Retrospective Study

Long-term Follow-up of Pulsed Radiofrequency Treatment for Trigeminal Neuralgia: Kaplan-Meier Analysis in a Consecutive Series of 149 Patients

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Background: At present, there is no ideal method for the treatment of trigeminal neuralgia (TN). The need for an easy, safe, non- or micro-neurodestructive, repeatable treatment, with a fairly satisfactory rate of pain relief, is paramount. Pulsed radiofrequency (PRF) as a minimally invasive and microdestructive technique has been reported to be an option for TN; however, no study has reported the long-term outcome of TN in a large case series.

Objectives: We aimed to investigate the efficacy, safety, and the long-term outcomes of PRF treatment for patients with TN.

Study Design: This was a long-term, large case series, retrospective study.

Setting: The study was conducted at Tiantan hospital,Beijing.

Methods: We retrospectively analyzed medical databases and follow-up data of 149 patients with TN from January 2008 through March 2021, who underwent PRF treatment, with a median follow-up time of 71.0 months (interquartile range, 20.0 months to 112.0 months). Baseline characteristics and intraoperative data of patients were retrospectively extracted; data about complications and side effects were also collected. The follow-up data were composed of the postoperative Barrow Neurological Institute Pain Intensity Score pain intensity at a different time, the onset time of PRF treatment, and the time when pain was recurrent.

Results: The initial pain relief rate was 75.17% after the procedure. The cumulative recurrence-free survival after the procedure was 75.00% at one month; 72.87% at 6 months; 70.59% at 12 months; 65.39% at 24 months; 61.63% 48 months; 56.73% at 96 months; and 49.64% at 144 months. The median recurrence-free time was 118 months according to the Kaplan-Meier estimator. Nineteen patients had pain recurrence with a median time of 15 months (range, 1.0 months to 96.0 months), among whom, 12 underwent a second PRF procedure and 9 patients experienced satisfactory pain relief. No serious complications or side effects occurred after the procedure.

Limitations: This was a single-center, retrospective study. Our study failed to conduct a stratified analysis on the effect of PRF treatment for classic and idiopathic TN. The most efficacious parameters of PRF applied for TN and studies trying to identify positive predictive factors of pain relief before PRF treatment have yet to be investigated.

Conclusions: The results of this study show the promising long-term effect of PRF on primary TN. The safety and repeatability might be more easily accepted by patients with TN and should be considered a preferred treatment option before choosing neurodestructive or more invasive methods.

Key words: Trigeminal neuralgia, pulsed radiofrequency, long-term follow up, Kaplan-Meier analysis

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Trigeminal neuralgia (TN) is defined as paroxysmal electric-shock-like painful attacks, confined to the somatosensory distribution of the trigeminal nerve, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve, and commonly evoked by innocuous stimulation like washing, shaving, smoking, or brushing the teeth et al (1,2). TN is a neurologic condition affecting 3-27 persons per 100,000 population (3,4); it has a significant impact on the quality of life and the socioeconomic functioning of the patient(5). The International Classification of Headache Disorders, 3rd edition, has formally classified TN into classic TN, secondary TN, and idiopathic TN(6). Unlike classic TN with microvascular compression, secondary TN is caused by an underlying disease and idiopathic TN is of unknown etiology.

Microvascular decompression (MVD) may be considered the most appropriate treatment after oral medication for classic TN (7,8). However, patients have the associated risks of cerebellar injury, hearing loss, cerebrospinal fluid leakage, etc (8). Some elderly patients with classic TN, or patients with comorbidities, patients with idiopathic TN, and some patients with secondary TN who are unwilling or unable to accept a more invasive approach, may choose a less-invasive treatment option when conservative treatments fail. These options include Gamma Knife radiosurgery (GKR)(9), or percutaneous procedures including glycerol rhizolysis, radiofrequency thermocoagulation (RFT), and percutaneous balloon compression (PBC) of the Gasserian ganglion (10,11). However, GKR has a pain relief rate lower than MVD and percutaneous procedures. Furthermore, the ideal dose that provides the best pain control balanced with minimum radiation complications is yet to be determined (12). Percutaneous procedures are now used more routinely in clinical pain management as outpatient procedures because of their simplicity, low cost, and the possibility of retreatment if pain returns (13). However, all these aforementioned percutaneous procedures are neurodestructive methods that present risks of sensory loss, dysesthesia, anesthesia dolorosa, corneal anesthesia, and masseter muscle weakness or paralysis (14,15). At present, there is no ideal method for the treatment of TN. Therefore, an easy, safe, non- or micro-neurodestructive, repeatable treatment, with a fairly satisfactory rate of pain relief, is needed.

Pulsed radiofrequency (PRF) is a minimally invasive, micro-destructive procedure for the treatment of TN. Van Zundert et al (16) first reported an excellent long-term effect, in 3 out of 5 patients with TN with a mean follow-up period of 19.2 months (range 10 months to 26 months). In a retrospective study of 34 patients with TN by Chua et al (17), the percentages of patients showing excellent pain relief after PRF at 2, 6, and 12 months were 73.5%, 61.8%, and 55.9%, respectively. We previously reported that the response rates of percutaneous PRF in the treatment of 28 patients with medically refractory TN was 85.7% at 6 months and 78.6% at both 12 months and 2 years (18). In contrast, Erdine et al (19) suggested that pain relief was not as satisfactory as RFT after PRF for idiopathic TN. Elawamy et al (20) found that, after PRF treatement, excellent pain relief was achieved in 82% of patients with classic TN after 6 months, but only 9.1% after 12 months and 0% after 24 months. However, no study has reported the long-term outcomes of PRF in a large TN series. Therefore, we retrospectively analyzed data from January 2008 through March 2021 in patients with TN with one or more divisions of the trigeminal nerve who underwent PRF, with the aim to investigate the initial efficacy, safety, and the long-term efficacy of PRF.

Methods

Patients

This study was approved by the Medical Ethics Committee of Beijing Tiantan Hospital, Capital Medical University before the retrospective collection of patients' data, and was conducted in compliance with the current version of the Declaration of Helsinki. This retrospective study analyzed the data of patients with TN who underwent PRF at the department of Pain Management, Beijing Tiantan Hospital, Capital Medical University from January 2008 through March 2021. Demographic and perioperative data were extracted from medical databases and follow-up data were collected from electronic records.

The inclusion criteria were as follows:

1. Age > 18 years
2. Diagnosed with TN in accordance with the International Classification of Headache Disorders 2nd edition, 3rd edition (beta version) and the 3rd edition (6,21,22)
3. Frequent pain episodes not relieved by medication management
4. Received percutaneous PRF treatment of the Gasserian ganglion

The exclusion criteria were as follows:

1. History of operation for TN such as MVD, GKR, PBC, RFT, glycerol injection, etc.
2. Incomplete medical records

Operation

Electrocardiograms (ECG), chest x-rays, blood routine, biochemical, and coagulation function were routinely obtained and evaluated by an anesthesiologist before surgery. Patients were placed supine on the computed tomography (CT) scanner bed with standard monitors: blood pressure, heart rate, ECG, and pulse oximeter were connected, and O_2 was administered via a nasal prong. The negative plate of the pain treatment generator (PMG-230, Baylis Medical Inc., Montreal, Canada) was attached to the skin on the patients' backs.

The puncture point was 3 cm lateral to the corner of the mouth on the affected side. After infiltrating the skin and subcutaneous tissues with 1% lidocaine local anesthesia, a 21-gauge, 10-cm treatment trocar with a 5-mm active tip (PMF-21-100-5, Baylis Medical Inc., Montreal, Canada) was used for the foramen ovale puncture. Following Hartel's forward approach, the puncture was performed towards the ipsilateral foramen ovale with the guidance of spiral CT (Somatom, Siemens Company, Munich, Germany) scanning (2 mm/layer) and 3-D reconstructed images (Fig. 1). Electrical stimulation of 0.1–0.2 V at 50 Hz was used to test sensory threshold and 2 Hz of electrical stimulation was used to test motor threshold. The depth and direction of the trocar were adjusted according to facial pain in the trigeminal nerve distribution and mandibular movements to ensure accurate puncture. The radiofrequency generator was set to automatic pulsed mode (42°C, 20 milliseconds, 2 Hz, 360 seconds) or manual pulsed mode with the upper temperature limit set at 42°C and a treatment duration of 360 seconds (23).

Definitions of Outcome

We used the modified Barrow Neurological Institute (BNI) pain intensity criteria (24) (Table 1) to evaluate treatment effect. Satisfactory pain relief level was defined as BNI I to BNI IIIb, and the first satisfactory pain relief after the PRF treatment was defined as initial pain relief. The onset time was recorded when the first satisfactory pain relief was observed after treatment. Complete pain relief was defined as being pain free without medicine (BNI I) after treatment. A

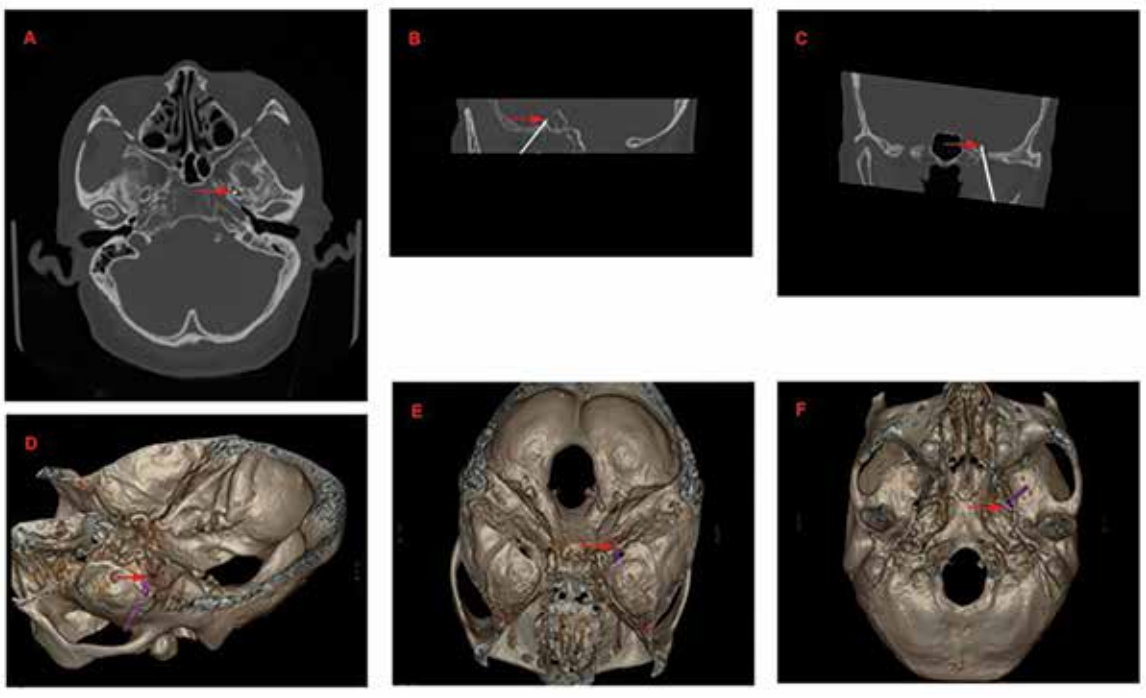

Fig. 1. *CT-guided foramen ovale puncture. Notes: (A) Base of the skull shows the needle (arrow) entering the foramen ovale. (B) Sagittal view shows the needle (arrow) entering the foramen ovale. (C) Coronal view shows the needle (arrow) entering the foramen ovale. (D, E, F) 3-D reconstruction of the skull base shows the needle (arrow) entering the foramen ovale.*

Table 1. *Modified Barrow Neurological Institute (BNI) pain intensity criteria.*

Degrees	Definition
BNI I	the trigeminal pain disappeared completely, requiring no drugs
BNI II	the trigeminal pain was mild, not requiring drugs
BNI IIIa	the trigeminal pain was disappeared, controlled with medication
BNI IIIb	the trigeminal pain was mild, controlled with medication
BNI IV	the trigeminal pain was moderate, not adequately controlled with medication
BNI V	the trigeminal pain was severe or not relieved

BNI grade that reached I-IIIb one month after treatment was defined as effective treatment, otherwise the treatment was considered ineffective. Patients who had responded to treatment (BNI I-IIIb) after PRF and increased to IV-V were defined as having pain recurrence. The effective rate after PRF were calculated as follows: [(BNI I+II+IIIa+IIIb)/total number of patients] × 100%.

Data Collection

Eligible patients were identified according to the inclusion and exclusion criteria. Baseline demographic characteristics were collected including each patient's age, gender, pain distribution side, branches affected, disease duration, baseline classification of BNI pain intensity, dose of carbamazepine, and concomitant disease. Intraoperative data of patients, including sensory stimulation voltage and motor stimulation voltage, operative duration, output voltage during treatment, and tissue resistance just before and after PRF treatment were retrospectively extracted from medical records. The data of perioperative complications and side effects, such as intraoperative bradycardia, facial hematoma, postoperative nausea, vomiting, dizziness, tinnitus, numbness in the distribution area of the trigeminal nerve, aggravating pain, etc. were also collected. Patients undergoing PRF treatment in our department were routinely followed-up via telephone for the purpose of medical quality improvement and all data were thoroughly recorded in electronic records. The follow-up data composed of postoperative BNI pain intensity at different times, onset of effectiveness of PRF treatment, and complications and side effects after treatment. The time when pain was recurrent (if the patient had pain recurrence) and any remedial treatments were also collected.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics version 20.0 (IBM Corporation, Armonk, NY). Normally distributed data are expressed as mean ± standard deviation (x ± SD) and compared using single-factor analysis of variance. Nonnormally distributed data are expressed as median (interquartile range, IQR) and differences were compared with the Mann–Whitney U test. A Kaplan-Meier plot was used to present recurrence-free survival curves. A value of $P < 0.05$ indicated a statistically significant difference.

Results

Patients' Demographics

From January 2008 through March 2021, 155 consecutive patients underwent a CT-guided PRF procedure for TN in the pain clinic of Beijing Tiantan hospital. Six patients were excluded according to the exclusion criteria because 3 had a history of MVD and 3 had incomplete medical records. Ultimately, 149 patients were included in this study and their medical records were collected and analyzed. The follow-up duration ranged from 2 to 152 months, with a median length of 71.0 months (IQR, 20.0 months–112.0 months). During the follow-up period, 4 patients were lost due to lack of telephone contact and 2 patients died due to unrelated causes. The patients' characteristics are listed in Table 2.

Intraoperative data

The mean operative duration was 38.44 ± 9.34 minutes. The median 50 Hz sensory stimulation voltage and 2 Hz motor stimulation voltage were both 0.1 V (IQR 0.1-0.1) and the mean output voltage during the treatment was 54.27 ± 16.58V. The mean tissue resistance just before PRF treatment was 250.60 ± 3 6.79 Ω, while it was 249.56 ± 33.17Ω immediately after treatment.

Treatment Effect

The initial pain relief rate was 75.17%. The average onset of effectiveness of PRF treatment was 2 days (range 0 to 30 days). When evaluated one month after treatment, 112 patients (75.17%) experienced at least satisfactory pain relief and among them, 64 patients (42.95%) experienced complete pain relief. Two months after the treatment, 108 patients (72.48%) experienced at least satisfactory pain relief and the complete pain relief rate had no statistical difference between one and 2 months ($P > 0.05$). Noneffective treatment was observed on a total of 37 patients (24.83%) one month

after treatment; among whom 3 patients had secondary TN. Twenty-three of them selected RFT treatment, 4 patients chose MVD, and the others accepted PBC treatment.

The cumulative recurrence-free survival of 149 patients after the first PRF treatment is presented as a Kaplan-Meier actuarial curve in Fig. 2. After the procedure, the cumulative recurrence-free survival was 75.00% at one month, 72.87% at 6 months, 70.59% at 12 months, 65.39% at 24 months, 61.63% at 48 months, 56.73% at 96 months and 49.64% at 144 months. The median follow-up time of the 149 patients was 71.0 months (IQR, 20.0 months-112.0 months), with a median recurrence-free time of 118 months according to the Kaplan-Meier estimator (Fig. 2).

Pain recurrence was reported in a total of 19 patients (16.96%) at one, 4.5, 5, 6, 8, 10, 11, 14, 15, 15, 15, 22, 22, 29, 40, 41, 52, 55 and 96 months after PRF treatment. Among the 19 patients with recurrent pain, 3 (15.79%) patients chose MVD, one (5.26%) patient chose RFT treatment, 3 (15.79%) patients chose PBC treatment and 12 (63.16%) patients selected repeat PRF treatment. Among the patients receiving the second PRF treatment, the follow-up time ranged from 17 to 137 months (median, 92.5 months; IQR, 40.25 months-106.75 months) and after the second PRF treatment, 9 patients achieved satisfactory pain relief and 4 of them got complete pain relief with an initial responsive rate of 75.00%. The remaining 3 patients who did not respond to the second PRF treatment chose RFT treatment afterwards. Three of those who underwent a second PRF treatment had pain recurrence again at 6, 31, and 43 months after the second procedure and underwent a third PRF procedure. Based on the last available data by telephone, these 3 patients were followed-up for 11, 50, and 80 months without pain recurrence (Fig. 3).

Intra- and Post-operative Side Effects and Complications

During the operation, transient bradycardia occurred in 12 patients (8.05%) while the trocar was near the foramen ovale; they recovered spontaneously without treatment. Five patients (3.36%) suffered local facial hematoma at the puncture site, which was absorbed spontaneously 2-3 weeks after the operation. Five patients (3.36%) suffered from postoperative dizziness. Twelve patients (8.05%) reported postoperative nausea and 2 of them (1.34%) suffered from vomiting after the procedure. All these

Table 2. *Baseline patients' characteristics.*

Variable	Primary TN (n = 146)	Secondary TN (n = 3)
Age (years)	57.42 ± 13.77	33 ± 7.81
Gender (Women/Men)	88/58	1/2
Side (Right/Left)	101/45	1/2
Branches affected (n, %) V1 V2 V3 V1, V2 V2, V3 V1, V2, V3	 7 (4.79%) 12 (8.22%) 59 (40.41%) 3 (2.05%) 57 (39.04%) 8 (5.48%)	 1 (33.33%) 2 (66.67%)
Duration of pain (months)	49.98 ± 58.47	12 ± 11.79
BNI before PRF (n, %) BNI IV BNI V	 86, 58.90% 60, 41.10%	 2, 66.67% 1, 33.33%
Preoperative carbamazepine dose (mg/d, median [interquartile range])	600 (400,875)	800 (550,800)
Comorbidities (n, %) Hypertension Diabetes Stroke	 37 (25.34%) 7 (4.79%) 4 (2.74%)	 1 (33.33%)

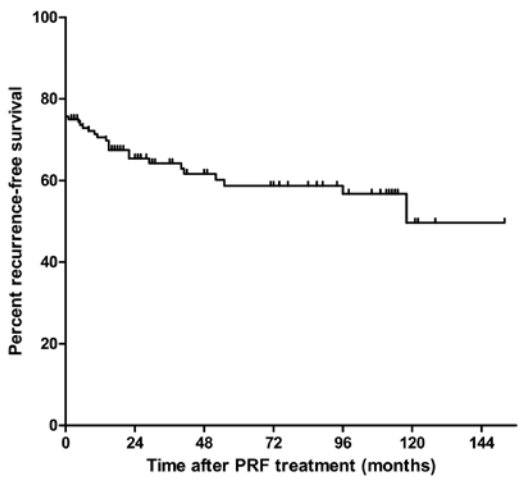

Fig. 2. *Kaplan-Meier recurrence-free survival curves for patients with TN who underwent PRF treatment.*

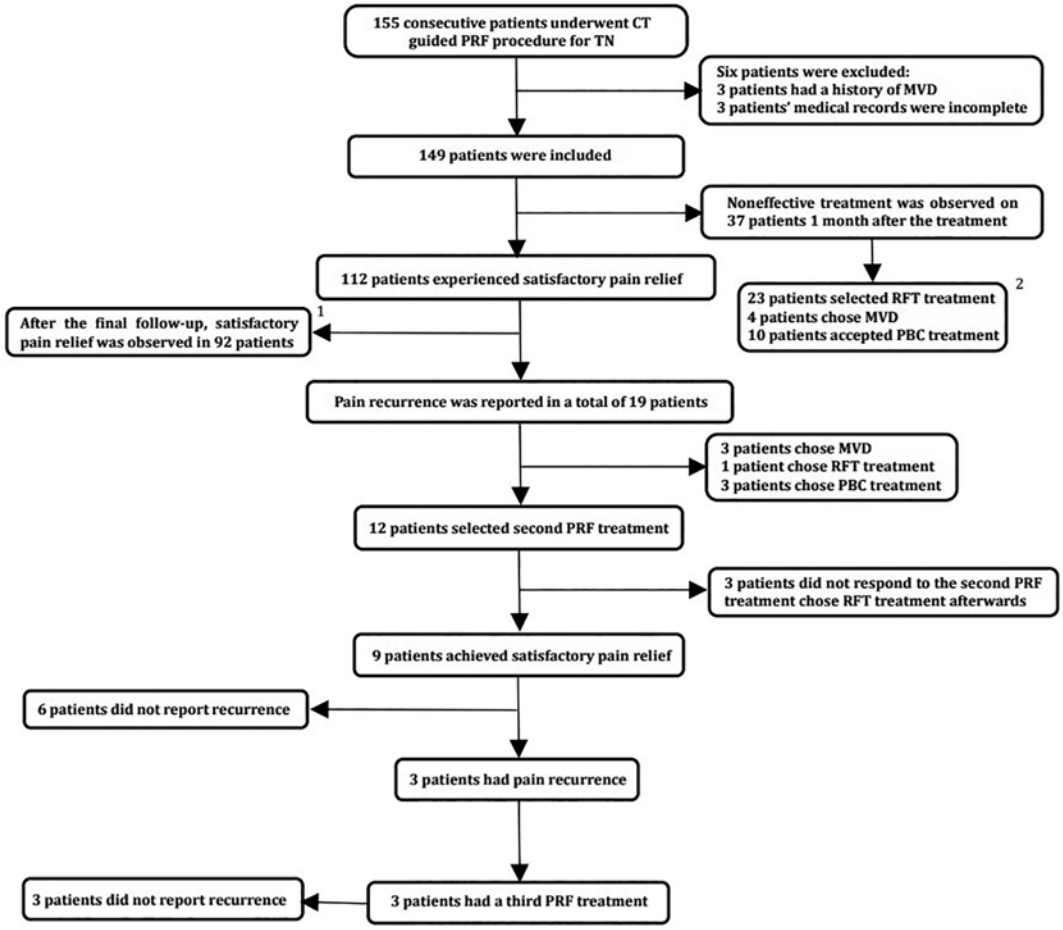

Fig. 3. *Flow chart of the study populations. 1: one patient lost owing to lack of telephone contact; 2: 3 patients lost owing to lack of telephone contact and 2 patients died.*

side effects disappeared within 4 hours after treatment. One patient (0.67%) suffered from tinnitus after PRF which disappeared 2 weeks later. Twenty-two patients (14.77%) felt pain aggravation and even needed to increase the dosage of analgesic for pain control, among whom 16 patients showed pain relief 1-2 weeks after treatment and the other 6 patients did not respond to treatment. Six patients (4.03%) experienced a mild numbness in the trigeminal nerve innervation area, and they all came back to normal gradually within one month. No patient experienced serious complications such as masticatory muscle weakness, corneal anesthesia, ulcer, or perioperative death.

Discussion

This study retrospectively reports the efficacy and safety of 149 patients with TN who underwent PRF treatment from January 2008 through March 2021, with a median follow-up length of 71.0 months (IQR, 20.0 months–112.0 months). There were several small case series studies reporting the short-term efficacy of PRF on TN with the initial pain relief rate ranging from 60% to 85.7% (1,12,13,17,22,25). In this study, the initial pain relief rate was 75.17% which was similar to Chua et al's report (17). The initial pain relief rate of PRF treatment was significantly inferior to RFT treatment, which had an initial success rate of 97.6% to 99% for TN (14,26). However, the adverse effects of

PRF were not serious compared to the possible adverse effects of RFT, such as facial numbness and masticatory muscle strength decline. Sharma et al (27) performed a systematic review and showed that the initial success rate with MVD for medically refractory TN was 96% (95% confidence interval 93.3% to 98.6%), which was also higher than that of PRF. But as a minimally invasive percutaneous technique, the PRF procedure is undoubtedly easier and safer to perform compared to MVD. After a single PRF treatment, 75.17% patients avoided neurodestructive or more invasive surgical options, which suggests that PRF is a promising treatment option for TN and perhaps should be considered a first-line minimally invasive choice in clinical practice.

The present study also proposes that patients experienced satisfactory pain relief with a median remission length of 118 months after PRF. After a single PRF treatment, the cumulative recurrence-free survival was 65.39%, 61.63% and 56.73% at 24, 48, and 96 months, respectively. With the extension of time, recurrence-free survival reduced to 49.64% at 144 months after the procedure. Kanpolat et al (14) reported that after a single RFT treatment, a neurodestructive technique, pain relief was achieved in 57.7% of the patients at 5 years and 52.3% at 10 years. Other researchers have reported that RFT could provide an average pain-free rate of 50.4% for a mean 5-year follow-up (28). However, prospective clinical studies comparing the long-term efficacy of PRF with other microinvasive techniques such as RFT are lacking.

A total of 19 patients (16.96%) had pain recurrence, with a median time of 15 months (range, 1.0-96.0) after the first PRF treatment in this study and 12 (12/19, 63.16%) of them were willing to accept a second PRF procedure. After undergoing the second procedure, 9 patients (9/12, 75.00%) experienced satisfactory pain relief. Three (3/9, 33.33%) out of 9 patients had a second pain recurrence after the second procedure and they all chose a third PRF treatment and got satisfactory pain control. These results suggest that, although there is a certain recurrence rate after PRF treatment, patients can receive PRF again in case of recurrence and for some patients PRF will still be effective. Therefore, this neuromodulative technique has the characteristic of repeatability.

Previous literature reporting the effects of PRF treatment on TN show inconclusive results. We recently identified the predictors of the analgesic efficacy of PRF targeting the Gasserian ganglion in patients with idiopathic TN and found that previous positive responses to peripheral branch nerve block of the trigeminal nerve with steroid and local anesthetic was an independent predictor of a positive outcome of PRF treatment(29). Factors such as age, gender, disease duration, laterality of the affected branch, comorbidities, and preoperative pain degree were not independent predictors of good efficacy of PRF. In this retrospective study, not all patients underwent a high-resolution imaging with 3-dimensional reconstruction, and for this reason we could not clarify the diagnosis of classic TN from their medical records. Therefore, our study was unable to clarify if the effect of PRF treatment for classic TN or idiopathic TN patients is different. Only 3 patients with secondary TN caused by intracranial small benign tumor were included in this study and their only symptom was TN. Noneffective treatment was observed in all 3 patients with secondary TN perhaps indicating that PRF may not be an effective treatment option for secondary TN.

Some researchers have proposed that the treatment timing and intraoperative parameters (the dose of PRF) might have a major impact on clinical effects. Tanaka et al (30)reported that PRF treatment (on the sciatic nerve) was more effective when applied in the early stages of mechanical allodynia and increasing exposure time of the PRF current from 2 minutes to 6 minutes has shown a more effective pain relief effect in a neuropathic pain model in rats. Another animal study also proved that increasing the exposure time of PRF current from 2 minutes to 6 minutes shows a significantly better antiallodynia effect. In a prospective, randomized, double-blinded study by Erdine et al (19) that evaluated the effect of PRF in comparison with RFT in the treatment of idiopathic TN, the authors described that PRF was not effective (19). In Erdine's study (19), the rather shorter duration of PRF (2 minutes) might have been one of the reasons why PRF was ineffective. Different from Erdine's study (19), both in our study and Chua's study (17), the duration of PRF was 6 minutes. We suspect that one of the main reasons for this discrepancy of effect among the various published studies may be due to an insufficient PRF dose used in most studies, and the efficacy of pain relief of PRF may be improved by adjusting these parameters. So far, there has been no standard optimal parameters to maximize pain relief and minimize complications. Other parameters, such as waveform, temperature, frequency, pulse width, output voltage or combined PRF, and 60°C or 65°C RFT treatment of the gasserian ganglion, which have been reported to be effective in

patients with idiopathic TN, should also be investigated through prospective clinical trials in the future.

Although the exact pain relief mechanisms of PRF remain unclear, we previously reported that PRF relieved neuropathic pain in rats with the mechanisms of upregulation of transcription and translation of glial cell line-derived neurotrophic factor in a compressed sciatic nerve (31). Vallejo et al (32) reported the pain regulatory gene expression in the spared nerve injury (SNI) model in rats after PRF, and found the expression of many proinflammatory gene expression, such as tumor necrosis factor-α and interleukin-6, returned to baseline values following PRF therapy. They also found that the up-regulation of sodium – potassium adenosine triphosphatase and c-Fos was found in the spinal cord following PRF treatment relative to the SNI group (32). Up to now, there has been no study reporting the mechanisms of PRF involved in an animal model of TN and further research is necessary.

Improper foramen ovale penetration may result in severe complications, such as cerebrospinal fluid leakage, carotid-cavernous fistula, and even monocular blindness (14,33,34). In this study, all patients' operations were performed with the help of an advanced CT imaging guidance technology; the success rate of puncture was 100%. No puncture-related serious complications occurred in our study. During the procedure, only 8.05% patients experienced bradycardia, especially during foramen ovale puncture, which was mild and did not require treatment. Meng et al (35) reported that trigeminal reflex occurred in 15.8% patients who underwent RFT treatment for primary TN which was controlled by using atropine before puncture (35). The occurrence rate of bradycardia during the PRF procedure may be lower than RFT but should be monitored carefully during each procedure. Five patients (3.36%) experienced dysesthesia in the distribution of TN after PRF treatment, 22 patients (14.77%) reported increased pain intensity immediately after treatment. These complications may be associated with puncture lesions, but fortunately, the dysesthesia disappeared within one month and the pain aggravation was transient and could be controlled by symptomatic treatment. Masseter dysfunction and facial numbness did not occur after PRF treatment, and as a simple, minimally invasive, and micro-destructive technique, PRF would be more easily accepted by patients when compared to destructive treatment and more invasive surgery.

Limitation

The limitations of this study are inherent to retrospective studies. Our study failed to realize a stratified analysis on the effect of PRF treatment for classic and idiopathic TN. Further evaluation from a larger sample of prospective, randomized, multicenter clinical trials is necessary to confirm the benefits of PRF treatment in patients with TN and to facilitate clinical decisions in the future. The most efficacious parameters of PRF applied for TN and studies trying to identify positive predictive factors of pain relief before PRF treatment have yet to be investigated.

Conclusion

To our knowledge, this is a retrospective study that reports the outcomes of PRF treatment in patients with TN with the largest sample size and the longest follow-up period. PRF treatment is a minimally invasive, micro-destructive, and effective treatment for patients with TN, especially those with primary TN. Such a minimally invasive procedure could be considered a preferred treatment option before a neurodestructive method or a major intracranial surgery.

References

1. Cheshire WP. Trigeminal neuralgia: For one nerve a multitude of treatments. *Expert Rev Neurother* 2007; 7:1565-1579.
2. Shah SA, Khan MN, Shah SF, Ghafoor A, Khattak A. Is peripheral alcohol injection of value in the treatment of trigeminal neuralgia? An analysis of 100 cases. *Int J Oral Maxillofac Surg* 2011; 40: 388-392.
3. Hall GC, Carroll D, Parry D, McQuay HJ. Epidemiology and treatment of neuropathic pain: The UK primary care perspective. *Pain* 2006; 122:156-162.
4. Rozen TD. Trigeminal neuralgia and glossopharyngeal neuralgia. *Neurol Clin* 2004; 22:185-206.
5. Van Kleef M, van Genderen WE, Narouze S, et al.1. Trigeminal neuralgia. *Pain Pract* 2009; 9: 252-259.
6. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018; 38:1-211.
7. Apfelbaum RI. Neurovascular decompression: The procedure of choice? *Clin Neurosurg* 2000; 46:473-498.
8. McLaughlin MR, Jannetta PJ, Clyde BL, Subach BR, Comey CH, Resnick DK. Microvascular decompression of cranial nerves: Lessons learned after 4400 operations. *J Neurosurg* 1999; 90:1-8.
9. Cohen J, Mousavi SH, Faraji AH, et al. Stereotactic radiosurgery as initial

surgical management for elderly patients with trigeminal neuralgia. *Stereotact Funct Neurosurg* 2017; 95:158-165.

10. Burchiel KJ, Slavin KV. On the natural history of trigeminal neuralgia. *Neurosurgery* 2000; 46:152-154; discussion 154-155.
11. Lee KH, Chang JW, Park YG, Chung SS. Microvascular decompression and percutaneous rhizotomy in trigeminal neuralgia. *Stereotact Funct Neurosurg* 1997; 68:196-199.
12. Young B, Shivazad A, Kryscio RJ, St Clair W, Bush HM. Long-term outcome of high-dose - knife surgery in treatment of trigeminal neuralgia. *J Neurosurg* 2013; 119:1166-1175.
13. Tronnier VM, Rasche D, Hamer J, Kienle AL, Kunze S. Treatment of idiopathic trigeminal neuralgia: Comparison of long-term outcome after radiofrequency rhizotomy and microvascular decompression. *Neurosurgery* 2001; 48:1261-1267; discussion 1267-1268.
14. Kanpola Y, Savas A, Bekar A, Berk C. Percutaneous controlled radiofrequency trigeminal rhizotomy for the treatment of idiopathic trigeminal neuralgia: 25-year experience with 1,600 patients. *Neurosurgery* 2001; 48:524-532; discussion 532-534.
15. Apfelbaum RI. A comparison of percutaneous radiofrequency trigeminal neurolysis and microvascular decompression of the trigeminal nerve for the treatment of tic douloureux. *Neurosurgery* 1977; 1:16-21.
16. Zundert JV, Brabant S, de Kelft EV, Vercruyssen A, Buyten JPV. Pulsed radiofrequency treatment of the Gasserian ganglion in patients with idiopathic trigeminal neuralgia. *Pain* 2003; 104:449-452.
17. Chua NHL, Halim W, Beems T, Vissers KC. Pulsed radiofrequency treatment for trigeminal neuralgia. *Anesth Pain Med* 2012; 1:257-261.
18. Meng L, Jia Z, Shen Y, Ren H, Luo F. Efficacy and safety of CT-guided percutaneous pulsed radiofrequency treatment of the Gasserian ganglion in patients with medically intractable idiopathic trigeminal neuralgia. *J Pain Res* 2018; 11:2877-2885.
19. Erdine S, Ozyalcin NS, Cimen A, Celik M, Talu GK, Disci R. Comparison of pulsed radiofrequency with conventional radiofrequency in the treatment of idiopathic trigeminal neuralgia. *Eur J Pain* 2007; 11:309-313.
20. Elawamy A, Abdalla EEM, Shehata GA. Effects of pulsed versus conventional versus combined radiofrequency for the treatment of trigeminal neuralgia: A prospective study. *Pain Physician* 2017; 20:873- 881.
21. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders. *Cephalalgia* 2004; 1:9-160.
22. The International Classification of Headache Disorders, 3rd edition (beta version). Headache Classification Committee of the International Headache Society (IHS). *Cephalalgia* 2013; 33:629-808.
23. Kim JH, Yu HY, Park SY, Lee SC, Kim YC. Pulsed and conventional radiofrequency treatment: Which is effective for dental procedure-related symptomatic trigeminal neuralgia? *Pain Med* 2013; 14:430-435.
24. Rogers CL, Shetter AG, Fiedler JA, Smith KA, Han PP, Speiser BL. Gamma knife radiosurgery for trigeminal neuralgia: The initial experience of The Barrow Neurological Institute. *Int J Radiat Oncol Biol Phys* 2000; 47:1013-1019.
25. Luo F, Shen Y, Wang T, Meng L, Yu X, Ji N. 3D CT guided pulsed radiofrequency treatment for trigeminal neuralgia. *Pain Pract* 2014; 14:16-21.
26. Fraioli B, Esposito V, Guidetti B, Cruccu G, Manfredi M. Treatment of trigeminal neuralgia by thermocoagulation, glycerolization, and percutaneous compression of the gasserian ganglion and/ or retrogasserian rootlets: Long-term results and therapeutic protocol. *Neurosurgery* 1989; 24:239-245.
27. Sharma R, Phalak M, Katiyar V, Borkar S, Kale SS, Mahapatra AK. Microvascular decompression versus stereotactic radiosurgery as primary treatment modality for trigeminal neuralgia: A systematic review and meta-analysis of prospective comparative trials. *Neurol India* 2018; 66:688-694.
28. Zheng S, Li X, Li R, et al. Factors associated with long-term risk of recurrence after percutaneous radiofrequency thermocoagulation of the gasserian ganglion for patients with trigeminal neuralgia: A multicenter retrospective analysis. *Clin J Pain* 2019; 35:958-966.
29. Ren H, Zhao C, Jia Z, Bian J, Luo F. Predictors of the analgesic efficacy of CT-guided percutaneous pulsed radiofrequency treatment of Gasserian ganglion in patients with idiopathic trigeminal neuralgia. *Pain Pract* 2020; 20:850-858.
30. Tanaka N, Yamaga M, Tateyama S, Uno T, Tsuneyoshi I, Takasaki M. The effect of pulsed radiofrequency current on mechanical allodynia induced with resiniferatoxin in rats. *Anesth Analg* 2010; 111:784-790.
31. Jin H, Ren H, Jia Z, Ji N, Luo F. Pulsed radiofrequency improves neuropathic pain in chronic constriction injury rats through the upregulation of the transcription and translation levels of glial cell line-derived neurotrophic factor. *Pain Physician* 2018; 21:33-40.
32. Vallejo R, Tilley DM, Williams J, Labak S, Aliaga L, Benyamin RM. Pulsed radiofrequency modulates pain regulatory gene expression along the nociceptive pathway. *Pain Physician* 2013; 16:601-613.
33. Ugur HC, Savas A, Elhan A, Kanpolat Y. Unanticipated complication of percutaneous radiofrequency trigeminal rhizotomy: Rhinorrhea: Report of three cases and a cadaver study. *Neurosurgery* 2004; 54:1522-1524; discussion 1524-1526.
34. Egan RA, Pless M, Shults WT. Monocular blindness as a complication of trigeminal radiofrequency rhizotomy. *Am J Ophthalmol* 2001; 131:237-240.
35. Meng Q, Zhang W, Yang Y, Zhou M, Li X. Cardiovascular responses during percutaneous radiofrequency thermocoagulation therapy in primary trigeminal neuralgia. *J Neurosurg Anesthesiol* 2008; 20:131-135.