

## Observational Study

# e Analysis of the Risk Factors and a Prediction Model for Postherpetic Trigeminal Neuralgia Recurrence After Extracranial Nonsemilunar Ganglion Radiofrequency Thermocoagulation

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**Background:** Extracranial nonsemilunar ganglion radiofrequency thermocoagulation in the treatment of postherpetic trigeminal neuralgia has significant clinical effects. However, the related risk factors for its recurrence have not been studied.

**Objective:** This study aimed to investigate the risk factors for the recurrence of postherpetic trigeminal neuralgia after extracranial nonsemilunar ganglion radiofrequency thermocoagulation, and to construct a recurrence prediction model.

**Study Design:** This is a single-center, retrospective observational study.

**Setting:** The study was conducted in the Department of Pain, Affiliated Hospital of Jiaxing College, Jiaxing, People's Republic of China.

**Methods:** A total of 76 patients with postherpetic trigeminal neuralgia admitted to the First Hospital of Jiaxing from July 2013 through October 2021 were retrospectively analyzed. All patients were treated with computed tomography-guided extracranial nonsemilunar segment radiofrequency therapy. The Kaplan-Meier method was used for survival analysis, the log-rank test was used, and the Cox proportional hazards regression model was used to analyze the clinical factors affecting postherpetic trigeminal neuralgia recurrence after extracranial nonsemilunar ganglia radiofrequency thermocoagulation; in addition, a recurrence prediction model was established.

**Results:** Patients were followed-up for 12 months. A univariate analysis showed that age and disease duration are the factors affecting postherpetic trigeminal neuralgia recurrence after extracranial nonsemilunar ganglion radiofrequency thermocoagulation ( $P < 0.05$ ). A multivariate Cox proportional hazards regression analysis showed that age and disease duration were independent influencing factors. The recurrence risk function model is expressed as follows.  $H(t) = h_0 \exp(1.116 X_1 + 1.340 X_2)$ , where  $X_1$  and  $X_2$  represent age and disease duration, respectively. The likelihood ratio of the model was tested, and the likelihood ratio was 195.776, showing statistical significance.

**Limitations:** We look forward to increasing the sample size in subsequent studies and exploring relevant conclusions in randomized controlled trials.

**Conclusion:** A short disease duration and young age can reduce the risk of recurrence after extracranial nonsemilunar ganglia radiofrequency thermocoagulation in patients with postherpetic trigeminal neuralgia. Our established recurrence prediction model can provide a reference for clinical diagnosis and treatment.

**Key words:** Postherpetic trigeminal neuralgia,; radiofrequency ablation, recurrence, risk factors, prediction model

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**H**erpes zoster is an infectious disease caused by the reinfection of varicella-zoster virus in the human body. The accompanying pain is called herpetic neuralgia (1-3). If the acute phase of herpes zoster cannot be effectively relieved, herpetic neuralgia may be transformed into postherpetic neuralgia. A specific type of postherpetic neuralgia is postherpetic trigeminal neuralgia (PHTN). It has pain patterns similar to acupuncture, knife cutting, burning and others, which seriously affects a patient's activities of daily living, such as sleep, teeth brushing, face washing, eating and others, leading to a poor quality of life and interference with a patients' normal life (4).

Pain during a PHTN attack is severe and unbearable, and the treatment is difficult (5,6). Conventional treatment methods for PHTN include drug therapy; however, but long-term treatment not only often results in poor outcomes, but it also cause induce serious side effects that cannot be tolerated by patients (7). Nerve blocks have an immediate effect, but the effect is short (8). Although spinal cord stimulation is effective in treating herpetic neuralgia's early stages, and can effectively reduce the incidence of postherpetic neuralgia, its efficacy rate in the treatment of postherpetic neuralgia is not high (9). In addition, since electrodes are implanted into the spinal canal, the risk of epidural infection is positively correlated with the implantation; there is also a risk of electrode displacement or even rupture. Importantly, its high expense limits its clinical application (10).

Studies have shown that radiofrequency ablation is effective in treating head and face pain (11,12). Since there has been no report on the postoperative recurrence of PHTN treated by extracranial nonsemilunar ganglia radiofrequency thermocoagulation, our study retrospectively analyzed the clinical data of 69 patients diagnosed with PHTN. Furthermore, the risk factors for recurrence are discussed. The risk factors for recurrence are explored, and a recurrence prediction model was constructed.

## **METHODS**

### **Inclusion Criteria and Exclusion Criteria**

The records of 74 patients with PHTN admitted to the First Hospital of Jiaxing from July 2013 through October 2021 were retrospectively collected. The general information, diagnosis, and treatment of these patients were obtained by searching their medical records.

Inclusion criteria: 1) Patients who satisfied the

diagnostic criteria for PHTN 2) a Numeric Rating Scale (NRS-11) score > 3.

Exclusion criteria: 1) The puncture site had an infection or tumor; patients with serious cardiovascular or cerebrovascular diseases; liver or kidney dysfunction; or abnormal coagulation function; 2) patients with diabetes mellitus who had poor blood glucose control; 3) long-term use of immunosuppressive agents or systemic failure; 4) patients suffering from mental diseases or unable to cooperate with the operation.

### **Surgical Procedure**

Our study team used awake computed tomography (CT)-guided transcranial nonsemilunar ganglion radiofrequency to treat PHTN.

The specific steps were as follows: during treatment, the patient's blood pressure, heart rate, electrocardiogram, and oxygen saturation were closely monitored and recorded. A nasal catheter was used for oxygen inhalation, thin pillows are placed under the patient's shoulders, secured with wide tape, and the neck is protected with a shield. After a successful puncture was confirmed by an electrophysiological test, a routine intravenous infusion of fentanyl 0.05 mg (50 µg) was used to increase the pain threshold. If the blood pressure of the patient increased by more than 20% of the basal value, the patient was given a 12.5 mg intravenous infusion of pirenidine. The above drug dosages were adjusted accordingly to maintain hemodynamic stability.

For patients with pain in the first branch of the trigeminal nerve, a CT-guided radiofrequency puncture of the supraorbital foramen was performed (Figs. 1 and 2) and then high and low frequency (50 Hz, 2 Hz) current was applied and a motor electrical stimulation test were administered. When a 0.2–0.5 mA current could induce skin numbness and muscle movement in the original painful area, then radiofrequency thermocoagulation at 95°C for 180 seconds was performed. The treatment was terminated if the pain resolved in the original affected area, as well as skin numbness.

CT-guided foramen ovale radiofrequency was performed for patients with branch II pain of the trigeminal nerve (Fig. 3), and CT-guided foramen ovale radiofrequency was performed for patients with branch III pain (Fig. 4). For the first and second branch pain, the radiofrequency puncture of the supraorbital foramen and round foramen were performed simultaneously. The round foramen and foramen ovale puncture were performed simultaneously for patients with branch

II + III pain. For patients with branch I + II + III pain, radiofrequency treatment of the supraorbital foramen, round foramen, and foramen ovale were performed concurrently (13). The tests and surgical procedures were the same as that of the first branch of the trigeminal nerve. If there is no pain in the original area and the skin is numb, the treatment should be terminated, the radiofrequency needle removed, the sterile dressing covered, and finally the patient returned to the ward.

### Follow-up

The patients were followed up through an evalu-

ation of their inpatient medical records, outpatient follow-up, or telephone calls. Data on the recurrence of PHTN after extracranial nonsemilunar ganglia radiofrequency thermocoagulation were obtained, such as recurrence and the time of recurrence. The day of extracranial radiofrequency ablation for PHTN was used as the starting point for follow-up, and the end time was October 31, 2022. The diagnostic criterion for recurrence was an NRS-11 > 3.

### Statistical Method

IBM SPSS Statistics 21.0 (IBM Corporation) software



Fig. 1. For patients with pain of the first branch of trigeminal nerve, CT-guided radiofrequency puncture of supraorbital foramen was performed.



Fig. 3. CT-guided foramen ovale radiofrequency was performed for patients with pain of branch II of trigeminal nerve.



Fig. 2. Radiofrequency needle was used to puncture into the supraorbital foramen under the guidance of CT.



Fig. 4. CT-guided foramen ovale radiofrequency was performed for patients with pain of branch III.

was used for statistical analysis. The Kaplan–Meier method and log-rank test were used for survival analysis. A Cox proportional hazards regression model was used for multivariate analysis, and a recurrence prediction model was established. Test level  $\alpha = 0.05$ .

## RESULTS

### Basic Patient Information

The records of 74 patients with PHTN who underwent radiofrequency thermocoagulation were collected. Among them, 2 patients were excluded due to incomplete data analysis, 2 patients were lost to follow-up due to the inability to contact them through repeated telephone calls, and one patient died. A total of 69 eligible patients with PHTN were finally included.

### Univariate Analysis of Postoperative Recurrence

Disease duration and age were related to the recurrence of PHTN after radiofrequency ablation ( $P < 0.05$ ). Gender, affected side, branch, concomitant diseases, length of hospital stay, and preoperative NRS-11 score were not associated with postoperative recurrence of PHTN after extracranial nonsemilunar ganglia radiofrequency thermocoagulation ( $P > 0.05$ ), as shown in Table 1.

### Multivariate Step-by-Step Cox Proportional Hazards Regression Model

With postoperative recurrence as the survival outcome and statistically significant factors as covariates by univariate test, a multivariate stepwise Cox proportional hazards regression model was used for analysis (variable screening method; forward: LR,  $\alpha_{in} = 0.05$ ,  $\alpha_{out} = 0.10$ ). The results showed that age and disease duration were independent risk factors for recurrence of PHTN after extracranial nonsemilunar ganglion radiofrequency thermocoagulation as shown in Table 2.

### Multivariate Prediction Model for Recurrence

According to the results of the multivariate Cox proportional hazards regression model, the recurrence risk function model for PHTN after extracranial nonsemilunar ganglion radiofrequency thermocoagulation was fitted as follows:  $h(t) = h_0 \exp(1.116X_1 + 1.340X_2)$ ;  $X_1$  and  $X_2$  represent age and disease duration, respectively.

## DISCUSSION

Extracranial nonsemilunar ganglion radiofre-

quency thermocoagulation in the treatment of primary trigeminal neuralgia has a good effect, high selectivity, and high precision. It is minimally invasive and has been widely used in clinical practice (14-16). In our study, we used extracranial nonsemilunar ganglia radiofrequency thermocoagulation for the treatment of PHTN. The radiofrequency target was located on the corresponding responsible nerve trunk, owing to the radiofrequency thermocoagulation's high selectivity. Thus, the standard radiofrequency thermocoagulation at 95°C and 180 seconds could be directly used. There was significant alleviation of pain after surgery and numbness in the affected area of the skin.

In this study, variables with  $P < 0.05$  were screened by univariate analysis, and relevant variables were further screened by Cox multivariate regression. The results showed that age and disease duration were independent influencing factors for the recurrence of PHTN after extracranial nonsemilunar ganglia radiofrequency thermocoagulation. These results indicate that older and long-term patients with PHTN are more likely to relapse; hence, vigilance should be exercised. However, the side, branch, concomitant disease, length of hospital stay, and preoperative NRS-11 score were not associated with the recurrence of PHTN after extracranial nonsemilunar ganglia radiofrequency thermocoagulation.

Herpes zoster mainly affects patients over 50 years old, with a quarter of them experiencing some type of herpes zoster-related complication (17). The preponderance of elderly patients to having postoperative recurrence may be due to their increased age, the cell-mediated immune response to varicella zoster virus is reduced, self-repair function is weakened, nerve involvement is more serious, and peripheral and central sensitization is more likely (18,19). In addition, with a prolonged disease course, central sensitization becomes more serious (20), and long-term pain stimulation causes patients to generate pain memory (21). Radiofrequency ablation for herpetic neuralgia may induce new-onset neuropathic pain and may also be one of the causes of recurrence.

The pathogenesis of herpetic neuralgia is complex. For patients with postoperative recurrence, it is necessary to combine drug therapy, psychological treatment, and other interventions. The patient should also be informed of the possible recurrence factors before surgery to avoid disputes.

### Limitations

Our study is limited by its being a single-center

## Postherpetic Trigeminal Neuralgia

Table 1. Univariate analysis of recurrence after radiofrequency ablation in 69 patients with postherpetic trigeminal neuralgia.

Variable	No Recurrence	Recurrence	P
Gender			0.977
Men	23	14	
Women	20	12	
Age			0.014
≤ 65	19	4	
> 65	24	22	
Affected side			0.215
Left	28	13	
Right	15	13	
Medical history (M)			0.001
≤ 24	38	14	
> 24	5	12	
Accompanying disease			
Hypertension	18	10	0.781
Diabetes	7	2	0.305
Heart disease	2	2	0.600
Branch Involved			
I	22	18	0.103
I, II	4	3	
I, II, III	0	1	
II	13	3	
II, III	0	1	
III	4	0	
Hospital stays (T)			
< 10	35	19	0.417
≥ 10	8	7	
Preoperative NRS-11			0.353
Mild	28	14	
Severe	15	12	

NRS-11, Numeric Rating Scale

Table 2. Multivariate STEP-D-Cox proportional hazards regression model was used to analyze 69 patients with postherpetic trigeminal neuralgia.

Risk factors	$\beta$	SE	Wald	P	OR	95% CI
Age	1.116	0.544	4.202	0.040	3.053	1.050-8.876
Medical history (M)	1.340	0.397	11.378	0.001	3.819	1.753-8.319

retrospective observational study; the reliability of the conclusions may need to be confirmed by multicenter, randomized controlled trials. Secondly, the follow-up time was short. In addition, the sample size was small.

### CONCLUSION

Disease duration and age are the influencing factors for the recurrence of PHTN after extracranial non-semilunar ganglia radiofrequency thermocoagulation. Our recurrence prediction model can provide a certain reference for clinical diagnosis and treatment.

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