Retrospective Study

Risk Factors for Recurrence After Radiofrequency Surgery of the V2 Branch of the Trigeminal Nerve

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Background: The factors influencing relapse after radiofrequency operation of the V2 branch of the trigeminal neuralgia are yet to be identified.

Objectives: The risk factors affecting recurrence after radiofrequency operation of the V2 branch of the trigeminal neuralgia were analyzed, and a curative effect prediction model was constructed.

Study Design: A retrospective study.

Setting: This study was conducted at the Affiliated Hospital of Jiaxing University, People's Republic of China.

Methods: The records of patients with maxillary nerve pain in the V2 branch of the trigeminal nerve who underwent computed tomography-guided foramen rotundum radiofrequency treatment at the Pain Department of the Affiliated Hospital of Jiaxing College from April 2014 through December 2020 were collected and randomly divided into training (n = 137) and test (n = 59) groups at a 7:3 ratio. The outcome variable was whether or not recurrence was observed 2 years postsurgery. Independent predictors were screened by LASSO (least absolute shrinkage and selection operator) regression analysis. Based on these findings, a nomogram prediction model was explored further and developed using multifactor logistic regression analysis. Also, the feasibility of the nomogram prediction model for recurrence after radiofrequency was assessed using a validation group. Finally, the discriminatory power, accuracy, and clinical utility of the prediction model were evaluated using the receiver operating characteristic (ROC), area under the curve (AUC), calibration curve, and decision curve analysis (DCA), respectively.

Results: LASSO regression, combined with multifactorial logistic regression analysis, identified factors such as age, duration, branches, and numbness that influence V2 trigeminal nerve pain recurrence in patients 2 years post-radiofrequency surgery ($P < 0.05$). The above variables were used to construct the nomogram prediction models. The AUC of the nomogram prediction model predicted that the recurrence post V2 radiofrequency was 0.726 in the training group and 0.611 in the test group. The DCA showed that the columnar plot prediction model predicted the risk of recurrence post-radiofrequency of the V2 branch of the trigeminal nerve had a threshold probability of 0 – 0.9.

Limitations: This was a single-center study.

Conclusion: A highly accurate nomogram prediction model (predictor variables include age, duration, branches, and numbness) was developed to improve the early identification and screening of patients at high risk of recurrence after V2 trigeminal nerve radiofrequency surgery.

Key words: Trigeminal neuralgia, maxillary neuralgia, radiofrequency, risk factors, prediction model

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Trigeminal neuralgia is a painful facial disorder affecting the trigeminal nerve. It is described as a sudden, intense jarring that can last from a few seconds to a few minutes (1). Although it is a rare condition, trigeminal neuralgia significantly affects quality of life (2). Specifically, the V2 branch of the trigeminal nerve is one of the most commonly affected branches in trigeminal neuralgia. However, traditional radiofrequency (RF) treatment of the trigeminal ganglion results in low success rates and numerous complications due to its nonselective nature (3).

Recent studies have aimed to improve the understanding and treatment of trigeminal neuralgia. One promising approach is computed tomography (CT)-guided foramen rotundum RF for highly selective dissection of the maxillary nerve of the V2 branch, resulting in a stable surgical outcome and no damage to other adjacent nerves (4). The CT-guided foramen rotundum RF has been shown to be a safe and effective surgical option for the treatment of pain in the V2 branch of the trigeminal nerve (5).

The procedure involves applying RF energy to the upper nerve of the foramen rotundum exiting the trigeminal nerve to destroy the nerve fibers responsible for transmitting pain signals (6). This minimally invasive procedure can provide long-term pain relief for patients with trigeminal neuralgia. However, a proportion of patients who undergo RF ablation of the V2 branch experience a recurrence of pain within 2 years of the procedure (7). Therefore, predicting the risk of recurrence is crucial to optimize treatment outcomes and provide an accurate prognosis for patients.

A nomogram is a statistical model that predicts the likelihood of a specific outcome based on a set of predictor variables. In our study, we aimed to develop a nomogram to predict trigeminal neuralgia's recurrence risk after RF ablation of the V2 branch. The data collected from a large cohort of patients who underwent this procedure were used to develop a nomogram that could accurately predict the risk of recurrence. Thus, we hoped to provide clinicians with a valuable tool for predicting the likelihood of recurrence and for guiding patient management decisions. The current results are valuable for the management of trigeminal neuralgia and contribute to the ongoing efforts to improve the understanding and treatment of this debilitating condition.

Methods

The inpatient data of patients with maxillary nerve pain of the V2 branch of the trigeminal nerve who underwent CT-guided foramen rotundum RF treatment in the Pain Department of the Affiliated Hospital of Jiaxing University from April 2014 through December 2020 were collected retrospectively. This study was approved by the Ethics Committee of the Affiliated Hospital of Jiaxing University (LS2021KY357). All patients first received regular conservative medical treatment with poor results. They voluntarily underwent RF treatment, and signed an informed consent form. The inclusion criteria were as follows: a diagnosis of trigeminal neuralgia with maxillary branch pain (8) and successful foramen rotundum RF surgery. The exclusion criteria were incomplete information, patient unavailability, and patient unwillingness to cooperate with follow-up.

Surgical Procedures

Each patient was admitted to the CT operating room, fitted with a nasal cannula for oxygen, and intravenous access obtained. Heart rate, blood pressure, and peripheral oxygen saturation were monitored. The patient was placed supine on the CT table with a pillow under the shoulder and the head was tilted back to approximately 20°.

The optimal puncture route was identified based on the CT scan, and the puncture site was marked on the affected side. After disinfection and towel spreading, the puncture site was locally anesthetized with 2% lidocaine (1 mL) and 0.05 mg (50 μg) fentanyl by intravenous injection, and an 18G RF needle with a 5 mm working end was inserted into the foramen rotundum under CT guidance (Fig. 1). After electrical impedance testing at 250–500 Ω, a sensorimotor test was conducted using a high-frequency (50 Hz, 500 μs) and a low-frequency current (2 Hz, 1,000 μs) for motor testing, with the needle tip position adjusted to within 0.5 mA. The parameters were as follows: temperature 95°C for 180 seconds, intravenous propofol one-2 mg/kg, followed by RF coagulation (5). The patient was observed for 20 minutes after regaining consciousness; if he had no complaints, he was returned to the ward.

Data Collection

The following parameters were collected by telephone follow-up: Numeric Rating Scale (NRS-11) 2 years postoperatively, numbness (whether numbness was still present) at 3 months postoperatively, gender, age, body mass index (BMI [kg/m^2]), history (invasive treatment received preoperatively, including microvascular decompression [MVD], percutaneous balloon compres-

sion [PBC], RF, and nerve block), complications (including conditions requiring long-term medication, such as hypertension and diabetes mellitus), sides (left or right), duration (duration of disease), branches (single and multiple branches), and NRS-11 (preoperative). The outcome indicator was recurrence: (preoperative NRS-11–postoperative NRS-11)/preoperative NRS < 50% (9).

Statistical Analysis

R 4.1.3 software (The R Foundation) was used for statistical analysis. The Kolmogorov–Smirnov normality test was used for continuous variables, mean ± standard deviation for normally distributed measures, t test for comparison between 2 groups, median (interquartile range) for nonnormally distributed data, and the rank-sum test for comparison between groups. The χ^2 test was used for analyzing enumeration data.

Following rigorous data filtering and preprocessing, eligible patients (n = 196) were randomized in a 7:3 ratio in the training (n = 137) and test (n = 59) groups. The independent predictors were screened using the least absolute shrinkage and selection operator method (LASSO regression) (10,11). Whether recurrence occurred at 2 years postsurgery was the outcome variable in the training group data; based on this phenomenon, the prediction model was further explored using multifactorial logistic regression analysis, and a nomogram prediction model was established.

The receiver operating characteristic (ROC) and area under the curve (AUC) were used to verify the predictive power of the predictive model. The Hosmer–Lemeshow test was used to determine the goodness-of-fit of the model and plot the calibration curve (12), while decision curve analysis (DCA) (13) was used to predict the 2-year postoperative risk of recurrence for trigeminal nerve V2 branch maxillary neuralgia foramen rotundum RF. $P < 0.05$ was considered statistically significant.

Results

Patients' Characteristics

Two years post-RF surgery, of the 196 patients with trigeminal branch V2 pain, 143 had no recurrence, while 53 had a recurrence. The differences in gender, BMI, medical history, complications, side effects, and NRS-11 between the no recurrence and recurrence groups were not statistically significant ($P > 0.05$). The differences in age, duration, branches, and numbness between the no recurrence and recurrence groups were statistically significant ($P < 0.05$) (Table 1).

Fig. 1. *An 18G radiofrequency needle was used to puncture into the foramen rotundum under CT guidance.*

All patients (n = 196) were randomly divided into the training group (n = 137) and the test group (n = 59) in a 7:3 ratio. There were no significant differences in the baseline characteristics between the 2 groups (all $P > 0.05$; Table 2).

Risk Factors for Recurrence

Recurrence at 2 years post-RF surgery in patients with trigeminal nerve V2 pain in the training group (assignment: yes = 1, no = 0) was used as the dependent variable, while gender (assignment: men = 1, women = 0), age (assignment: ≥ 65 years = 1, < 65 years = 0), BMI (assignment: ≥ 25 = 1, < 25 = 0), history (assignment: yes = 1, no = 0), complications (assignment: yes = 1, no = 0), sides (assignment: right = 1, left = 0), duration (years), branches (assignment: multiple = 1, single = 0), NRS-11 (assignment: ≥ 7 = 1, < 7 = 0), numbness (assignment: yes = 1, no = 0) were independent variables for LASSO regression analysis (Fig. 2), with the variation of the penalty coefficient λ.

The variables included in the model were declined gradually. Finally, the 10-fold cross-validation error was selected as the minimum λ+1 (1SE = 0.050 for the minimum value of λ), which was the optimal value of the model (Fig. 3), i.e., the filtered predictor variables included age, duration, branches, and numbness. The filtered predictor variables were included in a multifactor logistic regression analysis; the results showed that age, duration, branches, and numbness were the

Table 1. *Comparison of general information between the no recurrence and recurrence patients.*

Variables	Total (n = 196)	No recurrence (n = 143)	Recurrence (n = 53)	*P*	Statistic
Gender, n (%)				0.709	0.139
women	117 (60)	87 (61)	30 (57)		
men	79 (40)	56 (39)	23 (43)		
Age(year), n (%)				0.034	4.498
< 65	89 (45)	72 (50)	17 (32)		
≥65	107 (55)	71 (50)	36 (68)		
BMI, n (%)				1	0
< 25	148 (76)	108 (76)	40 (75)		
≥25	48 (24)	35 (24)	13 (25)		
History, n (%)				0.373	0.792
no	19 (10)	16 (11)	3 (6)		
yes	177 (90)	127 (89)	50 (94)		
Complications, n (%)				0.63	0.232
no	85 (43)	64 (45)	21 (40)		
yes	111 (57)	79 (55)	32 (60)		
Sides, n (%)				0.278	1.176
left	82 (42)	56 (39)	26 (49)		
right	114 (58)	87 (61)	27 (51)		
Duration (years), Median (Q1,Q3)	3 (1, 7)	3 (1, 6)	3 (1.5, 10)	0.04	3070.5
Branches, n (%)				0.012	6.284
single	175 (89)	133 (93)	42 (79)		
multi	21 (11)	10 (7)	11 (21)		
NRS-11, n (%)				0.871	0.026
< 7	122 (62)	90 (63)	32 (60)		
≥7	74 (38)	53 (37)	21 (40)		
Numbness, n (%)				0.032	4.581
No	41 (21)	24 (17)	17 (32)		
Yes	155 (79)	119 (83)	36 (68)		

BMI = body mass index (kg/m^2); NRS-11 = Numeric Rating Scale

factors that influence the recurrence 2 years post-RF surgery in patients with trigeminal nerve V2 branch pain (Table 3).

Constructing a Nomogram Prediction Model

The variables screened by the results of the above multifactor logistic regression analysis were included in the nomogram prediction model. The risk of recurrence 2 years after RF surgery in patients with V2 trigeminal branch pain was used to create the nomogram by selecting the outcome index. (Fig. 4). According to the scale described above, the nomogram corresponding to each risk factor, the individual score of that factor, and the total score were obtained by adding all the risk factor scores. The higher the total score, the greater the likelihood of recurrence 2 years post-RF surgery in patients with V2 trigeminal nerve pain.

Predictive Value of the Occurrence of Postoperative RF Recurrence in the Training and Test Groups

The ROC curve was plotted to assess the accuracy of the nomogram prediction. The area under the ROC curve of the training group nomogram prediction model was 0.726 (95% CI, 0.626 – 0.827), with a diagnostic threshold of 0.787, sensitivity of 87.9%, and specificity of 52.6%; the AUC of the predicted nomogram was 0.611 95% CI, 0.441 – 0.780], with a diagnostic threshold of 0.825, sensitivity of 79.5%, and specificity of 46.7%. Figure 5 shows that the prediction model had good predictive discrimination in both the training and test groups of the population.

Correction Curves for Recurrence Post-Trigeminal Nerve RF Surgery in the Training and Test Groups

In the training data set, the calibration curves for the nomogram showed that the predictions coincide with the observations. The Hosmer–Lemeshow goodness-of-fit test indicated that the model was not significant ($P > 0.05$), indicating that the model fits the observations satisfactorily (Fig. 6). The validation with the test set of data also showed a good fit between predictions and observations, with the Hosmer–Lemeshow goodness-of-fit test indicating that the model

was not significant (P > 0.05), indicating a good fit between the model and the observed data (Fig. 7).

DCA for the Occurrence of Post-Trigeminal RF Recurrence

The DCA of the screened variables for 2-year postoperative RF recurrence based on the nomogram prediction model (Fig. 8) showed that the net benefit of using the nomogram to predict the risk of 2-year postoperative RF recurrence in patients with V2 trigeminal nerve branch pain was high when patients had a threshold probability of 0 – 0.9, such that the wide range of alternative threshold probabilities deemed the model as a good assessment tool.

Table 2. *Basic clinical features in training and testing groups.*

Variables	Total (n = 196)	Training (n = 137)	Test (n = 59)	P	Statistic
Gender, n (%)				0.585	0.298
women	117 (60)	84 (61)	33 (56)		
men	79 (40)	53 (39)	26 (44)		
Age (years), n (%)				0.474	0.513
< 65	89 (45)	65 (47)	24 (41)		
≥65	107 (55)	72 (53)	35 (59)		
BMI, n (%)				0.458	0.552
< 25	148 (76)	106 (77)	42 (71)		
≥25	48 (24)	31 (23)	17 (29)		
History, n (%)				0.143	2.142
no	19 (10)	10 (7)	9 (15)		
yes	177 (90)	127 (93)	50 (85)		
Complications, n (%)				0.519	0.417
no	85 (43)	59 (43)	26 (44)		
yes	111 (57)	78 (57)	33 (56)		
Sides, n (%)				0.797	0.066
left	82 (42)	56 (41)	26 (44)		
right	114 (58)	81 (59)	33 (56)		
Duration (years), Median (Q1,Q3)	3 (1, 7)	3 (1, 7)	3 (1.5, 7)	0.806	4131
Branches, n (%)				0.155	2.018
single	175 (89)	119 (87)	56 (95)		
multi	21 (11)	18 (13)	3 (5)		
NRS-11, n (%)				0.475	0.511
< 7	122 (62)	88 (64)	34 (58)		
≥7	74 (38)	49 (36)	25 (42)		
Numbness, n (%)				0.952	0.004
no	41 (21)	28 (20)	13 (22)		
yes	155 (79)	109 (80)	46 (78)		
Status, n (%)				0.874	0.025
no relapse	143 (73)	99 (72)	44 (75)		
relapse	53 (27)	38 (28)	15 (25)		

BMI = body mass index (kg/m^2); NRS-11 = Numeric Rating Scale

Discussion

The current results show that age, duration, branches, and numbness were 4 independent risk factors for recurrence after trigeminal nerve V2 branch RF surgery, and that the probability of recurrence was low for those aged < 65 years, who had a shorter duration of the disease, had a single branch onset, and who had persistent numbness at 3 months postoperatively. This finding suggests a need for vigilance in elderly patients with chronic multibranch trigeminal neuralgia treated with RF. The recurrence rate did not correlate significantly with gender, comorbidity, history of preoperative treatment, right and left laterality, or preoperative pain score; this is consistent with previous clinical experience in managing trigeminal neuralgia (9,14-16). Based on these findings, we can screen patients who may have a poor prognosis in the early stage, adjust their treatment plans in time, or add some interventions to achieve better clinical outcomes. We can also communicate with patients to explain the situation, build consensus, and reduce patient expectations.

Furthermore, trigeminal neuralgia in the elderly is often associated with hypertension. Long-term hypertension can lead to thickening, hardening, and even calcification of the vessel walls, resulting in compression of the trigeminal meniscus and triggering trigeminal neuralgia, which is one of the most widely accepted

hypotheses of pathogenesis and the basis of the surgical theory of MVD (17). The older the age, the more severe vascular sclerosis and the more severe the compression of the trigeminal ganglion, with the sclerotic vessel wall exerting constant pressure on the trigeminal ganglion after a single operation, eventually leading to recurrence (18).

Minimally invasive surgery is now a widely accepted and effective surgical procedure for elderly patients who cannot tolerate surgery and have fewer surgical options (19). RF thermocoagulation is the destruction of a segmented nerve by thermal coagulation, causing degeneration and necrosis of the cytosol of the primary afferent neuron, loss of axon disruption, and disruption of nerve continuity, thereby blocking Aδ and C fibers from transmitting pain signals (20). Percutaneous balloon compression uses physical compression of the intracranial trigeminal ganglion to cause neuronal necrosis and eliminate pain. This phenomenon is closely related to the pressure within the balloon and is a significant factor in the treatment outcome (21); hence, for older patients, percutaneous balloon compression may be a better option (22).

Duration of disease is an independent risk factor for recurrence post-RF. Thus, prolonged pain leads to central (23) and peripheral sensitization (24). Also, RF has an optimal effect on peripheral sensitization but may be less effective on central sensitization, leading to the higher recurrence rate reflected in our results. Repeated stimulation of chronic pain over a prolonged period creates a pain memory (25). A proportion of patients with a long history of their condition have been treated for trigeminal neuralgia several times before surgery, including surgically; postoperative tissue adhe-

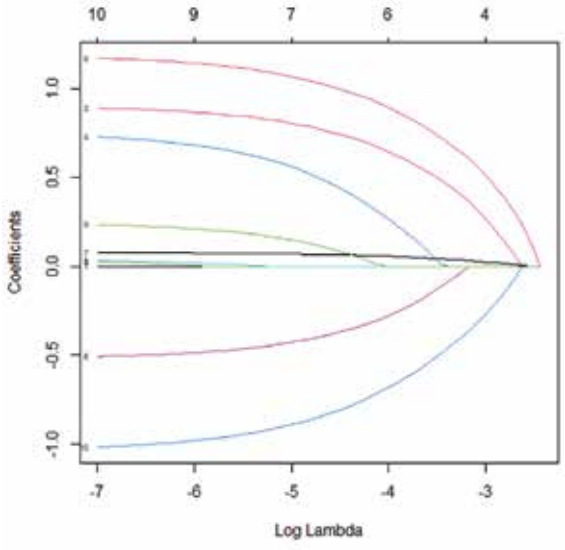

Fig. 2. *The variation of LASSO coefficients for different texture parameters as the super parameter (λ value) changes.*

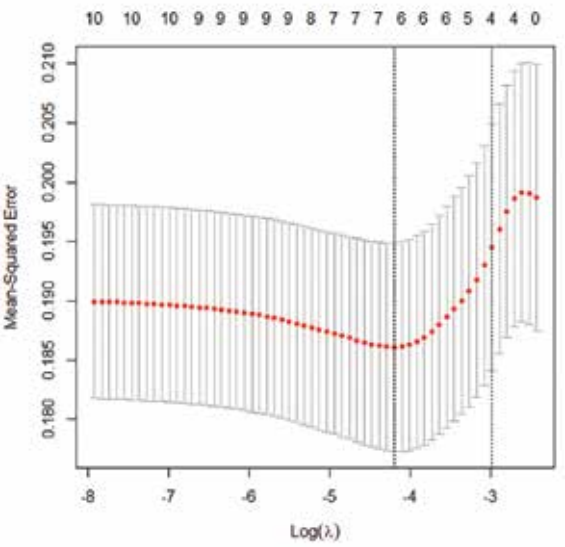

Fig. 3. *Texture feature selection in the LASSO model, showing the different super-parameters (λ value) corresponding to the diagnostic biases of the different models. The vertical dashed line on the left represents the minimum deviation of the log (λ) at the optimal λvalue, and the dashed line on the right represents the optimal logarithmic value of λ. The number at the top of the figure is the feature number.*

Table 3. *Multivariate logistic regression analysis of influencing factors of recurrence 2 years after radiofrequency surgery.*

	β	SE	Wald	*P* Value	OR	95% CI	
Age	0.977	0.368	7.046	0.008	2.656	1.291	5.462
Duration	0.077	0.033	5.526	0.019	1.080	1.013	1.152
Branches	1.158	0.499	5.377	0.020	3.184	1.196	8.476
Numbness	-0.898	0.395	5.163	0.023	0.407	0.188	0.884

OR = odds ratio

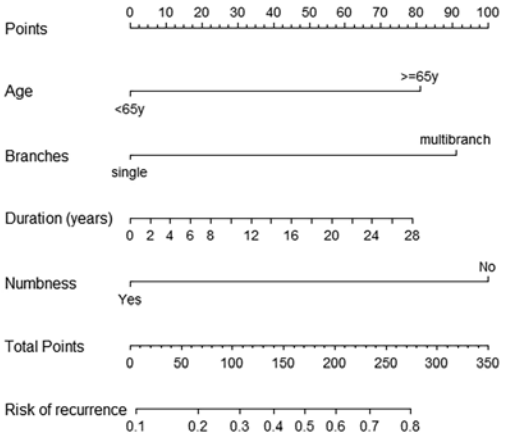

Fig. 4. *Nomogram predicting recurrence after trigeminal radiofrequency surgery.*

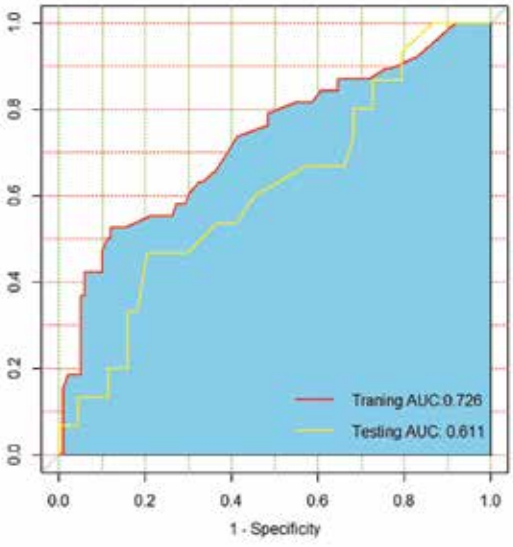

Fig. 5. *Receiver operating characteristic curve of the predictive nomogram for the risk of recurrence after trigeminal radiofrequency surgery.*

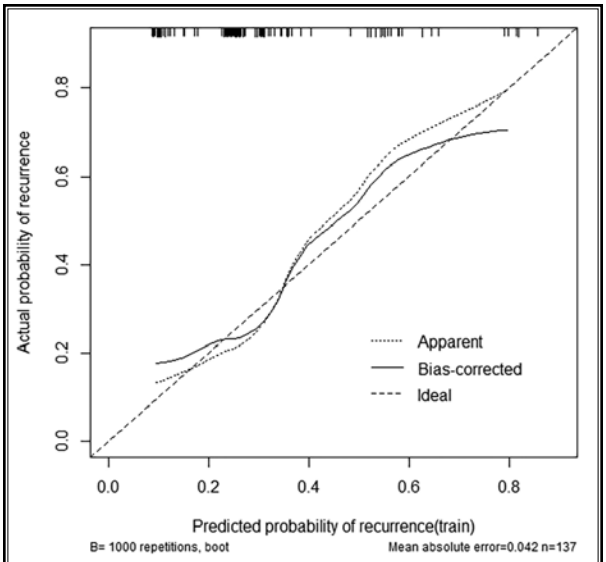

Fig. 6. *Calibration curve of the training group for predicting the risk of recurrence after trigeminal radiofrequency surgery by the predictive nomogram.*

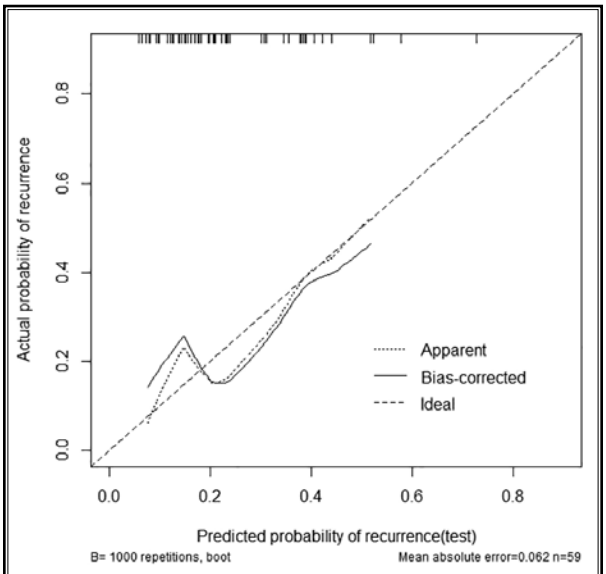

Fig. 7. *Calibration curve of the test group for predicting the risk of recurrence after trigeminal radiofrequency surgery by the predictive nomogram.*

sions and edema scars from repeated surgical irritation may contribute to the increased postsurgery recurrence rate (26).

The reason painful multiple branches treated with RF are prone to recurrence (27) may be that the targets are dispersed (V1+V2, V2+V3, or V1+V2+V3). The V1 branch in the supraorbital foramen, the V2 branch in the foramen rotundum, and the V3 branch in the foramen ovale deliver RF peripherally without entering the intracranial trigeminal ganglion; another reason may be the difference in diagnosis and differential diagnosis in patients with pain in both branches (V1+V2 or V2+V3). Supposedly, both targets achieve immediate pain relief after RF, but the lesion remains in the untreated branch, raising the recurrence rate (28). Furthermore, the choice of RF target may be less accurate in cases where the trigger point and the pain site are not in the same branch innervation area (29). For example, if V3 is the trigger

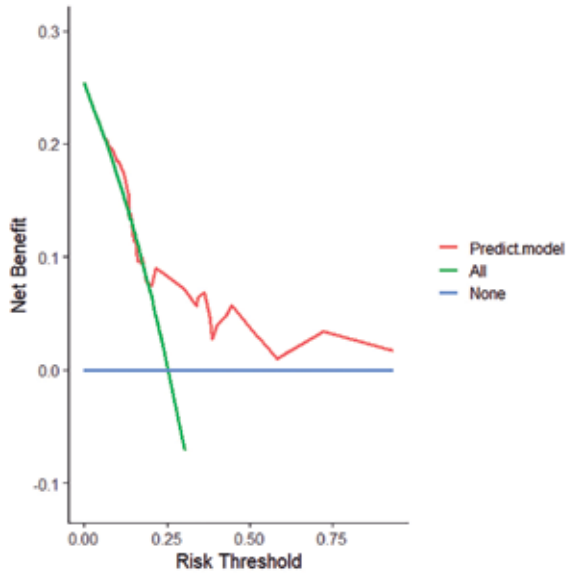

Fig. 8. *Decision curve analysis for predicting the risk of recurrence after trigeminal radiofrequency surgery by the predictive nomogram.*

point and the pain is in V1+V2, and if RF is only applied to V1+V2, leaving the V3 nerve intact, the immediate result will be very good; however, there is a high probability of recurrence in the long term.

The presence or absence of numbness at 3 months postoperatively is largely representative of the rate of nerve repair after RF. The absence of numbness at 3 months postoperatively indicates that the nerves in this group are capable of repair, and the purpose of RF nerve transection is to prevent the nerve from conducting pain signals (30). Although the conduction of sensation and pain do not co-occur, and we should strive for no pain or numbness in the future, this goal seems impossible with the current state of medical science (31). Nonetheless, the resolution of pain by RF causes loss of sensation (32). Thus, the presence or absence of numbness at 3 months postoperatively can also be used as an indicator to assess the likelihood of recurrence.

Nevertheless, the shortcomings of this study are that it was conducted at a single center, had a small sample size, and was not externally validated. Telephone follow-up did not provide an objective picture of a patient's condition. A subsequent prospective, double-blind, randomized controlled multicenter study needs to be designed to validate this model.

Conclusion

In conclusion, patients > 65-years-old, with prolonged disease duration and multiple painful branches, are likely to experience postoperative pain recurrence after RF in the V2 branch of the trigeminal nerve. Also, numbness at 3 months postoperatively can be used to predict the likelihood of recurrence.

This study successfully developed and validated a highly accurate predictive model for columnar maps (predictive variables include age, duration, branches, and numbness), which improves early identification and screening of patients at a high risk of pain recurrence after RF surgery.

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Author Contributions

Conception/design (FLW, ZFM, and KYX); data acquisition (FLW and ZFM); data analysis (KYX); data interpretation (FLW, ZFM, and KYX); drafting or revising (FLW, ZFM, and KYX); final approval (KYX). The authors agree to be accountable for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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