Percutaneous radiofrequency ablation (RFA) of the trigeminal Gasserian ganglion via the foramen ovale is still one of the classic treatments for primary trigeminal neuralgia. However, the Gasserian ganglion is deep in the middle cranial fossa. Although it is a structure outside the brain tissue, the puncture needle must enter the encephalic to reach the Gasserian ganglion and so it is difficult to completely avoid the risk of intracranial hemorrhage and infection caused by puncture damage to intracranial blood vessels. It is not clear whether it is possible for RFA at the extracranial non-gasserian-ganglion site via the exit of the cranial channel (foramen ovale) for patients with V3 trigeminal neuralgia (TN).

**Study Design:** Prospective, clinical research study

**Setting:** Department of Anesthesiology and Pain Medical Center, Jiaxing, China.

**Methods:** One hundred and seven patients with isolated mandibular branch trigeminal neuralgia were included. Radiofrequency thermocoagulation was performed by CT-guided percutaneous puncture through the foramen ovale. The puncture target was the midpoint of the horizontal transverse diameter of the oval foramen. If the tingling sensation in the mandibular nerve innervation area could be detected, the radiofrequency thermocoagulation (90°C, 120 sec) under intravenous anesthesia would be performed. We investigated the inclination angle, puncture angle and depth, puncture operation time, intraoperative complications and short-term and long-term results after operation.

**Results:** After radiofrequency thermocoagulation, the pain in the mandibular branch dominant area was completely diminished in 104 patients. Two patients were cured after the second radiofrequency treatment. No intracranial hemorrhage or infection complications occurred, except for facial hematoma during operation in 21 cases. After 12-24 months of follow-up, 9 patients had recurrence and were still effective after receiving additional extracranial radiofrequency treatment.

**Limitations:** A control group should be established and more clinical data should be collected in future work.

**Conclusion:** Extracranial non-Gasserian-ganglion RF can achieve satisfactory results and improve the safety of radiofrequency treatment for trigeminal neuralgia.

**Key words:** Trigeminal neuralgia, foramen ovale, trigeminal ganglion

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Trigeminal neuralgia (TN) is often described as a condition characterized by recurrent electric shocks or sharp shooting pain caused by nonpainful facial movement or stimuli, such as speaking, brushing teeth, washing face, eating, and similar daily activities (1-3). Oral antiepileptic drugs are...
the conservative treatment for TN. If this treatment approach is ineffective or unbearable, alternative invasive methods are used, such as craniotomy with microvascular decompression (4), balloon compression (5), radiofrequency therapy of the Gasserian ganglion (6), and Gamma Knife (7). These invasive methods have different indications, contraindications, advantages and disadvantages. Percutaneous radiofrequency ablation (RFA) of the trigeminal Gasserian ganglion via the foramen ovale remains one of the classic treatments for primary TN (8-10). However, the Gasserian ganglion is deep in the middle of the cranial fossa. Although it is a structure outside of the brain tissue, the puncture needle must enter the brain to reach the Gasserian ganglion. It is difficult to completely avoid the risk of intracranial hemorrhage and infection caused by puncture damage to intracranial blood vessels. In our previous clinical study, we found that the satisfactory curative effect of V2 TN treatment could be achieved by RFA through the foramen rotundum (FR) for patients with trigeminal nerve maxillary branch pain (11-13). However, for patients with V3 TN, the feasibility of RFA at the extracranial non-Gasserian-ganglion site via the exit of the cranial channel (foramen ovale) remains indefinite. Therefore, we investigated the effect of RFA treatment through the foramen ovale in patients with V3 TN.

**METHODS**

**Clinical Research**

We treated 107 patients with V3 TN from January 2016 to December 2017. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Jiaxing University. All cases were conducted in the same institution, and the diagnosis of TN was confirmed according to the International Headache Society guidelines. Potential secondary causes of TN were ruled out. Of the 107 patients, 50 were men and 57 were women, with a mean age of 68.22 ± 10.99 years (range: 38 - 88 years). The course of the disease is 7 - 39 months, with an average of 25 ± 14 months. The pain degree during the pain attack is 5 - 9 points visual analog score (VAS), with an average of 7.5 ± 1.2 points. See Table 1 for details.

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Time from diagnosis of V3 (Month)</th>
<th>VAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>68.22 ± 10.99</td>
<td>50</td>
<td>25.0 ± 14.4</td>
<td>47</td>
</tr>
<tr>
<td>68.22 ± 10.99</td>
<td>57</td>
<td>25.0 ± 14.4</td>
<td>60</td>
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**Percutaneous RFA Approach through the Foramen Ovale**

Equipment needed are RFA needle, electrode standby, other related drugs, and patient monitor and rescue facilities. The RF apparatus was Baylis (REF PMG-230, Baylis, Canada). Patients fasted for 4 to 6 hours before the operation, were placed on intravenous infusion, and sent to the computed tomography (CT) room.

After checking the patient's information, the patient was positioned supine on the CT scaffold, with thin pillows under the shoulders to keep the head slightly backward. The eyes, neck, and chest were covered with a radiation shield. A nasal cannula was fixed for oxygen inhalation, and a CT positioning grid was placed on the affected side to fix the head on the head frame of the CT table with wide tape (Fig. 1). After taking the lateral positioning image of the patient's head by CT, a 3-mm layer thickness scan was performed using a semi-coronal plane. The scanning frame overlapped with the ligature of the porus acusticus externus and mandible, and from the upper to the lower edge of the zygomatic arch (the inclination angle of the CT rack was the angle between the bottom of the scanning frame and the coronal plane; Fig. 2). The CT layer with the largest transverse diameter of the foramen ovale was identified as the puncture layer. To design the puncture path, we used the middle point of the transverse diameter of the inner orifice of the foramen ovale as the puncture target, and then we drew a straight line from the target point against the mandible coronal process to the surface of the skin, marked the outer mark as the puncture point, and measured the length of the line from the puncture point to the target point by a CT software tool ruler. The length of the line was the puncture depth, and the angle between the line segment and the sagittal plane was the puncture angle (Fig. 3). After setting the puncture path, the rack inclination angle and the puncture angle and depth were recorded. Local anesthesia was administered on the puncture point. With the position puncture guide (13), an RF needle with a bare 5-mm end was inserted from the puncture point and punctured at the medial edge of the coronal process of the mandible according to the designed puncture path to the target point (the mid-
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point of the horizontal diameter of the inner orifice of the foramen ovale; Fig. 4). We pulled out the RF needle core, inserted the matching electrode, and applied high- and low-frequency (50 Hz and 2 Hz, respectively) currents for sensation and motor stimulation test. If 0.1 - 0.5 mA currents induced mandibular tingling sensation and mandibular rhythmic twitch, propofol (1 - 2 mg/kg) was then injected intravenously, and continuous RFA was performed at 90°C for 120 seconds after the patient fell asleep. If 0.5 mA current did not induce tingling sensation and rhythmic twitch in the mandibular region, the needle tip position was adjusted properly and then tested until the outcome was satisfactory. After awakening, the pain was tested by needling the skin of the mandibular pain area. If the area felt numb, the RF needle was pulled out and the treatment was over. If the horizontal diameter of the foramen ovale was larger than 8 mm, the patient was treated by bipolar RF therapy with double needles (see Figs. 5, 6).

During the treatment period, patients’ vital signs were monitored and oxygen was given via a nasal cannula. If the blood pressure increased by more than 20% of the baseline value, intravenous injection of urapidil (12.5 mg) was given and repeated as appropriate to maintain hemodynamic stability depending on the blood pressure monitoring. If the heart rate dropped to 50 beats/min, atropine (0.3 - 0.75 mg) was injected intravenously and the therapy was paused until the heart rate returned to the baseline level. The puncture operation time (from local anesthesia of puncture point to puncture needlepoint to target time) was recorded. If hematoma occurred in the puncture site during the operation, we applied pressure on the site for several minutes to stop the bleeding and applied a cold compress for several hours after the operation. We recorded the curative effect of patients in the hospital and evaluated the long-term effect by telephone follow-up once a month. If pain and all sensation completely disappeared in the
area of the mandibular nerve innervation area, the treatment was considered effective. Otherwise, it was considered ineffective. Recurring pain was considered, but the pain in the original mandibular area reappeared during the subsequent follow-up period.

**Statistical Methods**

Data are presented as means ± standard deviation (x ± s). Analyses were performed using the software package GraphPad Prism 6 (GraphPad Software, San Diego, USA). Student’s t-test was used to analyze statistical differences, where P < 0.05 was considered statistically significant.

**RESULTS**

In all 107 patients, under CT localization, the RF puncture needle was accurately inserted to the midpoint of the horizontal diameter of the foramen ovale. Of the 107 patients, 83 patients had mandibular tingling and mandibular twitching induced by 0.1 ~ 0.5 mA current and 15 had satisfactory results after adjusting the position of the tip of the needle. In the remaining 9 patients, the horizontal diameter of the foramen ovale was more than 8 mm; hence, a double-needle probe bipolar RF was used. Numbness and jaw jitter could be detected by current stimulation below 0.5 mA for each of the 18 needles.

The parameters of RFA in all patients were 90° for 120 seconds. After RFA, the pain in the mandibular branch area diminished completely and the sensation in this area disappeared completely. Residual pain in the temporal region of the anterior ear was noted in 2 patients, and residual pain at the tip of the tongue, which diminished after a second RF treatment, was noted in one patient. The TN effects of RF therapy were “all or nothing,” and the patients stopped medication use completely after effective RF. No complications of intracranial

Fig 3. Design of the route, the angle, and the distance of the RFA needle insertion. Line 1 was drawn from the mid of the foramen ovale to the skin entry point. The needle insertion depth (distance: 7.37 cm) and the puncture angle (the angle between line 1 and the sagittal plane, β = 13) were then calculated.

Fig 4. Puncture to target was based on the design path (the tip should not cross the inner orifice of the foramen ovale).
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hernorrhage and infection occurred, except for 21 cases of facial hematomas during operation. After 12 to 24 months of follow-up, 9 cases had recurrence, which occurred in both groups of patients: 8 cases in single-needle therapy and one case in the double-needle therapy. After taking pregabalin for several weeks, 5 cases of recurrence with a foramen ovale diameter ≥ 6 mm underwent double-needle therapy as a secondary procedure, while the remaining cases with a foramen ovale diameter < 6 mm had single-needle therapy; all remained effective after receiving additional extracranial RF therapy (see Table 2 for the timeline of recurrence and management).

The rack tilt angle (angle between puncture needle and coronal plane) and puncture angle (angle between puncture needle and sagittal plane) were 18.2 ± 7.6° and 15.9 ± 4.6°, respectively. The average puncture depth was 63.48 ± 11.7 mm, and the average puncture operation time was 13.6 ± 5.7 minutes. The blood pressure of 23 patients increased above the baseline value during the puncture operation. In 20% of the patients, the heart rate decreased to 50 beats/min during RFA and recovered to normal after intravenous injection of atropine. Oxygen therapy by nasal cannula was given to all patients during the operation. SpO₂ decreased to less than 90% after propofol injection in 7 patients and recovered to normal after mandibular support and abduction of upper limbs. No auxiliary ventilation with the high-pressure mask was used to assist ventilation.

**Discussion**

At present, there are many clinical interventions for TN. TN can be divided into primary or secondary TN according to the existence of corresponding lesions. Oral antiepileptic drugs are often the first choice for primary TN, while secondary TN is generally treated based on the primary cause. When conservative treatment is ineffective or unbearable due to the side effects, surgical treatment is considered
(15-18). RFA has advantages of less trauma, high efficiency, and wide adaptation. Therefore, RFA of the Gasserian ganglion of the trigeminal nerve becomes one of the main methods for TN treatment. However, because the trigeminal Gasserian ganglion is an intracranial structure, the puncture needle must enter into the cranium to complete the operation during the trigeminal Gasserian ganglion RF. The risk of serious complications such as intracranial infection and hemorrhage exists. Our previous study found that if the target of RFA for V2 TN was transferred from the intracranial Gasserian ganglion to the extracranial hole (FR), a satisfactory effect was also achieved (10,19-21).

In the present study, we have successfully transferred the traditional target of RFA from the Gasserian ganglion to the exit cranial passage of each branch of the trigeminal nerve. Here we reported that 97.2% (104 cases) of V3 TN were treated with RFA at 90° for 120 seconds. Recurrence rate was only 8.41% (9/107) within 2 years, and nondangerous complications (facial hematomas) were only 19.6% (21/107). The satisfactory clinical effect was achieved completely. Our findings suggest that extracranial non-semilunar ganglion RFA is a highly selective treatment of trigeminal nerve branches. For the ophthalmic branch, maxillary branch, and mandible branch pain, the supraorbital foramen (22), FR, and foramen ovale are used as therapeutic targets, respectively. If neuralgia of multiple branches occurs at the same time, multiple targets could be combined to treat all branches of the trigeminal nerve without entering the cranium. Therefore, extracranial non-Gasserian ganglion RFA is a development of RF treatment of the trigeminal nerve, because it avoids the occurrence of serious complications such as intracranial hemorrhage or intracranial infection potentially caused by Gasserian ganglion RFA (23,24).

A major difference between this technique in the treatment of V3 TN and the traditional RFA is that the needle tip reaching the inner orifice of the foramen ovale is at the Gasserian ganglion through the foramen ovale. To confirm the site, we applied the high- and low-frequency electrical stimulation tests before the RFA treatment. Only if the 0.5 mA current induces the sense of mandibular needling and twitching would RFA be carried out. The traditional RFA method of TN requires the puncture needle to cross the foramen ovale 5 - 10 mm (see Fig. 7) until it reaches the TN Gasserian ganglion before electrophysiological test and RFA.

Other modifications of our method are RFA temperature and time parameters. In the traditional RF treatment, the needle tip is located at the Gasserian ganglion in which the neurons and nerve fibers are interwoven. To prevent damage to the non-responsible branches in the Gasserian ganglion, stepwise heating from 55° to 75° was done. The initial temperature is 55°, one step for every 5° lasting for 30 seconds. There were 4 - 6 steps, lasting 2 - 3 minutes in total (25-28). The stepwise increase of temperature avoids damaging the non-responsible branches of the trigeminal nerve in the Gasserian ganglion. After all, the nerve fibers in the Gasserian ganglion are extremely close and intertwined. The stepwise heating method can be used to test the sensory changes of the non-responsible branch dominating the region during RFTC. The advantage of stepped heating is that it is possible to test the sensory changes in the innervating area of the patient's non-responsible branch during RFA. Once the non-responsible branch is found to be affected, the needle tip position can be adjusted in time to avoid further damage to the non-responsible branch. During this period, it is necessary to communicate with the patient to confirm that there is no more injury to the non-responsible branches. But these temperature and time course parameters are obtained based on the RF of the intracranial Gasserian ganglion. Once the non-responsible branch is found to be involved, the tip of the needle must be adjusted in time to avoid further damage. However, if a highly selective extracranial non-Gasserian ganglion RFA is performed, there is no need to worry about damaging non-responsible branches, and thus stepwise heating is not required. Our team has carried out more than 500 extracranial non-Gasserian ganglion RFA treatments in recent years. All of them directly used continuous RFTC at 90°C for 120 seconds and no complications in the eye were observed (10,12,20-24), although it was thought that the incidence of facial numbness and ocular complications were high if the temperature was above 90°C during traditional Gasserian ganglion RFA (29).

During the traditional RF, because intravenous anesthesia cannot be used, patients usually feel strong
pain. When our extracranial non-Gasserian ganglion RF technique is implemented, the RF needle tip carries on the highly selective extracranial non-Gasserian ganglion in the foramen ovale. Therefore, the injury of the non-responsible branches could be avoided and our RFA can be directly applied at 90° for 120 seconds under intravenous anesthesia, which improves the treatment experience of the patients and takes a step forward to comfortable medical treatment.

The puncture operation of this technique is carried out under CT guidance. According to the puncture path designed in this group, the angles between the needle direction and the sagittal plane and coronal plane were 15.9 ± 4.6° and 18.2 ± 7.6°, respectively. The average puncture depth is 63.48 ± 11.7 mm. The skin puncture point was similar to the injection point of the Hartel approach. Because the puncture direction and depth had been measured with the help of the CT tool ruler before puncture, the operation is not time-consuming (the mean puncture operation time is 13.6 ± 5.7 min). Furthermore, because this puncture needle does not enter the cranium, it will not cause intracranial hemorrhage due to the puncture injury of intracranial blood vessels. However, the patients may have elevated blood pressure due to anxiety during the puncture operation. And since most patients are elderly (the average age is 68.22 ± 10.99 years old), they should be closely monitored and inhale oxygen (19) in order to prevent the occurrence of critical cerebrovascular complications in the operation center (20).

The limitation of this study is that there is no control group for traditional semilunar ganglion RFA. Because our RF was applied outside of cranium and only affected the responsible branch of trigeminal nerve, it did not cause any cranial hematomas or damage of non-responsible branches. Since traditional RFA still has the potential risk of cranial hematomas, it was not set as the control treatment. Besides, multicenter and large sample investigations are still needed.

In summary, RFA for primary TN mandibular branch pain can be achieved by transferring the target from the ganglion to the mandibular nerve exits (through the foramen ovale). In this way, the risk of intracranial hemorrhage or infection will decrease, and the safety of TN RF would be improved. Our present study suggests the advantage of extracranial non-Gasserian ganglion RFA in the treatment of TN.

Declarations

Ethics Approval and Consent to Participate
Institutional review board/ethics committee approval was obtained from the Institutional Review Board of the Jiaxing First Hospital.

Consent for Publication
All patients have consented to the submission of the study results.

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Competing Interests
The authors declare that they have no conflict of interests.

Authors’ Contributions
Huidan Lin and Bing Huang had the original idea for the manuscript and collected the data. Gang Cao, Guanjun Jin, Zhaodong Yang, Jinghan Shao, and Changshun Huang analyzed the data. Huidan Lin reviewed the literature for the introduction and drafted the manuscript. Ming Yao revised the manuscript. Bing Huang assisted in drafting the manuscript, revision of the text, and approved the final manuscript. All authors read and approved the final manuscript.

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