Systematic Review

Radiofrequency Thermocoagulation Through the Foramen Rotundum Versus the Foramen Ovale for V2 Primary Trigeminal Neuralgia: A Systematic Review and Meta-analysis

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Background: Percutaneous radiofrequency thermocoagulation (RFT) through the foramen rotundum (FR) is a new approach for the treatment of V2 trigeminal neuralgia (TN). Some studies have shown the novel method seems to have advantages over traditional RFT through the foramen ovale (FO). The optimal interventional surgical strategy for isolated V2 TN remains controversial.

Objectives: The purpose of our study was to perform a systematic review and meta-analysis to evaluate the clinical results of RFT through the FR and the traditional FO puncture approach.

Study Design: A systematic review of randomized controlled trials for thermocoagulation through the foramen rotundum versus the foramen ovale for V2 primary trigeminal neuralgia.

Methods: Randomized controlled trials or nonrandomized controlled trials published from January 2000 through October 2022 that compared RFT through the FR and the FO for V2 primary TN were found through a comprehensive search in 3 electronic databases (PubMed, EMBASE, Cochrane library). A total of 3 studies (105 patients) were included in this systematic review and meta-analysis.

Results: The results indicate that there are no statistically significant differences between the FR group and the FO group in terms of postoperative immediate effect rate (postoperative one week) ($P > 0.1$; standardized mean difference [SMD] = 0.67 [0.26- 1.71]) and recurrence rate ($P > 0.1$; SMD = 0.67 [0.26 - 1.71]). The long-term effect rate (postoperative one year) was significantly higher in the FR group ($P < 0.05$; SMD = 0.12 [0.01 - 0.22]).The FO group had a significantly higher total complication rate compared with the FR group ($P < 0.01$; SMD = 0.12 [0.03 - 0.53]).

Limitations: The limitations of this systematic review and meta-analysis include the small range of study populations. Heterogeneity caused by inconsistent follow-up time, outcome measurements, and RF parameters are other limitations.

Conclusion: In conclusion, RFT of the maxillary nerve through the FR for the treatment of primary V2 TN had a better long-term effect rate and fewer complications in comparison with thermocoagulation of the Gasserian ganglion through the FO. No differences were found between both interventions in terms of immediate effect rate and recurrence rate.

Key words: Radiofrequency thermocoagulation, primary trigeminal neuralgia, foramen rotundum, foramen ovale, systematic review, meta-analysis

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Trigeminal neuralgia (TN) is one of the most severe facial pain syndromes. It is characterized by severe, episodic pain in the distribution of one or more trigeminal nerve branches (1). Primary TN is diagnosed when a patient fits the criteria, however the pathogenesis of TN is unknown (2,3).

The V1, V2, and V3 branches of the trigeminal nerve originate from the gasserian ganglion and leave the skull through the superior orbital fissure, the foramen rotundum (FR), and the foramen ovale (FO), respectively. The maxillary branch (V2) is most frequently involved in primary TN (4). Gasserian ganglion ablation with percutaneous radiofrequency thermocoagulation (RFT) through the FO is the most commonly used treatment for primary TN. RFT through the FO is considered a minimally invasive, safe, and effective method for patients with primary TN refractory to or intolerant of drug treatment (5-8). However, in the Gasserian ganglion, the 3 nerve fiber divisions of the trigeminal nerve, are in close contact and partially interconnected (9). Therefore, when the Gasserian ganglion is punctured through FO, the V2 division is difficult to accurately locate. This approach can easily involve the ophthalmic division (V1) or the mandibular division (V3), resulting in complications (10).

In recent years, some studies have reported on the technique of computed tomography-guided selective RFT via the FR for isolated V2 TN. Huang, et al (11), and Ding, et al (10) performed initial prospective studies to assess the effectiveness of a new approach for RFT through the FR for the treatment of V2 primary TN. These studies showed promising results for this novel method (10-12). Some retrospective studies have shown that RFT through the FR seems to have advantages in terms of clinical efficacy and safety (13-15).

Therefore, we conducted this systematic review and meta-analysis to compare the effectiveness and safety of RFT through the FR vs the FO V2 primary TN.

Methods

Inclusion Criteria and Exclusion Criteria

Studies were included if they met the following criteria: 1)a randomized or non-randomized controlled study; 2) included patients with V2 primary TN; 3) pain was not controlled after standard drug treatment; 4) RFT through the FRand RFT through the FO were compared; 5) the mean follow-up periods were > 1 year.

Studies were excluded if: 1) they were noncontrolled; 2) the full text was not available; 3) the studies had TN as a secondary diagnosis; 4) they used treatment modalities other than RFT; 5) TN involved V1 or V3 divisions; (6) the patients had prior surgery for TN.

Search Methods and Selection of Studies

Relevant literature searches were performed using PubMed, EMBASE, and Cochrane library. The key words for literature searches included "radiofrequency thermocoagulation," "primary trigeminal neuralgia," "foramen rotundum," and "foramen ovale." The search was performed with limiting factors of "human" and "English language," published from January 2000 through October 2022. Each article selected for inclusion was reviewed by the junior authors to ensure proper selection. In cases of disagreement, the senior author arbitrated for the final inclusion or exclusion.

Data Extraction and Management

The following information was collected from each study using a standardized form: 1) study ID; 2) study design; 3) main inclusion/exclusion criteria; 4) patient demographics; 5) length of follow-up; 6) surgical approach for each group; 7) Visual Analog Score or Numeric Rating Scale scores pre-and postsurgery; 8) efficacy rate; (9) number of complications, type of complications, and rate of complications; (10) recurrence rate.

Statistical Analysis

Heterogeneity was tested using the χ^2 test and quantified by calculating the I^2 statistic, for which a *P* value less than 0.1 and an I^2 value greater than 50% was considered to be statistically significant. For the pooled effects, the weighted mean difference or standard mean difference was calculated for continuous variables according to the consistency of measurement units, and the odds ratio (OR) was calculated for dichotomous variables. Continuous variables are presented as mean differences and 95% CIs, whereas dichotomous variables are presented as OR and 95% CIs. Random-effects or fixed-effects models were used depending on the heterogeneity of the studies included. All statistical tests were performed with IBM SPSS Statistics 19.0 (IBM Corporation) and RevMan 5.3 (The Nordic Cochran Centre for the Cochrane Collaboration).

Results

Search Results

A total of 391 titles and abstracts were screened after removing irrelevant studies, case reports, and noncomparative studies. The secondary stage screening of abstracts was based on study design, population, purpose of interventions, and outcome index. A total of 22 articles were retrieved in full and screened, yielding a total of 3 articles for this systematic review and meta-analysis. The selection process is shown in Fig. 1.

Table 1 provides a summary of the studies included

in the review. A total of 277 patients were included in this meta-analysis. The study sample size ranged from 27 to 80. These studies were published from 2014 through 2022.

Risk of Bias Assessment and Trial Characteristics

All 3 included studies were prospective controlled trials; 2 were randomized and one was nonrandomized. One article had some concern risk of bias, one had an overall high risk of bias, and one had an overall low risk of bias (Fig. 2). The major baseline characteristics of each study (study design, number of patients, patient age and gender statistics, follow-up time, and surgical approach) are presented in Table 2.

Clinical Outcome

Postoperative Immediate Effect Rate

The immediate effect rate (postoperative one week) was reported in 2 studies that had a total sample size of 107. It showed no significant heterogeneity among the studies (heterogeneity: $P > 0.1$; $I^2 = 27\%$) therefore, a fixed-effects model was adopted. The immediate effect rate (postoperative one week) showed no difference between the FR group and the FO group ($P > 0.1$; SMD = 0.67 [0.26 - 1.71]) (Fig. 3).

Postoperative Long-term Effect Rate

The long-term effect rate (postoperative one year) was reported in all 3 studies that had a total sample size of 175. It showed no significant heterogeneity among the studies (heterogeneity: $P > 0.1$, $I^2 = 0\%$) therefore, a fixed-effects model was adopted. The long-term effect rate (postoperative one year) was significantly higher in the FR group compared with the FO group ($P < 0.05$; SMD = 0.12 (0.01 - 0.22]) (Fig. 4).

Recurrence Rate

The recurrence rate was reported in all 3 studies that had a total sample size of 171. The recurrence rate showed no significant heterogeneity among the studies (heterogeneity: $P > 0.1$; $I^2 = 27\%$) therefore, a fixed-effects model was adopted. The recurrence rate was not different between the FR group and FO group ($P > 0.1$; SMD = 0.67 [0.26, 1.71]) (Fig. 5).

Complication Rate

The 3 studies (n = 173 patients; 90 in the FR group and 83 in the FO group) all reported the 3 most common postoperative complications: hematoma, corneal involvement, and masticatory weakness.

We created 3 subgroups for each complication. In subgroup A, the hematoma complication rate was not different between the FR and FO groups ($P > 0.1$; SMD = 0.68 [0.31 - 1.15]). In subgroup B, the FO group had a significantly higher corneal involvement complication rate compared with the FR group ($P < 0.05$; SMD =

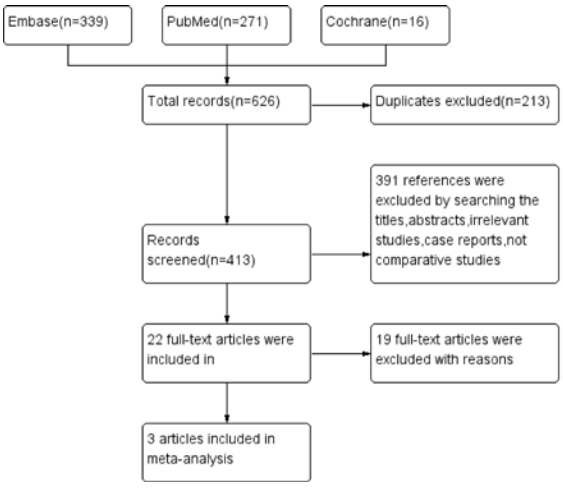

Fig. 1. *Flow diagram.*

Table 1. *Study characteristics.*

Author		Huang 2014	Xue 2019	Ding 2022
Study Design		RCT	RCT	Non-RCT
Number of patients (n)	FR	15	40	35
	FO	12	40	35
Age (y, range)	FR	(65.0 (±9.8)	64.95 ± 12.50	57.79 ± 6.29 (34-76)
	FO		64.28 ± 11.89	57.56 ± 6.43 (33-73)
Gender (W/M)	FR	12/15	24/16	21/14
	FO		16/24	20/15
Affected side(R/L)	FR	8/19	NR	21/14
	FO			22/13
Preoperative Pain Duration (m, range)	FR	31.9 m (± 10.2)	NR	11.38 ± 5.61 (3-21)
	FO			11.24 ± 5.37 (3-–22)
RF needle sizes	FO	22G, 2 mm naked tip	21G, 10 mm naked tip	21G, 5 mm naked tip
	FR			
RF parameters	FO	85°C, 90x2 s	75°C, 240 s	50°C-68°C, 180 s
	FR		90°C, 240 s	

0.07 [0.01 - 0.67]). In subgroup C, the FO group had a significantly higher masticatory weakness complication rate compared with the FR group ($P < 0.01$; SMD = 0.03 (0.00 - 0.35]). Finally, the FO group had a significantly higher overall total complication rate compared with the FR group ($P < 0.01$; SMD = 0.12 (0.03 - 0.53]) (Fig. 6).

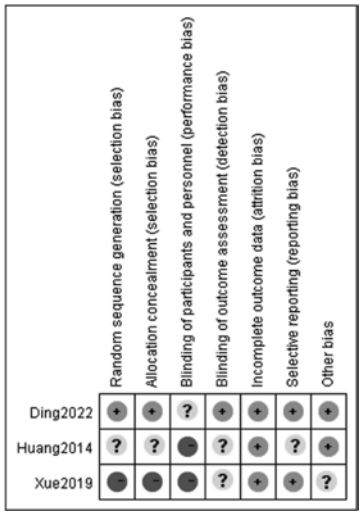

Fig. 2. *Risk of bias assessment.*

Table 2. *Number of relief, recurrence and complications between the 2 groups.*

Study			Huang 2014	Xue 2019	Ding 2022
Pain Relief (/Total Patients)		FR	15/15	40/40	28/35
		FO	9/12	33/36	26/35
Recurrence		FR	0/15	0/40	8/35
		FO	1/10	3/36	7/35
Complication	Hematoma	FR	2	14	1
		FO	2	15	3
	Corneal involvement	FR	0	0	0
		FO	1	22	2
	Masticatory weakness	FR	0	0	0
		FO	5	31	2

Discussion

This comparative, systemic review and meta-analysis assessed the efficacy and safety of RFT through the FR and FO for primary TN. We found no difference between both approaches in terms of immediate effect rate and recurrence rate. There is a small tendency for FR RFT to have a better long-term effect rate. The complication rate of hematoma had no difference between the groups. The complication rate of corneal involvement and masticatory weakness was significantly higher in the FO group. In general, The FO group had a higher overall complication rate.

RFT is a neuro-selective disruptive technology. The high frequency current generated by the RF instrument causes ions in the tissue to oscillate, which in turn heats the tissue, causing a local temperature rise. The heated target tissue coagulates conductive pain neurofibrils (Aδ and C-type), whereas conductive tactile neurofibrils (Aα and Aβ-type) can tolerate relatively high temperatures and will not be destroyed. Therefore, gradual heating can selectively destroy the sensory nerves, while relatively preserving the tactile fibers. Pain relief can be achieved, and the sense of touch can partially or completely be preserved (16,17).

Percutaneous trigeminal rhizotomy for the treatment of TN was first attempted by Hartel as early as 1914. Radiofrequency ablation was introduced by Sweet in the 1970s. The Hartel technique describes a method of reaching the Gasserian ganglion by passing a needle from the external side of the mouth, inserting it at the level of the upper mid-molar tooth, and passing it cephalad and inward until

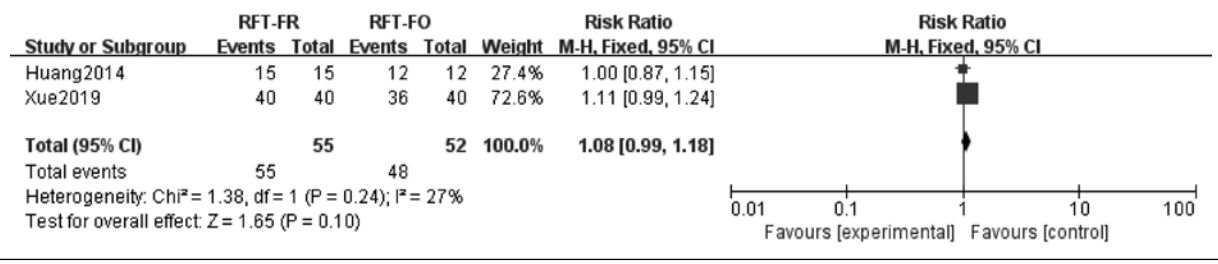

Fig. 3. *Immediate effect rate forest plot.*

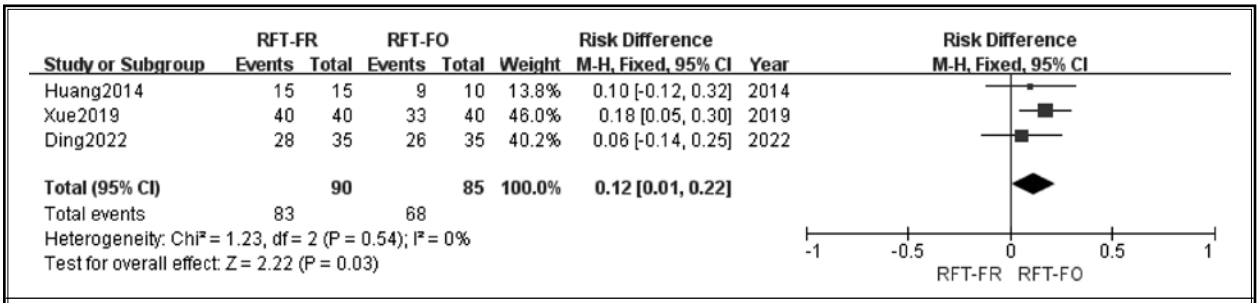

Fig. 4. *Long-term effect rate forest plot rate.*

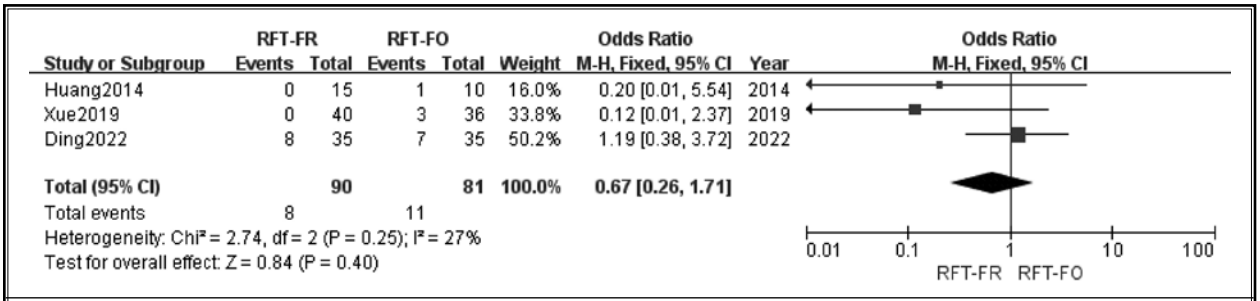

Fig. 5. *Recurrent rate forest plot.*

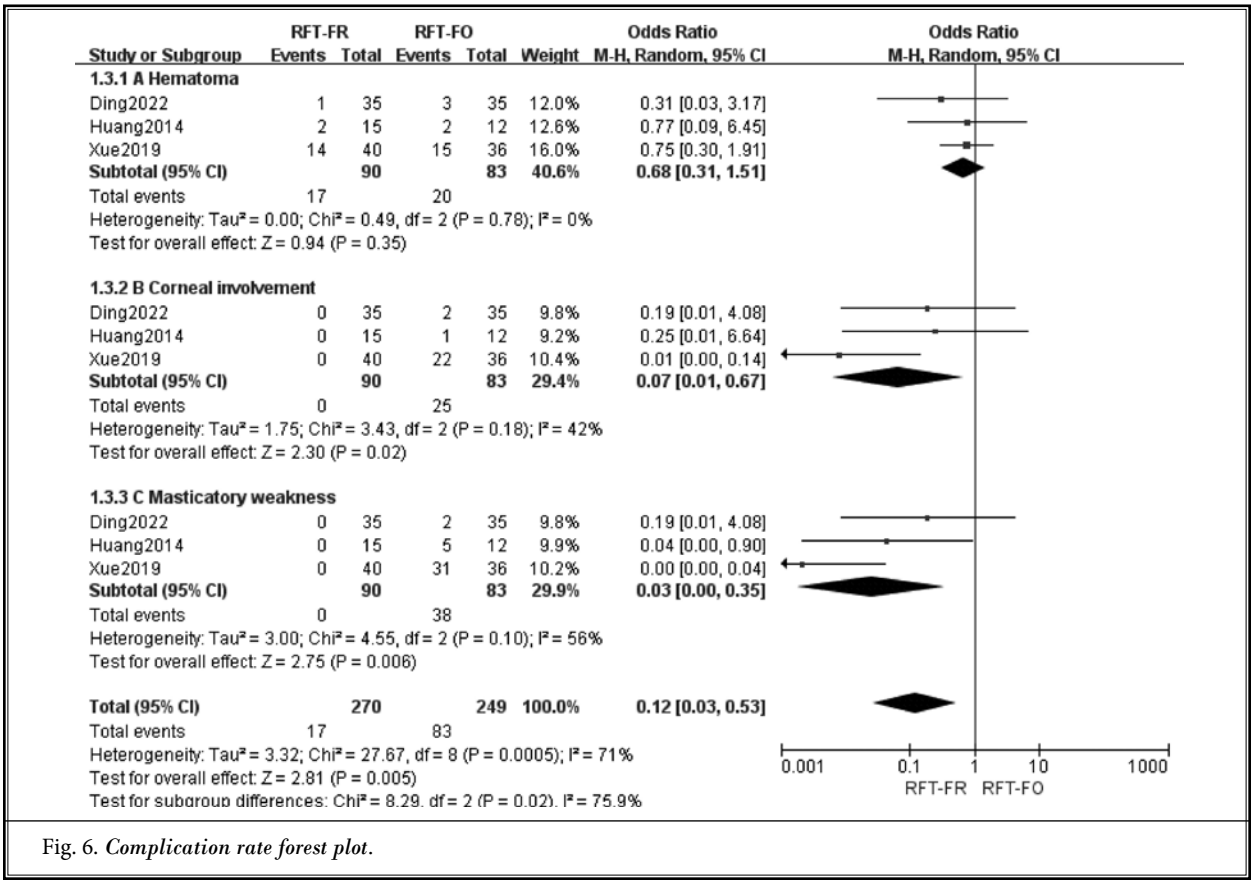

Fig. 6. *Complication rate forest plot.*

the needle tip reaches the temporal bone in front and to the outer side of the FO. This allows the needle to further advance into the inner side of the FO to finally reach the Gasserian ganglion (5,18,19). The procedure has been an established treatment for TN for many decades with successful pain relief in about 80% – 98% of patients (6,20,21).

The V3 nerve that exits through the FO could be easily injured when the RF needle goes through the FO, leading to masticatory weakness along the V3 dermatome. When the needle tip goes too deep into the FO, it may cause V1 injury, leading to corneal involvement, corneal hypesthesia, diminished corneal reflex, and even blindness in severe cases (22,23). Once the needle is inside Meckel's cave, it is often difficult to differentiate the subbranches from each other; repeated adjustments are often required until the electrical stimulation induces V2 area paresthesia (6,24).

Only the maxillary nerve is located at the external orifice of the FR. It is not adjacent to the V1 and V3 divisions. Therefore, at this location, there is no risk of injury to other nerves. Moreover, the entrance through the FR does not enter Meckel's cave, and no loss of cerebrospinal fluid occurs, thereby reducing the chance of low intracranial pressure headache, meningitis, and intracranial infection. The V2 division passes out of the skull through the external orifice of the FR. The position of the nerve trunk is fixed and no branch is issued. There is no anatomical variation. The bony landmarks are exact, and RFT of the V2 division can be completely performed without entering the FO. The depth of the puncture needle through the FR is short, and there is no need to repeatedly adjust the orientation and depth (10,25).

From a physiological perspective,both approaches achieve the goal of relieving pain by denaturing the conductive pain neurofibrils through RF. The FR approach selectively ablates the V2 branch of the Gasserian ganglion, while the FO approach directly acts on the Gasserian ganglion.

The regeneration of conductive pain neurofibrils determines whether pain relapses (26-28). Our results confirm that there is no difference in the surgical recurrence rate between the 2 groups.

Anatomically, the FR puncture approach seems to be more accurate and safer.

Our results also prove this to some extent. Both surgical methods have been proved to be effective in relieving patients' symptoms. FR seems to have a slight advantage in long-term efficacy, while in avoiding surgical complications FR has shown obvious advantages. However, many studies have shown that FR is smaller and deeper than FO, and there are more obstacles in the puncture path, which makes the FR puncture path more difficult than FO, and the technical requirements for surgical operators are more strict (29-31).

Limitations

The results of this review should be interpreted with some limitations. First, both the number of the included studies and the sample size were small, which might affect the outcome. Second, the inconsistency among the studies in reporting outcomes limited our meta-analysis. Third, there was substantial heterogeneity due to the inconformity regarding the duration of follow-up. Fourth, our article used summary data instead of individual patient data, which might lead to the loss of some covariates at the individual patient level. Finally, due to the difference in RF parameters, the results might be influenced and need to be carefully applied.

Conclusion

In conclusion, RFT through the FR for the treatment of primary V2 TN had a better long-term effect rate and fewer complications in comparison with thermocoagulation of the Gasserian ganglion through the FO. No difference between both intervention in terms of immediate effect rate and recurrence rate were found. RFT of the maxillary nerve through FR may be safer than the FO approach. We recommend more studies with a larger sample size and longer follow-up to have stronger conclusions and to assess the long-term effectiveness and safety of the FR approach.

References

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018; 38:1-211.
2. Lambru G, Zakrzewska J, Matharu M. Trigeminal neuralgia: A practical guide. *Pract Neurol* 2021; 21:392-402.
3. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia - Diagnosis and treatment. *Cephalalgia* 2017; 37:648-657.
4. Cheng JS, Lim DA, Chang EF, Barbaro NM. A review of percutaneous treatments for trigeminal neuralgia.

Neurosurgery 2014; 1:25-33; discussion 33.

5. Gronseth G, Cruccu G, Alksne J, et al. Practice parameter: The diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. *Neurology* 2008; 71:1183-1190.
6. Kanpolat 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.
7. Son BC, Kim HS, Kim IS, Yang SH, Lee SW. Percutaneous radiofrequency thermocoagulation under fluoroscopic image-guidance for idiopathic trigeminal neuralgia. *J Korean Neurosurg Soc* 2011; 50:446-452.
8. Zhao Y, Zhang X, Yao J, Li H, Jiang Y. Microvascular decompression for trigeminal neuralgia due to venous compression alone. *J Craniofac Surg* 2018; 29:178-181.
9. Hayes DJ, Chen DQ, Zhong J, et al. Affective circuitry alterations in patients with trigeminal neuralgia. *Front Neuroanat* 2017; 11:73.
10. Ding Y, Yao P, Li H, Hong T. Comparison of efficacy and safety of CT-guided radiofrequency thermocoagulation through foramen rotundum versus foramen ovale for V2 primary trigeminal neuralgia. *Pain Physician* 2021; 24:587-596.
11. Huang B, Yao M, Feng Z, et al. CT-guided percutaneous infrazygomatic radiofrequency neurolysis through foramen rotundum to treat V2 trigeminal neuralgia. *Pain Med* 2014; 15:1418-1428.
12. Xue TQ, Zhang QX, Bian H, et al. Radiofrequency thermocoagulation through foramen rotundum versus foramen ovale for the treatment of V2 trigeminal neuralgia. *Pain Physician* 2019; 22:E609-E614.
13. Ran B, Wei J, Zhong Q, et al. Long-term follow-up of patients treated with percutaneous radiofrequency thermocoagulation via the foramen rotundum for isolated maxillary nerve idiopathic trigeminal neuralgia. *Pain Med* 2019; 20:1370-1378.
14. Wan Q, Zhang D, Cao X, Zhang Y, Zhu M, Zuo W. CT-guided selective percutaneous radiofrequency thermocoagulation via the foramen rotundum for isolated maxillary nerve idiopathic trigeminal neuralgia. *J Neurosurg* 2018; 128:211-214.
15. Zhao W, Yang L, Deng A, Chen Z, He L. Long-term outcomes and predictors of percutaneous radiofrequency thermocoagulation of Gasserian ganglion for maxillary trigeminal neuralgia: A retrospective analysis of 1070 patients with minimum 2-year follow-up. *Ann Med* 2022; 54:2420-2430.
16. Letcher FS, Goldring S. The effect of radiofrequency current and heat on peripheral nerve action potential in the cat. *J Neurosurg* 1968; 29:42-47.
17. Mittal B, Thomas DG. Controlled thermocoagulation in trigeminal neuralgia. *J Neurol Neurosurg Psychiatry* 1986; 49:932-936.
18. Taha JM, Tew JM, Jr., Buncher CR. A prospective 15-year follow up of 154 consecutive patients with trigeminal neuralgia treated by percutaneous stereotactic radiofrequency thermal rhizotomy. *J Neurosurg* 1995; 83:989-993.
19. Taha JM, Tew JM, Jr. Treatment of trigeminal neuralgia by percutaneous radiofrequency rhizotomy. *Neurosurg Clin N Am* 1997; 8:31-39.
20. Wu CY, Meng FG, Xu SJ, Liu YG, Wang HW. Selective percutaneous radiofrequency thermocoagulation in the treatment of trigeminal neuralgia: Report on 1860 cases. *Chin Med J (Engl)* 2004; 117:467-470.
21. Broggi G, Franzini A, Lasio G, Giorgi C, Servello D. Long-term results of percutaneous retrogasserian thermorhizotomy for "essential" trigeminal neuralgia: Considerations in 1000 consecutive patients. *Neurosurgery* 1990; 26:783-786; discussion 786-787.
22. Taha JM, Tew JM, Jr. Comparison of surgical treatments for trigeminal neuralgia: Reevaluation of radiofrequency rhizotomy. *Neurosurgery* 1996; 38:865-871.
23. Chivukula S, Kim W, Zhuo X, et al. Radiosurgery for secondary trigeminal neuralgia: Revisiting the treatment paradigm. *World Neurosurg.* 2017; 99:288-294.
24. Yoon KB, Wiles JR, Miles JB, Nurmikko TJ. Long-term outcome of percutaneous thermocoagulation for trigeminal neuralgia. *Anaesthesia* 1999; 54:803-808.
25. Koizuka S, Saito S, Sekimoto K, Tobe M, Obata H, Koyama Y. Percutaneous radio-frequency thermocoagulation of the Gasserian ganglion guided by high-speed real-time CT fluoroscopy. *Neuroradiology* 2009; 51:563-566.
26. Guest J, Santamaria AJ, Benavides FD. Clinical translation of autologous Schwann cell transplantation for the treatment of spinal cord injury. *Curr Opin Organ Transplant* 2013; 18:682-689.
27. Martin D, Robe P, Franzen R, et al. Effects of Schwann cell transplantation in a contusion model of rat spinal cord injury. *J Neurosci Res* 1996; 45:588-597.
28. Mira KM, Elnaga IA, el-Sherif H. Nerve cells in the intracranial part of the trigeminal nerve of man and dog. Anatomical study of the fifth cranial nerve. *J Neurosurg* 1971; 34:643-646.
29. Ding W, Chen S, Wang R, et al. Percutaneous radiofrequency thermocoagulation for trigeminal neuralgia using neuronavigation-guided puncture from a mandibular angle. *Medicine (Baltimore)* 2016; 95:e4940.
30. Candido KD, Germanovich A, Ghaly RF, Gorelick GH, Knezevic NN. Case report: Computed tomography scan-guided Gasserian ganglion injection of dexamethasone and lidocaine for the treatment of recalcitrant pain associated with herpes simplex type 1 infection of the ophthalmic division of the trigeminal nerve. *Anesth Analg* 2011; 112:224-227.
31. Kambadakone A, Thabet A, Gervais DA, Mueller PR, Arellano RS. CT-guided celiac plexus neurolysis: A review of anatomy, indications, technique, and tips for successful treatment. *Radiographics* 2011; 31:1599-1621.