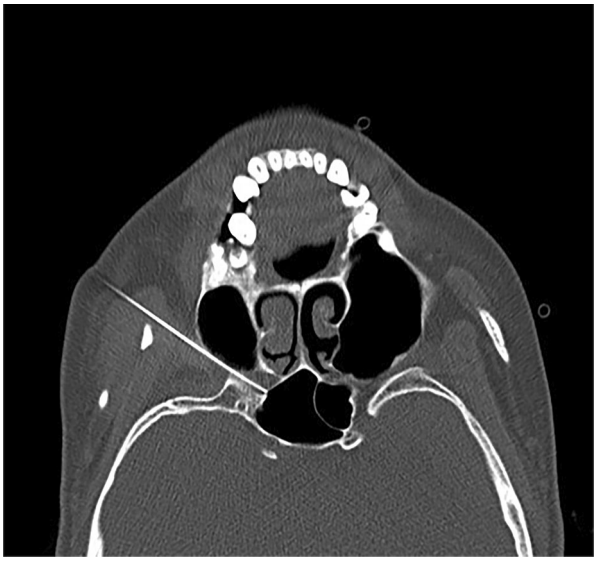

Fig. 4 Under CT guidance, the RF needle is inserted and advanced according to predetermined parameters, a process that requires repeated correction of the puncture direction and path by CT scan to ensure consistency with the designed optimal puncture path until the target SPG is reached

6, 12, and 24 months after surgery, respectively. The NRS score range was 0–10, with 0 indicating no pain and 10 as the most severe pain; the higher the score, the stronger the pain level. The NRS-weighted value (NRS-WV) was calculated as follows: WV = $(A - B)/A$, where A was the preoperative NRS score and B was the follow-up timepoint for NRS score. The efficacy was judged according to the weighted values that are specifically divided into ineffective, remission, and cure: NRS-WV < 50% was ineffective, 50% ≤ NRS-WV ≤ 75% indicated remission, and NRS-WV > 75% was a cure. The total effective rate = (remission + cure)/total cases × 100%. The patients were also observed for numbness at 1 day, 1 month, 3 months, 6 months, 12 months, and 24 months after surgery and classified into no, mild, moderate, and severe numbness according to the severity of facial numbness. Total incidence of numbness = (mild numbness + moderate numbness + severe numbness)/total number of cases × 100%.

Statistical Analysis

IBM SPSS26 software was utilized to analyze the data statistically. The measurement data conformed to a normal distribution and were expressed as mean ± standard deviation ($\bar{x}\pm s$), while the median (interquartile spacing) was used for non-normal distribution. Wilcoxon rank-sum test was used for comparison of non-normally distributed measurement data, and c^2 test was used for comparison of the enumeration data of the two groups. $P < 0.05$ indicated a statistically significant difference.

RESULTS

Clinical Features

From May 2019 to August 2021, 27 patients with refractory headaches were included (Fig. 5). Over the course of the study, 2/16 migraine cases and 1/11 CH cases were lost to follow-up. Among 24 patients, 14 with migraine and 10 with CH, including 10 males and 14 females, with an age range of 17–77 (mean 50.33 ± 15.19) years and an onset duration of 1 week to 30 years (mean 9.71 ± 8.79 years), completed the follow-up. The basic information of the patients is listed in Table 1.

Treatment Effects

NRS scores of the patients before and after surgery: the NRS scores at each postoperative timepoint were significantly lower than those before surgery ($P < 0.05$), as shown in Table 2.

Comparison of NRS scores at various timepoints in two groups of patients with migraine and CH (Table 3).

Frequency of headache attacks and duration of each attack before and after treatment in patients with migraine (Table 4).

Variations in the cluster phase and remission phase in patients with CH before and after treatment (Table 5).

Treatment results at different postoperative timepoints: the effective rates of patients with migraine at 1 day, 1 month, 3 months,

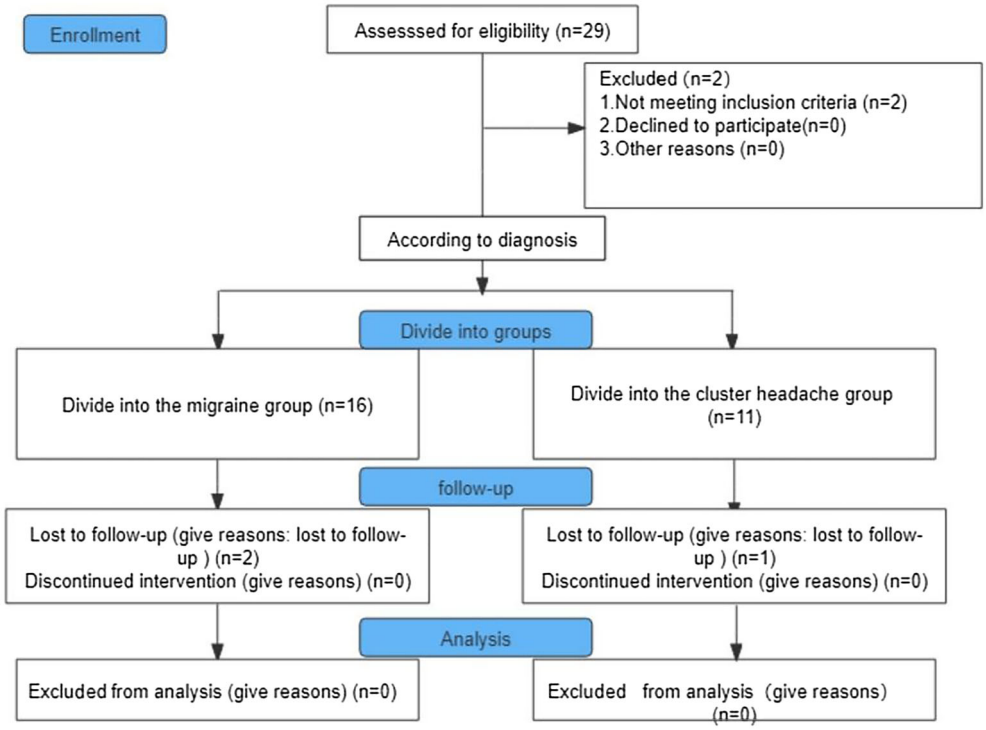

Fig. 5 Flow diagram

6 months, 12 months, and 24 months after surgery were 100.00%, 92.86%, 85.72%, 78.57%, 78.57%, and 71.42%, respectively, while the effective rates for patients with CH were 90.00%, 100.00%, 100.00%, 90.00%, 90.00%, and 100.00%, respectively (Table 6).

The cumulative recurrence-free survival for patients with migraine and CH is illustrated as a Kaplan–Meier actuarial curve in Fig. 6.

Postoperative Complications

Occurrence of facial numbness in patients at different timepoints after surgery: The total incidence of numbness in migraine patients at 1 day after surgery, 1 month after surgery, 3 months after surgery, 6 months after surgery, 12 months after surgery, and 24 months after surgery was 100.00%, 100.00%, 50.00%, 35.71%, 21.42%, and 7.14%, respectively, while that in patients with CH at these timepoints was 100.00%, 100.00%, 20.00%, 10.00%, 10.00%, and 0.00%, respectively. Strikingly, the total incidence of numbness in the patients decreased gradually, and the difference in the rate of numbness between the two groups was not statistically significant ($P > 0.05$; Table 7).

The quality of sleep (PSQI score) at each timepoint in both groups is shown in Fig. 7.

A Modified 2D-Visual Analog Scale

Changes in headache frequency and intensity before and after treatment were assessed simultaneously according to the modified 2D-VAS proposed by Dones et al. [15]. In 14 patients with migraine (Fig. 8), scores ranged from 2–6 before radiofrequency thermocoagulation (RFTC) treatment to 1–2 after RFTC treatment.

DISCUSSION

In this study, we investigated the difference in clinical efficacy and complications of the same treatment modality and CT-guided RFTA of the SPG for the two diseases, migraine and CH. No significant difference was detected in the

Table 1 Basic information sheet

Patient no.	Clinical characteristics					
	Age	Sex	Course (years)	NRS	Diagnosis	Complications
1	46	Male	30	6	Migraine	
2	50	Male	1	7	Migraine	
3	52	Female	10	7	Migraine	
4	71	Female	10	6	Migraine	Hypertension and arthrolithiasis
5	52	Male	30	7	Migraine	
6	72	Female	0.03	7	Migraine	Hypertension and ophthalmoparalysis
7	36	Male	10	6	Migraine	
8	57	Male	20	5	Migraine	
9	55	Female	0.04	6	Migraine	
10	43	Female	20	6	Migraine	
11	17	Female	3	5	Migraine	
12	45	Female	10	6	Migraine	
13	54	Female	3	6	Migraine	
14	51	Female	1	6	Migraine	
15	32	Male	0.02	6	CH	
16	63	Female	10	6	CH	
17	72	Female	0.08	5	CH	Hypertension
18	32	Male	10	8	CH	
19	53	Male	20	6	CH	
20	32	Male	10	7	CH	
21	49	Female	10	7	CH	
22	65	Male	5	5	CH	
23	32	Female	10	7	CH	
24	77	Female	10	6	CH	Hypertension

efficiency of the two diseases in the short term, while the efficiency of CH was significantly better than that of migraine in the long term.

Accumulating evidence has indicated that neuromodulation has an impact on patients suffering from intractable severe craniofacial pain. Some studies recommended steroid injections combined with local anesthetics to block the SPG [16], electrical stimulation of the SPG [17], and neurolytic agents (ethanol) [18] or RFTA [12] to remove the SPG, which have improved the symptoms in patients with headache. In 2011, Chua et al. [19] first performed non-ablative pulsed radiofrequency therapy (PRFT) on three patients with a history of CHs for > 10 years. Among these patients

Table 2 Comparison of NRS scores at different timepoints before and after surgery

	Preoperative NRS	1 day after surgery	1 month after surgery	3 months after surgery	6 months after surgery	12 months after surgery	24 months after surgery
Migraine	6 (7–6)	2 (2–1)	1 (2.25–0.75)	1.5 (3–0)	3 (3–0)	2 (3–0.75)	3 (3–1.5)
Z		−3.322b	−3.307b	−3.311b	−3.311b	−3.311b	−3.317b
P		0.001	0.001	0.001	0.001	0.001	0.001
Cluster headache	6 (7–5.75)	1 (2–1)	1 (2–0)	0.5 (2.25–0)	0.5 (3–0)	1 (2–0)	1 (2–0)
Z		−2.842b	−2.820b	−2.816b	−2.814b	−2.820b	−2.820b
P		0.004	0.005	0.005	0.005	0.005	0.005

Table 3 Comparison of NRS scores between the two groups at each timepoint

	Preoperative NRS	1 day after surgery	1 month after surgery	3 months after surgery	6 months after surgery	12 months after surgery	24 months after surgery
Z	0.000b	−0.707c	−1.265c	−0.680c	−1.242c	−1.208c	−2.200c
P	1	0.48	0.206	0.496	0.214	0.227	0.028

Table 4 Frequency of headache attacks and duration of each attack

	n	Frequency of headache attacks (number per 90 days)	Duration of headache (hours)
Pre-RFTC	14	9 (26–7)	4 (5–4)
Post-RFTC	14	5 (6–5)	4 (5–4)
Z		−4.536b	0.000c
P		< 0.001	1

Table 5 Variations in the cluster phase and remission phase in patients

	Duration of remission (months)	Duration of clusters (months)
Pre-RFTC	2.0 (2.5–1.5)	10.0 (10.5–9.5)
Post-RFTC	0.5 (1.1–0.0)	11.5 (12.0–10.9)
Z	−2.375b	−2.375c
P	0.018	0.018

who were treated conservatively with limited pain relief and after PRFT, two patients showed complete pain relief and one patient showed partial pain relief with no neurological side effects or complications. Garcia-Isidoro et al. [20] mentioned different neuromodulation

Table 6 The effective rates at different timepoints after surgery

	1 day after surgery	1 month after surgery	3 months after surgery	6 months after surgery	12 months after surgery	24 months after surgery
Migraine	100.00%	92.86%	85.72%	78.57%	78.57%	71.42%
CH	90.00%	100.00%	100.00%	90.00%	90.00%	100.00%
Chi-square	3.522	0.747	1.565	0.857	0.857	8.623
P	0.172	0.688	0.457	0.651	0.651	0.013

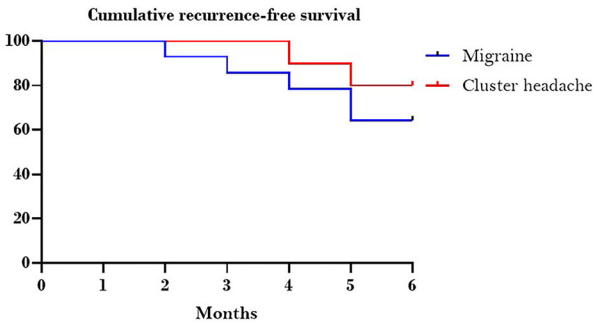

Fig. 6 Kaplan–Meier curve indicates the cumulative recurrence-free survival for 14 and 10 patients with migraine and CH, respectively, after CT–guided SPG RFTA. The blue and red lines represent cumulative recurrence-free survival in patients with migraine and CH, respectively. The horizontal coordinates 1, 2, 3, 4, 5, and 6 represent 1 day after surgery, 1 month after surgery, 3 months after surgery, 6 months after surgery, 12 months after surgery, and 24 months after surgery, respectively

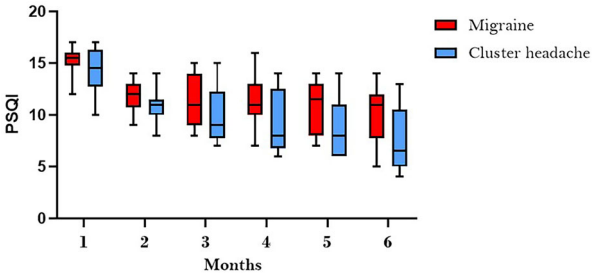

Fig. 7 The box plots in red and blue represent the sleep quality scores of the two groups of patients at different time points, respectively. The horizontal coordinates 1, 2, 3, 4, 5, and 6 represent preoperative, 1 month after surgery, 3 months after surgery, 6 months after surgery, 12 months after surgery, and 24 months after surgery, respectively

techniques, including radiofrequency ablation, pulsed radiofrequency, continuous radiofrequency (radiofrequency thermocoagulation), laser therapy, transcutaneous electrical nerve stimulation (TENS), etc. The effects of invasive neuromodulation were studied from different perspectives. Other neuromodulation therapies, such as the use of ultrasound, magnetic therapy, deep brain stimulation, or motor cortex stimulation, are also mentioned. The interventional treatment by minimally invasive neuromodulation techniques is preferable to neurosurgical

Table 7 Incidence of facial numbness in patients at different timepoints after surgery

	1 day after surgery	1 month after surgery	3 months after surgery	6 months after surgery	12 months after surgery	24 months after surgery
Migraine	100.00%	100.00%	50.00%	35.71%	21.42%	7.14%
CH	100.00%	100.00%	20.00%	10.00%	10.00%	0.00%
Chi-square	0.549	0.549	3.056	2.194	0.549	0.745
P	0.459	0.459	0.217	0.334	0.459	0.388

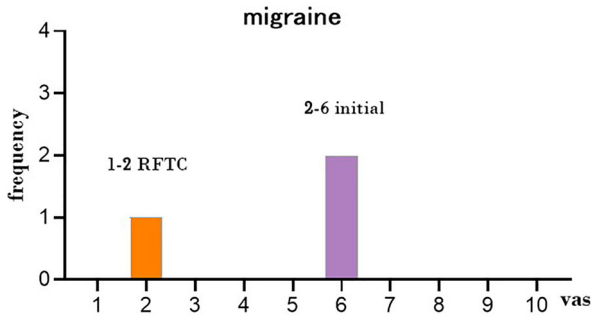

Fig. 8 Improvement on both frequency and intensity of pain in patients affected by migraine after RFTC treatment. The modified VAS grades on the X-axis the intensity of pain from 0 (no pain) to 10 (maximal pain ever experienced) as in the conventional VAS while on the Y-axis are 4 degrees of percentage of time/day in which patients experienced pain. Grade 1 (from 0 to 20% of the day), Grade 2 (from 21 to 40% of the day), grade 3 (from 41 to 60% of the day) and Grade 4 (never-ending pain). The day time is intended to 24 h period

interventions in the deep brain [21] or hypothalamus. Recent studies [22] have elucidated that the SPG located within the PPF plays a critical role in cerebrovascular autonomic neurophysiology and the pathophysiology of various headache disorders (CH, migraine, and trigeminal autonomic headache). Therefore, the neuromodulation of autonomic fibers (parasympathetic and sympathetic) may play a key role in the treatment of headache, stroke, or cerebrovascular spasms [23].

For the long-term efficiency of CT-guided RF of SPG in CH over migraine, it is speculated that CH is a trigeminal autonomic headache involving simultaneous abnormal activity of the hypothalamus, trigeminal vascular system, and autonomic system with ipsilateral autonomic symptoms. Although the exact pathogenesis remains unclear, these specific clinical manifestations are strongly related to the involvement of the parasympathetic component of SPG.

The long-term follow-up results of SPG RF showed that its therapeutic effects persist over time. This treatment may be a good option for patients with chronic refractory headaches. Thus, we need additional data and large sample size to assess its potential use in other forms of cephalofacial pain. RF thermocoagulation of SPG may provide a safe and effective treatment for the resolution of various forms of head and facial pain.

CONCLUSION

In conclusion, CT-guided RFTA of the SPG significantly relieves the headache symptoms in patients with refractory migraine and CH. It has the advantages of rapid onset, long duration, and a safe and reliable treatment process, making it worthy of clinical application.

ACKNOWLEDGEMENTS

Funding. This study and Journal's Rapid Service Fee were supported by the National Natural Science Foundation of China (81901124), Natural Science Foundation of Zhejiang Province of China (LY20H090020, LGF20H090021, LQ19H090007), Medical and Health Science and Technology Research Program of Zhejiang Province (2020RC124, 2020RC122, 2019KY687), Science and Technology Project of Jiaxing City (2021AD30164), Emergency Science and Technology Special Fund of Jiaxing City (2020GZ30001), Construction Project of Anesthesiology Discipline Special Disease Center in Zhejiang North Region (201524), Key Discipline Established by Zhejiang Province and Jiaxing City Jointly–Pain Medicine (2019-ss-ttyx), Key Discipline of Anesthesiology of Jiaxing City (2019-zc-06) and Jiaxing Key Laboratory of Neurology and Pain Medicine.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Author Contributions. Bingyue Xin and Keyue Xie designed the experimental, and drafted the manuscript. Ge Luo participated in acquisition and analysis of data. Ming Yao

reviews articles and provides surgical support. All authors read and approved the final manuscript.

Disclosures. Bingyue Xin, Keyue Xie, Ge Luo and Ming Yao have nothing to disclose.

Compliance with Ethics Guidelines. This study was approved by the Ethics Committee of the First Affiliated Hospital of Jiaxing University, located in Jiaxing City, Zhejiang Province, China(LS2021-XJS-142). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. The data sets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Robbins MS. Diagnosis and management of headache: a review. JAMA. 2021;325(18):1874–85.
2. Goadsby PJ, Lipton RB and Ferrari MD. Migraine–current understanding and treatment. N Engl J Med. 2002; 346: 257–70.
3. Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. Headache. 2015;55(Suppl 2):103–26.
4. Robbins MS, Starling AJ, Pringsheim TM, et al. Treatment of cluster headache: the American Headache Society evidence-based guidelines. Headache. 2016;56:1093–106.
5. Hoffmann J, May A. Diagnosis, pathophysiology, and management of cluster headache. Lancet Neurol. 2018;17:75–83.
6. Rozen TD, Fishman RS. Cluster headache in the United States of America: demographics, clinical characteristics, triggers, suicidality, and personal burden. Headache. 2012;52:99–113.
7. Nilsson Remahl AI, Laudon Meyer E, Cordonnier C, et al. Placebo response in cluster headache trials: a review. Cephalalgia. 2003;23:504–10.
8. Schulman EA, Lake AE 3rd, Goadsby PJ, et al. Defining refractory migraine and refractory chronic migraine: proposed criteria from the refractory headache special interest section of the American Headache Society. Headache. 2008;48(6):778–82.
9. Silberstein SD, Dodick DW, Pearlman S. Defining the pharmacologically intractable headache for clinical trials and clinical practice. Headache. 2010;50(9):1499–506.
10. D'Antona L, Matharu M. Identifying and managing refractory migraine: barriers and opportunities? J Headache Pain. 2019;20(1):89.
11. Robbins MS, Robertson CE, Kaplan E, et al. The sphenopalatine ganglion: anatomy, pathophysiology, and therapeutic targeting in headache. Headache. 2016;56:240–58.
12. Narouze S, Kapural L, Casanova J, et al. Sphenopalatine ganglion radiofrequency ablation for the management of chronic cluster headache. Headache. 2009;49:571–7.
13. Yarnitsky D, Goor-Aryeh I, Bajwa ZH, et al. 2003 Wolff Award: possible parasympathetic contributions to peripheral and central sensitization during migraine. Headache. 2003;43:704–14.
14. Zhu J, Luo G, He Q, et al. Evaluation of the efficacy of unipolar and bipolar spinal dorsal root ganglion radiofrequency thermocoagulation in the treatment of postherpetic neuralgia. Korean J Pain. 2022;35:114–23.
15. Dones I, Messina G, Nazzi V, et al. A modified visual analogue scale for the assessment of chronic pain. Neurol Sci. 2011;32(4):731–3.

16. Penarrocha-Diago M, Boronat A, Penarrocha-Oltra D, et al. Clinical course of patients with episodic cluster headache treated with corticosteroids inproximity to the sphenopalatine ganglion: a preliminary study of 23 patients. Med Oral Patol Oral Cir Bucal. 2012;17:e477–82.

17. Ansarinia M, Rezai A, Tepper SJ, et al. Electrical stimulation of sphenopalatine ganglion for acute treatment of cluster headaches. Headache. 2010;50: 1164–74.

18. Devoghel JC. Cluster headache and sphenopalatine block. Acta Anaesthesiol Belg. 1981;32:101–7.

19. Chua NH, Vissers KC, Wilder-Smith OH. Quantitative sensory testing may predict response to sphenopalatine ganglion pulsed radiofrequency treatment in cluster headaches: a case series. Pain Pract. 2011;11:439–45.

20. Garcia-Isidoro S, Castellanos-Sanchez VO, Iglesias-Lopez E, et al. Invasive and non-invasive electrical neuromodulation in trigeminal nerve neuralgia: a systematic review and meta-analysis. Curr Neuropharmacol. 2021;19(3):320–33.

21. Maniam R, Kaye AD, Vadivelu N, et al. Facial pain update: advances in neurostimulation for the treatment of facial pain. Curr Pain Headache Rep. 2016;20:24.

22. Schmidt RF, Theofanis TN, Lang MJ, et al. Sphenopalatine ganglion stimulation is a reversible and frequency-dependent modulator of the blood–brain barrier. Brain Res. 2019;1718:231–41.

23. Baker TS, Robeny J, Cruz D, et al. Stimulating the facial nerve to treat ischemic stroke: a systematic review. Front Neurol. 2021;12:1–15.