Retrospective Study

Nomogram for Predicting the Recurrence Rate in Selective Radiofrequency Thermocoagulation of the Trigeminal Nerve Based on Regression via Least Absolute Shrinkage and Selection Operator

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Background: Computed tomography-guided percutaneous selective radiofrequency thermocoagulation (RFT) of the trigeminal nerve is a novel, minimally invasive technique for the treatment of trigeminal neuralgia, but the high recurrence rate after surgery might pose a serious problem.

Objectives: The purpose of this study was to explore the risk factors affecting the recurrence rate after RFT and to predict the recurrence rate and provide evidence for the early prediction.

Study Design: A single-center retrospective study.

Setting: This study was carried out in the Affiliated Hospital of Jiaxing University in China.

Methods: One hundred thirty-nine patients were included in this study. The cumulative survival rates according to temperature and type of pain were estimated by the Kaplan-Meier analysis. The least absolute shrinkage and selection operator Cox regression model was used to build the nomogram. Time-independent receiver operating characteristic curve analysis confirmed the signature's predictive capacity. A calibration curve was generated to judge the accuracy of absolute risk predictions, and Brier scores were used to quantitatively evaluate the calibration. Decision curve analysis was applied to comprehensively evaluate the clinical effectiveness of the model. A multiparameter nomogram was used to analyze the scores and predict the risk of relapse.

Results: Three predictors were screened by multivariate Cox regression analysis. Pain grade (refit hazard ratio [HR]: 1.6807; 95% confidence interval [CI]: 1.1963-2.3613) and type of pain (HR: 6.2802; 95% CI: 3.3705-11.7021) were considered to be risk factors affecting the recurrence rate after RFT, while temperature (HR: 0.5203; 95% CI: 0.2859-0.9468) was identified as a protective factor. The recurrence rate within 2 years in 85°C group was 51.09%, while that in 95°C group was 29.79%. The nomogram exhibited good discrimination and calibration. Compared with the preoperative period, all of the patients' postoperative Numeric Rating Scale scores (NRS-11) decreased significantly ($P < 0.05$). The main postoperative complication was numbness, with a gradual decrease in the Barrow Neurological Institute score over time. Autonomic symptoms and decrease of masticatory muscle function were the secondary postoperative complications, and no other adverse events were observed. Overall patient satisfaction at 2 years postoperatively was 7.83 ± 1.93.

Limitations: This study contains a small sample size from a single center and the conclusion of randomized controlled trials will be more convincing.

Conclusions: Increasing temperature can effectively reduce the recurrence rate after RF, and the combination of atypical pain and higher NRS-11s could be a risk factor increasing the recurrence rate. The novel nomogram exhibited favorable survival stratification accuracy and shown a great potential for screening high-risk groups and evaluating the risk of recurrence rate.

Key words: Radiofrequency, trigeminal neuralgia, chronic pain, neuropathic pain

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Trigeminal neuralgia (TN) refers to transient and severe facial pain on one or more branches of the trigeminal nerve. This pain often lasts from a few seconds to several minutes. The nature of the pain varies and can be described as acupuncture, electric shock, and burning and can be induced by brushing teeth, touching, or eating (1,2). Population-based studies (3,4) have shown that the prevalence of TN is approximately 0.3%. Severe paroxysmal pain can significantly affect daily work and quality of life. At the same time, an increasing number of studies (1,5,6) have shown that TN can cause serious emotional disorders, even suicidal thoughts. Approximately 20% of patients with TN are likely to suffer from persistent attacks of severe pain (7), undoubtedly increasing the physical and mental burden on patients. Based on its severe clinical symptoms, the treatment of TN is a top priority. Currently, carbamazepine is the most effective drug in the treatment of TN (8). If the effect of drug treatment is not good, surgery can be considered (9). Computer tomography (CT)-guided percutaneous radiofrequency thermocoagulation (RFT) is a novel, safe, and highly selective minimally invasive operation that has proved effective in many studies (10-12). A related study (13) has shown that nearly 40% of patients relapse after receiving RFT, and we believe that, with the extension of follow-up time, the recurrence rate might be higher. The high recurrence rate after RFT is an objective problem that must urgently be solved. This study analyzed patients with TN diagnosed in the pain department who selectively underwent CT-guided RFT of the trigeminal nerve to explore the risk factors affecting the recurrence rate, to better predict the postoperative recurrence probability, to complete model construction and overall evaluation, and to systematically analyze the curative effect 2 years after the operation.

Methods

Patients

This study was reviewed by the Medical Ethics Committee of the Affiliated Hospital of Jiaxing University (LS2020-137). All participating patients signed informed consent forms. In this single-center cohort study, we reviewed the medical records of 139 consecutive patients undergoing extracranial RFT to treat TN between 02/2016 and 08/2019.

Inclusion and Exclusion Criteria

The inclusion criteria were the following. 1) The diagnosis of TN is based on 3 main criteria: pain restricted to the territory of one or more divisions of the trigeminal nerve; paroxysms of pain that are sudden, intense, and very short (< 1 second to 2 minutes, but usually a few seconds) and are described as a "shock" or an "electric sensation"; and pain triggered by innocuous stimuli on the face or in the intraoral trigeminal territory (14). 2) The patient fully understood the risks of surgery and agreed to undergo RFT. 3) Serious pain affected daily work and sleep. 4) Numeric Rating Scale scores (NRS-11s) $\geq$ 4. 5) The effect of drug treatment was not good.

The exclusion criteria were: 1) Herpes zoster-related TN. 2) History of minimally invasive surgery, such as RF or balloon compression. 3) The ophthalmic nerve (V1) or multiple branches affected. 4) Inability to understand or use the relevant scales. 5) Refusal to provide personal information or medical records for scientific research.

Figure 1 shows the enrollment of the patients in this cohort.

Surgical Procedure

All of the operations were performed by a pain physician with more than 10 years of clinical experience. Patients were positioned supine with their shoulders supported on a soft pillow. After selecting the appropriate body surface puncture point, 1% lidocaine was injected for local anesthesia, and then 22G RF needles were advanced to the foramen rotundum or transforamen ovale under the guidance of CT. If the patient complained of an abnormal sensation, the puncture needle was pushed to approximately 0.5 cm, and CT was scanned again to ensure that the tip of the needle reached the target (Fig. 2). After confirming that there was no evidence of blood, cerebral spinal fluid, or paresthesia, the needle core was removed, and the matching electrode was inserted along the casing. The sensory test was performed at 50 Hz with a pulse width of 500 μs and amplitude of 0.2-1.0 mA, and it could be considered positive when paresthesia concordant with the patient's usual TN pain was generated. A motor test was then performed by stimulating the probes at 2 Hz and 0.1-0.5 V to confirm that the probe was not in proximity to other adjacent nerves (12). Then, 0.5-11 mL of 1% lidocaine were injected 2 minutes before the procedure, followed by the implementation of RFT by the operator. The temperature of the RF needle was set to 85°C or 95°C, and the corneal reflex was tested every 15 seconds during the operation. A reduction in NRS-11s by more than 50% was considered to be successful. After extracting the needle, the puncture point was

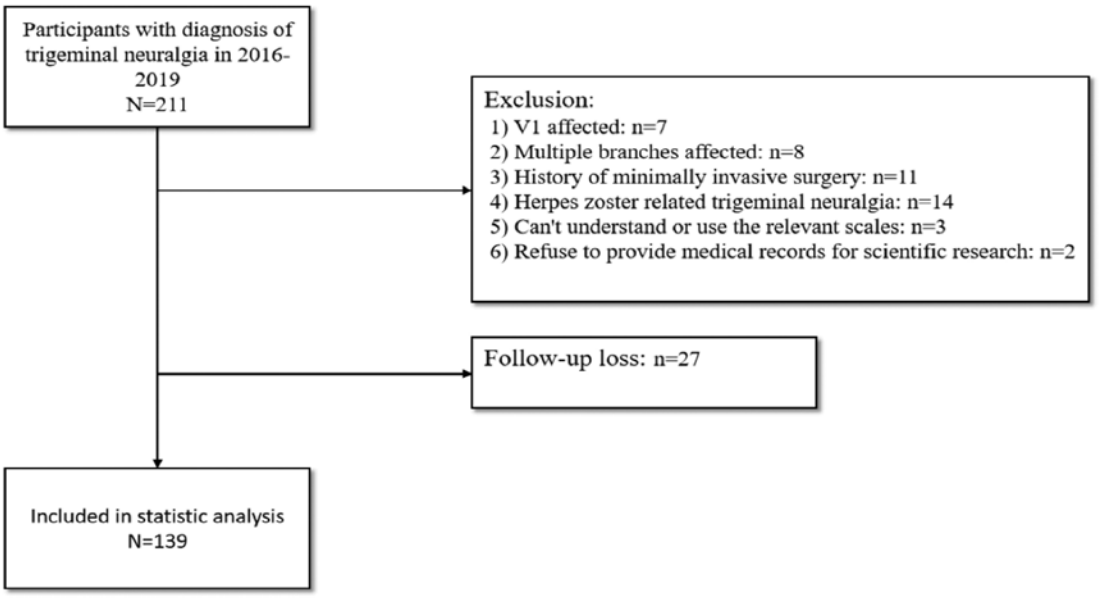

Fig. 1. *Flow chart depicting the patients' inclusion and exclusion.*

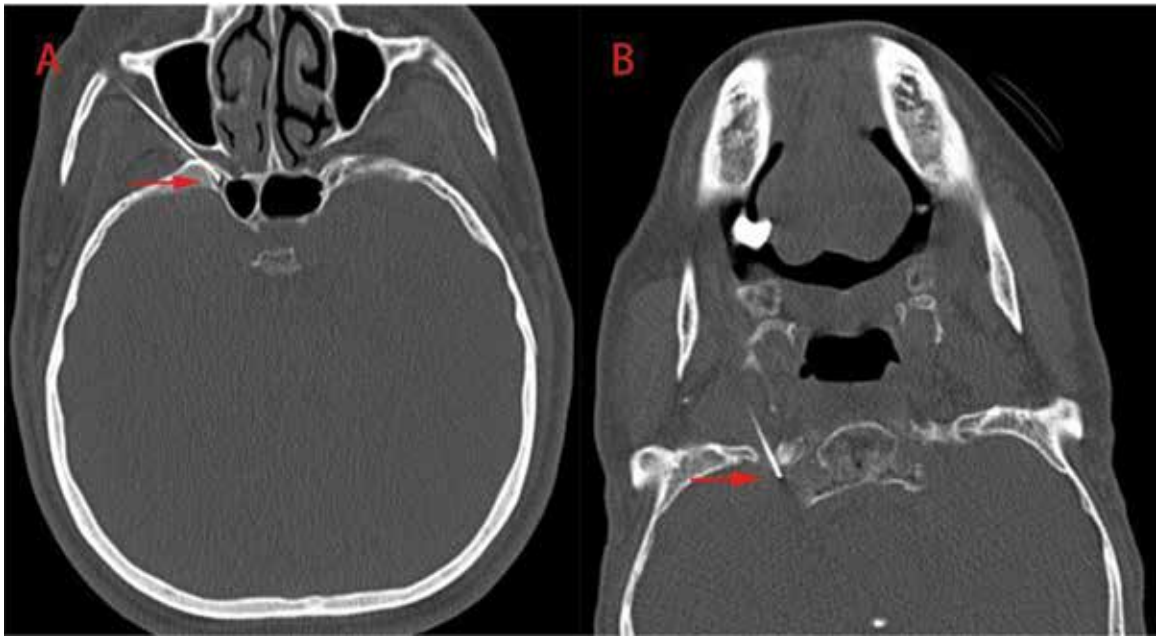

Fig. 2. *The puncture needle was punctured to the foramen (A) or trans-foramen ovale (B). The red arrow indicates the position of the needle tip.*

locally pasted with an aseptic application. After the vital signs were measured again and observed in the treatment room for 20 minutes, if there was no obvious discomfort, the patients returned to the ward.

Surgical Instruments

Some instruments involved in this study following: 1) CT machine, Siemens Somatom Emotion System (Siemens HealthCare, Malvern, PA, United States); 2)

puncture needle (Inomed Health Ltd, Hopwood Lane, Halifax, United Kingdom); and 3) RF machine (Baylis Medical Company Inc., Toronto, Canada).

Outcome Definitions

The primary endpoint was the recurrence rate, and the number and time of occurrence of outcomes during the follow-up period were recorded. Censoring was defined as loss to follow-up or no positive outcome during the follow-up period. NRS-11s were used to assess the intensity of pain caused by TN. The NRS-11s are 0-10 points, 0 points is painless pain, 10 points is severe pain, the higher the score, the more severe the pain degree. Sensation was evaluated by the Barrow Neurological Institute (BNI) numbness grade (I-IV) as follows: I, no numbness; II, mild numbness, causing no impact; III, moderate numbness, somewhat bothersome; and IV, severe numbness, very bothersome (15). The other secondary endpoints included adverse events and patient satisfaction.

Statistical Analysis

Data analysis was partially performed using SPSS software, Version 26.0 (IBM Corporation, Armonk, NY, United States). The Shapiro-Wilk test was used to determine whether the collected data had a normal distribution. Normally distributed data are expressed as the mean ± standard deviation, while nonnormally distributed data are expressed as the median (interquartile range).

A number of studies (2,7) have analyzed the risk factors affecting the postoperative efficacy of TN. On the basis of previous studies, combined with the guidance of experts, we included factors, such as age, gender, duration of disease, affected branch, complications, pain grade, type of pain, and RF temperature (Table 1). Patients with V1 affected were excluded, and then the affected branches were divided into binary variables. To reflect the similarity of the data in the same category as much as possible, the duration of disease was divided into 2 clusters with 10 iterations based on K-means clustering. The type of pain, age, and RF temperature were also regarded as binary variables according to the specific restrictions. Complications refer to at least one of the diseases in patients with hypertension, diabetes, cerebral infarction and so on. The International Headache Society classifies type of TN pain into 2 categories: "typical (type 1)" and "atypical (type 2)". Typical pain causes sporadic pain characterized by severe burning facial pain that lasts up to 2 minutes per episode. Sometimes, episodes of pain may occur in clusters that last for several hours at a time. In contrast, atypical pain presents with a constant, typical burning, and stabbing pain that is less severe than typical pain (2).

The proportional hazard assumption makes a preliminary assessment by calculating the Schoenfeld residual (Suppl. Fig.). The cumulative survival rates of the RF temperature and type of pain were estimated by the Kaplan-Meier analysis and compared with the log-rank test (Fig. 3). Based on significance of 0.20, we drew a simple directed acyclic graph and adjusted the relationship between the included variables for univariate Cox regression. Variables with P values < 0.20 were considered in the multivariate analysis. The risk factors were screened by interval censored multivariate Cox regression analysis, and the corresponding hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. Multivariate analysis was based on the least absolute shrinkage and selection operator (LASSO) regression. We constructed a penalty function to shrink the regression coefficient to achieve variable screening and built an optimal model through cross-validation. Due to the small regression coefficient shrunk by the screening procedure, we adjusted the HR and 95% CI after refitting the model, calculated the linear predictors and predicted probability, and used a histogram to describe the distribution (Suppl. Figs. 2 and 3. The model diagnosis was based on the analysis of multicollinearity and influential cases. The multicollinearity diagnosis between independent variables was evaluated by the variance inflation factor (VIF). If the VIF of each variable was < 5, it showed that there was no multicollinearity. A time-independent receiver operating characteristic (ROC) curve was drawn, and the C-index was calculated to evaluate the model discrimination; the calibration curve was performed to test the consistency between the predicted probability and the observed probability, the Brier score was obtained by $(Y\text{-}p)^2$, and the calibration of the model was evaluated quantitatively. The regression coefficients of the Cox regression model were transformed into scores and plotted as a nomogram.

The NRS-11s and BNI score of each time interval were tested by repeated- measures analysis of variance (ANOVA). Pairwise comparisons were performed with Bonferroni's test, and the significance was adjusted.

R Packages

Rstudio software (version: 1.4.1106, Boston, MA) was mainly used to perform the data visualization and analy-

sis. Descriptions of cumulative hazards, survival probability, and ROC curves were based on the packages survminer_0.4.9, survival_3.2-12, and tidyverse_1.3.1, respectively. Nomograms and violin plots were generated by the addition of VRPM_1.2, rms_6.2-0, and ggpubr_0.4.0. After downloading stdca.R from www.mskcc.org/sites/default/files/node/4509/documents/decisioncurveanalysis.zip, the source function was loaded in Rstudio to complete the drawing of the decision curve. Besides, rms_6.2-0 and survival_3.2-12 were used to complete the calibration curve, and the analysis of influential cases and proportionality was mainly based on survminer_0.4.9. A line segment dynamic nomogram was created with regplot_1.1.

Results

Baseline Characteristics

Based on the inclusion and exclusion criteria, 211 patients diagnosed with idiopathic TN in 2016-2019 were included. There were 7 cases of V1 affected and 8 cases of multibranch involvement, 11 cases had a history of minimally invasive surgery, 14 cases were herpes zoster-related TN, 3 cases had inability to understand or use relevant scales, 2 patients refused to provide medical records for scientific researchers, 27 cases were lost to follow-up, and 139 patients were finally included in the data analysis. The baseline characteristics of all of the included patients are shown in Table 2.

Interval-Censored Multiple Cox Regression

Of the 139 patients, 61 recurred during the follow-

Table 1. *Risk factors associated with relapse after RFT.*

Independent Variables	Crude HR [95% CI]	Adjusted HR [95% CI]
Age, y		
< 60	1.067 [0.622-1.831]	1.368 [0.778-2.405]
≥ 60		
Gender		
Women	1.070 [0.648-1.768]	0.932 [0.547-1.587]
Men		
Complications		
No	1.229 [0.737-2.048]	0.959 [0.553-1.663]
Yes		
Duration of Disease, y		
Cluster-1	1.320 [0.716-2.433]	0.966 [0.488-1.912]
Cluster-2		
Branch		
V2	0.948 [0.576-1.560]	0.937 [0.560-1.565]
V3		
Pain Grade	1.753 [1.251-2.457]	1.670 [1.171-2.382]
Type of Pain		
Typical	5.740 [3.125-10.543]	6.057 [3.175-11.553]
Atypical		
Temperature, °C		
85	0.484 [0.267-0.879]	0.506 [0.273-0.938]
95		

Duration: This variable was divided into cluster-1 and cluster-2 based on K-means clustering; Branch: V2-maxillary nerve, V3-mandibular nerve.

Abbreviatons: RFT, radiofrequency thermocoagulation; HR, hazard ratio; CI, confidence interval; y, year.

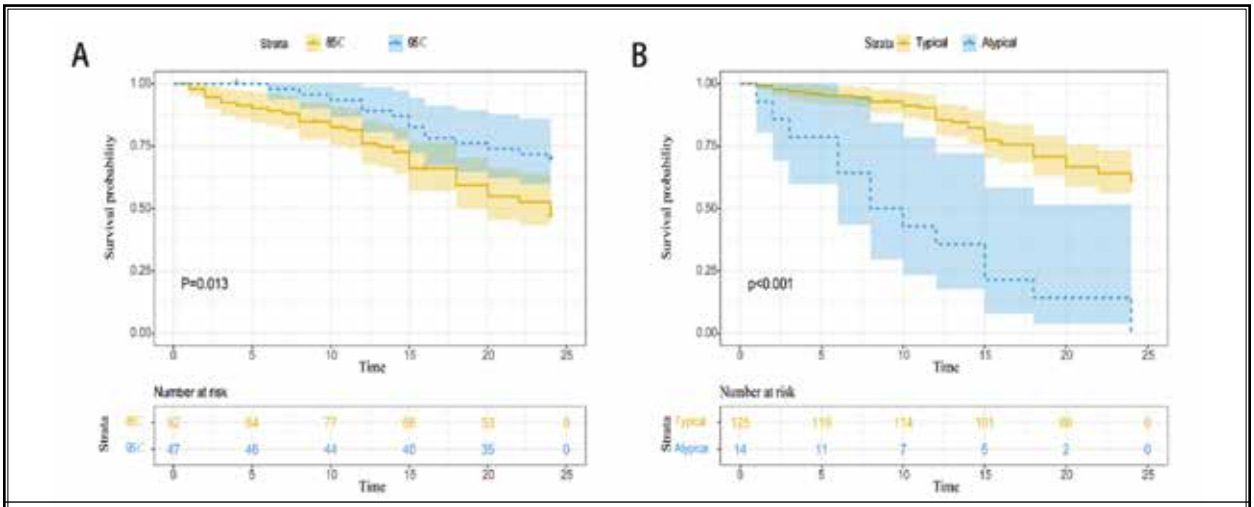

Fig. 3. *Kaplan-Meier analysis was performed to calculate the cumulative survival rates of temperature (A) and type of pain (B) (log-rank test).*

Table 2. *Baseline characteristics of patients with total cohort.*

Variables	Total cohort (n=139)
Age, n (%)	
< 60	42
≥ 60	97
Gender, n (%)	
Women	81
Men	58
Height, Mean ± SD, cm	161.13 ± 7.59
Weight, Median (IQR), kg	60 (53.00-69.00)
BMI, Mean ± SD, kg/m²	23.37 (21.36-25.33)
Complications, n (%)	
No	58
Yes	81
ASA, n (%)	
II	124
III	15
Side, n (%)	
Left	58
Right	81
Hospital Stay, Median (IQR), d	4 (3.00-6.00)
Branch, n (%)	
V2	69
V3	70
Type of pain, n (%)	
Typical	125
Atypical	14
Temperature, n (%)	
85°C	92
95°C	47
Pain Grade, Median (IQR)	6.00 (6.00-7.00)
Duration of Disease, Median (IQR), y	3.00 (1.00-7.00)

Abbreviations: n, number; SD, standard deviation; IQR, interquartile; BMI, body mass index; ASA, American Society of Anesthesiologists; d, day; y, year.

up period, including 47 in the 85°C group (51.09%) and 14 in the 95°C group (29.79%). The results of Kaplan-Meier and cumulative hazards results are shown in Figs. 3 and 4, respectively. Compared with the 85°C group, RFT at 95°C could significantly reduce the risk of recurrence within 2 years ($P < 0.05$, log-rank test). Compared with type 1 TN (preponderance of shock-like pain), type 2 TN (preponderance of constant pain) significantly increased the risk of recurrence ($P < 0.05$). Table 1 shows the HRs and 95% CIs after univariate analysis of related variables and adjustment and control of confounding factors in SPSS. After using Cox regression to shrink the regression coefficient, 3 predictors were selected: pain grade (original HR: 1.1048; refit HR [95% CI]: 1.6807 [1.1963-2.3613]), type of pain (original HR: 3.1789; refit HR [95% CI]: 6.2802 [3.3705-11.7021]), and temperature (original HR: 0.9533; refit HR [95% CI]: 0.5203 [0.2859-0.9468]). Figure 5 shows that, with the increase in penalty coefficient, the regression coefficient continues to shrink, the number of variables in the model decreases gradually, and cross-validation was used to find the optimal model (Fig. 6). In the process of model diagnosis, the distribution of influential cases (Suppl. Fig. 4) was further analyzed. In the results of the study, the overall evaluation of the model was performed from 3 aspects. The C-indices at 6, 12, 18, and 24 months of the model were 0.787, 0.705, 0.672, and 0.689, respectively. Figure 7 shows time-independent ROC curve analysis and areas under the curves. The results of the calibration curve (Fig. 8) indicate that the model overestimated the risk of recurrence to some extent when the observed probability was < 90%, but when the observed probability was > 90%, the model underestimated the risk, and the Brier score was approximately 0.14. Finally, Suppl. Fig. 5 shows that the net return of threshold probability was higher in a certain range. On the basis of multivariate analysis, according to the contribution of each factor to the outcome in the model, each level of factor was assigned a score, and the risk of recurrence was predicted according to the total score. Figures 9 and 10 show 2 types of nomograms drawn based on LASSO regression. One is a line segment dynamic nomograph (Fig. 10), assuming that pain grade was 8, the frequency temperature was 85°C, and the pain type was type 1 TN, with a total score of 0.851; then, the predicted probability of recurrence within 2 years was 74.1%.

Repeated Measures ANOVA for the NRS-11s and BNI Scores

The results of Mauchly's test of sphericity suggested that $P < 0.05$, and Greenhouse-Geisser was used to correct the significance. After pairwise comparison of the NRS-11s of each time interval, the results showed that the difference between T0 and other time intervals was statistically significant ($P < 0.05$), and there were significant differences of T4, T5, and T6 with other time intervals ($P < 0.05$). The results of the BNI score analysis showed that there was no significant difference between T5 and T6, but the multiple comparisons of other time intervals were statistically significant ($P <$

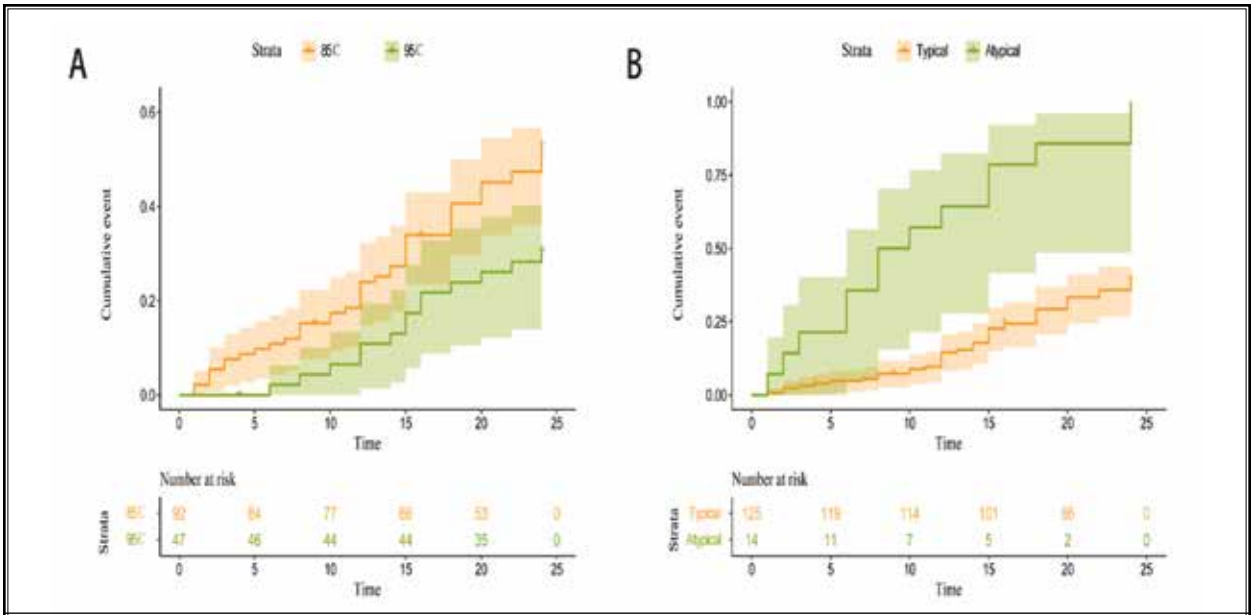

Fig. 4. *Cumulative hazards with temperature (A) and type of pain (B) within 24 months.*

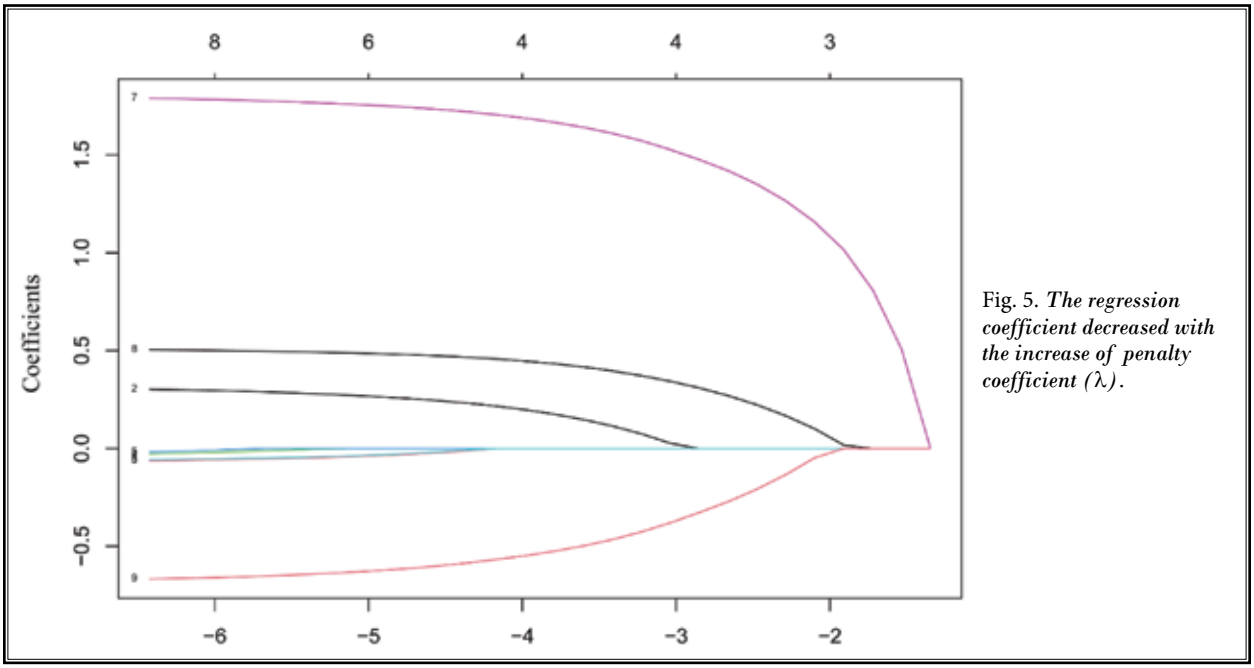

Fig. 5. *The regression coefficient decreased with the increase of penalty coefficient (λ).*

0.05). Figure 11 describes the changes in the BNI score and NRS-11s at each time interval.

Secondary Outcomes

Numbness is a common and persistent complication after RFT. Nine patients had BNI scores of 3 or more, and the other patients showed mild numbness 2 years after the operation. In addition, a total of 6 patients had autonomic nerve symptoms (such as nasal congestion and tears), and one of them had the above 1-2 symptoms during pain attacks. However, there were approximately 15 cases of obvious salivation and masticatory muscle dysfunction after RFT, and there were no other adverse events, such as hematoma, after the

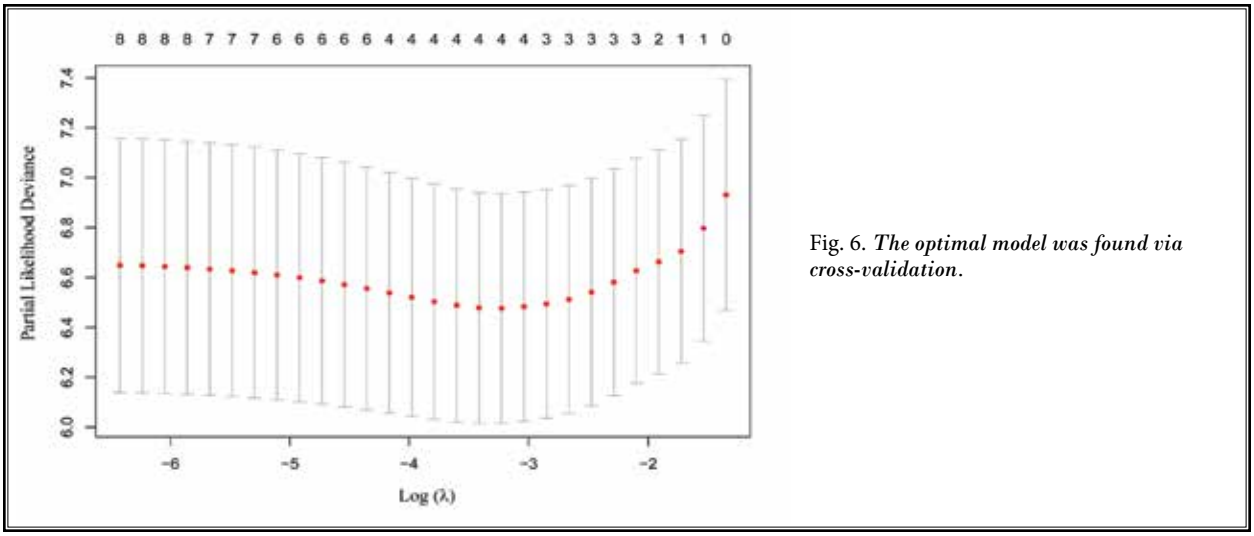

Fig. 6. *The optimal model was found via cross-validation.*

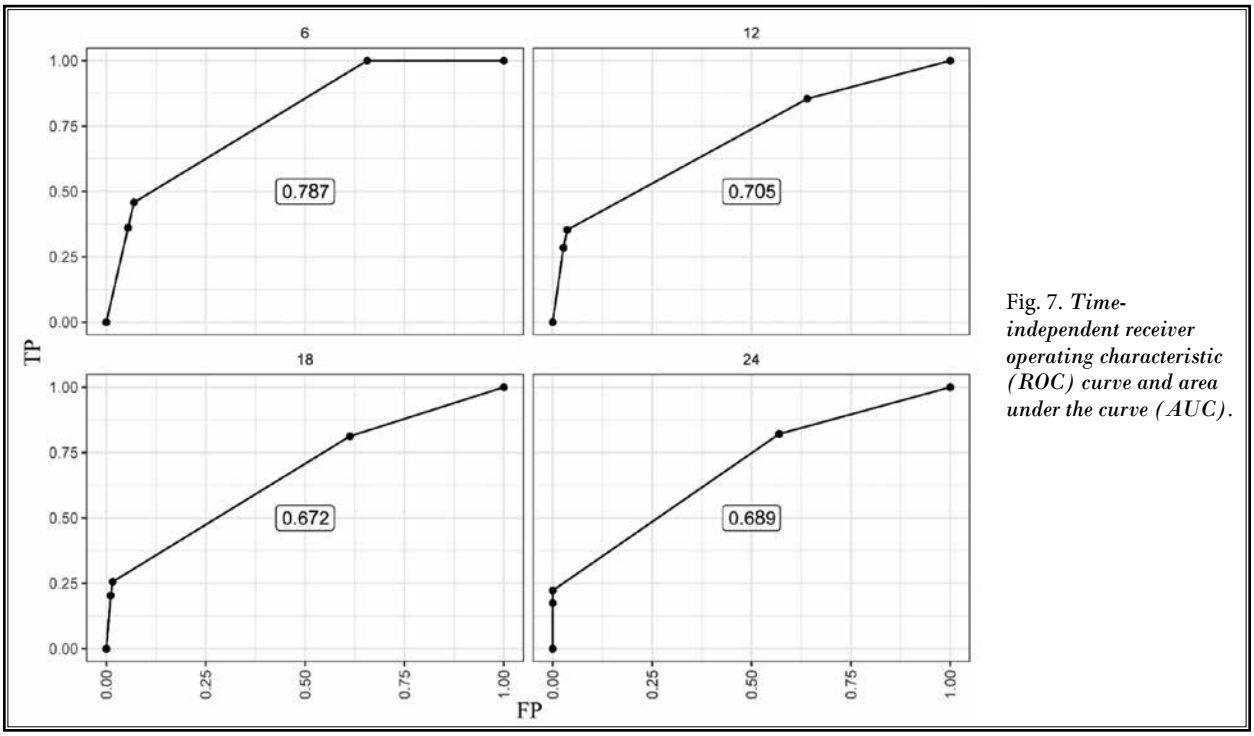

Fig. 7. *Time-independent receiver operating characteristic (ROC) curve and area under the curve (AUC).*

operations. The overall satisfaction of patients 2 years after the operation was 7.83 ± 1.93.

Discussion

The trigeminal nerve is the largest cranial nerve and is responsible for sensation in the face and certain motor functions, such as biting and chewing. It consists of 3 branches: the V1, the maxillary nerve (V2), and the mandibular nerve (V3) (16). Classic TN is a sudden, transient, and stereotyped attack of usually intense, sharp, or stabbing pain in the distribution of one or more branches of the trigeminal nerve (2). TN can be divided into 3 types: classical, idiopathic, or secondary. The cause of idiopathic TN is unknown. Compared with patients with typical TN, idiopathic TN patients are more likely to be women, and the onset age is younger (17,18,21). Such debilitating neuropathic pain conditions will affect basic human psychological devel-

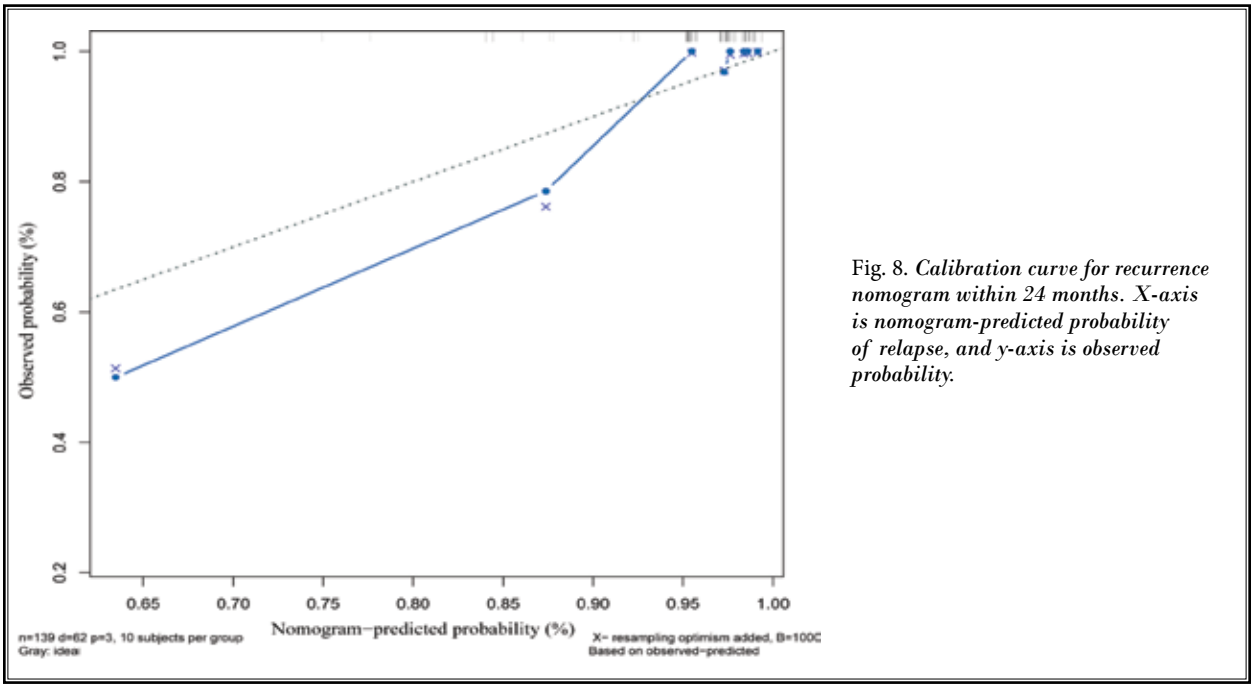

Fig. 8. *Calibration curve for recurrence nomogram within 24 months. X-axis is nomogram-predicted probability of relapse, and y-axis is observed probability.*

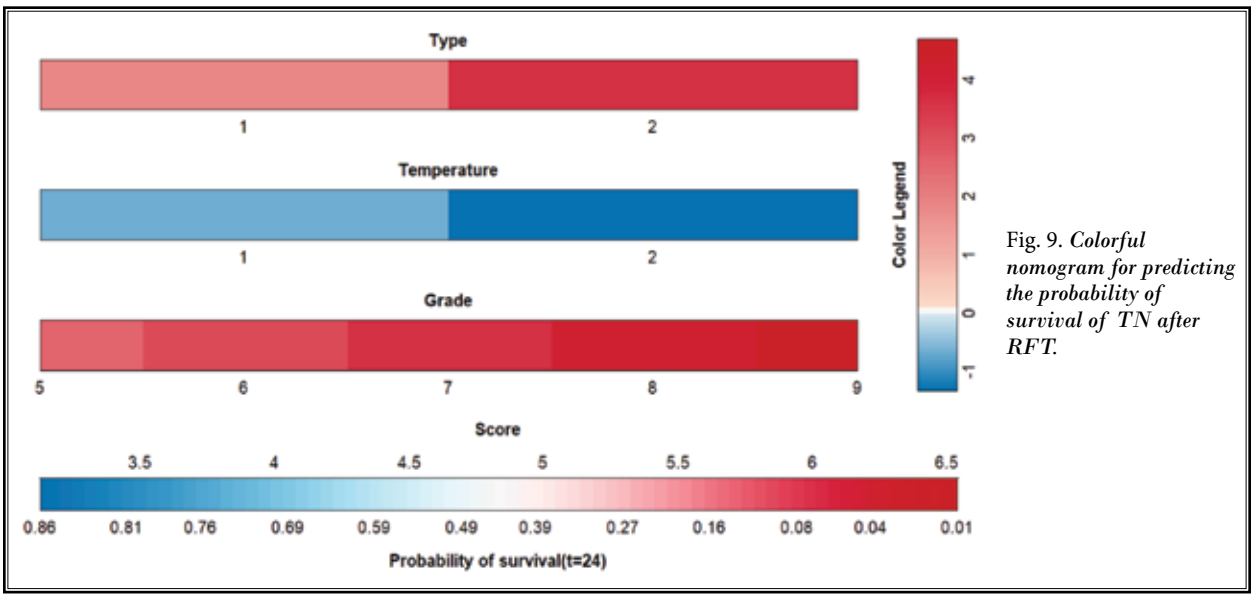

Fig. 9. *Colorful nomogram for predicting the probability of survival of TN after RFT.*

opment, physical health, and activities, such as talking and eating (2). It is not difficult to diagnose TN with typical clinical manifestations, but it must be distinguished from other diseases, such as migraine, postherpetic neuralgia, and glossopharyngeal neuralgia (1). Currently, the understanding of idiopathic TN remains insufficient, but some studies have pointed out that TN might be related to ion channel functional variation, neural inflammation, and nonmultiple sclerosis lesions (19-21). The decrease in the nociceptive stimulation threshold encoded by Aδ and C fibers can cause local sensory abnormalities (1,29). In-depth understanding of etiology and pathophysiology could bring new therapeutic targets and provide individualized treatment for TN (22). Carbamazepine achieves a therapeutic effect by blocking sodium channels to stabilize the cell membrane. Although they are widely used in the clinic, drugs when used for a long time can cause many side

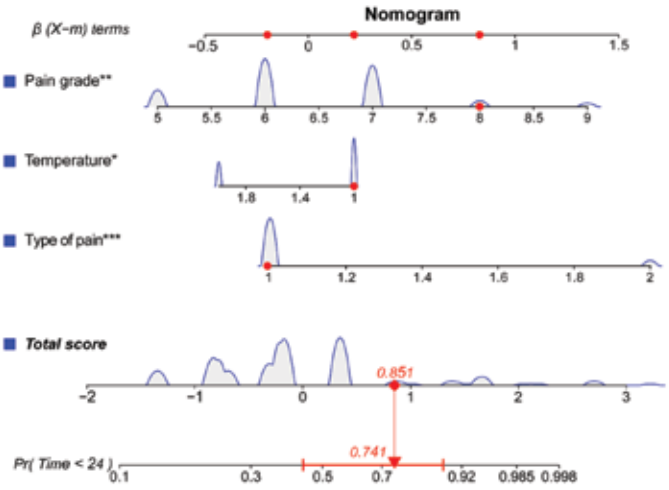

Fig. 10. *Line segment dynamic nomograph. Pain grade, temperature, and type of pain were the 3 selected predictors. When the pain grade was 8, the temperature was 85°C, and with type 2 TN, the total score was 0.851, the predicted probability of recurrence within 2 years was 0.741.*

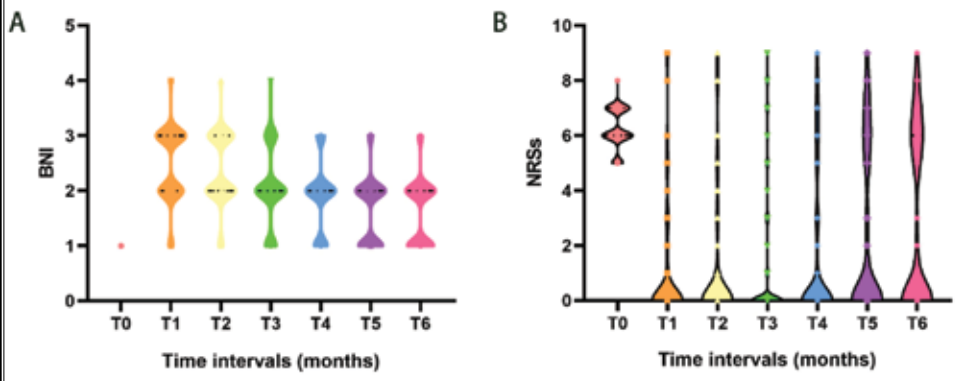

Fig. 11. *Distribution of Numeric Rating Scale scores (NRSs) (A) and Barrow Neurological Institute (BNI) score (B) {AU: "[Distribution of NRSs (A) and BNI score (B)]"?} for each time interval during 24 months.* T0: before operation; T1: 3 months after operation; T2: 6 months after operation; T3: 9 months after operation; T4: 12 months after operation; T5: 18 months after operation; T6: 24 months after operation.

effects (1,23), constituting a common reason for stopping the taking of medicine.

CT-guided percutaneous selective RFT of TN is a highly selective neuromodulation technique. The safety and effectiveness of its clinical application have been confirmed in many studies (24,25). Although the short-term effect after surgery is relatively accurate, the high long-term recurrence rate remains concerning.

In this study, 139 patients who underwent selective RFT of the trigeminal nerve were analyzed in an attempt to construct a highly stable clinical prognosis model to screen for risk factors affecting the postoperative recurrence rate to predict the probability of recurrence and to screen the high-risk group and guide clinical treatment (Table 1).

Multivariate Cox regression analysis was based on the LASSO method. By regulating the penalty coefficient and shrinking the regression coefficient to screen predictors, we screened out 3 variables: temperature, type of pain, and pain grade. The temperature parameter was a factor to which we paid close attention. In a study (16) involving 15 patients with V2 affected, it was found that selective RFT of the trigeminal nerve at 85°C resulted in no recurrence within one year after the operation. However, we believe that the conclusion based on a small sample size and short follow-up time might not be accurate. Zheng et al (13) found that, of the 1,481 patients who underwent RF, approximately 35.18% relapsed during long-term follow-up in a multicenter, retrospective study, and all of the patients received RF temperatures < 80°C in this study. We could not directly attribute the high recurrence rate to the

insufficient RF temperature, but to a certain extent, increasing the RF temperature can accelerate the destruction of the target nerve and reduce the time of pain during thermocoagulation. In addition, the higher that the temperature of the bare segment of the RF needle is, the larger that the range of damage caused by the settled RF time and cycle is, ensuring the thoroughness of the target nerve damage.

The results of multivariate analysis suggested that higher RF temperature was a protective factor against relapse (refit HR [95% CI]: 0.5203 [0.2859-0.9468]), also supporting our conjecture. In addition, the researchers did not find that patients in the 95°C group had more serious postoperative complications. However, under the premise that the diameter of the puncture needle and the length of the bare segment were fixed, how increasing the RF temperature will affect the damage range could be an interesting question. We hope to achieve the goal of target nerve destruction as soon as possible, while reducing damage to surrounding tissue as much as possible.

Subtypes of TN are based on the preponderance of shock-like or constant pain (26). Miller et al (27) pointed out that patients with type 1 symptoms were more likely to have their pain relieved and were less likely to relapse after surgery. In this study, the results of LASSO regression supported the above point of view (type of pain, refit HR [95% CI]: 6.2802 [3.3705-11.7021]). After adjusting for the regression coefficient, the recurrence rate of patients with type 2 symptoms was 5.28 times higher than that of patients with type 1 symptoms. These authors also reported that type 2 TNs were considered to be a worse stage of TN development, and in their study, most patients with type 2 symptoms worked well after microvascular decompression (MVD), and these patients had significantly longer symptoms before treatment.

We performed cluster analysis of the duration of disease and produced 2 cluster centers, which ensured the similarity of the dataset in the group, but there was no significant difference in the course of disease between the 2 groups (the proportion of type 1 TN: type 2 TN in the long duration group = 15.2%:21.4%). Our results suggested that the duration of disease might not be the main cause of type 2 TN. Watson (28) pointed out that the subtype of TN has nothing to do with the duration of disease. Obermann et al (29) used the nociceptive blink reflex and pain-related evoked potentials to detect damage to nociceptive fibers and observed central facilitation of trigeminal nociceptive processing in type 2 TN, indicating overactivation of central sensory transmission. There was a definite mechanism of central sensitization in type 2 TNs, and selective RFT of the trigeminal nerve might not block central facilitation. It is worth mentioning that the conclusions drawn from the lack of sufficient samples might have overestimated the probability to some extent, so the exploration and understanding of type 2 TNs are expected to be supported by more research evidence.

In addition, pain grade seemed to be correlated with recurrence (refit HR [95% CI]: 1.6807 [1.1963-2.3613]), but the overall contribution to the model was not significant. It was not clear whether central sensitization was involved in the deterioration of pain, but we suspect that there might be an association between these factors.

In addition, a retrospective study (30) based on a cohort of 92 patients indicated that the presence of autonomic symptoms in the TN correlated with a worse prognosis for pain relief after MVD. However, only 6 patients with autonomic symptoms were observed in this study, so the statistical analysis based on this sample was meaningless. On the whole, NRS-11s tend to decrease at first and then increase, and with the extension of follow-up time, the numbness of most patients will gradually decrease. In addition, obvious salivation or masticatory muscle dysfunction caused by damaged motor fibers after RF surgery of the V3 branch can be expected. Thus, patients must be informed of the relevant complications before the operation to ensure that they are fully aware of them. There were no other complications caused by puncture in this study.

Limitations

Considering that internal validation after random splitting will reduce the sample size, we will perform external validation in subsequent studies to further increase the credibility of the model. In addition, the results of multicenter, randomized, controlled trials could increase the persuasiveness of the conclusions.

Conclusions

In this study, a novel model was established to predict the recurrence rate after CT-guided selective RFT of the trigeminal nerve. Temperature, type of pain, and pain grade were selected after shrinking the regression coefficients. The high predictive accuracy and survival stratification performance of the multiparametric nomogram demonstrated great potential for screening high-risk groups and evaluating the risk of recurrence rate.

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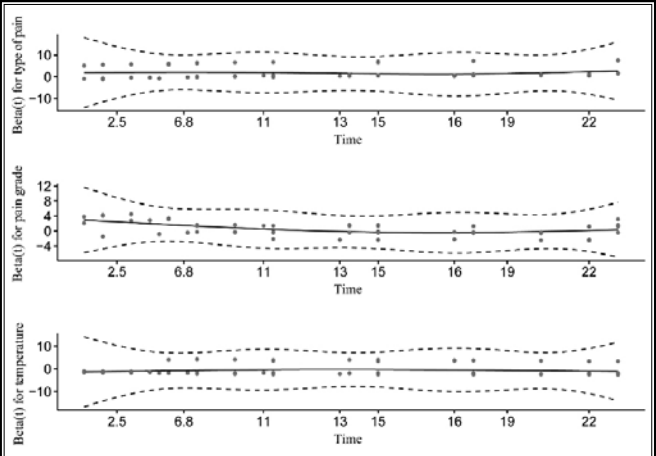
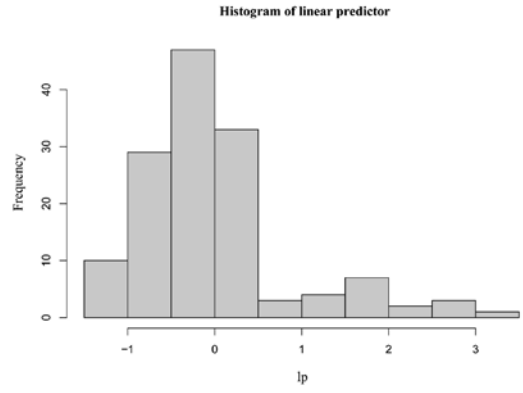
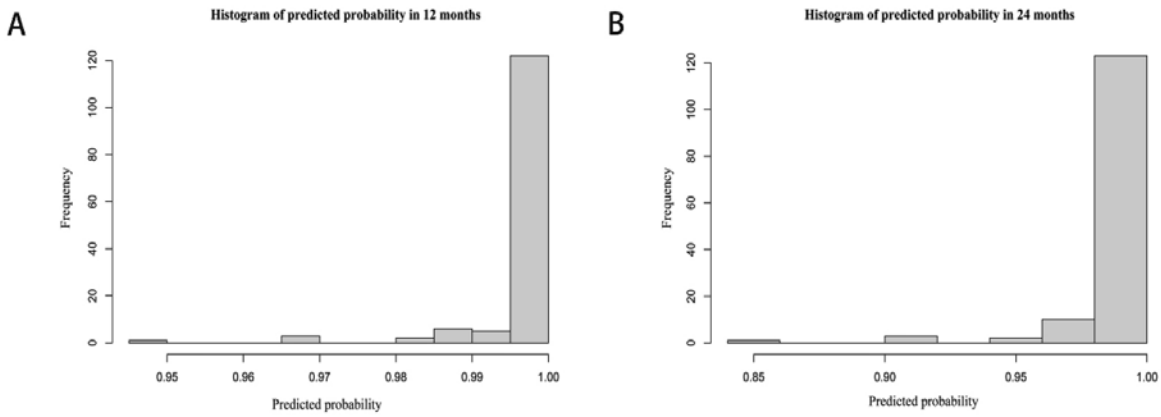


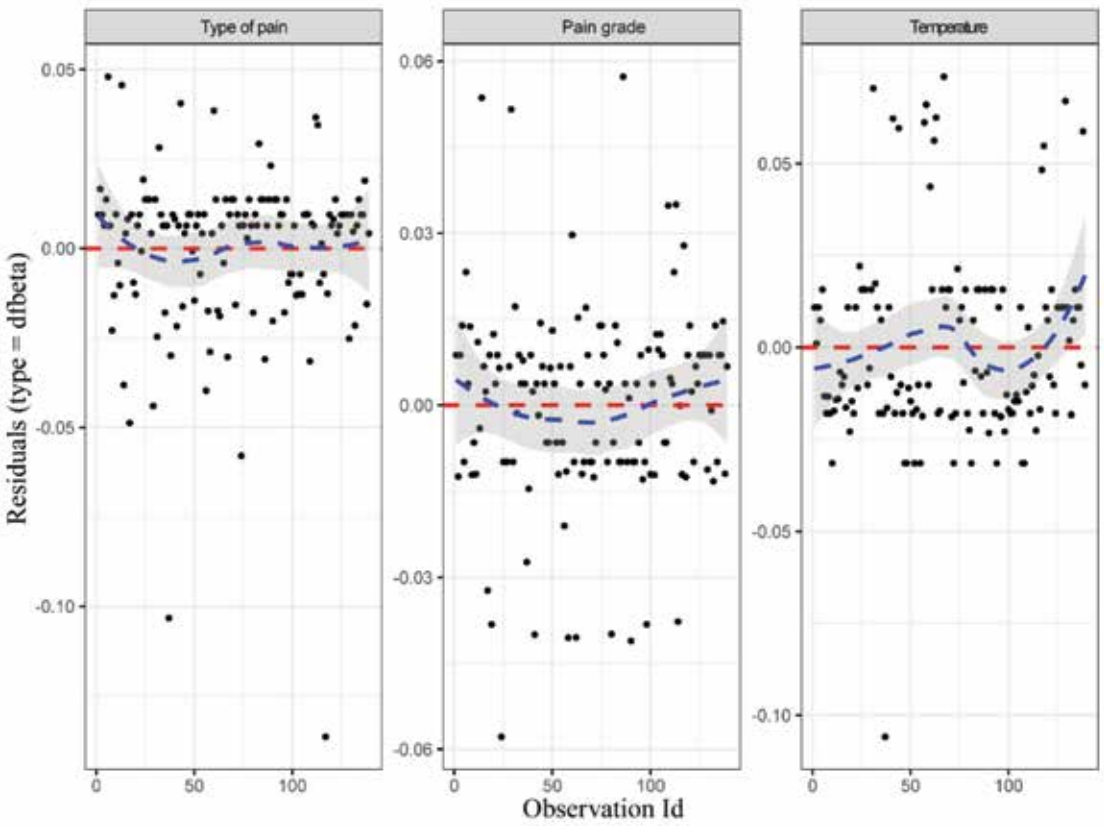
Suppl. Fig 1. *Schoenfeld residual with 3 predictors*.



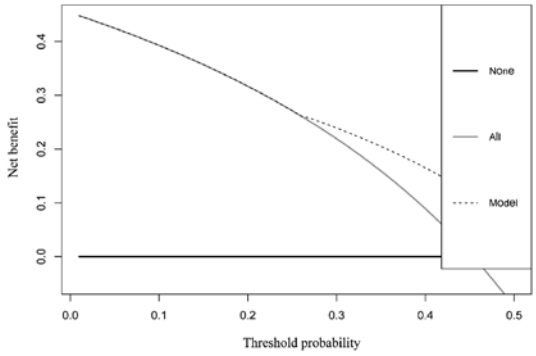
Suppl. Fig 2. *Linear predictors performed by histogram*.



Suppl. Fig 3. *Predicted probability performed by histogram in 12 and 24 months*.



Suppl. Fig 4. *Distribution of influential cases in 3 predictors.*



Suppl. Fig 5. *Decision curve analysis of 24 months recurrence risk prediction model for patients underwent radiofrequency thermocoagulation of trigeminal neuralgia.*