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Original Article

CT-guided radiofrequency treatment of trigeminal neuralgia at different temperatures through foramen rotundus

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Abstract: Objective: To compare the efficacy and safety of CT-guided radiofrequency therapy in the treatment of trigeminal neuralgia (TN) through foramen rotundus at different temperatures. Methods: A total of 60 patients with TN in our hospital were selected and randomly divided into the control group and the observation group, with 30 cases in each group. CT or MRI was routinely performed before the operation to exclude intracranial space-occupying lesions. The round hole of both groups of patients was targeted under CT guidance. The puncture needle position and depth were determined according to CT images and radiofrequency electrical stimulation. The control group gradually increased the radiofrequency temperature to 75°C, and the observation group gradually increased to 90°C for damage treatment. Both groups of patients were treated with radiofrequency for 360 s. The clinical efficacy was evaluated by BNI classification criteria. At the same time, the visual analog scale (VAS) score, the total score of Pittsburgh sleep quality index (PSQI) and the incidence of complications were compared between the two groups. The Kaplan-Meier method in survival analysis was used to calculate the pain recurrence rate at 1 and 2 years after the operation. Results: One week after the operation, there was no significant difference in the total effective rate between the two groups (χ^2=0.089, P=0.766). After 2 months, the total effective rate of the observation group was higher than that of the control group (χ^2=4.043, P=0.044). One day and one week after the operation, the VAS score of the observation group was higher than that of the control group (t=7.365, 6.269; P=0.007, 0.012), and the total score of PSQI was significantly higher than that of the control group (t=8.026, 5.447; P=0.002, 0.015). There was no significant difference in VAS score and PSQI total score between the two groups 1 month and 2 months after operation (P>0.05). There was no significant difference in the incidence of postoperative complications between the two groups (P>0.05). Kaplan-Meier survival analysis was used to calculate the recurrence rate of pain at 1 and 2 years after operation. The recurrence rate of the observation group was significantly lower than that of the control group (χ^2=4.219, 4.021; P=0.039, 0.044). Conclusion: CT-guided radiofrequency at 90°C through foramen rotundus is effective in the treatment of trigeminal neuralgia without increasing the incidence of complications.

Keywords: CT-guided, transforaminal, different temperature, radiofrequency therapy, trigeminal neuralgia, curative effect

Introduction

Trigeminal neuralgia (TN) is a common neurological disease in neurosurgery. It is mainly caused by the lesion of unilateral facial trigeminal nerve and characterized by recurrent and paroxysmal severe pain in the area dominated by one or more branches. The pain feels like knife-cut, electric-shock, burning and tearing, with the characteristics of sudden happening and sudden stop. It often occurs when washing the face, brushing teeth, talking or when the face suffers from hot and cold stimulation. The pain usually lasts for several seconds to several minutes, and the degree is heavy or even intolerable [1]. At present, there are many treatment options for TN, including drugs, acupuncture, gamma knife, decompression and ganglion closure. These treatments may have a certain curative effect but they also have disadvantages and adverse reactions, which are difficult to tolerate in some patients [2]. With the development of minimally invasive treatment technology, radiofrequency thermocoagulation of tri-

Table 1. Comparison of general data between the two groups (n, $\bar{x} \pm sd$)

Groups	Control group (n=30)	Observation group (n=30)	χ^2/t	P
Gender (Male/Female)	12/18	11/19	χ^2=0.071	0.791
Age (years)	61.3±10.7	61.7±10.5	t=0.263	0.852
Course of diseases (years)	5.4±3.9	5.5±4.0	t=0.647	0.706
Location of the disease (n)			χ^2=0.634	0.426
Left side	10	13		
Right side	20	17		
Branches of affected trigeminal nerve			χ^2=0.077	0.781
I	3	2		
II	9	9		
III	5	4		
I+II	3	3		
II+III	9	10		
I+II+III	1	2		

geminal ganglion has become a popular treatment method for TN, with the advantages of minimally invasive, simple and obvious curative effect [3]. Among them, accurate puncture and positioning are the key points of radiofrequency treatment, and CT-guided puncture through a round hole can greatly improve the positioning accuracy [4]. Clinical studies have found that radiofrequency thermocoagulation uses the therapeutic principle of protein coagulation and denaturation caused by high temperature, which can also cause a certain degree of nerve damage [5]. Therefore, how to reduce the complications of nerve injury and ensure the analgesic effect has become the key to the technical breakthrough of radiofrequency thermocoagulation. At present, the treatment temperature of radiofrequency thermocoagulation is generally controlled at 75°C-90°C, and different temperatures have their treatment advantages and disadvantages [6]. However, there is no guiding standard for different temperature selection of radiofrequency thermocoagulation for TN, and its efficacy and safety are still controversial. Therefore, this study compared the efficacy and safety of CT-guided radiofrequency treatment at different temperatures through the foramen rotundus to provide a reference for clinical treatment options.

Materials and methods

General information

A total of 60 cases of TN patients in Shanghai Pudong Hospital, Fudan University Pudong Medical Center from February 2016 to June 2018 were selected. Inclusion criteria: (1) All of them met the diagnostic criteria of the International Society for pain (IASP) [7]; (2) Intracranial space-occupying lesions were excluded by routine CT or MRI; (3) All patients were under the relevant treatment indications of radiofrequency thermocoagulation, including those who were ineffective or intolerable by strict and regular drug treatment, and those who were ineffective or unwilling to accept other surgical treatments; (4) The therapy was invalid or patients could not tolerate after oral medication, physical therapy and closed treatment, etc.; (5) All of them voluntarily participated in the study and signed the informed consent. Exclusion criteria: (1) Patients with secondary TN caused by intracranial cholesteatoma; (2) Patients who received decompression, nerve root resection or gamma knife surgery in the past; (3) Patients with a history of spinal or brain injury or nervous system diseases; (4) Patients combined with serious cardiovascular and cerebrovascular diseases, liver, kidney and lung diseases. They were randomly divided into the control group and the observation group, with 30 cases in each group. There was no significant difference in gender, age, course of the disease, location of disease, and number of trigeminal nerve branches between the two groups. So results are comparable (**Table 1**). This study was approved by the Ethics Committee of Shanghai Pudong Hospital, Fudan University Pudong Medical Center.

Radiofrequency therapy

When patients enter the CT intervention room, routine ECG, blood oxygen saturation, brain CT

scanning, blood and urine routine and liver and kidney function tests were performed. After ensuring that the patient had no foramen rotundus dysfunction, anatomical abnormalities and intracranial space-occupying lesions, skin preparation, routine disinfection and towel laying were carried out. Patients lied supine on the CT scanning table for spiral scanning. The technicians put a thin pillow on the shoulder position, adjusted the angle of the CT frame, and tilted the CT frame to the side of the patient's foot about 20 degrees. Firstly, the puncture side and puncture point were initially located with a metal tag. Then the exact coordinates of the foramen rotundus were analyzed when the CT scanning data were input into the data system. Foramen rotundus was usually located 2.0-2.5 cm away from the angle of the mouth on the affected side and 0.5-1.0 cm downward. After the puncture point was determined, the face was disinfected and injected with 1.0% lidocaine (Shandong Luhua Pharmaceutical Co., Ltd., China) under local anesthesia. COSMAN RFG-1B neuro-radiofrequency pain treatment instrument and radiofrequency needle (Cosman Medical, Inc.) were used. The exposed part of the radiofrequency needle tip was 5 mm. Technicians performed puncture under CT guidance and adjusted the angle of the needle according to the coordinates of the foramen rotundus. After the needle successfully entered the foramen rotundus, the puncture needle first reached the indentation of the trigeminal semilunar ganglion, and then an electrical stimulation test was performed by connecting the radiofrequency hyperthermia apparatus. The electrical stimulation was performed at 0.2-0.3 V and 50 Hz for about 1 ms. If the numbness or pain in the trigeminal innervation area can be reproduced, it is suggested that the puncture position is accurate, otherwise, it is necessary to fine-tune the puncture needle depth to achieve the precise position. After the puncture position was determined, 2 mg/kg propofol (Sichuan Guorui Pharmaceutical Co., Ltd., China) and 0.05 mg fentanyl (Yichang Humanwell Pharmaceutical Co., Ltd., China) were injected intravenously. After complete anesthesia, patients were treated with radiofrequency thermocoagulation, whose temperature increased gradually. The patients in the control group were treated at 65°C for ablation for 60 s, 70°C for 240 s, and then gradually heated to 75°C for 60 s. Patients in the observation group were treated at 65°C for ablation for 60 s, 70°C for 240 s, and then gradually heated to 90°C for 60 s. Eye movement, facial sensation, corneal reflex and other conditions were closely observed in both groups.

Outcome measures

Main outcome measures: (1) The total effective rate was compared between the two groups at 1 week and 2 months after operation. The total effective rate = (number of cured patients + number of markedly effective patients + the number of patients improved)/total number of patients ×100%; (2) Visual analog scale (VAS) scores were compared between the two groups at 1 day, 1 week, 1 month and 2 months after the operation; (3) The incidence of complications such as facial numbness, decreased masticatory power, keratitis, diplopia, cerebrospinal fluid leakage and death were observed. The total complication rate was the sum of the incidence of each complication.

Secondary outcome measures: (1) Pittsburgh sleep quality index (PSQI) scores were compared between the two groups at 1 day, 1 week, 1 month and 2 months after the operation; (2) After 2 years of follow-up, the pain recurrence rate of 1 year and 2 years after operation was compared between the two groups. The pain recurrence rate = the number of pain recurrence cases/total number of cases ×100%. In the first year after discharge, the doctor conducted a telephone follow-up once a month. The patient was followed up in the outpatient department every six months. In the second year after discharge, the doctor made a telephone follow-up every three months, and the patient was followed up in the outpatient department every six months.

Efficacy criteria and test methods

The efficacy standard was evaluated according to the BNI classification after treatment, which was divided into grade I, grade II, grade III, grade IV and grade V [8]. Grade I was painless; grade II was occasional pain, but no medication was needed; grade III was mild pain, but pain was well controlled after medication; grade IV was moderate pain, which was still not improved after drug treatment; grade V was severe pain and could not be relieved by drugs. The

Table 2. Comparison of total effective rate of two groups at 1 week after operation (n, %)

Groups	Cure	Effective	Improvement	Ineffective	Total effective rate (%)
Control group (n=30)	10 (33.33)	6 (20.00)	6 (20.00)	8 (26.67)	73.33
Observation group (n=30)	11 (36.67)	5 (16.67)	7 (23.33)	7 (23.33)	76.67
χ^2					0.089
P					0.766

Table 3. Comparison of the total effective rate of patients in the two groups at 2 months after operation (n, %)

Groups	Cure	Effective	Improvement	Ineffective	Total effective rate (%)
Control group (n=30)	12 (40.00)	9 (30.00)	4 (13.33)	5 (16.67)	83.33
Observation group (n=30)	15 (50.00)	7 (23.33)	7 (23.33)	1 (3.34)	96.66
χ^2					4.043
P					0.044

curative effect was divided into four levels, including cure: BNI grade I after treatment; significant effect: BNI grade II after treatment; improvement: BNI grade III after treatment; ineffective: BNI grade IV-V after treatment. The total effective rate = (cured number + markedly effective number + improved number)/total number ×100%. VAS scores ranged from 0 to 10, including 0 for no pain, 1-3 for mild pain, 4-6 for moderate pain and 7-10 for severe pain. PSQI was used to evaluate the sleep quality of patients. The scale contains 7 factors, and each factor has 0-3 grades, corresponding to 0-3 points, with a full score of 21 points. The higher the score, the worse the sleep quality [9]. Criteria for recurrence of pain: after treatment, the same kind of pain appeared again in the original pain area innervated by the trigeminal nerve [10].

Statistical methods

All statistical data were analyzed by SPSS 21.0 professional statistical software. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd), and a t-test of independent samples was used for comparison between groups. VAS score and PSQI total score were compared at multiple time points by repeated measurement analysis of variance combined with post Bonferroni test. All the count data were expressed in cases (percentages). The chi-square test was used to compare among the groups. The log-rank method in Kaplan Meier analysis was used to calculate the postoperative recurrence rate. The difference was statistically significant with $P<0.05$.

Results

Comparison of the total effective rate of the two groups 1 week after the operation

One week after the operation, the total effective rate of the observation group was 76.67%, while that of the control group was 73.33%. There was no significant difference between the two groups ($\chi^2=0.089$, $P=0.766$). See **Table 2**.

Comparison of the total effective rate of patients in the two groups after 2 months of treatment

Two months after the operation, the total effective rate of the observation group was 96.66% while that of the control group was 83.33%. The total effective rate of the observation group was significantly higher than that of the control group ($\chi^2=4.043$, $P=0.044$). See **Table 3**.

Comparison of VAS scores in patients between the two groups at different time points after operation

One day and one week after the operation, the VAS scores of patients in the observation group were significantly higher than those of the control group (t=7.365, 6.269; P=0.007, 0.012). There was no significant difference in VAS scores of patients between the two groups 1 month and 2 months after the operation (t=0.490, 0.166; P=0.723, 0.892). See **Table 4** and **Figure 1**.

Table 4. Comparison of VAS scores of patients between the two groups at different time points ($\bar{x} \pm sd$)

Groups	One day after operation	One week after operation	One month after operation	Two months after operation
Control group (n=30)	3.46±1.07	3.20±1.15	2.68±0.74	2.55±0.91
Observation group (n=30)	4.39±1.25	4.03±1.42	2.77±0.69	2.63±0.82
t	7.365	6.269	0.490	0.166
P	0.007	0.012	0.723	0.892

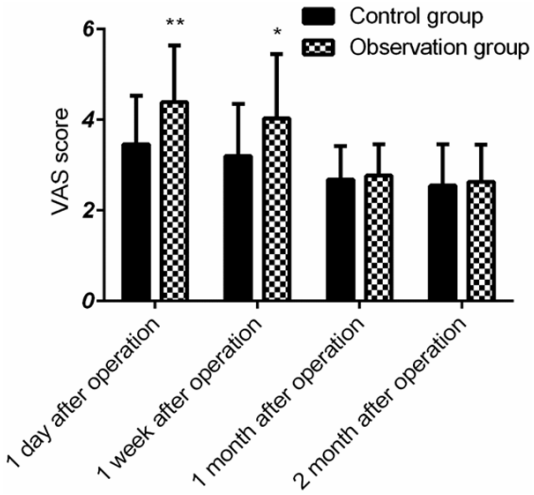

Figure 1. Comparison of VAS scores of patients between the two groups at different time points. Compared with the control group, *P<0.05; compared with the control group, **P<0.01. VAS: visual analog scale.

Comparison of PSQI total score in patients between the two groups at different time points

At 1 day and 1 week after the operation, the total score of PSQI in the observation group was significantly higher than that in the control group (t=8.026, 5.447; P=0.002, 0.015). There was no significant difference in the total score of PSQI in patients between the two groups 1 month and 2 months after the operation (t=1.246, 0.783; P=0.271, 0.468). See **Table 5** and **Figure 2**.

Comparison of the incidence of postoperative complications between the two groups

There was no significant difference in the incidence of complications such as facial numbness, decreased masticatory power, keratitis, diplopia, cerebrospinal fluid leakage and death between the two groups (P>0.05). See **Table 6**.

Comparison of the recurrence rate in patients between the two groups 1 year and 2 years after the operation

The recurrence rate of the observation group was significantly lower than that of the control group (χ^2=4.219, 4.021; P=0.039, 0.044). See **Table 7** and **Figure 3**.

Discussion

At present, the exact etiology of TN is still unclear. The main accepted pathogenesis theories include microvascular compression and neurodegeneration. It was considered that demyelination occurred in the 5-10 mm segment of the entry area of the trigeminal nerve root (REZ). Microvascular compression and pulsation caused pain [11]. The middle- and old-age population is the most common group catching TN. The incidence rate has been increasing year by year in recent years. The main manifestation of patients is intermittent facial irritation pain, and the longer the course of the disease, the frequency and degree of pain attack are significantly increased. TN is difficult to self heal and seriously reduce the quality of life of patients. How to treat TN is also a clinical concern. At present, there are many treatment methods for TN, which can be divided into oral medication and surgical treatment. Drug treatment includes adriamycin, while surgical treatment can be roughly divided into microvascular decompression and nerve root destruction, which includes glycerin damage, gamma knife and radiofrequency thermocoagulation [12]. Since sweet et al. first proposed radiofrequency thermocoagulation for the treatment of TN, with the development of minimally invasive technology at this stage, it has been vigorously promoted in the clinical treatment of TN, and its effectiveness and safety have also been recognized. Radiofrequency thermocoagulation is based on the differ-

Table 5. Comparison of total PSQI scores in patients between the two groups at different time points ($\bar{x} \pm sd$)

Groups	One day after operation	One week after operation	One month after operation	Two months after operation
Control group (n=30)	8.96±2.87	6.25±2.01	5.40±1.75	5.56±1.47
Observation group (n=30)	11.41±2.82	8.84±2.18	5.32±1.58	5.69±1.63
t	8.026	5.447	1.246	0.783
P	0.002	0.015	0.271	0.468

Note: PSQI: Pittsburgh sleep quality index.

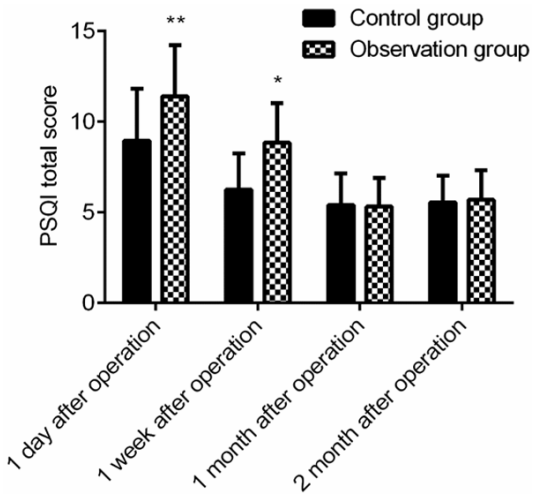

Figure 2. Comparison of total PSQI scores in patients between the two groups at different time points. Compared with the control group, *P<0.05; compared with the control group, **P<0.01. PSQI: Pittsburgh sleep quality index.

ence in temperature tolerance between conduction pain and tactile nerve fibers. By damaging the pain nerve fibers and retaining the tactile nerve fibers, radiofrequency thermocoagulation can achieve the purpose of relieving pain and reserving the corresponding position tactile. In the pathogenesis of TN, the medium of pain conduction is myelin-free fibers Aδ and C. The diameter of these fibers is relatively small, the temperature tolerance is relatively poor, and the sensitivity to RF current is high. When the temperature rises to 60-75°C, these fibers begin to degenerate [13]. However, the tactile and thermal conducting fibers are myelinated coarse fibers Aα and Aβ, which have a larger diameter and have higher thermal tolerance. Generally, when the temperature is less than 75°C, there is no damage, and even when the temperature is higher than 80°C, fibers can maintain good functions [14]. Radiofrequency thermocoagulation reaches the semilunar ganglion of the trigeminal nerve through a puncture needle, and the radiofrequency current releases a lot of heat. The temperature range is controlled by a thermistor, and the temperature tolerance principle of conduction touch and pain nerve fiber is used to achieve the selective damage of pain nerve fiber, achieve the treatment purpose of pain relief, and greatly improve the treatment effectiveness.

Temperature control is the key factor affecting the therapeutic effect of radiofrequency thermocoagulation. However, there is no clear guideline for temperature control at home and abroad, and there is great clinical controversy. At present, it is considered that the radiofrequency temperature should be controlled at 75±5°C. Under this temperature range, the conduction pain nerve fibers gradually degenerate, while the conduction tactile has myelin sheath and the nature of crude fiber is stable. So radiofrequency thermocoagulation can achieve the purpose of selective thermal damage. At the same time, the study points out that in radiofrequency thermocoagulation, the field strength and voltage can also alleviate the pain to a certain extent [15]. Blindly increasing the temperature can cause serious complications such as nerve scald. However, if the temperature is too low, the damage is incomplete and the recurrence rate is high. The temperature of about 75°C is helpful to distinguish the electrode distance, scar degree near nerve fiber and improve the accuracy of selective damage [16]. Zhao et al. found that there was no significant difference in the degree of pain relief and the incidence of complications in patients with TN treated by radiofrequency thermocoagulation at 70°C and 75°C [17]. It was pointed out that there was no significant difference in efficacy and safety between 70°C and 80°C. Recently, more and more doctors

Table 6. Comparison of the incidence of postoperative complications between the two groups (n, %)

Groups	Control group (n=30)	Observation group (n=30)	χ^2	P
Facial numbness	7 (23.33)	6 (20.00)	0.098	0.754
Decreased masticatory power	2 (6.67)	2 (6.67)	0.000	1.000
Keratitis	0 (0.00)	1 (3.33)	1.017	0.313
Diplopia	2 (6.67)	0 (0.00)	2.069	0.150
Cerebrospinal fluid leakage	0 (0.00)	0 (0.00)	0.000	1.000
Death	0 (0.00)	0 (0.00)	0.000	1.000
Total incidence	11 (36.67)	9 (30.00)	0.300	0.584

Table 7. Comparison of the recurrence rate in patients between the two groups 1 year and 2 years after operation (n, %)

Groups	Recurrence rate one year after operation	Recurrence rate two years after operation
Control group (n=30)	7 (23.33)	11 (36.67)
Observation group (n=30)	3 (10.00)	5 (16.67)
χ^2	4.219	4.021
P	0.039	0.044

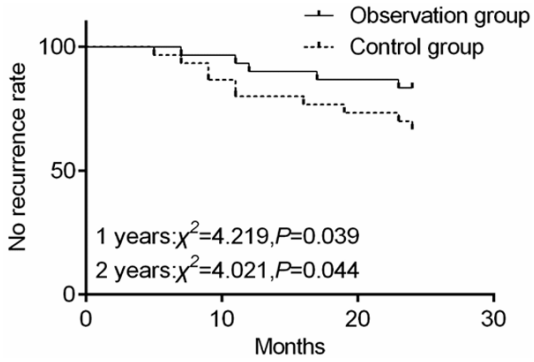

Figure 3. Comparison of non-recurrence rate in patients between the two groups after operation.

have raised the temperature to 85°C or even 90°C, and confirmed that this temperature range is safe and reliable, and can damage the ganglion more thoroughly. Ding et al. confirmed that it was relatively safe to control the temperature below 90°C, which will not cause sequelae such as corneal hyporeflexia [18]. In this study, we compared the efficacy and safety of radiofrequency thermocoagulation for TN at 75°C and 90°C. During the treatment, the temperature increased gradually from 65°C. The results showed that there was no significant difference in the total effective rate of the two groups one week after the operation, while the total effective rate of the observation group was significantly higher than that of the control group 2 months after the operation. The VAS score of the observation group was significantly higher than that of the control group at 1 day and 1 week after operation. However, there was no significant difference in VAS score between the two groups at 1 month and 2 months after the operation, but they were significantly improved compared with those before treatment. At the same time, the total score of PSQI also showed the same results. The results showed that the analgesic effect of 90°C was slightly better than that of 75°C. However, some studies hold the opposite attitude, which believed that the highest temperature of 85°C can meet the requirements of TN treatment [19]. If the temperature is too high, the nerve fibers will be damaged too much, which will lead to the deformation and rupture of axons. In the later stage, the proliferation of small fibers will cause an increase of axon volume, which may lead to the recurrence of pain.

Complications and recurrence rate are important criteria for evaluating radiofrequency thermocoagulation. Because radiofrequency thermocoagulation applies the principle of heating the exposed part of the puncture trocar, dehydration, degeneration and coagulative necrosis of the ganglion appear, it has achieved the purpose of destroying the diseased nerves and relieving pain [20]. The range of coagulative necrosis of ganglion is closely related to the curative effect and complications, and the temperature is an important factor affecting the range of necrotic foci. The too high or too low temperature will affect the postoperative curative effect, so it is very important to control the optimal temperature range [21]. The trigeminal nerve, as a mixed nerve fiber for conduction of sensation and pain, is difficult to achieve absolute selectivity in thermal damage without damaging Aα and Aβ nerve fibers. Therefore, numbness caused by injury is also the most common complication of radiofrequency ther-

mocoagulation [22]. The results of this study showed that there was no significant difference in the incidence of postoperative facial numbness, decreased masticatory force and other complications between the two groups, and there was no serious complication such as cerebrospinal fluid leakage. It was safe and reliable. The 2-year follow-up showed that the recurrence rate of the observation group was significantly lower than that of the control group 1 and 2 years after the operation, which indicated that the lesion ganglion was more completely damaged at the highest temperature of 90°C, and the curative effect was more firm. However, the results of this study may be affected by individual factors such as small sample size and limited follow-up time. The long-term safety of the selected 90°C temperature remains to be observed, and the experimental results need to be further verified by increasing the sample size and research depth.

In conclusion, CT-guided radiofrequency thermocoagulation with the highest temperature of 90°C through the foramen rotundus has a significant effect in the treatment of TN, which can effectively reduce the pain of patients, reduce the recurrence rate of long-term pain, but does not increase the incidence of complications. It is safe and reliable, which is worthy of clinical promotion.

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Disclosure of conflict of interest

None.

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