Observational Study

A Novel Sequential Percutaneous Radiofrequency Treatment Strategy for Drug-refractory Trigeminal Neuralgia: A Propensity Score–matched Study

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Disclaimer: H. Ren, Y. Wang, and Z. Chen contributed equally. This study was supported by the Capital's Funds for Health Improvement and Research (2020-2-2046).

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

Article received: 12-02-2022
Revised article received: 03-21-2024
Accepted for publication: 05-22-2024

Free full article: www.painphysicianjournal.com

Background: Gasserian ganglion-targeted conventional and pulsed radiofrequency treatments are percutaneous procedures performed for drug-refractory trigeminal neuralgia. However, ideal outcomes are not always achieved with these procedures; frequent postprocedural complications and therapeutic ineffectiveness are also of major concern.

Objectives: This study was conducted to investigate a novel strategy for effective, uncomplicated pain relief in patients with drug-refractory trigeminal neuralgia.

Study Design: A multicenter, retrospective, observational study.

Setting: Participating centers were Beijing Tiantan Hospital and Sanbo Brain Hospital.

Methods: From January 2010 through December 2019, a total of 2,087 patients with drug-refractory trigeminal neuralgia were included in the current study. Of them, 143 underwent sequential conventional radiofrequency treatment and 1,944 underwent conventional radiofrequency treatment only. The primary outcome was being pain free at 24 months postprocedure; multiple secondary outcomes were compared between treatments before and after propensity score matching.

Results: At the 24-month follow-up, sequential radiofrequency treatment provided a higher pain-free outcome than conventional radiofrequency treatment (0.93 [95% CI, 0.92–0.94]) vs 0.89, (95% CI, 0.84–0.94; $P = 0.04$); hazard ratio, 1.703 (95% CI, 1.01–2.86). For the 124 propensity score–matched pairs, there was no significant difference between groups, although pain-free outcomes were numerically higher in the sequential radiofrequency treatment group (0.93 [95% CI, 0.89–0.98]) vs 0.90 (95% CI, 0.85–0.96; $P = 0.3$); hazard ratio, 0.653 (95% CI, 0.27–1.60). Notably, sequential radiofrequency treatment correlated with fewer overall postprocedural complications than conventional radiofrequency treatment, despite propensity score matching analysis (14/143 vs 723/1944, relative risk, 0.69 (95% CI, 0.65–0.74; $P < 0.001$); 11/124 vs 45/124, relative risk 0.69 (95% CI, 0.60–0.80; $P < 0.001$).

Limitations: Procedural parameters and quality of life evaluation by treatment were not analyzed and cost data were not collected.

Conclusion: Sequential radiofrequency treatment has the potential to provide effective, uncomplicated, pain-free outcomes.

Key words: Trigeminal neuralgia, pulsed radiofrequency treatment, conventional radiofrequency treatment, propensity score matching

Pain Physician 2024: 27:E785-E794

Trigeminal neuralgia (TN) is a chronic pain syndrome characterized by recurrent episodes of excruciating, electric-shock-like facial pain along the trigeminal dermatomes with an abrupt onset and termination. The incidence of TN is approximately 12.6 to 28.9 per 100,000 person-years, which increases with age and peaks at 67 years old (1,2). Extreme pain results in decreased quality of life and increased suicide attempts (3).

Anticonvulsant agents are recommended as the first-line treatment for paroxysmal attacks of TN (4). However, unbearable side effects and drug interactions result in a 25% drug withdrawal rate, which limit administering anticonvulsants (4).

There is a lack of strong evidence supporting a specific type of surgery for drug-refractory TN. Microvascular decompression, gamma knife surgery, glycerol rhizolysis, balloon compression, and radiofrequency (RF) ablation treatment are all surgical options; however, each has its own advantages and disadvantages. A patient's physical condition, personal wishes, and other factors must be considered when choosing any of these surgeries (4,5).

Percutaneous RF treatment is a minimally invasive local procedure that involves puncturing the foramen ovale with an electrode and discharging a RF electric current (6-8). Conventional RF treatment is an effective technique that has been used for managing TN for more than 30 years (3,4). The mechanisms of conventional RF treatment mainly involve ablative lesioning and heat-induced nerve ablation. This block nociceptive transduction and relieves trigeminal pain. The initial success rate of conventional RF treatment is from 94% to 100%, as suggested by previous literature (9-11). Therefore, conventional RF treatment is one of the recommended options to manage TN in drug-refractory or drug-intolerant patients, especially in elderly patients (12).

Nonetheless, nonselective ablative lesioning of the trigeminal nerve and the gasserian ganglion is associated with unwanted incidental complications, such as dysesthesias, trigeminal motor weakness, anesthesia dolorosa, corneal anesthesia, and additional rarely occurring events. Postprocedural complications impair a patient's quality of life and are attributed to an overall unsatisfactory lifestyle (10).

Pulsed RF treatment is a minimally destructive neuromodulatory technique that was first applied for TN in 2003 (13). In pulsed RF treatment, a 45 V electrical stimulus is applied at 2 Hz, with 20 millisecond stimulation periods separated by 480 millisecond intervals with no current (14). These intervals allow heat dissipation and prevent the temperature of the electrode tip from exceeding 42°C (14,15). A reliance on neuromodulation rather than neuronal ablation makes pulsed RF treatment a relatively safe technique with few severe adverse events compared to conventional RF treatment (16,17), although its therapeutic effectiveness remains controversial (13,18). In our previous investigations, 3-dimensional computed tomography guidance with individualized RF parameters improved the efficacy of pulsed RF treatment (19-22). The pulsed RF treatment produced an uncomplicated success rate of 65% at 24 months (22). The results indicate that pulsed RF treatment is a potential treatment option for drug-refractory TN to try before moving on to invasive treatments.

Based on our clinical experiences, we hypothesized that a novel sequential RF strategy involving initial pulsed RF treatment followed by any necessary conventional RF treatment would improve a patient's overall prognosis compared to conventional RF treatment alone. The rescue procedure, conventional RF treatment, would not be applied unless the pulsed RF treatment failed or TN recurred following the pulsed RF treatment. Consequently, we conducted this retrospective study to investigate the efficacy and safety of sequential RF treatment and examine the hypothesis that sequential RF treatment can decrease the incidence of postprocedural complications compared to conventional RF treatment while providing comparable effectiveness.

Methods

Study Design and Ethical Approval

This was a multicenter, retrospective data analysis involving patients with drug-refractory TN who underwent percutaneous RF treatment at Beijing Tiantan Hospital and Sanbo Brain Hospital Capital Medical University, from January 2010 through December 2019. Data collection and analysis took place from March through June of 2022. Ethics approval was granted by the institutional Medical Ethics Committee before data collection was initiated. All patients were asked before surgery whether their de-identified data could be used for noninterventional research, and were asked to sign an informed consent form if they agreed. Data from patients without this scientific data use agreement were not used in this study.

The study was performed in accordance with the Strengthening the Reporting of Observational Studies

in Epidemiology (STROBE) guidelines (23). Propensity scores were calculated according to the methodological approach reported by Guo and Fraser (24) to detect undesirable demographic bias and identify comparable individuals.

Patient Population and Data Collection

Eligible adult patients were included in our study. As there was no prospective definition of the sequential RF strategy, included patients were deemed to have followed the sequential RF strategy if they: 1) received a successful pulsed RF treatment as their initial percutaneous RF intervention with no pain recurring in the first 2 postprocedural years; 2) received a successful pulsed RF treatment as their initial percutaneous RF intervention and received a subsequent conventional RF treatment for recurrent TN in the first 2 postprocedural years; or 3) did not respond to pulsed RF treatment and underwent conventional RF treatment one month post the initial procedure.

The exclusion criteria were: 1) patients with incomplete information or follow-up data; 2) a history of any invasive treatment for TN; 3) having received an invasive treatment at another medical facility during the study period; 4) had undergone invasive treatments other than conventional RF treatment.

The included patients were divided into sequential and conventional RF groups based on the treatments received. After obtaining permission for data extraction, we searched the institutional information system for patients' sociodemographic and baseline information. The recorded characteristics included age, gender, affected nerve division(s), laterality, etiology (secondary or nonsecondary TN), pretreatment pain intensity, and disease course length. The definition of secondary TN was based on the ICHD-3 (25) as follows:

A) Recurrent paroxysms of unilateral facial pain fulfilling the criteria for TN, either purely paroxysmal or associated with concomitant continuous or near-continuous pain.
B) An underlying disease has been confirmed to cause or explain the neuralgia.
C) Not better accounted for by another ICHD-3 diagnosis.

We also checked outpatient records and departmental follow-up notes (for clinical use, routine follow-up was conducted through outpatient visits, social media, or telephone calls to assess therapeutic effectiveness and safety issues).

Procedures

Either pulsed or conventional RF treatment was performed on all included patients under 3-dimensional computed tomography scanning guidance. Continuous monitoring of blood pressure, heart rate, electrocardiogram features, pulse, and blood oxygen saturation was routinely established before the procedure began. The negative electrode of a PMG-230 RF generator (Baylis Medical Inc.) was placed on each patient's lower back. All procedures were carried out in accordance with the methods described previously (21,26). Manual pulse RF mode was set for pulsed RF treatment. The upper pulsed RF temperature limit was set to 42°C. The output voltage was gradually increased to the highest voltage that the patient could tolerate (with no obvious discomfort) for 360 seconds (27-29). For conventional RF treatment, the temperature and RF time were set as per the physician's evaluation (26). Each mode of RF treatment was adjusted according to the operators' evaluation and the patients' response in order to maximize efficacy and safety.

Therapeutic Effectiveness Definition and Outcome Observation

The therapeutic effectiveness was determined using the Barrow Neurological Institute Pain Inventory (BNI [BNI I - no pain without medications, BNI II – mild pain without medications, BNI IIIa – no pain with medication, BNI IIIb – endurable pain with medication, BNI IV – intensified pain inadequately controlled by medication, BNI V – persistent pain with medication]). Postprocedural pain graded as BNI I-IIIb was defined as a responsive intervention;, BNI scores of IV-V were defined as a failed procedure. Recurrence was defined as deteriorated pain relief (BNI IV-V) after a responsive initial intervention (26). The primary outcome was being pain-free at 24 months postprocedurally. Secondary outcomes were the success rate of either procedure at 6, 12, and 24 months postprocedurally as well as any incidence of postprocedural complications.

Sample Size Estimation and Statistical Analyses

Since there was a scarcity investigating being pain-free from sequential RF treatment at 24 months postprocedurally, the sample size of our study was beyond estimation. The sample size of this study was evaluated based on feasibility. We therefore included all available patients to improve the statistical power.

Data are presented as the mean and SD for normally distributed continuous variables and the median and interquartile range for skewed continuous variables. Categorical variables are presented as counts and percentages. Considering the potential confounding factors in a prespecified analysis, we used propensity score analysis to compare outcomes of the sequential RF group and conventional RF group. Initially, logistic regression analysis was performed using predetermined baseline characteristic variables to compute the propensity score for every patient. Variables included in the propensity model were age, gender, laterality, BNI score before intervention, etiology, length of disease, and affected division. Patients were paired following a 1:1 nearest neighbor matching without replacement by treatment. The maximal permissible calliper width was 0.1 during propensity score matching. A blinded independent biostatistician, unaware of treatment allocation and clinical outcome data, conducted the propensity score analyses.

After correcting for these confounding factors, the Kaplan–Meier curves were delineated for time-to-recurrence outcomes. Between-group comparisons were performed with the Kruskal–Wallis test and the Wilcoxon signed-rank test for continuous variables; the χ^2 test, the McNemar test, and conditional logistic regression for categorical variables; and the log-rank test for survival variables. The Cox model was applied to estimate hazard ratios with corresponding 2-sided 95% CIs. A P value < 0.05 was taken to indicate statistical significance. The computations for all statistical analyses and propensity score matching were performed using RStudio 2021.09.0+351 Ghost Orchid (Posit Software).

Results

We identified an initial cohort of 3,094 patients who underwent percutaneous RF treatment in the study settings from January 2010 through December 2019. We excluded 436 patients who were invasively treated for TN before receiving RF treatment. Incomplete demographic and clinical data were noted in 517 patients, who were also excluded from the study. Consequently, 143 patients were included in the sequential RF group. On the other hand, 1,944 patients receiving conventional RF treatment were included in this analysis.

The propensity score was calculated for each individual included in the study. We matched 124 patients into pairs on the basis of similar propensity scores (Fig. 1).

Regarding sociodemographic characteristics, statistical significance was detected in most items (Table 1). Compared to those in the sequential RF group, patients in the conventional RF group were older (P < 0.001), experienced greater pain (P < 0.001), and were more frequently affected on the right side (P = 0.025). Additionally, patients in the conventional RF group had TN for a longer duration (P < 0.001), and had a higher incidence of primary TN (P = 0.042). More women were treated in the conventional RF group (P < 0.001).

In order to offset the imbalance in patients' demographic information, we estimated propensity scores with a logistic regression model. All demographic characteristics were considered confounding factors and were included in the logistic regression model as covariates. We matched 124 pairs of patients by treatment. Statistical significance was not detected in baseline demographic characteristics between the matched pairs (Table 2).

In the sequential RF treatment group (n = 143), 57 patients received an extra Gasserian ganglion puncture for conventional RF treatment. In 42 of the patients in this group (29.4%), conventional treatment was performed because the patients did not respond to pulsed RF treatment; in the other 15 (10.5%) cases, it was performed because trigeminal pain recurred. All conventional RF treatment performed after sequential RF treatment elicited a clinical response. Recurrence was reported in 4 (2.8%), 7 (4.2%) and 11 (7.7%) patients at 6, 12, and 24 months postprocedure.

Of patients who underwent conventional RF treatment (n = 1,944), the initial procedure failed in 33 patients, leading to an initial success rate of 98.3%. A higher recurrence rate was detected in patients receiving this treatment, with 6.3%, 10.2%, and 14.6% of patients developing TN at 6, 12, and 24 months postprocedure.

Sequential RF treatment showed a higher recurrence-free rate than conventional treatment; the difference by treatment was statistically significant (0.93; 95% CI, 0.92–0.94) vs 0.89; (95% CI, 0.84–0.94; P = 0.04), hazard ratio, 1.703 (95% CI, 1.01–2.86), (Fig. 2a). For the 124 matched pairs, 12 patients in the conventional RF group and 8 in the sequential RF group had TN recurrence at the end of follow-up. The effectiveness rate of the sequential RF group was still greater than that of the conventional RF group at each time point, although the intergroup difference in the recurrence-free rate was not statistically significant (0.93; 95% CI, 0.89–0.98) vs 0.90 (95% CI, 0.85–0.96; P = 0.3); hazard

ratio, 0.653 (95% CI, 0.27–1.60), (Fig. 2b).

For safety considerations (Fig. 3), the incidence of puncture-associated complications, including intraoperative transient bradycardia, local facial hematoma, self-limited tinnitus, or other rarely occurring events, were not statistically significant between treatments (overall incidence: 3.2% for sequential RF treatment vs 2.6% for conventional RF treatment), although the puncture per patient ratio was higher in the sequential RF treatment (200 punctures in 143 patients, 1.4 punctures per patient).

Regarding postprocedural safety issues, sequential RF treatment significantly decreased the incidence of 2 major complications: dysesthesia (8 of 143 vs 311 of 1,944, relative risk [RR], 0.88 95% CI, 0.85–0.93) among the patient population, compared to conventional RF treatment, (6 of 124 vs 25 of 124, RR 0.84 [95% CI, 0.76–0.92] after propensity score matching); and trigger motor weakness (13 of 143 vs 422 of 1,944, RR 0.86 [95% CI, 0.81–0.91]) among the patient population, 34 of 124 vs 11 of 124, RR 0.79 (95% CI, 0.70–0.89 after propensity score matching).

In the sequential RF group, the incidence of other uncommon postprocedural events, including anaesthesia dolorosa, corneal anesthesia and facial herpes, were also decreased. None of the included patients developed diplopia or aseptic meningitis. Sequential RF treatment correlated with a decreased incidence of overall postprocedural complications compared to conventional RF treatment, regardless of propensity score matching analysis (14 of 143 vs 723 of 1,944, RR 0.69 [95% CI, 0.65–0.74; $P < 0.001$]); 11 of 124 vs 45 of 124, RR 0.69 (95% CI, 0.60–0.80; $P < 0.001$).

Discussion

Our analysis investigated the effectiveness and safety of a novel sequential percutaneous RF strategy (involving pulsed and, if necessary, conventional RF treatment) for drug-refractory TN. The propensity score was estimated for each included patient based on their demographic baseline information to achieve more convincing study outcomes. Compared to conventional RF treatment, sequential treatment provided a superior recurrence-free rate at 24 months postprocedure among the included patients in general and in propensity score-matched pairs.

Statistical significance was detected between treatments until the patients were matched. Furthermore, sequential RF treatment significantly decreased the overall incidence of postprocedural complications

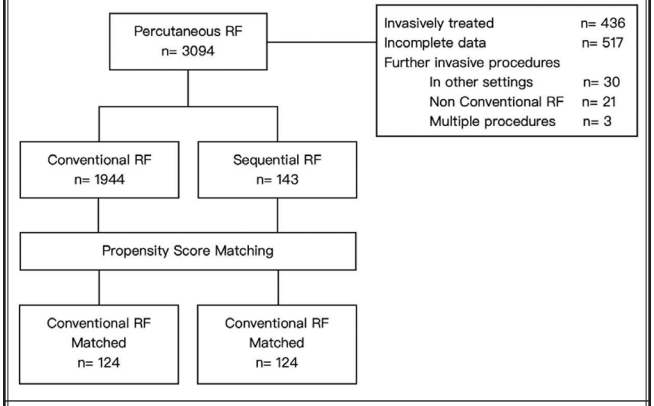

Fig. 1. *Study profile. RF denotes radiofrequency.*

Table 1. *Patient demographics by treatment group before propensity score matching.*

	Conventional n = 1944	Sequential n = 143	*P* value
Age1	71.1 [56.4-85.8]	53.5 [46.7-61.3]	< 0.001
Gender[2]			
Women	1,315 (68%)	73 (51%)	< 0.001
Men	629 (32%)	70 (49%)	
Laterality[§]			
Right	1,079 (56%)	65 (46%)	0.025
Left	865 (44%)	78 (54%)	
BNI before intervention[2]			
IV	692 (36%)	113 (79%)	< 0.001
V	1,252 (64%)	30 (21%)	
Etiology[2,3]			
Secondary	84 (4%)	12 (8%)	0.042
Primary	1,860 (96%)	131 (92%)	
Length of disease[1](mos)	110.6 [59.3-161.9]	58.1 [26.3-89.9]	< 0.001
Affected division(s)[2,4] (%)			
I	192 (10%)	16 (11%)	0.116
II	223 (12%)	12 (8%)	
III	523 (27%)	48 (34%)	
I+II	294 (15%)	14 (10%)	
I+III	17 (1%)	3 (2%)	
II+III	386 (19%)	33 (23%)	
I+II+III	309 (16%)	17 (12%)	

Data are presented as the median (interquartile range) or n (%). BNI = Barrow Neurological Institute Pain Inventory. [1]Kruskal–Wallis test. [2]χ^2test or Fisher's exact test. [3]Per the International Classification of Headache Disorders, 3rd edition, by the Headache Classification Committee of the International Headache Society (IHS). [4]Trigeminal division: I for ophthalmic, II for maxillary and III for mandibular.

Table 2. *Baseline demographics by treatment (propensity score matched).*

	Conventional n = 124	Sequential n = 124	*P* value
Age[1]	53.8 [46.4-62.2]	54.5 [48.0-61.0]	0.429
Gender[2]			
Women	67 (54%)	65 (52%)	0.899
Men	57 (46%)	59 (48%)	
Laterality[2]			
Right	62 (50%)	60 (48%)	0.899
Left	62 (50%)	64 (52%)	
BNI before intervention[2]			
IV	90 (73%)	96 (77%)	0.463
V	34 (27%)	28 (23%)	
Aetiology[2,3]			
Secondary	9 (7%)	12 (10%)	0.648
Non-secondary	115 (93%)	112 (90%)	
Length of disease[1](mos)	60.6 (28.0-93.2)	62.5 (31.2-93.8)	0.638
Affected division(s)[2,4] (%)			
I	11 (8.9%)	12 (9.7%)	0.964
II	14 (11.3%)	11 (8.9%)	
III	38 (30.6%)	41 (33.1%)	
I+II	12 (9.7%)	13 (10.5%)	
I+III	3 (2.4%)	3 (2.4%)	
II+III	26 (21.0%)	29 (23.4%)	
I+II+III	20 (16.1%)	15 (12.1%)	

Data are presented as the mean (SD), median [interquartile range] or n (%). BNI = Barrow Neurological Institute Pain Inventory. [1]Wilcoxon signed-rank test. [2]McNemar test for paired 2 x 2 categorical data, conditional logistic model for 2 x N (N > 2) categorical data. [3]Per the International Classification of Headache Disorders, 3rd edition, by the Headache Classification Committee of the International Headache Society (IHS). [4]Trigeminal division: I for ophthalmic, II for maxillary and III for mandibular.

before and after propensity score matching. To the best of our knowledge, our study is the first to demonstrate a sequential strategy of percutaneous RF interventions.

Our team reported in prior studies, the initial response rate of pulsed RF treatment was above 70% for drug-refractory TN (21,22). For patients who did not respond to pulsed RF treatment, conventional treatment was still relatively effective, although the exact success rate was not examined (22). We therefore speculated that the effectiveness of sequential RF treatment would be comparable to that of the conventional form. In the current study, all patients who underwent sequential RF interventions showed responsiveness to pulsed RF treatment and/or subsequent conventional RF treatment; the latter was performed if patients did not respond to pulsed treatment or if TN recurred after pulsed treatment.

The initial success rate of sequential RF treatment was 100%. For patients receiving conventional RF treatment, the initial response rate was 98.3%. This outcome was consistent with previous investigations (9-11). By the end of the study period, a total of 11 in the sequential RF treatment group and 283 patients in the conventional RF treatment experienced TN recurrence. The 2-year recurrence-free rate among those who received sequential RF treatment was 6.9% higher than those who received conventional RF treatments only. The difference was statistically significant (92.3% vs 85.4%, $P = 0.04$). For propensity score matched-patients, the overall recurrence-free survival at 2 years postprocedure was 90.3% for conventional RF treatment and 93.5% for sequential RF treatment. Although no significant difference was detected, the overall recurrence-free rate for sequential RF treatment was 3.2% higher than that of conventional RF treatment.

The incidence of overall postprocedural complications was 10% and 37% for sequential and conventional RF treatment, respectively (RR 0.69; 95% CI, 0.65–0.74; $P < 0.001$). Trigeminal motor weakness was the most frequent complication and was observed in nearly 22% of patients who received conventional RF treatment, which was approximately 14% higher than the rate among patients who received sequential RF treatment (RR 0.86; 95% CI, 0.81–0.91; $P < 0.001$). Facial dysesthesia developed in 16% of patients who received conventional RF treatment, which was 10% higher than the incidence in patients who received sequential RF treatment (RR 0.86; 95% CI, 0.81–0.91; $P < 0.001$). The safety profile of conventional RF treatment was consistent with previous investigations (30-32). The incidence of adverse events varied from 8% to 20% for dysesthesia and from 10% to 28% for trigeminal motor weakness (30-34).

Our results suggest that sequential RF treatment is associated with a reduced incidence of treatment-related and postprocedural complications. The reduction of adverse events with sequential RF treatment compared to conventional RF treatment was statistically significant both before and after propensity score matching. Compared to the conventional RF treatment group that only received neurodestructive surgery, sequential RF strategy enables a substantial number of patients with TN avoid or postpone the consequences of conventional RF treatment for at least 2 years. This also means that a subset of patients

may experience no or delayed neurodestruction-related adverse effects for up to 2 years after pulsed RF treatment.

Sequential RF treatment entails more puncture procedures, and may increase the number of puncture-related adverse events (35,36). The use of blunt trocar needles can reduce puncture-related adverse events (35); however, these are unavailable in some places. Although sharp trocar needles were used in our study, puncture-related events were rarely observed in either group, and the overall puncture incidence for sequential RF treatment was only slightly higher than that for conventional treatment. Lethal puncture-related events, such as accidental intraarterial stick, were not observed. Recoverable nonfatal complications, such as facial hematoma and self-limited tinnitus, occurred but were very low in both groups (3.2% for sequential RF treatment vs 2.6% for conventional RF treatment). This can be explained by the application of 3-dimensional computed tomography guidance, which provided optimal surgical vision to observe the full puncture process (29,37-40). In several previous studies performed by our team (19-21), CT-guided foramen ovale puncture demonstrated a very good safety profile without serious puncture-related complications. However, other hospitals that are not equipped with CT-guidance for puncture should use blunt trocar needles. Similarly, the incidence of puncture-associated events were comparable across groups, although patients who received sequential RF treatments received considerably more puncture attempts. The findings confirmed our hypothesis that sequential RF treatment would have a lower postprocedural complication rate than conventional treatment while producing favorable therapeutic effectiveness.

We proposed a sequential RF treatment strategy based on the expectation of an uncomplicated, pain-free experience and an increased overall postprocedural quality of life. In our study design,

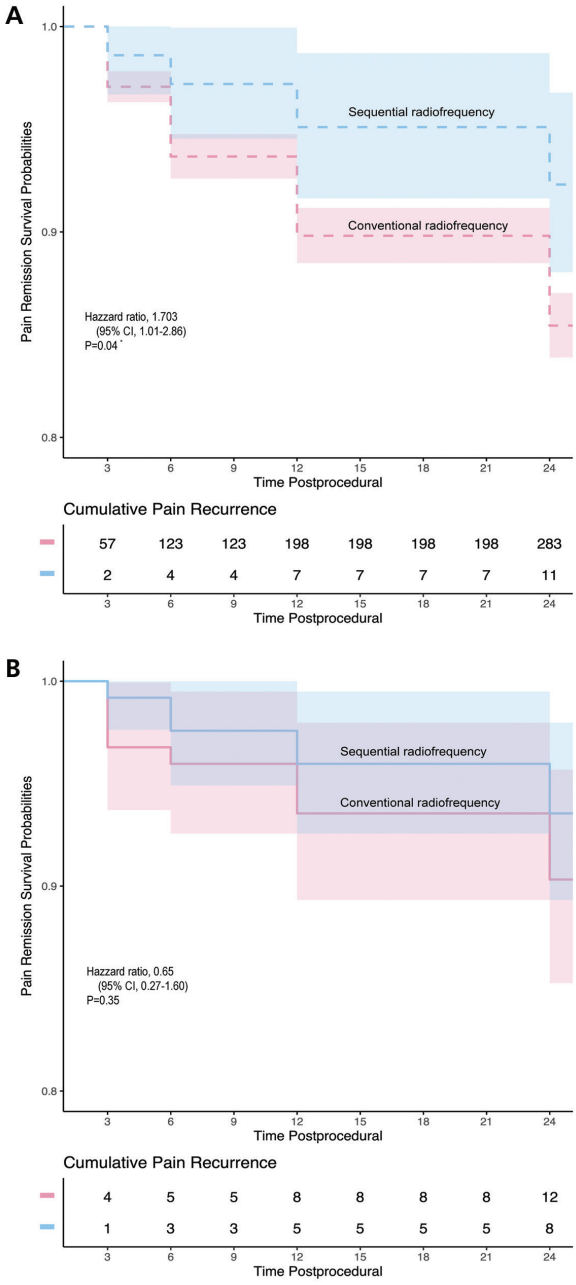

Fig. 2. *A) Kaplan–Meier curves for pain-free survival and cumulative recurrence in the overall sample.Blue and pink represent sequential and conventional radiofrequency treatment, respectively. The lines are Kaplan–Meier curves; the shaded areas denote 95% CIs. Survival comparison between sequential and conventional radiofrequency treatments. HR, 1.703 (95% CI, 1.01-2.86); P = 0.04 by the log-rank test. *:P < 0.05; B) Kaplan–Meier curves for pain-free survival and cumulative recurrence in propensity-matched pairs. Blue and pink represent sequential and conventional radiofrequency treatment. The lines are Kaplan–Meier curves; the shaded areas denote 95% CIs. Survival comparison between sequential and conventional radiofrequency treatment. HR, 0.65 (95% CI, 0.27-1.60); P = 0.35 by the log-rank test. *:P < 0.05*

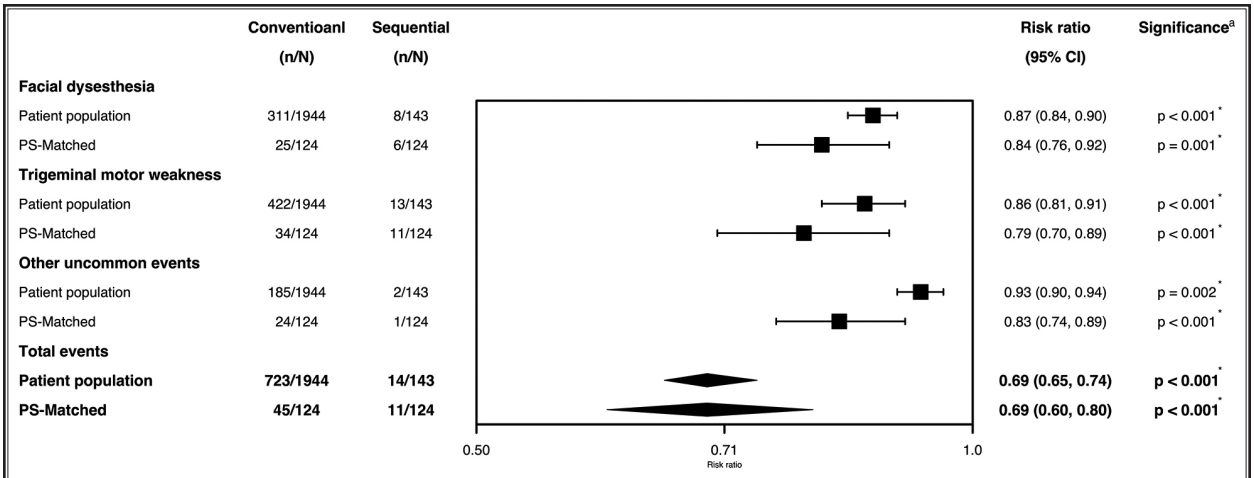

Fig. 3. *Forest plot for postprocedural complications*.
[a]: Significance by treatment, compared using the chi-square test and Fisher's exact test. *:$P < 0.05$

we used 3 types of clinical circumstances to illustrate the sequential RF strategy. Prospectively, conventional RF treatment as part of a sequential strategy was applied when pulsed RF treatment failed to provide sufficient pain relief. Thus, it could be performed shortly after the initial pulsed RF treatment or postponed until pain recurred.

Our recent longitudinal analysis revealed that 3-dimensional computed tomography–guided pulsed RF treatment with appropriate parameters provided uncomplicated long-term (more than 144 months) pain relief for up to 50% of treated patients, which ideally exempted approximately half of the patients from subsequent conventional RF treatment. Due to the retrospective nature of the study, we restricted the follow-up period to 24 months to obtain a sufficiently large sample size to support strong conclusions. The findings in the present study confirmed our expectations within the limited study period. Out of 143 patients who were treated according with a sequential strategy, 57 received subsequent conventional RF treatment within 2 years. The main concern for these patients was the underlying risk attributable to the repeated puncture. Nonetheless, we believe using 3-dimensional computed tomography guidance decreased the undesirable events attributed to the Gasserian ganglion puncture. The results concerning the puncture-associated events met our previous expectations (40).

Limitations

This study has several limitations. First, we managed the baseline characteristics with a propensity score estimation to even the differences in demographics. However, the baseline information of the matched patients was evidently shifted due to the matching process. Therefore, the matched cohort may not have accurately represented the general population. Nonetheless, due to the retrospective nature of the study, we did not perform a sensitivity analysis of procedural parameters and quality of life evaluation by treatment.

Another concern is the total treatment cost that the patients incurred. If sequential RF treatment is followed by conventional RF treatment, patients incur additional costs. Nonetheless, we were unable to collect cost data because of the retrospective nature of the study, changes in RF procedure fees and reimbursement policies, and other potential costs for treating TN and/or its complications.

In this retrospective study, all patients were treated using sharp needles because blunt needles are not commercially available in the People's Republic of China. Sharp needles are a risk for puncture-related adverse events such as hematomas, death, and hemorrhage. However, all puncture procedures in our study were performed under 3-dimensional reconstructed image guidance generated by spiral CT; serious puncture-related adverse events did not occur. In the future, prospective studies should be conducted using different kinds of needles. Further prospective, randomized clinical trials are warranted to investigate the effectiveness, safety, and cost-effectiveness of the sequential RF treatment strategy.

Conclusions

Sequential RF treatment is a potential treatment option for drug-refractory TN. Compared to conventional RF treatment, this novel strategy showed comparable overall medium-term effectiveness and a significantly decreased incidence of treatment-related and overall postprocedural complications. Given the retrospective nature of the study, further considerations involving cost-effectiveness analysis and quality-of-life evaluations were not included in our study. Therefore, the results of our investigation should be interpreted with caution. A further prospective multicenter randomized open-label study on sequential RF treatment is currently being conducted by our research team.

Role of the Sponsor

The sponsor had no role in the trial design, trial conduct, data handling, data analysis, or writing and publication of the manuscript.

Author Contributions

Hao Ren helped perform study analysis, figure generation, and wrote the main manuscript text.

Yang Wang helped prepare figures, analyze the study, and collect data.

Zheng Chen helped generate figures, supervise study conduction, and review the manuscript.

Yan Zhang helped review the manuscript, supervise study analysis, generate figures, and read and approved the final manuscript.

Guo Feng Ma helped analyze the study, supervise study conduction, and read and approved the final manuscript.

Fang Luo helped conceive the idea for this study, conduct the study, and read and approved the final manuscript.

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