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Percutaneous radiofrequency trigeminal rhizotomy benefits in patients with refractory trigeminal neuralgia

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Abstract

A significant number of patients suffers from refractory trigeminal neuralgia (TN) after receiving microvascular decompression (MVD) or other neuro-destructive procedure such as gamma knife radiosurgery (GKRS). This study aims to demonstrate a remediable, reproducible approach to treating refractory pain effectively by percutaneous radiofrequency trigeminal rhizotomy (RF-TR).

A total of 392 patients with TN were treated by RF-TR during the past 10 years. Among these patients, 48 cases who had received either MVD, GKRS alone, or a combination of both were assigned to group A. Those who had not received any form of treatment (125 patients) or failed to respond medically (130 patients) were assigned as the control group (group B). All the RF-TR were performed by a single surgeon with the aid of intraoperative computed tomography (iCT)-based neuronavigation with magnetic resonance (MR) image fusion. The outcome measure was the numerical rating scale (NRS) expressed subjectively by patients. The paired Student *t* test and the analysis of covariance (ANCOVA) were used for statistical analysis.

In group A, 21 of 24 patients (88%) had significant improvement (NRS change ≥5) in facial pain after RF-TR. The average NRS score was 9.75 ± 0.53 before the procedure and 1.92 ± 3.35 post-treatment (significant NRS decrease [$P = .000$]). On the other hand, in group B, 226 of 255 patients (89%) also had dramatic amelioration of facial pain after RF-TR. The average NRS score was 9.46 ± 0.69 before the procedure and 1.62 ± 2.85 post-treatment (7.84 ± 2.82 in NRS decrease [$P = .008$]). By using a univariate ANCOVA, no statistical significance was found in NRS score improvement between the two groups.

Repeated MVD and GKRS for refractory TN may be less desirable due to a greater risk of mortality (up to 0.8%) and morbidity (4% of serious complications). Conversely, RF-TR administration with the novel navigation technique by using iCT and MR image fusion is free from any remarkable and irreversible morbidities. In this study, RF-TR not only provided an alternative and effective strategy if TN recurred but also resulted in the same NRS score improvement regardless of the status of prior treatment.

Abbreviations: ANCOVA = analysis of covariance, GKRS = gamma knife radiosurgery, iCT = intraoperative computed tomography, MR = magnetic resonance, MVD = microvascular decompression, NRS = numerical rating scale, RF-TR = percutaneous radiofrequency trigeminal rhizotomy.

Keywords: gamma knife radiosurgery, intraoperative computed tomography, microvascular decompression, neuro-destructive procedure, radiofrequency trigeminal rhizotomy, refractory trigeminal neuralgia, tic douloureux, trigeminal neuralgia

1. Introduction

Trigeminal neuralgia (TN), also known as tic douloureux, is the most commonly seen cranial neuralgia.[1] The incidence of TN ranges between 4.5 and 28.9 per 100,000 per year, which rises with the increase in age and is more prevalent in women than men (male-to-female ratio 1:1.8).[2] Symptoms onset is mainly in middle age; young adults and children are less frequently affected.[3] TN is characterized by paroxysmal episodes of sharp pain confined to the dermatome of the trigeminal nerve, which can be triggered by non-noxious stimuli such as wind, chewing, talking, coldness and light touch, and may result in full sensory dysfunction.[4] Up to 44% of patients experience unsatisfactory level of pain relief while on standard medical treatment with

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The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

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anticonvulsants such as carbamazepine, thus requiring further intervention.[5]

Nowadays, there are several interventions other than medication available for TN, including microvascular decompression (MVD), percutaneous radiofrequency trigeminal rhizotomy (RF-TR), percutaneous glycerol rhizotomy (PGR), percutaneous balloon compression (PBC), and stereotactic radiosurgery (SRS), such as gamma knife radiosurgery (GKRS) or cyberknife.[6]

These procedures are characterized by different success rates and side effect profiles. However, there is no single, standard for the treatment of TN, which must be individualized in accordance with the risks and benefits.[1]

A significant proportion of patients still suffer from refractory TN even after receiving MVD or other neuro-destructive procedures such as GKRS, which are regarded as effective and definitive treatments for TN. The reported annual recurrence rate ranges from 1% to 5%.[7–9] The cure for patients suffering from refractory TN has been challenging. Repeated MVD or GKRS for refractory TN may be less desirable due to a greater risk of mortality and morbidity, which are caused by adhesion and radiation overdose, respectively. Conversely, percutaneous radiofrequency ablation of the trigeminal gasserian ganglion, has gained much more acceptance in TN patients who are refractory to other forms of therapy.

There is a lack of research focusing on PR-TR intervention for refractory TN. Therefore, this study aims to demonstrate the utility of RF-TR in treating patients with refractory TN who have failed MVD, GKRS, or both.

2. Materials and methods

This retrospective study has been approved by the Research Ethics Committee of Chang Gung Medical Foundation (IRB number: 201902111B0).

2.1. Study group selection

Between May 2010 and December 2016, a total of 392 patients with TN ranging from 20 to 90 years old (mean 63.7) were included. Among these patients, 24 cases had refractory TN in which 2 patients received MVD, 17 patients received GKRS, and 5 patients received both MVD and GKRS before the procedure. These patients were assigned to group A as shown in Table 1. Patients who had not undergone MVD or neuro-destructive treatment or had failed to respond medically (130 patients) were assigned to the control group (group B), as shown in Table 2. All the patients subsequently received RF-TR in our hospital. No patients in the study had a documented history of multiple sclerosis or associated magnetic resonance (MR) images of mass-occupying lesion.

2.2. Operative procedure

In this study, the patients were treated with RF-TR at our institution's Brain-SUITE Intraoperative computed tomography (iCT, Siemens Healthcare, Erlangen, Germany and Brainlab, Feldkirchen, Germany). All procedures were performed on an outpatient basis by a single surgeon (Jen-Tsung Yang). Briefly, the ENT reference array was strapped to the patient's forehead for registration on the neuronavigation system. A head CT scan was performed intraoperatively, and the acquired images were sent to the computer for planning. The MR images with the highlighted trigeminal cistern were fused with the iCT images. The instrument adaptor was attached to the hub of a 100-mm long, 20-gauge radiofrequency-insulated cannula with a 5-mm active tip. The entry point as defined by the landmarks of Hartel's technique was adjusted based on fusion image guidance for an unobstructed linear pathway toward the trigeminal cistern. Xylocaine (1%) was infiltrated, and cannulation was done under real-time guidance by neuronavigation with fusion images.

All patients were awake while cannulation took place under local anesthesia and fentanyl (25–50 μg every 5–10 minutes). After localization of the electrode tip by electrophysiological test stimulation, ablation was performed following light sedation with the administration of propofol (1%, 1–1.5 mg/kg). The pulse oximetry, continuous electrocardiography, and blood pressure of the patients were monitored throughout the procedure. Two consecutive lesions were made at a temperature

Table 1

Group A (comparator) patient characteristics (n=24).

Parameters	Values
Age	63.7 (20–90)
Sex	
Male	6 (25%)
Female	18 (75%)
Side of pain	
Right	19 (79%)
Left	5 (21%)
Pain distribution	
V2	2 (8%)
V3	5 (21%)
V2, V3	17 (71%)
Previous treatment	
Only MVD	2 (8%)
Only GKRS	17 (71%)
MVD + GKRS	5 (21%)
Pre-RF-TR NRS score (mean)	9.75

GKRS = gamma knife radiosurgery, MVD = microvascular decompression, RF-TR = percutaneous radiofrequency trigeminal rhizotomy.

Table 2

Group B (control) patient characteristics (n=255).

Parameters	Values
Age	63.2 (20–87)
Sex	
Male	95 (37%)
Female	160 (63%)
Side of pain	
Right	152 (60%)
Left	103 (40%)
Pain distribution	
V2	52 (20%)
V3	62 (24%)
V2, V3	141 (55%)
Previous treatment	
Medications	130 (51%)
None	125 (49%)
Pre-RF-TR NRS score (mean)	9.46

RF-TR = percutaneous radiofrequency trigeminal rhizotomy.

Table 3

NRS score data.

Group	Study design	N	Intervention	Mean	SD	SEM
A	Had received GKRS or MVD	24	Pre-RF-TR NRS score	9.75	0.53	0.108
			Post-RF-TR NRS score	1.92	3.35	0.683
B	Had *not* received GKRS or MVD	255	Pre-RF-TR NRS score	9.46	0.69	0.043
			Post-RF-TR NRS score	1.62	2.85	0.179

Both group A (NRS: 9.75–1.92, $P=.000$) and group B (NRS: 9.46–1.62, $P=.008$) had immediate drastic improvement of the trigeminal neuralgia symptoms.

GKRS = gamma knife radiosurgery, MVD = microvascular decompression, NRS = numerical rating scale, RF-TR = percutaneous radiofrequency trigeminal rhizotomy, SD = standard deviation, SEM = standard error mean.

of 70 to 95°C for 100 seconds. The temperature in this study was higher than our previous procedures by 5 to 10°C. After completing the procedure, the patients were awakened from the anesthesia to assess the efficacy of the procedure.

2.3. Analytic technique

The postoperative follow-up period ranged from 26 to 95 months. A satisfaction survey was conducted by telephone interview. The numerical rating scale (NRS) expressed subjectively by each patient was used to evaluate the severity of pain before and after the RF-TR. Statistical Package for the Social Sciences (SPSS) version 25 for Mac was used for analysis. The Wilcoxon signed-rank test was used for acknowledging the effect of RF-TR in group A; whereas the paired Student *t* test was used for group B; the univariate analysis of covariance (ANCOVA) was used for differentiating the striking results of NRS improvement between Group A and Group B (control group). The differences were considered statistically significant when $P<.05$.

3. Results

3.1. Clinical outcomes

In group A, 21 of 24 patients (88%) had marked improvement (NRS change ≥5) of facial pain after RF-TR. The average NRS score was 9.75 ± 0.53 before and 1.92 ± 3.35 after treatment (Significant NRS decrease [$P=.000$]). There were still three patients (12%) who had no pain relief postoperatively. No patients developed diplopia, keratitis, or anesthesia dolorosa at long-term follow-up. On the other hand, 226 of 255 patients (89%) in group B had dramatic amelioration of facial pain after RF-TR. The average NRS score was 9.46 ± 0.69 before and 1.62 ± 2.85 after treatment (7.84 ± 2.82 in NRS decrease [$P=.008$]). There were 29 patients (11%) without proper pain

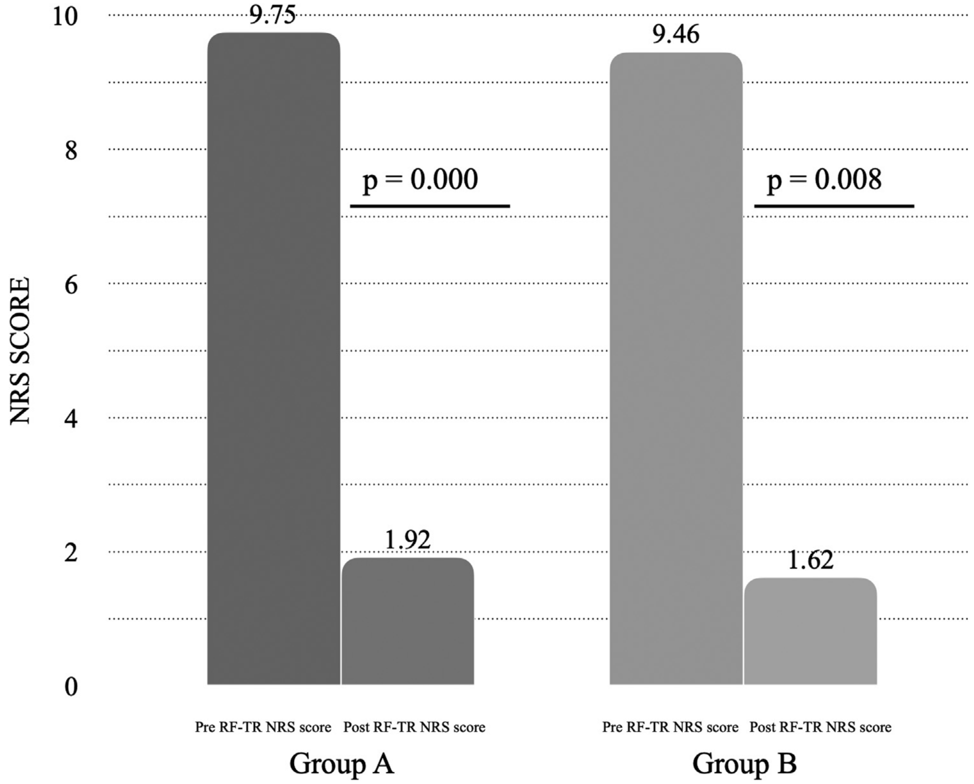

Figure 1. The desirable outcome of both group A and group B in graphics.

Table 4

NRS score improvement (pre-RF-TR NRS score–post-RF-TR NRS score).

Group	Study design	Analysis	Result	*P*-Value	Interpretation
Group A	Had received GKRS or MVD	Wilcoxon signed-rank test	Reject null hypothesis (RF-TR NRS: pre = post)	.000	Significant NRS improvement
Group B	Had *not* received GKRS or MVD	Paired Student *t* test	NRS improvement 7.84 ± 2.82	.008	Significant NRS improvement
Group A vs group B		Analysis of covariance	NRS improvement group A ≠ group B	.891	No statistical difference in NRS improvement between group A and B

There is no difference in the degree of clinical improvement between the two groups (*P* = .891).
GKRS = gamma knife radiosurgery, MVD = microvascular decompression, NRS = numerical rating scale, RF-TR = percutaneous radiofrequency trigeminal rhizotomy.

relief postoperatively. Data are shown in Tables 3 and 4 and Figure 1.

3.2. NRS score improvement

Significant improvements were observed in both group A and B. The difference in the degree of clinical response between the two groups was analyzed by the ANCOVA, which showed no statistical significance (*P* = .891), shown in Table 4. Thus dramatic improvements could be achieved by RF-TR in patients who relapsed following MVD, GKRS, or both, to the same degree as patients who had no prior treatment except for medication alone.

4. Discussion

4.1. RF-TR for TN

Percutaneous neuro-destructive procedures use a needle to precisely access the gasserian ganglion. Lesioning is facilitated by thermocoagulation, chemical ablation, or mechanical compression. With a 25-year experience involving 1600 patients, the clinical analysis by Kanpolat et al show initial response rates of 97.6% to 99%, with 41% of patients maintaining complete pain control after 20 years.[1] Recurrence rates differ from 38.2% at 1 year[10] to 10% at 6.5 years of follow-up.[11] Complications of RF-TR include hypesthesia with 3.3% of patients experiencing symptoms for more than 1 month.[12] There is a 5.7% to 17.3% rate of loss of corneal sensation and a 0.6% to 1.9% rate of keratitis.[1,10,11] 4% of patients experience masseter weakness,[1] and a 0.6% to 0.8% rate of anesthesia dolorosa.[1,10] Higher temperatures may be related to the prevalence of postoperative hypesthesia.[13]

In TN, our RF-TR procedure can provide significant pain relief immediately for a patient who had not received any previous invasive treatments (group B); a satisfying average of 7.84 NRS improvement was found in this patient group.

As for refractory TN, a nationwide study revealed most patients had an RF-TR as a secondary procedure after MVD or GKRS.[14] The head-to-head comparisons of initial success rate, recurrence rate and rate of adverse events between RF-TR and MVD, as well as RF-TR and GKRS are discussed below.

4.2. RF-TR versus MVD for refractory TN

MVD for TN is associated with an immediate symptom relief rate of 80.3% to 96%,[15–17] and 72% to 85% at 5 years.[17] Evidence of arterial or venous compression is linked with a better outcome.[18,19] However, because MVD is more invasive than other surgical procedures for TN, its efficacy and safety in older patients have been widely debated. The mortality rate is reported to be between 0.15% and 0.8%.[13,20,21] Complications including facial weakness, occur in 0.6% to 10.6%, with some deficits improving with time,[9,22] along with a 1.2% to 6.8% rate of hearing loss.[15,18,22,23] The rate of cerebrospinal fluid (CSF) leak reported is 1.5% to 4%.[23] Anesthesia dolorosa, the most serious complication, develops in 4% of patients especially in those who received internal neurolysis during MVD.[8] In the hand of experienced surgeons at high-volume centers, the complication and mortality rate could be reduced significantly.[20]

Several studies on re-operation after previous failed MVD indicate that surgeons have to deal with challenges from arachnoid adhesions and abnormal anatomical relationships,[24] which can be associated with higher complications rates than the initial surgery.[25] One of the many great advantages of RF-TR over MVD for refractory TN is that it provides more selective targeting of the trigeminal nerve distributions than other percutaneous procedures, especially with the aid of our iCT and fusion MR image. In a study of 41 patients having poor outcomes after MVD received CT-guided RF-TR procedure, among them, 37 (90.2%) patients achieved immediate pain relief, and 34 (82.9%) received multiple repeated procedures and remained satisfied with their pain relief during the follow-up period. Neither mortality nor life-threatening complications were observed.[26] RF-TR is also useful if TN recurs at an older age, when the risks of general anesthesia may outweigh the benefit of MVD.[14]

4.3. RF-TR versus GKRS for refractory TN

GKRS is associated with initial pain relief in 79% to 91.8% of patients.[27–31] Pain improvement after GKRS is always delayed and usually takes 10 days to 3.4 months.[27–34] Median duration of pain relief is reported at 32 months to 4.1 years.[27] Radiation dose may be correlated with the response from repeated GKRS.[35] Hypesthesia occurs in 6% to 42% of patients after GKRS,[27–29,32,33] which is dose-dependent and may correlate with the proximity of the lesioning target to the brainstem.[31,34] Anesthesia dolorosa has been reported in 0.2%.[29] The morbidity increases with repeated GKRS, with the rate of hypesthesia ranging from 11% to 80%[31,36] and corneal dryness at 6.6%.[37]

Regarding the dosimetry of GKRS treatment, a minimum of 70 Gy is necessary for efficacy, which was firstly established in 1996 by a multicenter trial.[38] A study of a baboon model suggested that necrosis of neurons occurred at 100 Gy, which turned out to be the maximum dose of GKRS.[39] Within this dose range, higher doses result in better efficacy. A study shows that radiation dose >60 Gy in the second GKFR is significantly associated with better pain control outcomes (*P* = .018). A cumulative dose >140 to 150 Gy is significantly associated with a more satisfying pain control outcome (*P* = .033).

However, the major side effect of trigeminal nerve deficit is linked with a cumulative brainstem edge dose of >12 Gy (*P* = .077).[40] To date, there is no established cut-off for dose, and there was a tendency to decrease the dose at second GKRS in most studies to avoid dysfunction.[36] Although both RF-TR and GKRS provide convincing pain relief without the need for general anesthesia, there are still some advantages of RF-TR over GKRS for refractory TN.

5. Limitations

The sample size of the intervention group (group A) was small, with only 24 patients. Another limitation was the loss of long-term following-up data for patients who underwent RF-TR surgery may lead to undocumented TN recurrence.

6. Conclusions

In this study, although relatively small in sample size, RF-TR has a similar initial success rate for patients with refractory TN whether they had received MVD, GKRS, or not. The NRS score improvement between group A (having previous surgical interventions with MVD, GKRS, or both) and group B (having medication alone) showed no significance. Hence, RF-TR should be considered for patients with relapsing pain following MVD, GKRS, or both.

Repeated treatments such as MVD or GKRS for refractory TN may be less desirable due to a greater risk of mortality and morbidity. Given the efficacy and safety of RF-TR using neuronavigation with iCT and MR imaging, it should be considered a practical treatment option for recurrent TN, especially in patients with a poor health condition or who refuse to receive further craniotomy or gamma knife surgery. In conclusion, RF-TR provided an alternative and effective strategy if TN recurred, regardless of the form of intervention the patient had before.

Author contributions

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