Retrospective Study

A Predictive Model for the Risk of Postsurgery Pain Recurrence in the V1 Branch of the Trigeminal Nerve

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Background: The factors influencing pain recurrence following V1 trigeminal nerve surgery are still unknown.

Objective: We aimed to analyze the risk factors affecting pain recurrence following surgery in the V1 branch of the trigeminal nerve, construct a nomogram-based therapeutic efficacy prediction model using logistic regression analysis, and validate the model's predictive performance.

Study Design: A retrospective study.

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

Methods: Data were retrospectively collected from 131 patients with trigeminal neuralgia and V1 branch algesia who underwent either radiofrequency thermocoagulation through the supraorbital foramen or percutaneous balloon compression at the Pain Department of the Affiliated Hospital of Jiaxing University from March 2017 through January 2021. The patients were randomly divided into a training group (n = 92) and a testing group (n = 39) in a 7:3 ratio. A least absolute shrinkage and selection operator (LASSO) regression was used to screen independent predictive factors. The outcome variable was whether the patient experienced pain recurrence within 2 years postsurgery. Those results were used to construct a nomogram-based predictive model, followed by a multivariate logistic regression analysis. The feasibility of the nomogram-based predictive model was evaluated by the validation group. Finally, the predictive model's discrimination ability, accuracy, and clinical usability were evaluated using a receiver operating characteristic curve, calibration curves, and decision curve analysis, respectively.

Results: The results indicate that among the total 131 patients, 76 patients did not experience pain recurrence within 2 years postsurgery, while 55 patients suffered a pain recurrence. The results of the LASSO regression, combined with a multivariate logistic regression analysis, showed that age, pre-Numeric Rating Scale score, and surgery type were the influencing factors for patients with V1 branch pain who experienced pain recurrence within 2 years postsurgery ($P < 0.05$). From this data a nomogram-based predictive model was established. The area under the curve of the nomogram-based predictive model for the training group was found to be 0.890 (95% CI, 0.818 - 0.961); in the test group it was 0.857 (95% CI, 0.748 - 0.965) in the test group. The Hosmer-Lemeshow goodness-of-fit test revealed an excellent fit ($P > 0.05$), while the decision curve analysis showed that the net benefit of using the nomogram-based predictive model to predict the risk of recurrence after 2 years was higher when the patient's threshold probability was 0 to 0.990.

Limitations: This was a single-center study.

Conclusion: A high-precision nomogram-based predictive model was successfully established and validated (with predictive variables including age, pre-Numeric Rating Scale score, and surgery type). We envisage this model will help improve the early identification and screening of high-risk patients for postsurgery pain recurrence of the V1 trigeminal nerve branch.

Key words: Trigeminal neuralgia, risk factors, prediction model

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Trigeminal neuralgia (TN) is a common neurogenic pain disorder characterized by severe electric shock-like pain in the head and facial areas, innervated by the trigeminal nerve and usually divided into 3 branches: V1, V2, and V3 (1,2). The pathogenesis of TN is complex and as yet unclear. Moreover, studies on V2- and V3-associated nerve disorders are numerous, but research on the V1 branch is relatively scarce (3,4).

The treatment modalities for V1 branch-associated pathologies include the use of radiofrequency thermocoagulation (RFT) and percutaneous balloon compression (PBC) (5,6). The former utilizes high temperatures generated as a result of RFT to induce protein denaturation at the target point, thereby blocking pain signal transmission (7), while the latter employs the principle of physical compression to induce degeneration and necrosis of the ganglion, resulting in blocking pain (8). Although both procedures can effectively alleviate pain, they encounter pain recurrence, compromising patients' compliance and confidence (9). This failing necessitates developing a predictive model to identify high-risk patients, make preparations, and choose appropriate interventions.

Our study aimed to retrospectively analyze the relevant conditions of patients with TN involving the V1 branch who underwent minimally invasive surgery and assess risk factors affecting V1 branch pain recurrence to provide a reference in selecting the best-suited TN treatment plans.

Methods

Study Patients

Data were retrospectively collected from the hospital records of 131 patients who visited the Department of Pain Management of Jiaxing University Affiliated Hospital from March 2017 through January 2021 for TN V1 branch pain. These patients underwent either computed tomography (CT)-guided supraorbital foramen RFT or PBC surgery.

All patients had received standard drug conservative treatment and had poor outcomes. They voluntarily accepted surgical treatment, and signed a consent form. All patients who were diagnosed with TN V1 branch pain and completed a surgical procedure were selected for our study (10); those patients who either had incomplete data, were unable to be were contacted, or were unwilling to cooperate with follow-up were excluded.

After strict data filtering and preprocessing, eligible patients (n = 131) were randomly divided into a training (n = 92) and a test group (n = 39) in a 7:3 ratio (using R 4.1.3 software [The R Foundation]). The study protocol was duly approved by the Ethics Committee of Jiaxing University Affiliated Hospital (2023KY034). The proceduralists were all pain physicians.

Surgical Methods

All patients fasted for at least 6 hours presurgery. They were put on nasal oxygen via a nasal catheter upon entering the CT treatment room. A venous access was opened, and heart rate, blood pressure, and peripheral oxygen saturation were monitored. Patients were positioned supine on the CT table for CT scanning.

Following the CT scan, the optimal puncture path was determined, and the puncture point on the affected side of the face was marked for demarcation. Percutaneous puncture of the supraorbital foramen with a 2 mm, 18G radiofrequency puncture needle was performed under CT guidance. After testing the impedance at 250-500 Ω, sensory-motor testing was carried out using high-frequency currents (50 Hz, 500 μs) for sensory testing and low-frequency currents (2 Hz, 1,000 μs) for motor testing. The needle tip position was adjusted to below 0.5 mA, and the sensory test covered the original pain area, while muscle twitching was observed in the orbital area during motor testing.

The parameters were set to a temperature of 95°C for 180 seconds. All patients were anesthetized with an intravenous injection of 1-2 mg/kg of propofol, followed by RFT. The patient was kept under observation for an additional 20 minutes following recovery from anesthesia and only transferred to the ward when no discomfort was reported.

Microballoon compression of the trigeminal ganglion was then performed under CT guidance. Briefly, the puncture needle was inserted into the foramen ovale, and after confirming its position, 1 mL of 2% lidocaine was injected. A guide wire was then inserted into the puncture needle, and a balloon catheter was slowly placed into the needle to pass through the needle tip and enter Meckel's cave, confirmed by CT scanning. This was then followed by slowly injecting 0.35 to 0.70 mL of 30% iodized oil contrast medium into the balloon through the guide wire to fill the balloon, and a 3-way valve was used to seal the injection port to prevent contrast medium reflux. The balloon's correct position and pear shape appearance were confirmed

using CT scanning. The patients were asked during the surgery about their pain level and numbness in the affected side. Balloon removal followed after 180 to 200 seconds of trigeminal ganglion compression. The puncture needle was removed, and the puncture site was compressed for a few minutes before being covered with a dressing; then, the patient was transferred to the ward.

Data Collection

The data about age, gender, symptoms duration, primary diagnosis (whether it was primary or secondary), preoperative pain level measured using the Numeric Rating Scale (NRS-11), type of surgical procedure (PBC or RFT), and affected side (left or right) were collected from the HaiTai electronic medical record system version 3.0 (Nanjing Haitai Medical Information System Co. LTD.). Follow-up calls were made to collect NRS-11 scores 2 years postsurgery. The outcome measure of pain recurrence was defined as a postoperative NRS-11 score less than 50% of the preoperative score (11).

Statistical Analysis

All data were statistically analyzed using R 4.1.3 software (The R Foundation). A χ^2 test used to analyze count data. Using whether pain recurrence occurred 2 years postsurgery in the training group as the outcome variable, a least absolute shrinkage and selection operator (LASSO) regression was used to screen for independent predictive factors, and then multiple logistic regression was used to explore further and establish a nomogram prediction model, which was validated using the testing group data. The prediction model performance was evaluated using a receiver operating characteristic (ROC) curve to verify the predictive effect of the model and the Hosmer-Lemeshow goodness-of-fit test to determine the model's goodness of fit. A calibration curve was also constructed, and a decision curve analysis (DCA) was used to predict the risk of pain recurrence 2 years postsurgery. Differences with a *P* value less than 0.05 were considered statistically significant.

Results

General Information

Our general information data analysis showed that among the 131 patients, 76 did not experience any pain recurrence, while 55 suffered pain recurrence at 2 years postsurgery. Comparing demographic and clinical characteristics, namely gender, duration, primary, and affected side between the 2 groups, showed no significant difference ($P > 0.05$), while there was a significant difference in age, pre-NRS-11 score, and surgery type ($P < 0.05$) as shown in Table 1. Furthermore, the difference in the baseline characteristics of the 2 patient groups was not statistically significant ($P > 0.05$, Table 2).

Pain Recurrence Risk Factors

In the training group with TN V1 branch pain, risk factors were assessed by assigning definite scores to them, including pain recurrence as a dependent variable (one for yes and 0 for no) and independent variables including age (one for ≥ 65 years, and 0 for age < 65), gender (one for men, and 0 for women), duration (one for ≥ 5 years and 0 < 5 years), primary diagnosis (one for yes, and 0 for no), pre-NRS-11 score (one for an NRS-11 score ≥ 7 and 0 for an NRS-11 score < 7), surgery type (one for PBC, and 0 for RFT), and affected side (one for right, and 0 for left), followed by a LASSO regression analysis as shown in Fig. 1.

As the penalty coefficient λ changed, the variables included in the model gradually decreased. Finally, the value of 10-fold cross-validation error with the smallest $\lambda + 1$ (one standard error of the λ min = 0.082) was selected as the optimal value of the model, as shown in Fig. 2. The multiple logistic regression analysis included the selected predictive variables: age, pre-NRS-11 score, and surgery type. Results indicated that age, pre-NRS-11 score, and surgery type influenced TN V1 branch pain recurrence at 2 years postsurgery, as shown in Table 3.

Constructing a Nomogram Prediction Model

Our nomogram prediction model includes the variables selected from the multiple logistic regression analysis. The outcome measure was the risk of TN V1 branch pain recurrence at 2 years postsurgery. The created nomogram is shown in Fig. 3. It is based on the scale above for each risk factor on the nomogram; a single score for each factor was obtained. The total score was calculated by adding the scores for all risk factors, which could then be used to predict the probability of V1 branch pain recurrence at 2 years postsurgery for a given patient. The higher the total score, the greater the likelihood of pain recurring at 2 years postsurgery in TN V1 branch pain.

Table 1. *Comparison of general information between patients without pain recurrence and patients with pain recurrence.*

Variables	Total (n = 131)	Nonrecurrence (n = 76)	Recurrence (n = 55)	*P*	Statistic
Age, n (%)				0.007	7.322
< 65 y	42 (32)	32 (42)	10 (18)		
≥ 65 y	89 (68)	44 (58)	45 (82)		
Gender, n (%)				1	0
Women	71 (54)	41 (54)	30 (55)		
Men	60 (46)	35 (46)	25 (45)		
Duration, n (%)				0.305	1.051
< 5years	70 (53)	44 (58)	26 (47)		
≥ 5years	61 (47)	32 (42)	29 (53)		
Primary Diagnosis, n (%)				0.307	1.043
No	47 (36)	24 (32)	23 (42)		
Yes	84 (64)	52 (68)	32 (58)		
Pre-NRS-11, n (%)				< 0.001	19.548
< 7	69 (53)	53 (70)	16 (29)		
≥ 7	62 (47)	23 (30)	39 (71)		
Surgery Type, n (%)				< 0.001	21.182
RFT	89 (68)	39 (51)	50 (91)		
PBC	42 (32)	37 (49)	5 (9)		
Affected Side, n (%)				1	0
Left	48 (37)	28 (37)	20 (36)		
Right	83 (63)	48 (63)	35 (64)		

NRS-11 = Numeric Rating Scale

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

The prediction accuracy of the column chart model was evaluated using a ROC curve. The area under the curve of the ROC curve for the training group was found to be 0.890 (95% CI, 0.818 - 0.961), and 0.857 for the test group (95% CI, 0.748 - 0.965), as shown in Fig. 4. This indicates that the prediction model had good discriminative ability in both the training and validation populations.

Correction Curves for Postoperative Pain Recurrence in Patients in the Training and Test Groups

The nomogram's training dataset calibration curve showed good agreement between predicted and observed values; the Hosmer-Lemeshow goodness-of-fit test indicated that the model was not significant ($P > 0.05$), indicating a good fit of the model to the observed data (Fig. 5). Similar results were observed on the validation dataset, with good agreement between predicted and observed values; the Hosmer-Lemeshow goodness-of-fit test did not indicate significance ($P > 0.05$), suggesting a good fit of the model to the observed data (Fig. 6).

The Decision Curves of Postsurgery Pain Recurrence in the Training and Test Groups

Based on the nomogram predictive model, a DCA was performed on the variables selected for postoperative recurrence at 2 years. The results are shown in Fig. 7. The results reveal that the net benefit of using the nomogram to predict the risk of postoperative pain recurrence in patients with TN V1 branch pain was higher when the threshold probability ranged from 0 to 0.990, where the wide range of alternative threshold probabilities proved to be a good evaluation ability of the model.

Discussion

TN is a common neurological disorder causing severe facial pain, and significantly compromising patients' social and work well-being (12,13). The treatment options for TN, especially for V1 branch involvement, are limited (14).

Although drug therapy may be effective in the

Table 2. *The baseline characteristics of the 2 groups.*

Variables	Total (n = 131)	Test Group (n = 39)	Training Group (n = 92)	*P*	Statistic
Age, n (%)				0.219	1.512
< 65y	42 (32)	9 (23)	33 (36)		
≥ 65y	89 (68)	30 (77)	59 (64)		
Gender, n (%)				0.312	1.023
Women	71 (54)	18 (46)	53 (58)		
Men	60 (46)	21 (54)	39 (42)		
Duration, n (%)				0.896	0.017
< 5years	70 (53)	20 (51)	50 (54)		
≥ 5years	61 (47)	19 (49)	42 (46)		
Primary Diagnosis, n (%)				0.548	0.361
No	47 (36)	16 (41)	31 (34)		
Yes	84 (64)	23 (59)	61 (66)		
Pre-NRS-11, n (%)				0.454	0.562
< 7	69 (53)	23 (59)	46 (50)		
≥ 7	62 (47)	16 (41)	46 (50)		
Surgery Type, n (%)				0.681	0.169
RFT	89 (68)	28 (72)	61 (66)		
PBC	42 (32)	11 (28)	31 (34)		
Affected Side, n (%)				0.269	1.224
Left	48 (37)	11 (28)	37 (40)		
Right	83 (63)	28 (72)	55 (60)		
Status, n (%)				0.41	0.677
Nonrecurrence	76 (58)	20 (51)	56 (61)		
Recurrence	55 (42)	19 (49)	36 (39)		

NRS-11 = Numeric Rating Scale

early stages, drug tolerance development with the disease's progression is a significant drawback, necessitating dose increases, often resulting in adverse effects (15,16). Minimally invasive surgical treatments for pain management, such as RFT and PBC, are associated with a high pain recurrence rate (17). Therefore, our study aimed to investigate the risk factors for postoperative pain recurrence of TN involving the V1 branch and establish a prediction model to identify high-risk patients, improve treatment effectiveness, and reduce pain recurrence rates.

The significance of our study lies in its analysis of risk factors, which can better guide individualized treatment for patients and improve surgical outcomes while reducing pain recurrence rates, thereby improving patients' quality of life.

The results show that age, pre-NRS-11 score, and surgery type are 3 independent risk factors affecting the 2-year pain recurrence rate, where patients under the age of 65, with pre-NRS-11 scores less than 7, and who underwent PBC, had a lower pain recurrence rate. These results suggest that caution should be exercised while performing minimally invasive surgical treatment

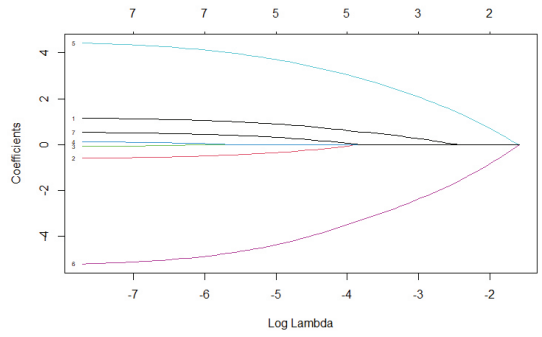

Fig. 1. *The variation of LASSO coefficients for different texture parameters as the super parameter (λ value) changes.*

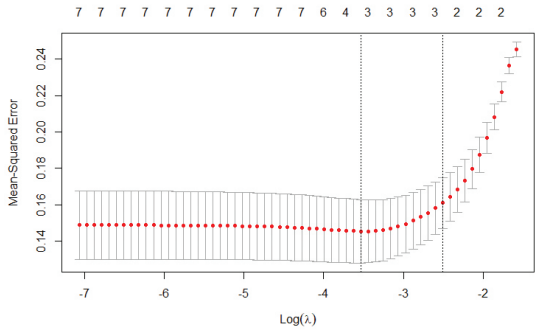

Fig. 2. *Texture feature selection in the LASSO model, showing the different super-parameters (λ value) corresponding to the diagnostic biases of the different models. The vertical dashed line on the left represents the minimum deviation of the log (λ) at the optimal λvalue, and the dashed line on the 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 postsurgery pain recurrence in patients with trigeminal nerve branch V1 pain.*

	β	SE	Wald	*P* value	OR	95% CI	
Age	1.836	0.523	12.321	< 0.001	6.274	2.250	17.494
Pre-NRS	3.341	0.626	28.460	< 0.001	28.261	8.280	96.460
Type	-2.678	0.476	31.688	< 0.001	0.069	0.027	0.174

NRS-11, numeric rating scale; SE, standard error; Wald, chi-square value, OR, odds ratio

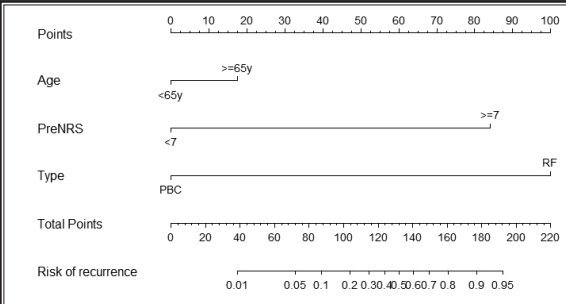

Fig. 3. *Nomogram for predicting the risk of postsurgery pain recurrence.*

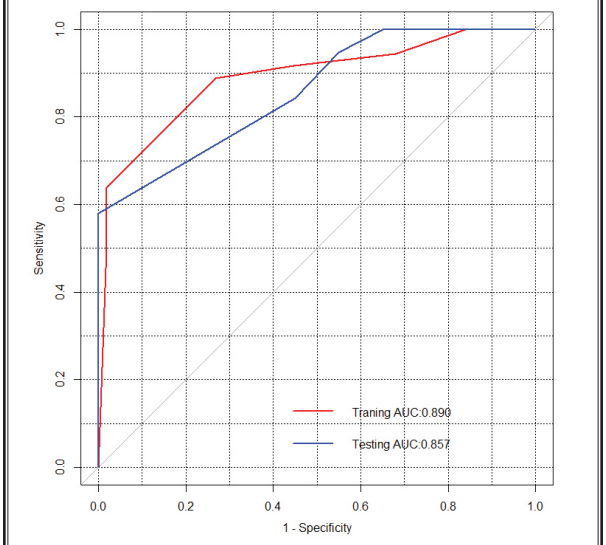

Fig. 4. *Receiver operating characteristic curve of the predictive nomogram for the risk of postsurgery pain recurrence.*

on elderly patients with severe TN. There was no significant correlation between pain recurrence rate and gender, disease duration, whether it was primary TN, or the affected side, which is similar to previous findings on the overall treatment of TN (18,19).

Elderly patients with TN often suffer from other comorbidities, which might increase their postoperative pain recurrence risk (20). A study reported that in elderly patients with TN, multiple sclerotic lesions could already be detected on magnetic resonance imaging before the TN symptoms appeared (21). Hypertension is another more common age-related disease that may contribute to TN pathogenesis, where vascular nerve compression causes TN (22). The blood vessels and nerves exist in close proximity, but TN is usually rare in the younger population; as the blood vessels thicken and harden with age due to hypertension, pressure gradually increases on the nerve, translating into TN (23).

Both RFT and PBC procedures aim to destroy a part of the nerve, thereby hindering pain signal transmission, resulting in pain alleviation. Still, these procedures fail to resolve the underlying cause, where continuous compression stimulation leads to postoperative pain recurrence (24). Although microvascular decompression (MVD) surgery can fundamentally resolve the problem of vascular compression, elderly patients often have a poor tolerance to craniotomy, contraindicating MVD surgery; currently, minimally invasive RFT and PBC are the best options for such patients (25,26).

Severe preoperative pain scores may also indicate a more severe condition (27), where such patients urgently need surgery and have higher expectations for postoperative outcomes. Severe and persistent pain

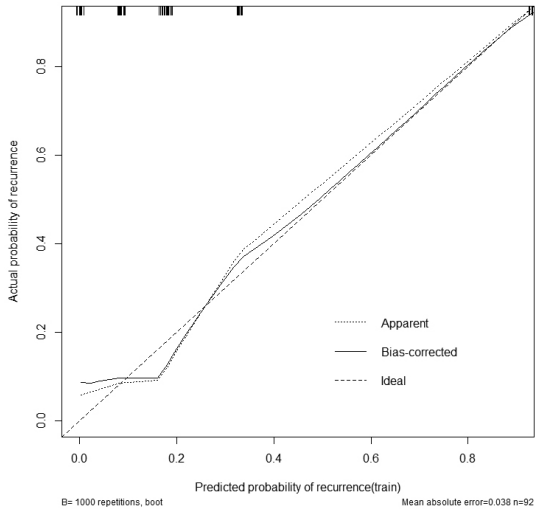

Fig. 5. *Calibration curve of the training group for predicting the risk of postsurgery pain recurrence by the predictive nomogram.*

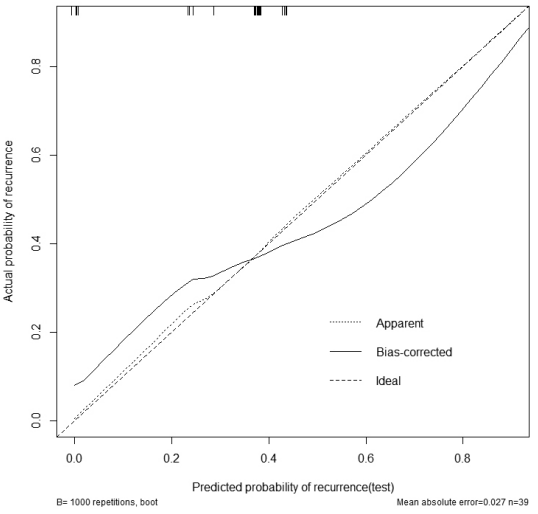

Fig. 6. *Calibration curve of the test group for predicting the risk of postsurgery pain recurrence by the predictive nomogram.*

can result in anxiety and depression (28), which often lead to a series of chain reactions (29), including insomnia, anorexia, and social problems, all of which cannot be resolved together with postoperative pain relief. Thus, long-term psychological problems may lead to an increase in the pain recurrence rate.

Some studies have reported that changing the puncture direction can improve the RFT's effectiveness for the trigeminal nerve V1 branch (30). However, temperature is the most critical factor affecting RFT success, where high temperatures can cause enough degeneration and nerve tissue necrosis within an acceptable range and distance of the target site, thereby preventing nerve regeneration (31). Treatment of the V2 and V3 branches with high-temperature RFT is usually performed at the foramen ovale, which has very stable therapeutic effects, but V1 being a particular branch, high-temperature RFT at the semilunar ganglion site may cause corneal ulcers, with the most severe cases leading to blindness. Therefore, high-temperature RFT for V1 branch treatment can only be performed at the more distant orbital fissure (32). Moreover, the key factors affecting the procedure's effectiveness in PBC are the compression time and balloon pressure (33). In our study, all included cases were treated using standardized surgical criteria (34) to reduce the bias caused by human factors.

A nomogram is a statistical model for creating a personalized prediction analysis of clinical events.

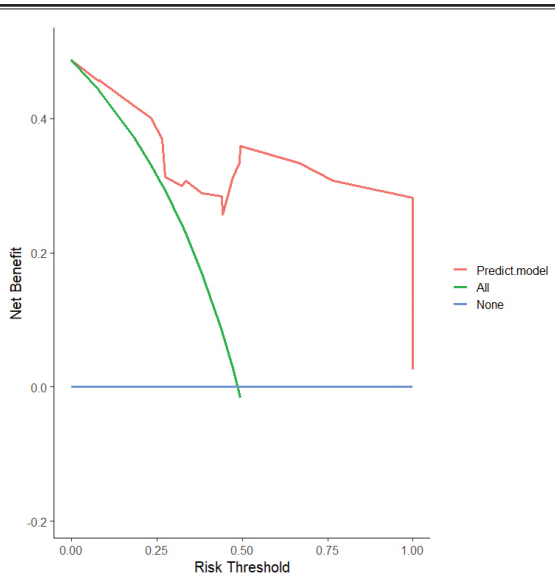

Fig. 7. *Decision curve analysis for predicting the risk of postsurgery pain recurrence by the predictive nomogram.*

Compared with other predictive statistical methods, the nomogram analysis provides better-personalized risk assessment through intuitive and visual means (35). In our study, 3 easy-to-collect patient clinical variables were analyzed using LASSO regression combined with multiple logistic regression analysis. All patients who met the inclusion criteria were randomly divided into

a training group (n = 92) and a testing group (n = 39) to evaluate predictive model performance. The results showed that the training group had an area under the ROC curve of 0.890 for predicting the nomogram, indicating high performance. When the established predictive model was validated, it showed good performance in terms of prediction accuracy, calibration curve, and DCA, indicating the excellent predictive ability of the model.

Limitations

This study had certain limitations, such as being a single-center study with a small sample size and a lack of external validation. Secondly, phone follow-up may not objectively reflect a patient's condition. Subsequent multicenter studies should be designed to validate the model.

Conclusion

This study successfully developed and validated a highly accurate nomogram prediction model (with age, pre-NRS-11 score, and surgery type as predictor variables) and envisaged improving early identification and screening for high-risk patients with postoperative pain recurrence in patients with TN V1 branch pain.

Author Contributions

Conception/design (KX); data acquisition (DY); data analysis (KX); data interpretation (DY and KX); drafting or revising (DY and KX); final approval (DY and KX). We agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved by all authors.

References

1. Terrier LM, Hadjikhani N, Destrieux C. The trigeminal pathways. *J Neurol* 2022; 269:3443-3460.
2. Freddi TAL, Ottaiano AC, Lucio LL, et al. The trigeminal nerve: Anatomy and pathology. *Semin Ultrasound CT MR* 2022; 43:403-413.
3. Ge X, Wang L, Pan L, et al. Amplitude of low-frequency fluctuation after a single-trigger pain in patients with classical trigeminal neuralgia. *J Headache Pain* 2022; 23:117.
4. Hammad Y, Mootz A, Klein K, et al. Trigeminal nerve repair: Is the trigeminocardiac reflex a concern? *J Oral Maxillofac Surg* 2021; 79:2355-2357.
5. Xie K, Liu S, Huang B, et al. Effects of supraorbital foramen variations on the treatment efficacy of radiofrequency therapy for V1 trigeminal neuralgia: A retrospective study. *Pain Res Manag* 2020; 2020:8142489.
6. Lu Z, Wang J, Cao Y, et al. Treatment of third branch trigeminal neuralgia with a balloon inflated in the foramen ovale. *Front Neurol* 2022; 13:826653.
7. Zhang H, Ni H, Liu S, et al. Supraorbital nerve radiofrequency for severe neuralgia caused by herpes zoster ophthalmicus. *Pain Res Manag* 2020; 2020:3191782.
8. Xia Y, Yu G, Min F, et al. The focus and new progress of percutaneous balloon compression for the treatment of trigeminal neuralgia. *J Pain Res* 2022; 15:3059-3068.
9. Radoš I. Treatment options for trigeminal neuralgia. *Acta Clin Croat* 2022; 61:96-102.
10. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia* 2018; 38:1-211.
11. Wang Z, Wang Z, Li K, et al. Radiofrequency thermocoagulation for the treatment of trigeminal neuralgia. *Exp Ther Med* 2022; 23:17.
12. Kc E, Islam J, Park YS. Trigeminal ganglion itself can be a viable target to manage trigeminal neuralgia. *J Headache Pain* 2022; 23:150.
13. Cruccu G, Di Stefano G, Truini A. Trigeminal neuralgia. *N Engl J Med* 2020; 383:754-762.
14. Diener HC, Tassorelli C, Dodick DW. Management of trigeminal autonomic cephalalgias including chronic cluster: A review. *JAMA Neurol* 2023; 80:308-319.
15. Finnerup NB. Trigeminal neuralgia and the merit of small clinical trials. *Lancet Neurol* 2022; 21:951-953.
16. Schott Andersen AS, Maarbjerg S, Noory N, et al. Safety and efficacy of erenumab in patients with trigeminal neuralgia in Denmark: A double-blind, randomised, placebo-controlled, proof-of-concept study. *Lancet Neurol* 2022; 21:994-1003.
17. Lv W, Hu W, Chi L, et al. Factors that may affect recurrence of trigeminal neuralgia after percutaneous balloon compression. *J Clin Neurosci* 2022; 99:248-252.
18. Zheng JH, Sun K, Zhang HT, et al. A study on the recurrence rate of trigeminal neuralgia after MVD and the related factors. *J Neurol Surg B Skull Base* 2020; 81:572-578.
19. Hong JH, Lee JY, Kim SJ, et al. Retrospective analysis of clinical feature in trigeminal neuralgia. *Pain Physician* 2023; 26:39-44.
20. Ge X, Wang L, Pan L, et al. Alteration of the cortical morphology in classical trigeminal neuralgia: Voxel-, deformation-, and surface-based analysis. *J Headache P*ain 2023; 24:17.
21. Dilwali S, Mark I, Waubant E. MRI lesions can often precede trigeminal neuralgia symptoms by years in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2022; 94:189-192.
22. Chen Q, Yi DI, Perez JNJ, et al. The Molecular basis and pathophysiology of trigeminal neuralgia. *Int J Mol Sci* 2022; 23:3604.
23. Zhang H, Liu M, Guo W, et al. The effect of trigeminal ganglion block on trigeminocardiac reflex in elderly patients with trigeminal neuralgia undergoing percutaneous balloon

compression: A randomized controlled study. *Ther Clin Risk Manag* 2022; 18:1091-1098.

24. Sadashiva N. Microvascular decompression for trigeminal neuralgia with concomitant persistent primitive trigeminal artery. *Neurology India* 2021; 69:826-828.
25. Andersen ASS, Heinskou TB, Rochat P, et al. Microvascular decompression in trigeminal neuralgia - A prospective study of 115 patients. *J Headache Pain* 2022; 23:145.
26. Ichimasu N, Nakajima N, Matsushima K, et al. Microvascular decompression for trigeminal neuralgia caused by trigeminocerebellar artery. *Neurosurg Focus Video* 2020; 3:V4.
27. Salis B, Svensson P, Exposto FG. Referred sensation location can be altered by a strong heterotopic nociceptive stimulus: Implications for clinical pain conditions. *Pain* 2023; 164:e242-e250.
28. Kendler KS. Melancholia as psychalgia: The integration of psychophysiological theory and psychopathologic observation in the mid-19th century. *Mol Psychiatry* 2022; 28:230-235.
29. Singhota S, Tchantchaleishvili N, Wu J, et al. Long term evaluation of a multidisciplinary trigeminal neuralgia service. *J Headache Pain* 2022; 23:114.
30. Wang T, Xu S, He Q, et al. Efficacy and safety of radiofrequency thermocoagulation with different puncture methods for treatment of V1 trigeminal neuralgia: A prospective study. *Pain Physician* 2021; 24:145-152.
31. Scott-Solomon E, Hsu YC. Neurobiology, stem cell biology, and immunology: An emerging triad for understanding tissue homeostasis and repair. *Annu Rev Cell Dev Biol* 2022; 38:419-446.
32. Mousavi SH, Gehling P, Burchiel KJ. The long-term outcome of radiofrequency ablation in multiple sclerosis-related symptomatic trigeminal neuralgia. *Neurosurgery* 2022; 90:293-299.
33. Ding Y, Wang Y, Wang Y, et al. A retrospective study to examine the association of different pear-shaped balloons with efficacy and postoperative complications in percutaneous balloon compression for trigeminal neuralgia. *Neurosurg Rev* 2023; 46:60.
34. Huang B, Yao M, Chen Q, et al. Awake CT-guided percutaneous stylomastoid foramen puncture and radiofrequency ablation of facial nerve for treatment of hemifacial spasm. *J Neurosurg* 2021; 135:1459-1465.
35. Jiang S, Fang J, Yu T, et al. Novel model predicts diabetic nephropathy in type 2 diabetes. *Am J Nephrol* 2020; 51:130-138.