

Percutaneous Radiofrequency Thermocoagulation in Trigeminal Neuralgia : Analysis of Early and Late Outcomes of 156 Cases and 209 Interventions

Hasan Burak Gunduz, Orhun Mete Cevik, Murad Asilturk, Muslum Gunes, Mustafa Levent Uysal, Ozden Erhan Sofuoglu, Erhan Emel

Department of Neurosurgery, Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Neurology, Neurosurgery and Psychiatry, Istanbul, Turkey

Objective : Trigeminal neuralgia is one of the most common causes of facial pain. Our aim is to investigate the efficacy and borders of percutaneous radiofrequency thermocoagulation in the treatment of trigeminal neuralgia.

Methods : Between May 2007 and April 2017, 156 patients with trigeminal neuralgia were treated with radiofrequency thermocoagulation. These 156 patients underwent 209 procedures. In our study, we investigated the early and late results of percutaneous radiofrequency thermocoagulation under guiding fluoroscopic imaging in the treatment of trigeminal neuralgia. Barrow Neurological Institute (BNI) pain scale was used for grading the early results. In addition, Kaplan-Meier survival analysis was used to assess long-term outcomes. Of the 156 patients who underwent radiofrequency thermocoagulation for trigeminal neuralgia, 45 had additional disease. Patients with this condition were evaluated with their comorbidities. Early and late results were compared with those without comorbidity.

Results : In 193 of 209 interventions BNI pain scale I to III results were obtained. Out of the 193 successful operation 136 patients (65.07%) were discharged as BNI I, 14 (6.70%) as BNI II, 43 (20.58%) as BNI III. Sixteen patients (7.65%) remained uncontrolled (BNI IV and V). While the treatment results of trigeminal neuralgia patients with comorbidity seem more successful in the early period, this difference was not observed in follow-up examinations.

Conclusion : Finally, we concluded that percutaneous radiofrequency thermocoagulation of the Gasserian ganglion is a safe and effective method in the treatment of trigeminal neuralgia. However, over time, the effectiveness of the treatment decreases. Nevertheless, the reappability of this intervention gives it a distinct advantage.

Key Words : Facial pain · Foramen ovale · Radiofrequency ablation · Trigeminal neuralgia.

INTRODUCTION

Trigeminal neuralgia (TN) is the most common of all cra-

nial neuralgias. According to the 3rd edition of the International Classification of Headache Disorders, TN is a disorder characterized by recurrent unilateral brief electric shock-like

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• Address for reprints : **Hasan Burak Gunduz**

Department of Neurosurgery, Bakirkoy Prof. Dr. Mazhar Osman Ruh Sagligi ve Sinir Hastaliklari Egitim ve Arastirma Hastanesi, Zuhuratbaba Mahallesi, Dr. Tevfik Saglam Cad 25/2, Bakirkoy/Istanbul 34147, Turkey

Tel : +905325733120, E-mail : bgunduz62@yahoo.com, ORCID : <https://orcid.org/0000-0003-0020-7928>

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pains, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve and triggered by innocuous stimuli. It may develop without apparent cause or be a result of another diagnosed disorder^{19,39}. Currently, the pathophysiology of TN remains unclear. According to the “ignition theory” TN is the result of abnormalities in the afferent neurons of the trigeminal root or ganglion¹. The incidence of TN is two to five patients per 100000 people^{6,8,15,20,35}.

Today, there are three major theories explaining the etiology of TN. The first is related to the disease (multiple sclerosis [MS], diabetes mellitus, hypertension) the other to the direct trauma to the nerve (neurovascular compression), and the third to the polyetiological origin of the disease. In selected cases, decompression of the vascular structure that presses on the fifth nerve has been shown to relieve pain^{12,13,33}. Additionally, The third factor can be explained as all possible aetiological factors that can affect the trigeminal nerve system and evoke demyelination and dystrophy. In spite of all these, no identifiable cause can be found for most TN patients^{25,36}.

There are many medical and surgical options available for the treatment of TN. Currently, many disciplines of clinical and basic sciences continue to investigate etiological factors and the most effective treatment methods for TN. In this article we investigated early and late results of TN which has been treated with radiofrequency thermocoagulation (RFT). We recorded the complications encountered during this period. We further searched into the relations between TN and accompanying diseases.

Treatment

The first step in TN treatment is the conservative medical treatment¹⁸. Initially, the response to medical therapy is 80%, which decrease to less than 50% over time¹⁰. In cases where medical treatment is ineffective or associated with significant side effects, surgical treatment options may be considered. These options include percutaneous glycerol rhizotomy, radiofrequency rhizotomy, balloon compression, peripheral nerve section, radiosurgery and microvascular decompression (MVD)¹⁸.

The foramen ovale puncture was first described by Härtel⁹ in 1913 as a percutaneous route to the Meckel Cave to treat TN^{11,21,24}. In 1974, Sweet and Wepsic²⁹ introduced radio frequency generated thermal energy to damage the preganglion-

ic trigeminal rootlets in the Meckel cave. Under appropriate conditions, percutaneous RFT is a viable treatment method because of the short application time, long effect time, the possibility of a reintervention and high patient satisfaction rate^{2,22,27,30-32,37}.

MATERIALS AND METHODS

Patient selection

Ethics Committee approval was obtained for this study (Date : December 1, 2016; approval document number : 514).

First of all, we preferred to include the patients who can be defined as typical TN into the RFT procedure. This group consisted of patients with pain on the face characterized by paroxysmal lancinating, shocklike pain confined to the somatosensory distribution of the trigeminal nerve¹⁴. We excluded TN cases with atypical features outside the RF group.

Cranial magnetic resonance (MR) imaging was performed in all patients who underwent intervention. RFT was recommended for patients who did not have an image of vascular compression. In addition, RFT was recommended for MS patients and patients who cannot be administered general anesthesia due to their comorbidities. In addition, during this period, MVD surgery was performed on 67 patients who were found to have significant vascular compression on the Trigeminal Nerve on MR imagination.

A total of 209 procedures were done in 156 patients between May 2007 and April 2017 in a single Neurosurgery clinic and the results were retrospectively analyzed. Patient profiles, the immediate outcome of the therapy, painless time margin, and complications were obtained from the hospital medical records, clinical follow-ups and questionnaires sent to patients

Table 1. Barrow Neurological Institute pain intensity scale

Pain score	Definition
I	No trigeminal pain, no medication
II	Occasional pain, not requiring medication
III	Some pain, adequately controlled with medication -IIIa : No pain, continued medication -IIIb : Persistent pain, controlled with medication
IV	Some pain, not adequately controlled with medication
V	Severe pain, no pain relief

after April 2017. Postoperative results of patients were graded using the Barrow Neurological Institute (BNI) pain scale (Table 1)⁴⁾. For assessing long term outcomes Kaplan-Meier survival analysis was used⁷⁾.

The study group consisted of 81 female (52.94%) and 75 male (47.06%) patients. The ages ranged between 27–86 where the average was 58.03 ± 14 . One hundred patients (64.10%) had right, 56 (35.90%) had left sided symptoms. The branches involved were isolated V1 in one patient (0.48%), isolated V2 in 57 patients (27.27%), isolated V3 in 40 patients (19.14%), V1 and V2 in 17 patients (8.13%), V2 and V3 in 70 patients (33.50%), and V1, V2 and V3 in 24 patients (11.48%) (Table 2).

Surgical course

The patient is taken to the operating table in supine position. Fluoroscopy is adjusted to show the cella turcica, clivus and petrous apex on the lateral image. The position is confirmed by seeing the aligned orbital roofs and anterior clinoid processes.

Härtel⁹⁾ anatomical landmarks are used for percutaneous procedures to the Gasserian Ganglion. The entry point is 2.5 cm lateral to the angle of the mouth. An 18-gauge needle cannula is inserted along the medial of the coronoid process of the mandible and aimed toward the plane intersecting a point 30 mm anterior to the external acoustic meatus along the zygomatic arch and the medial aspect of the pupil. A free-hand technique is then used to direct the needle toward the foramen ovale with a finger inside the oral cavity to prevent perforation of the ipsilateral buccal mucosa and to ensure that the needle traveled medial to the mandible. The imaging of the needle during the procedure is performed by lateral image fluoroscopy. In 32 (15.31%) of 209 interventions, we added oblique submental imaging in addition to lateral imaging (Fig. 1).

After foramen ovale is penetrated at the correct position, cerebrospinal fluid can be observed at the proximal end of the needle. Although this can be accepted as a sign of Meckel Cave penetration, following deciding that we have placed the electrode properly, we give motor and sensory stimuli. Then the RF device is switched to the stimulus mode and a low frequency stimulus (2 Mhz) is applied. If the masticatory response is observed when the stimulus is applied, the frequency is increased as the second step (75 Mhz). When re-stimulation is applied pain that mimics neuralgia is expected. The final localization of the needle is decided with the help of the character and localization of the pain produced by the radiofrequency generator supplied stimulation. Ineffective results of the stimulation point towards misplacement. Depending on the patient's response, a new position is given to the electrode. Additionally, pain around the eye on stimulation also points to a misplacement of the needle to a V1 zone. Lesion generation close to the V1 branch should be avoided due to increased risk of keratitis. After confirming the localization, three radiofrequency lesions are performed at 70°C each in 3–5 mm. After each replacement of the electrode, the accuracy of the position is checked by applying stimulation. In addition, corneal reflex control should be performed at each stage of the intervention.

Table 2. Demographics of patients and localization of pain with trigeminal neuralgia treated with percutaneous radiofrequency thermocoagulation

Characteristic	Value
Patients (n=156)	
Age (years)	58.03±14.01 (27–86)
Sex, F : M	81 (52.94) : 75 (47.06)
Affected side, R : L	100 (64.10) : 56 (34.90)
Procedures (n=209)	
Affected division (all interventions)	
V1	1 (0.48)
V2	57 (27.27)
V3	40 (19.14)
V1, V2	17 (8.13)
V2, V3	70 (33.50)
V1, V2, V3	24 (11.48)

Values are presented as mean±standard deviation (range) or number (%). F : female, M : male, R : right, L : left

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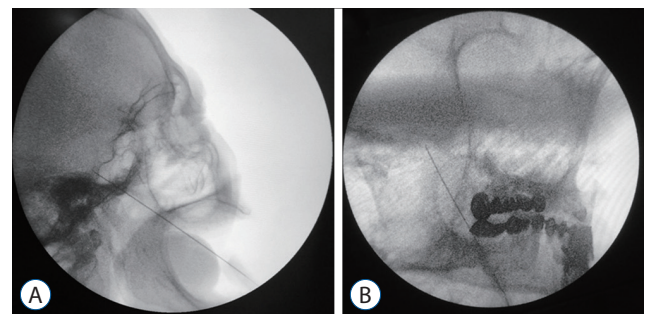


Fig. 1. Trajectory of the catheter needle in lateral (A) and oblique submental (B) cranial radiograph images.

Table 3. Early RFT results according to the BNI scale

BNI pain score	Value (n=209)
I	136 (65.07)
II	14 (6.70)
III	43 (20.58)
IIIa	29 (13.88)
IIIb	14 (6.70)
IV	13 (6.22)
V	3 (1.43)

Values are presented as number (%). RFT : radiofrequency thermocoagulation, BNI : Barrow Neurological Institute

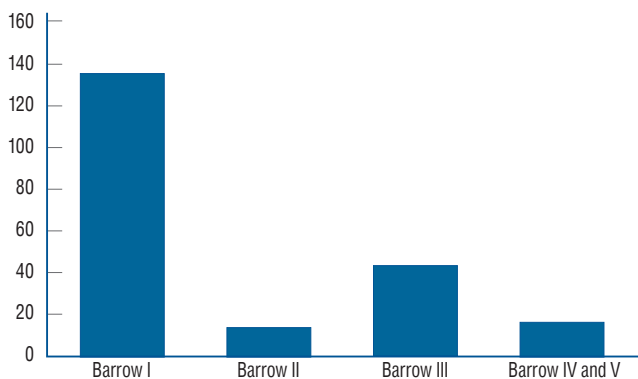


Fig. 2. Early period results according to Barrow Neurological Institute pain intensity scale.

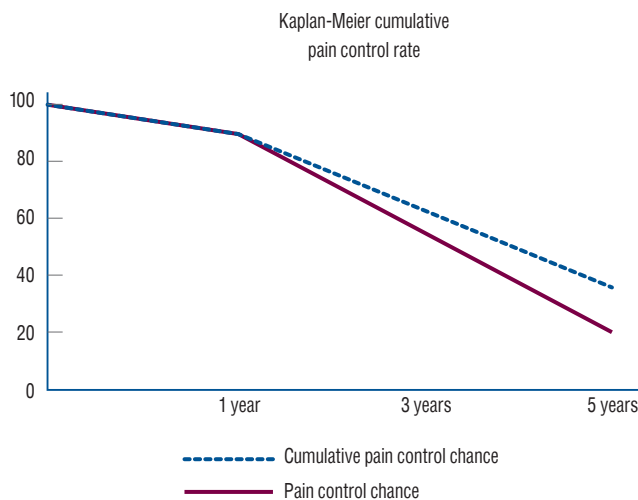


Fig. 3. A graph showing Kaplan-Meier analysis of the pain-free survival rate of 209 surgical procedures with trigeminal neuralgia treated by radiofrequency thermocoagulation. X-axis denotes pain-free survival in years and y-axis denotes cumulative survival.

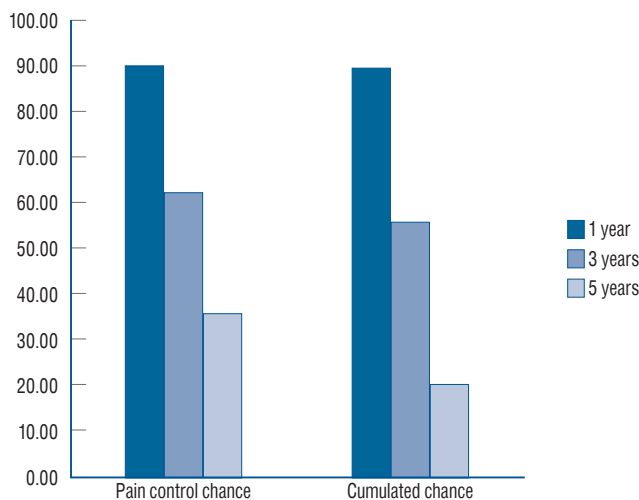
RESULTS

Early period results

A total of 209 procedures were done in 156 patients. BNI pain scale was used for grading the early results. One hundred ninety-three procedures out of 209 have achieved BNI I to III on early postoperative period. Out of the 193 successfully operated patients 136 patients (65.07%) were discharged as BNI I, 14 (6.70%) as BNI II and 43 (20.58%) as BNI III. Of the 43 patients, 29 (13.88%) were BNI IIIa and 14 were BNI IIIb (6.70%). Over 209 procedures, 16 patients (7.65%) remained uncontrolled (BNI IV and V) (Table 3 and Fig. 2).

Follow-up

The number of patients in the follow-up was decreased over time. In the 1 year follow up, 156 patients were in control out of the 174 patients. After the Kaplan-Meier analysis, both the controlled pain rate and the cumulative control rate of the group are 89.66%. In the 3rd year follow up, 81 out of the 130 eligible patients were in control. According to the Kaplan-Meier analysis the pain control rate is 62.3% and the cumulative control rate is 55.86%. For the 5th year follow up 29 out of the 81 eligible patients remained under control, which gave a controlled pain rate of 35.8% and a cumulative rate of 20% (Fig. 3). On the April 2016 follow up of the study, the longest controlled pain patient had 118 months of painless period.



Complications

In the postoperative period moderate intrabuccal hematoma was observed in 19 patients (9.10%). Varying postoperative hypoesthesia has been seen almost on all effective interventions. Hypoesthesia on the region is not interpreted as a complication by the surgical team. It was the expected result of Gasserian ganglion blockage. Detailed information was given to the patients before the procedures. One hundred ninety-three out of 209 procedures had facial hypoesthesia. The degree of hypoesthesia ranged from tactile hypoesthesia (n=182, 87.08%) to facial numbness (n=11, 5.26%). The early results of 193 patients who developed facial hypoesthesia after RF treatment were evaluated as BNI I in 136 (65.07%), BNI II in 14 (6.70%), and BNI III in 43 patients (20.57%).

In 13 patients (6.22%), sensory changes were uncertain. In patients whose sensory changes were uncertain, early BNI results were grade IV in eight patients (3.83%), grade V in five patients (2.39%). In addition to these sensory changes, dysesthesia was observed in three patients (1.43%). These three patients were in BNI V group (Table 4). Results showed a lower rate of early pain remission in patients without sensory changes.

Masseter muscle weakness and temporal muscle atrophy have been seen on five patients (2.39%) and one patient (0.48%), respectively. Corneal hypoesthesia have been seen on

Table 4. Sensory changes after RFT in early period

Sensory changes in all procedures (n=209)	
Facial hypoesthesia	193 (92.34)
Tactile hypoesthesia	182 (87.08)
BNI I	127 (60.77)
BNI II	13 (6.22)
BNI III	42 (20.10)
Facial numbness	11 (5.26)
BNI I	9 (4.31)
BNI II	1 (0.48)
BNI III	1 (0.48)
No sensory change	13 (6.22)
BNI IV	8 (3.83)
BNI V	5 (2.39)
Dysesthesia	3 (1.43)
BNI V	3 (1.43)

Values are presented as number (%). RFT : radiofrequency thermocoagulation, BNI : Barrow Neurological Institute

six patients and one patient had corneal reflex deficit (3.35%). Artificial tear drop has been prescribed to the seven patients. In the long term no keratitis has been observed in these patients (Table 5).

DISCUSSION

We analyzed our patients for pain relief, early and persistent complications, painless period and repeat interventions, and accompanying diseases.

Analysis of treatment and results

One hundred ninety-three (92.34%) of the 209 surgeries were in the first three scoring according to the BNI pain intensity score. Score I was a complete painless result and did not require additional medical support (136, 65.07%). There

Table 5. Complications occurred due to intervention in 209 procedures

Complication	Procedure (n=209)
Intrabuccal hematoma	19 (9.10)
Corneal hypoesthesia and reflex deficit	7 (3.35)
Dysesthesia	3 (1.43)
Masseter muscle weakness	5 (2.39)
Atrophy of temporal muscle	1 (0.48)

Values are presented as number (%)

Table 6. Trigeminal neuralgia and comorbidities

	Value
CVS, HT	23
Multiple sclerosis	5
DM	3
Thyroid diseases	3
Respiratory system diseases	2
Glaucoma	1
Gastrointestinal diseases	1
Coexisting diseases	
HT, DM	4
Parkinson's disease, HT	1
Renal disease, HT	1
GIS, HT, thyroid, CVS	1

CVS : cardiovascular system diseases, HT : hypertension, DM : diabetes mellitus, GIS : gastrointestinal system diseases

was occasional mild pain in score II. These patients also did not need medical support (14, 6.70%). In score IIIa and b, there was some pain and could be controlled by medical support (43, 20.58%). We have accepted scores IV and V as failure (16, 7.65%). In these two groups, the pain was not under complete control with supportive drug therapy.

The results in our study group seemed harmonious with other studies in the literature but were not the best. In order to prevent complications : 1) we avoided to make a lesion to V1 branch. 2) We avoided high temperature and long applications. 3) We avoided RF application for atypical TN. And 4) we closely monitored the quality of the pain, localization and masseter muscle response during stimulation.

We tried to follow up long-term results of the patients. Kaplan-Meier survival analysis method was used for the analysis of the results.

When we checked the results in other series, Son and colleagues²⁸⁾, recurrence rate at the end of 3rd year in 38 disease series was 29.1%. When we take out the pain control group, our 3-year recurrence rate was 44.3%. Taha and colleagues³⁰⁾ state that 35% of patients are out of follow-up during a 14-year period and that the rate of recurrence was 25% over this time period. Kanpolat and colleagues¹⁴⁾ have followed 719 patients for 5 years and pain control was 57% in a series of 2138 attempts. In our study at the end of the fifth year, the pain controlled patient rate was 35%.

Table 7. Data for patients with comorbidities

	Number of patients	Number of patients whose pain have started	Number of controlled patients at the end of the time margin	Pain control chance (%)	Cumulated chance (%)
1 year	43	2* (10.48%); 6.86 [†]	41* (32.52%); 2.21 [†]	95.35	95.35
3 years	41	21* (19.96%); 0.05 [†]	20* (21.04%); 0.05 [†]	48.78	46.51
5 years	20	13* (9.49%); 1.30 [†]	7* (10.51%); 1.17 [†]	35.00	16.28

*The calculated expected value. [†]Chi square statistic for the cell only

Table 8. Data for patients with no comorbidities

	Number of patients	Number of patients whom have pain started	Number of controlled patients at the end of the time margin	Pain control chance (%)	Cumulated chance (%)
1 year	158	47* (38.52%); 1.87 [†]	111* (119.48%); 0.60 [†]	70.25	70.25
3 years	111	53* (54.04%); 0.02 [†]	58* (56.96%); 0.02 [†]	52.25	36.71
5 years	58	24* (27.51%); 0.45 [†]	34* (30.49%); 0.40 [†]	58.62	21.52

*The calculated expected value. [†]Chi square statistic for the cell only

Table 9. Comparison for cumulative pain control between comorbidity group and no comorbidity group

	All patients (%)	Comorbid patients (%)	No comorbidity (%)	p-value
1 year	89.66	95.35	70.25	0.000678
3 years	55.86	46.51	36.71	0.703894
5 years	20	16.28	21.52	0.06812

Table 10. Comparison of p-values at the end of each year

	Chi-square statistic	p-value	Yates correction applied chi-square statistic	Yates correction applied p-value
End of 1st year	11.5473	0.000678	10.2261	0.001385
End of 3rd year	0.1445	0.703894	0.0389	0.843631
End of 5th year	3.3278	0.06812	2.4479	0.117685

TN and comorbidities

Of the 156 patients who underwent intervention, 45 (28.85%) had another disease. Cardiovascular system diseases and hypertension (n=23, 14.74%) were the most common comorbidities in all patients. This was followed by MS (n=5, 3.20%), diabetes mellitus (n=3, 1.92%), and thyroid diseases (n=3, 1.92%) (Table 6). In particular, the etiological linkage of hypertension, MS and diabetes mellitus to TN has been discussed in various studies^{3,16,23,26,34,38}.

When the patients with known comorbidities such as hypertensive disease, diabetes mellitus, MS, and Parkinson's disease are separated into a group and cumulative pain rates were compared to the group with no known comorbidities, the group with comorbidities had a higher rate of cumulated pain control at the first year as high as 95.35% compared to the patients with no comorbidities group of 70.25% (Tables 7-10). The other interesting finding was that the pain control chance between the years 3 and 5 for the patients with no comorbidities group was 58.62%. In this period, pain control rate decreased to 35.00% in the patient group with comorbidities (Fig. 4).

If the rates for pain control for all patients are taken as expected for the *p* value for the first-year comorbidities and no comorbidities patient group is calculated the result comes 0.000678 which is considerably significant if a *p*-values below 0.05 is taken as significant. However, when the groups are compared at the end of the third year and fifth year, the *p*-values calculated to be above 0.05. With the rates of each group is falling to same values at the long term, having a higher rate of control for the first year in the patients with the comorbidities group raises many questions, primarily if this finding is a statistical coincidence, and second what are the possible mecha-

nisms causing the difference in the pain control distribution. To check if this was a statistical coincidence despite the calculated *p*-value, Yates correction has been applied as well and the result still fell below 0.05 (0.001385). Yates correction applied results have been reported at Table 10 (Tables 7-10). Such higher control rate for the first year control may have a link to the etiology of disease itself. Since the etiology of the disease is not fully understood the comorbidities reported may have a link to the etiology and these etiologies linked with the comorbidities may respond better to the treatment. The other explanation could be the patient bias. The patients with the comorbidities also include patients who are not able to go into general anesthesia and know this treatment is the final option for them, which may lead them to a somewhat increased tolerance¹⁷. It is certain that further studies documenting the patients and their accompanying comorbidities are needed to further explore this deviation.

Analysis of complications

Facial hypoesthesia developed in all the patients in the first 3-level group. This hypoesthesia was defined as "not disturbing and not troublesome". Donnet and colleagues⁵ declare that pain relief is obtained at the "cost" of trigeminal hypoesthesia, which ideally is purely thermoalgesic but also includes an almost inevitable tactile hypoesthesia or facial numbness. This situation has already been explained to all patients before the intervention.

In three of the patients, sensory changes occurred in a disturbing manner (1.43%). In the series of Son and colleagues²⁸, one patient reported an occasional and moderate disturbance (12.5%), and one patient reported a frequent and severe disturbance (12.5%).

Masseter muscle weakness was observed in five patients (2.39%). Broggi and colleagues² reported 105 cases (10.5%) of masseter weakness with minor chewing impairment. Son et al.²⁸ described pterygoid or masseter muscle weakness in six patients (15.8%) after RFT.

Corneal hypoesthesia and anesthesia developed in 3.35% of our patients. In the Broggi et al.²'s results, there was a decrease in corneal reflex without any damage to the eye in 19.7% patients. Son et al.²⁸ wrote that there was no keratitis, weakness in the extraocular muscles, and no deficits in other cranial nerves.

Taha and colleagues³⁰ talk about "producing optimum le-

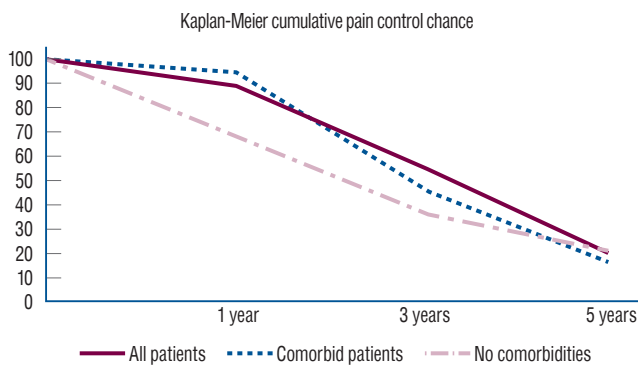


Fig. 4. Comparison of the cumulative pain control chances.

sion” while explaining their results. According to them, if the analgesia rates were high, the lowest recurrence rates and the highest rates of dysesthesia were observed. During the interventions, we were careful not to exceed 70 degrees centigrade when applying lesions. We can say that this restriction raises our recurrence rate but keeps our dysesthesia rate low.

Limitations of the study

One of the points that we want to draw attention to in this study is the decrease in the number of patients followed up in the 5-year period. The main reasons for this were the decrease in the number of patients who came to follow-up in the outpatient clinic and we could not reach them by telephone. We are aware of this shortcoming affects our long-term results and we want to emphasize that it would be appropriate to consider this in our article.

It is also noteworthy that TN patients with comorbidities in early post-RFT results have higher success rates. First, one of the factors that will affect the causes of this result is the pathophysiology of TN, which is still not fully understood today. Besides, the results we obtained in our study include a heterogeneous patient group. There are wide range of diseases in this group such as hypertension, MS and diabetes mellitus. To explain the reasons for our results, it is necessary to investigate the links of these diseases with TN separately.

CONCLUSION

In this study, we presented our intervention criteria, surgical technique we use, short- and long-term outcomes, comorbidities, complications, and reinterventions. Furthermore, we evaluated other articles about the topics we talked about. We aimed to achieve a high and long success rate and a low complication rate throughout our treatment process. To achieve these goals, our main landmarks were : 1) accurate diagnosis, 2) optimum operating room conditions including C-arm, 3) appropriate localization during intervention, 4) appropriate temperature and appropriate time for lesion generation, and 5) repeat intervention in recurrences. Finally, we conclude that percutaneous RFT of the Gasserian ganglion is a safe and effective method in the treatment of TN. However, over time, the effectiveness of the treatment decreases. Nevertheless, the repeatability of this intervention gives it a distinct advantage.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

INFORMED CONSENT

This type of study does not require informed consent.

AUTHOR CONTRIBUTIONS

Conceptualization : HBG, MA

Data curation : MG, MLU, OES

Methodology : HBG

Project administration : HBG

Visualization : EE

Writing - original draft : HBG, OMC, MA

Writing - review & editing : HBG, OMC, EE

ORCID

Hasan Burak Gunduz	https://orcid.org/0000-0003-0020-7928
Orhun Mete Cevik	https://orcid.org/0000-0001-9898-3807
Murad Asilturk	https://orcid.org/0000-0002-9782-0624
Muslum Gunes	https://orcid.org/0000-0003-4923-0889
Mustafa Levent Uysal	https://orcid.org/0000-0001-5562-6041
Ozden Erhan Sofuoglu	https://orcid.org/0000-0003-3787-6500
Erhan Emel	https://orcid.org/0000-0002-0584-9164

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