

Retrospective Study

Nomogram Model for Predicting the Risk of Recurrence after Surgery of the V3 Branch of the Trigeminal Nerve

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Background: Factors influencing recurrence after V3 trigeminal nerve surgery remain unknown.

Objectives: To analyze the risk factors affecting recurrence after trigeminal nerve branch V3 surgery, construct a nomogram prediction model, and verify the predictive efficacy of the model.

Study Design: A retrospective study.

Setting: This study was performed at the Affiliated Hospital of Jiaxing University, China.

Methods: Patients with mandibular nerve pain of the V3 branch of the trigeminal nerve treated with percutaneous puncture foramen ovale trigeminal mandibular nerve radiofrequency or trigeminal semilunar nerve microballoon compression at the Pain Department of the Affiliated Hospital of Jiaxing College, between January 2016 and April 2021, were enrolled and randomly divided into the training group (n = 108) and the test group (n = 47) according to the ratio of 7:3. The feasibility of the nomogram prediction model was further explored using multifactor logistic regression analysis based on the screening of independent predictors by the least absolute shrinkage and selection operator (LASSO) regression analysis using recurrence in one year after surgery as the outcome variable, and was assessed by the validation group. Finally, the discriminatory power, accuracy, and clinical utility of the prediction model were assessed using the area under the receiver operating characteristic curve (AUC), calibration curve, and decision curve analysis (DCA), respectively.

Results: Among the 155 patients with trigeminal V3 pain, 128 had no recurrence and 27 had recurrence one year after surgery. LASSO regression combined with multifactorial logistic regression analysis showed that age, procedure, and duration were factors influencing recurrence one year after surgery ($P < 0.05$). A nomogram prediction model was developed using the above variables. The AUC of the nomogram prediction model was 0.749 (95% CI [0.618, 0.879]) in the training group and 0.793 (95% CI [0.584, 0.980]) in the test group for postoperative recurrence of V3. The DCA showed that the net benefit of using the nomogram prediction model to predict the risk of postoperative recurrence of the V3 branch of the trigeminal nerve was higher when patients had a threshold probability of 0 to 0.486.

Limitations: This was a single-center study.

Conclusions: This study successfully developed and validated a highly accurate nomogram prediction model (with age, procedure, and duration as predictive variables), which can improve the early identification and screening of patients at high risk of recurrence after trigeminal nerve V3 branch surgery.

Key words: Trigeminal neuralgia, mandibular nerve, risk factors, prediction model

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Trigeminal neuralgia (TN) is a common form of neuropathic pain, typically characterized by severe electric shock-like pain in the cephalofacial distribution of the trigeminal nerve (1). The pathological process of TN is complex and the pathogenesis is unclear (2). The severe pain during attacks can seriously impact the patient's quality of life, leading to anxiety, depression, and even suicide (3). The V3 branch is the thickest of the 3 branches of the trigeminal nerve and has both sensory and motor functions. Surgery (4) or radiofrequency (RF) thermocoagulation of the trigeminal mandibular nerve by percutaneous puncture foramen ovale (5) is a minimally invasive surgical treatment, but some patients experience a recurrence of postoperative pain (6). In recent years, a few studies have investigated the efficacy of minimally invasive surgical treatment of the V3 branch of the trigeminal nerve and the recurrence factors. In this study, we reviewed patients who underwent minimally invasive surgery to treat mandibular nerve pain in the V3 branch of the trigeminal nerve and analyzed the risk factors affecting postoperative recurrence in the V3 branch, in order to provide a reference for the choice of treatment options for TN.

METHODS

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of the Affiliated Hospital of Jiaxing College (2023KY034)

Study Patients

The data of inpatients with mandibular nerve pain of the V3 branch of the trigeminal nerve who underwent computed tomography (CT)-guided foramen ovale RF or percutaneous microballoon compression (PBC) surgery at the Pain Department of the Affiliated Hospital of Jiaxing College, between January 2016 and April 2021, were retrospectively reviewed. This study was approved by the Ethics Committee of the Affiliated Hospital of Jiaxing College (2023KY034). All patients received regular medication as conservative treatment without relief, and voluntarily underwent surgery after signing a consent form. Inclusion criteria were as follows: consistent with the diagnosis of pain in the mandibular branch of the trigeminal nerve (7). The patients were admitted to the clinic and successfully completed the surgery. Exclusion criteria were as follows: incomplete information, unreachable, and unwilling to cooperate with follow-up.

Surgical Methods

The patient was admitted to the CT operating room with a nasal cannula for oxygen and intravenous access. The patient was placed supine on the CT table with a pillow under the shoulder to tilt the head back at an angle of approximately 20°. The optimal puncture route was decided after a CT scan, and the puncture site was marked on the affected side. Percutaneous foramen ovale RF dissection of the trigeminal mandibular nerve was conducted as follows: an 18-G RF needle with a working end of 10 mm was inserted into the foramen ovale under CT guidance and the electrical impedance was tested at 250-500 Ω . Sensory-motor testing was performed using high-frequency current (50 Hz, 500 μ s) and low-frequency current (2 Hz, 1000 μ s). The sensory test covered the original painful area, and the motor test showed obvious muscle movement of the lower lip. PBC of the trigeminal hemimelia was performed as follows: after confirming the position on CT, 1 mL of 2% lidocaine was injected and the balloon catheter with guide wire was slowly placed into the puncture needle so that the balloon portion of the catheter tip completely crossed the tip of the puncture needle into the Meckel's cavity and the position was confirmed on CT scan. The guide wire was then withdrawn and the balloon was slowly filled with 0.35-0.70 mL of 30% iodophoresis contrast agent, and the injection port was blocked with a T-tube to prevent backflow of the contrast agent. A second CT scan showed a well-positioned balloon with a "pear-shaped" balloon pattern. During the procedure, the patient was asked when the pain in the affected side had disappeared and numbness appeared, and then the balloon was emptied and the compression was stopped.

Data Collection

Age, gender, procedure (RF or PBC), duration, complications (including hypertension, diabetes, etc), pre-surgery (history of previous surgical treatment for TN, including RF, PBC, microvascular decompression [MVD], etc), and prepain (preoperative Numeric Rating Scale [NRS-11]) were retrieved from the Hitech Electronic Medical Record System 3.0. Postoperative NRS-11 was collected by telephone follow-up. Outcome indicator recurrence was defined as: (preoperative NRS-11-postoperative NRS-11)/ preoperative NRS-11 < 50% (8).

Statistical Analysis

Statistical analysis was performed using R 4.1.3 software (Institute for Statistics and Mathematics;

Vienna, Austria). Continuous variables were tested using the Kolmogorov-Smirnov normality test; measures conforming to a normal distribution were described by mean \pm SD and compared between 2 groups using the t test; nonnormally distributed data were described by median (IQR) and compared between 2 groups using the rank sum test; and count data were analyzed using the chi-square test. The eligible patients (n = 155) were randomly divided into the training group (n = 108) and the test group (n = 47) in the ratio of 7:3 by strict data filtering and preprocessing. The least absolute shrinkage and selection operator method (LASSO regression) was used to determine whether recurrence occurred one year after surgery as the outcome variable in the training group data (9,10). The independent predictors were screened, based on which the nomogram prediction model was further explored and developed using multivariate logistic regression analysis, and the constructed prediction model was validated using the test group data. To evaluate the efficacy of the prediction model, the area under the receiver operating characteristic (ROC) curve (AUC) was used to validate the prediction, and the prediction effect was verified by the Hosmer-Lemeshow test to determine the model's goodness of fit, and the calibration curve (11) was plotted using decision curve analysis (DCA) (12). The risk of recurrence of mandibular neuralgia in the V3 branch of the trigeminal nerve one year after surgery was predicted. The difference was considered statistically significant at $P < 0.05$.

RESULTS

General Information

Of the 155 patients with pain in the V3 branch of the trigeminal nerve one year after surgery, 128 had no recurrence and 27 had recurrence. There was no statistical difference in the gender, complications, presurgery, and prepain of patients between the nonrecurrence and recurrence groups. The differences in age, procedure, and duration were statistically significant between patients in the nonrecurrence and recurrence groups ($P < 0.05$) (Table 1).

All patients (n = 155) were randomly

divided into the training group (n = 108) and the test group (n = 47) 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 (assignment: Yes = 1, No = 0) was used as the dependent variable. Age (assignment: ≥ 65 years = 1, < 65 years = 0), gender (assignment: Men = 1, Women = 0), procedure (assignment: PBC = 1, RF = 0), duration (assignment: ≥ 5 years = 1, < 5 years = 0), and presurgery (assignment: Yes = 1, No = 0) were used as the dependent variables. Moreover, duration (≥ 5 years = 1, < 5 years = 0), complications (assignment: Yes = 1, No = 0), presurgery (assignment: Yes = 1, No = 0), and prepain (assignment: $\geq 7 = 1, < 7 = 0$) were used as independent variables in the LASSO regression analysis (Fig. 1). As the penalty coefficient λ changes, the number of variables included in the model decreases. The variables included in the model were gradually reduced, and finally, the 10-fold cross-validation error was selected

Table 1. Comparison of general information between the nonrecurrence and recurrence patients.

Variables	Total (n = 155)	Nonrecurrence (n = 128)	Recurrence (n = 27)	P value	Statistic
Age, n (%)				0.032	4.58
< 65y	66 (43)	60 (47)	6 (22)		
$\geq 65y$	89 (57)	68 (53)	21 (78)		
Gender, n (%)				0.373	0.793
women	95 (61)	81 (63)	14 (52)		
men	60 (39)	47 (37)	13 (48)		
Procedure, n (%)				0.007	7.333
RF	87 (56)	65 (51)	22 (81)		
PBC	68 (44)	63 (49)	5 (19)		
Duration, n (%)				0.021	5.299
< 5 years	91 (59)	81 (63)	10 (37)		
≥ 5 years	64 (41)	47 (37)	17 (63)		
Complication, n (%)				0.735	0.115
no	59 (38)	50 (39)	9 (33)		
yes	96 (62)	78 (61)	18 (67)		
Presurgery, n (%)				0.584	0.299
no	111 (72)	90 (70)	21 (78)		
yes	44 (28)	38 (30)	6 (22)		
Prepain, n (%)				1	0
< 7	97 (63)	80 (62)	17 (63)		
≥ 7	58 (37)	48 (38)	10 (37)		

Abbreviations: RF, radiofrequency; PBC, percutaneous balloon compression.

Table 2. The baseline characteristics in the 2 groups.

Variables	Total (n = 155)	Test Group (n = 47)	Training Group (n = 108)	P value	Statistic
Age, n (%)				0.379	0.773
< 65 years	66 (43)	23 (49)	43 (40)		
≥ 65 years	89 (57)	24 (51)	65 (60)		
Gender, n (%)				0.408	0.685
women	95 (61)	26 (55)	69 (64)		
men	60 (39)	21 (45)	39 (36)		
Procedure, n (%)				0.756	0.096
RF	87 (56)	25 (53)	62 (57)		
PBC	68 (44)	22 (47)	46 (43)		
Duration, n (%)				0.146	2.111
< 5 years	91 (59)	23 (49)	68 (63)		
≥ 5 years	64 (41)	24 (51)	40 (37)		
Complication, n (%)				0.888	0.02
no	59 (38)	17 (36)	42 (39)		
yes	96 (62)	30 (64)	66 (61)		
Presurgery, n (%)				0.951	0.004
no	111 (72)	33 (70)	78 (72)		
yes	44 (28)	14 (30)	30 (28)		
Prepain, n (%)				0.293	1.106
<7	97 (63)	26 (55)	71 (66)		
≥ 7	58 (37)	21 (45)	37 (34)		
Status, n (%)				1	0
nonrecurrence	128 (83)	39 (83)	89 (82)		
recurrence	27 (17)	8 (17)	19 (18)		

Abbreviations: RF, radiofrequency; PBC, percutaneous balloon compression.

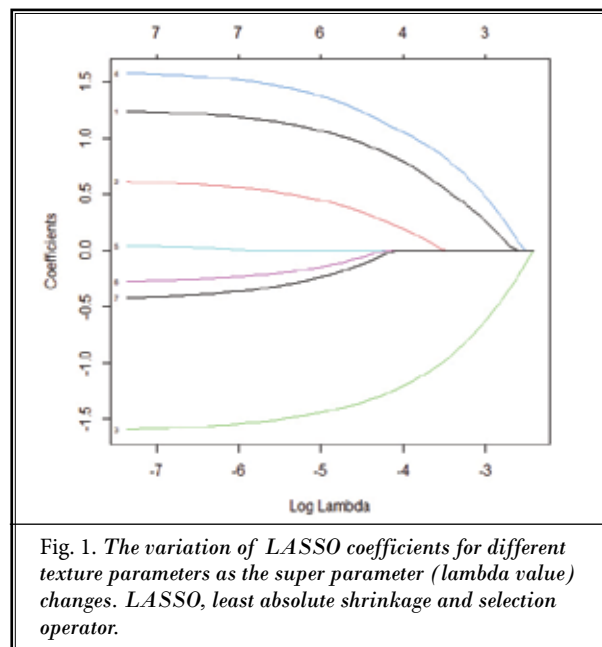


Fig. 1. The variation of LASSO coefficients for different texture parameters as the super parameter (lambda value) changes. LASSO, least absolute shrinkage and selection operator.

as the minimum $\lambda+1$ (1 SE = 0.067 for the minimum value of λ) as the optimal value of the model (Fig. 2), at which point the screened predictor variables included age, procedure, and duration. The screened predictor variables were included in the multivariate logistic regression analysis, and the results showed that age, procedure, and duration were the influencing factors for whether or not recurrence occurred one year after surgery in patients with trigeminal nerve branch V3 pain (Table 3).

Constructing a Nomogram Prediction Model

The variables selected from the results of the above multivariate logistic regression analysis were incorporated into the nomogram prediction model, and the outcome measure was selected as the risk of recurrence one year after surgery in patients with trigeminal V3 branch pain, and the nomogram was drawn (Fig. 3). The total score was obtained by summing all risk factors to obtain the incidence of recurrence of V3 pain one year after surgery in the corresponding patient.

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

The ROC curve for the prediction accuracy of the nomogram was plotted and the AUC for the nomogram prediction model was 0.749 (95% CI [0.618, 0.879]) in the training group and 0.793 (95% CI [0.584, 0.980]) when validated by the test group data, indicating that the prediction model had good predictive discrimination in both the training and validation group populations (Fig. 4).

Correction Curves for Postoperative Recurrence in Patients With Trigeminal Nerve Branch V3 Pain in the Training and Test Groups

In the training dataset, the calibration curves for the nomogram 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

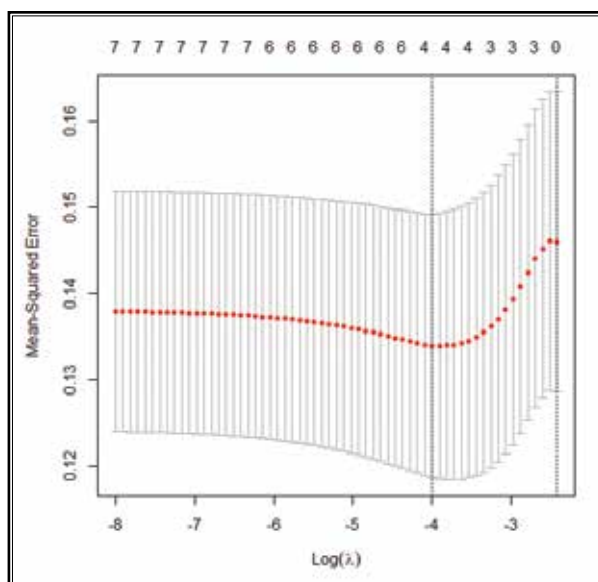


Fig. 2. Texture feature selection in the LASSO model, showing the different super-parameters (lambda value) corresponding to the diagnostic biases of the different models. The vertical dashed line on the left represents the minimum deviation of the log (lambda) at the optimal lambda value, and the dashed line on the right represents the optimal logarithmic value of lambda. The number at the top of the figure is the feature number. LASSO, least absolute shrinkage and selection operator.

Table 3. Multivariate logistic regression analysis of influencing factors of recurrence after surgery in patients with trigeminal nerve branch V3 pain.

	β	SE	Wald	P value	OR	95% CI	
Age	1.118	0.526	4.523	0.033	3.059	1.092	8.570
Procedure	-1.711	0.562	9.253	0.002	0.181	0.060	0.544
Duration	1.469	0.483	9.260	0.002	4.346	1.687	11.197

Abbreviation: OR, odds ratio.

between the model and the observations (Fig. 5). Validation with the test group dataset 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. 6).

The Decision Curves of Recurrence After Surgery of the V3 Branch of the Trigeminal Nerve in the Training Group and the Test Group

The DCA of the screened variables for recurrence

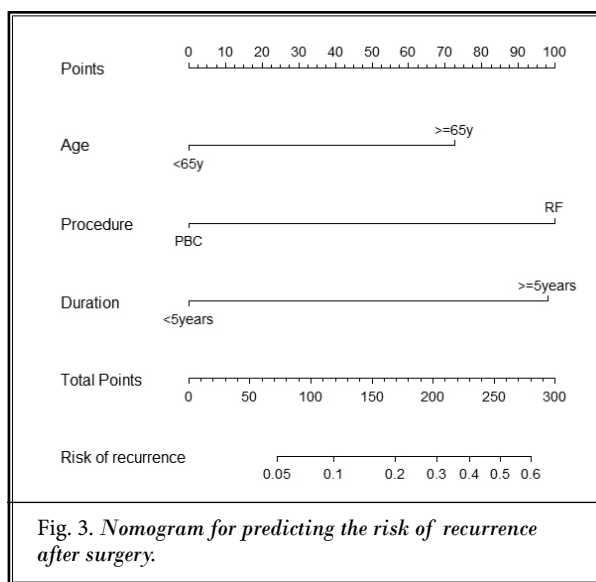


Fig. 3. Nomogram for predicting the risk of recurrence after surgery.

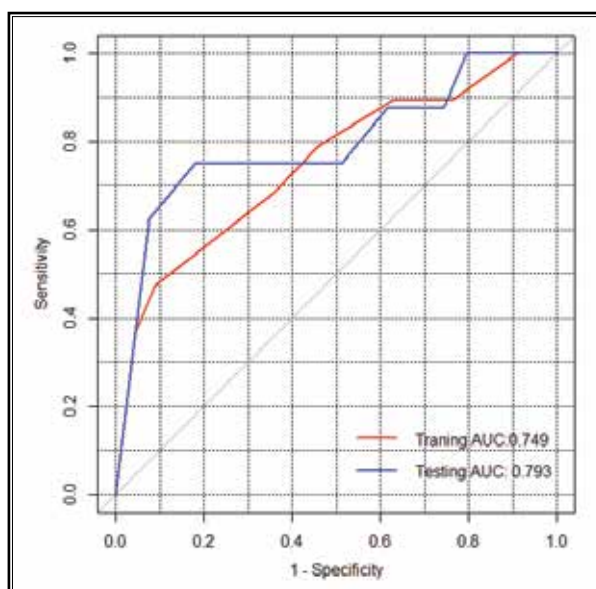


Fig. 4. ROC curve of the predictive nomogram for the risk of recurrence after surgery. ROC, receiver operating characteristic [curve].

1-year after surgery, based on the nomogram prediction model (Fig. 7), showed that the net benefit of using a nomogram to predict the risk of recurrence 1-year after surgery in patients with trigeminal nerve V3 branch pain was higher when patients had a threshold probability of 0-0.486. The wide range of alternative threshold probabilities suggests that the model is a good assessment tool.

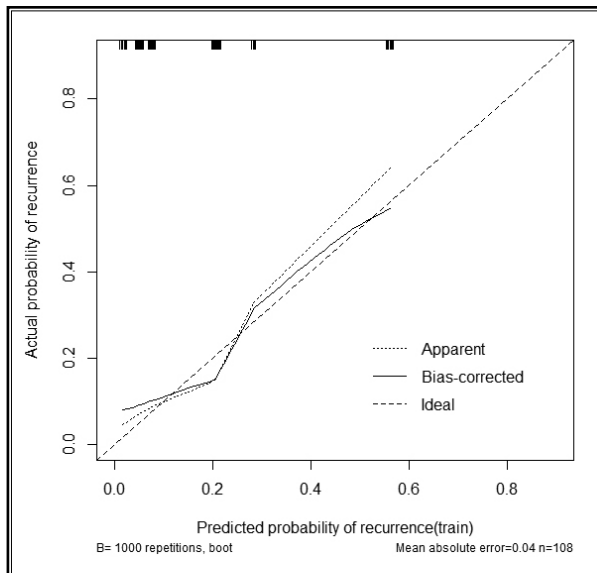


Fig. 5. Calibration curve of the training group for predicting the risk of recurrence after surgery by the predictive nomogram.

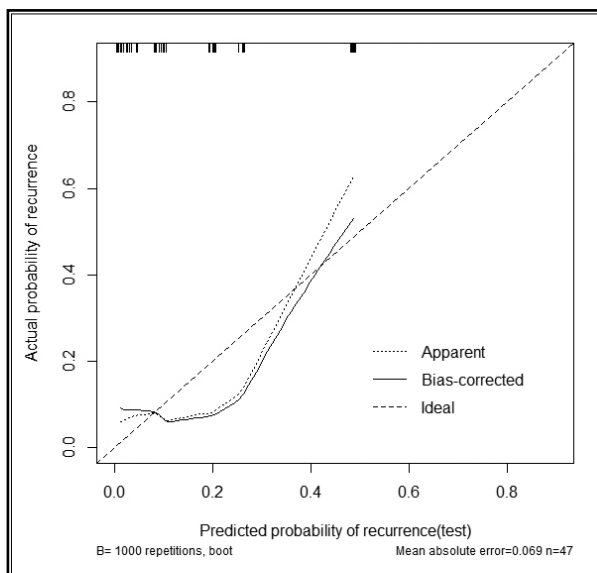


Fig. 6. Calibration curve of the test group for predicting the risk of recurrence after surgery by the predictive nomogram.

DISCUSSION

The results of this study showed that age, surgical procedure, and duration of disease were the independent risk factors for recurrence after trigeminal nerve V3 surgery, with a lower recurrence rate for patients aged < 65 years, undergoing balloon compression sur-

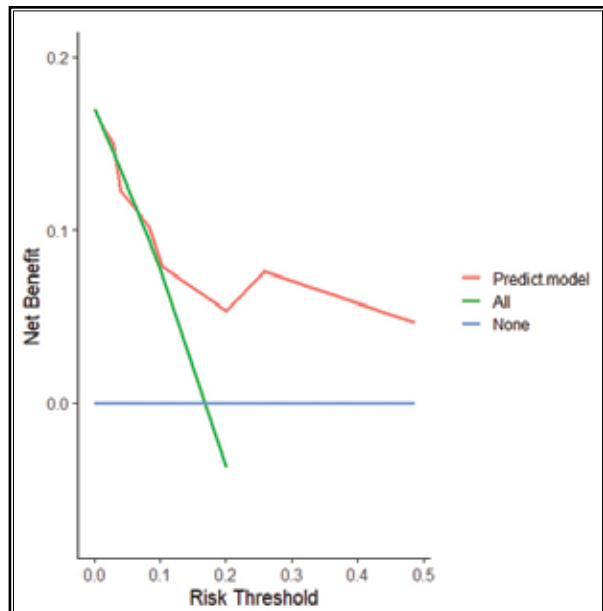


Fig. 7. DCA for predicting the risk of recurrence after surgery by the predictive nomogram. DCA, decision curve analysis.

gery and with a duration of disease < 5 years, suggesting the need for vigilance in the treatment of chronic TN patients of advanced age who undergo minimally invasive surgery. The recurrence rate did not correlate significantly with gender, comorbidity, history of surgery, or preoperative pain rating. This result is similar to previous treatments for TN in general (13-15).

Elderly patients with TN often have hypertension, and prolonged hypertension can lead to thickening and hardening of the blood vessel walls or even calcification, resulting in compression of the trigeminal meniscus and triggering TN (16).

This is one of the most widely accepted hypotheses for the pathogenesis of TN (17). It is also the surgical rationale for MVD (18,19). The older the patient, the more severe the vascular sclerosis and the more severe the compression of the trigeminal meningeal ganglion, and the continued compression of the meningeal ganglion by the sclerotic vessel wall after a single operation, eventually leading to recurrence (19). Minimally invasive surgery is a widely accepted and effective surgical option for elderly patients who are less tolerant of surgery and have fewer surgical options (20,21). RF procedures utilize high-frequency currents that alternate to interrupt or alter pain pathways. Continuous RF involves the use of a constant RF current to produce a thermal lesion in a targeted nerve, which interrupts

pain-afferent pathways, while pulsed RF utilizes rapidly changing electrical pulses to achieve the same intended effect (22). RF thermocoagulation is the destruction of a segmented nerve by heat coagulation, which causes degeneration and necrosis of the cytosol of the primary afferent neurons, loss of axonal disruption, and disruption of nerve continuity, thus blocking the A α and C fibers from transmitting pain signals (23). PBC is the physical compression of the intracranial meningeal ganglion, causing necrosis of some neurons within the ganglion to eliminate pain (24). This is closely related to the pressure inside the balloon, and is an important factor in the outcome of the procedure (25,26). The main reason why RF is more susceptible to recurrence is that the target of action is in the foramen ovale, which is more peripheral to the intracranial semilunar ganglion than the balloon compression (27). Another possibility is that the location of the balloon compression through the foramen ovale into the semilunar ganglion is relatively fixed; whereas, the size of the foramen ovale varies considerably with RF thermocoagulation performed at the mouth of the foramen ovale, with the possibility of a shift in the target site of RF, despite verification by CT scan and electrophysiological testing to confirm the position of the RF needle in relation to the nerve. It is possible that the target shift may occur during the continuation of the RF execution (28). The extracranial target can be a target of the nerve. The extracranial target has the advantage of being virtually free of intracranial hemorrhage and infection, although it may result in an increased recurrence rate (29,30). Central sensitization of pain may occur in patients with disease duration of > 5 years (31). In patients with chronic pain for > 5 years, pain memory is produced by repeated stimulation over a long period of time (32). Some patients who have had

TN for > 5 years have been treated several times before surgery, even surgically, and the postoperative tissue adhesions and edema scars caused by repeated surgical irritation may contribute to the increased recurrence rate after surgery (33). Based on these findings, it is clinically possible to predict the recurrence rate based on the patient's age, duration of disease, and type of surgery planned. However, this does not mean that PBC is necessarily superior to RF, and the actual clinical surgical plan must be considered in combination with the actual situation. We urge that early treatment of the V3 branch of the trigeminal nerve must be beneficial.

Limitation

The limitations of this study were that it was a single-center, small sample-size study, without external validation. The telephone follow-up did not provide an objective assessment of the patients' condition. A prospective, double-blind, randomized, controlled, multicenter study will be designed in the future to validate the model.

In summary, postoperative recurrence of trigeminal V3 pain is more likely to occur in patients > 65 years of age and with a disease duration of > 5 years. The choice of surgical approach should be made carefully, after considering the advantages and disadvantages of different surgical approaches.

CONCLUSIONS

This study successfully developed and validated a highly accurate nomogram prediction model (with age, procedure, and duration as predictive variables), which helps to improve the early identification and screening of patients at high risk of postoperative recurrence among patients with trigeminal nerve V3 branch pain.

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