Retrospective Study

Correlation Between Meckel's Cave Size and Iohexol Dosage in Percutaneous Microballoon Compression for Trigeminal Neuralgia of Aged Patients

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Background: Percutaneous microballoon compression (PMC) is a safe and effective method (1) for treating trigeminal neuralgia (TN). Though many surgeons have carried out this kind of surgery, practitioners who lack sufficient surgical experience may be unaware of this method of improving the clinical effectiveness of PMC for aged patients.

Objective: To investigate the relationship among the success of the PMC method, the size of a patient's Meckel's cave (MC), and the iohexol dosage in a pear-shaped balloon and form a mathematical model for the effectiveness of the treatment.

Study Design: Retrospective study.

Setting: Neurosurgery Department of Tongling People's Hospital, China.

Methods: One hundred eighteen patients (34 men and 84 women) undergoing PMC, aged 72.07 ± 7.10 years old, were collected retrospectively in the study. Fifteen of the patients were in Tongling People's Hospital from September 2022 to March 2024, and 103 were in Nanjing Drum Tower Hospital from January 2023 to October 2023, The sizes of all the patients' MCs were measured by 3D-Slicer software with preoperative cranial magnetic resonance imaging (MRI); all balloons were of the standardized pear shape, and intraoperative iohexol dosages were recorded. The patient's score on the Barrow Neurological Institute pain scale (BNI-P) was recorded at 3 time points: before the surgery (Pre_BNI), the first day after the surgery (BNI_1), and the seventh day after the surgery (BNI_7). Correlation analysis was carried out to determine the association between the intraoperative iohexol dosage and MC size.

Results: The overall effective rate of PMC was 97.46% (115/118). During the first postoperative day, 3 patients reported feeling pain scores of V on the BNI-P scale. None of the other patients reported an experience of pain. At the 7th day of post-operation, those 3 patients still felt no pain relief, whereas the others continue not to experience pain. There was a significant correlation between iohexol dosage (unit: mL) and MC size (expressed as MC volume, unit: mm^3): iohexol dosage (mL) = 0.54336 + 0.00060286 x MC Volume (mm^3) - 0.05654 x BNI_1*. (*The scores from 1 to 5 are equivalent to I to V on the BNI-P.)

Limitations: The study was retrospective, so we could not validate the accuracy of the model by analyzing the iohexol dosage used in the operation; additionally, the duration of the follow-up was short, and the sample size was relatively small.

Conclusions: The equation (iohexol dosage = 0.54336 + 0.00060286 x MC Volume - 0.05654 x BNI_1) yields a value at which operations have a very high success rate, regardless of whether the patients have received previous TN treatment. The equation can be used to guide the intraoperative usage of iohexol and to help surgeons without sufficient surgical experience for predicting patients' prognoses.

Key words: Trigeminal neuralgia, percutaneous microballoon compression, iohexol dosage, 3D Slicer, Meckel's cave

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Trigeminal neuralgia is defined as a unilateral disorder characterized by a sudden, recurrent, brief, shock-like, or stabbing episode of pain in the distribution of one or more divisions of the trigeminal nerve (2). This condition is one of the most painful disorders known (3). TN pain can be triggered by daily activities such as talking, brushing teeth, chewing, and touching the face (4). The 2 types of the condition are known as primary TN (PTN) and secondary TN (5). PTN is usually caused by neurovascular compression, which refers to the compression of blood vessels (6) on the trigeminal root near the brain stem. The closer the compression is to the brain stem, the more likely symptoms are to appear.

For gerontic patients who cannot tolerate major surgery or do not respond to medication, percutaneous microballoon compression (PMC) is a safe and effective method of treating TN (7). In PMC, a pear-like shape is usually the standard compression configuration for a balloon (8). However, a pear-like balloon alone is not enough to achieve a successful surgery for some patients because they experience postoperative pain (9), especially if the operation is carried out by surgeons without sufficient surgical experience (10).

Therefore, to help surgeons who lack much professional experience, this study aims to determine a standardized and objective approach to eliminate the expertise gap among doctors of different levels of abilities. Few studies have reported the correlations among MC size, iohexol dosage, and BNI-P score after PMC. In an effort to improve the effectiveness of PMC, we expect to explore the associations of iohoxel dosage with MC size and BNI-P score after PMC surgery from this study of 118 patients who have undergone the procedure.

Methods

Study Design and Setting

This study was a retrospective one meant to investigate 118 patients who were treated in 2 hospitals and underwent PMC from September 2022 to March 2024. The patients' BNI-P scores were routinely measured at pre-operation, the first postoperative day (POD1), and the seventh postoperative day (POD7). The requirement for informed consent was waived because of the retrospective nature of the study.

Inclusion criteria: (1) diagnosis of PTN; (2) preoperative BNI-P scores = V; (3) age of patients ≥ 60 years old; (4) strictly unilateral craniofacial pain; (5) no other comorbid chronic headache disorder, such as migraine or tension-type headache.

Exclusion criteria: (1) STN diagnosis; (2) preoperative BNI-P scores < V; (3) inability to accurately comprehend or respond to the questionnaire; (4) preoperative blood routine, coagulation function, liver and kidney function, electrocardiogram, etc. indicating surgical contraindications.

Instruments and Equipment

Tongling People's Hospital: Digital subtraction angiography machine, disposable balloon catheter kit for brain surgery.

Nanjing Drum Tower Hospital: C-arm, disposable balloon catheter kit for brain surgery.

MC Size Measurement

MRI images in DICOM format were transferred to 3D Slicer software for the reconstruction of MC images and the calculation of each MC's volume (Fig. 1).

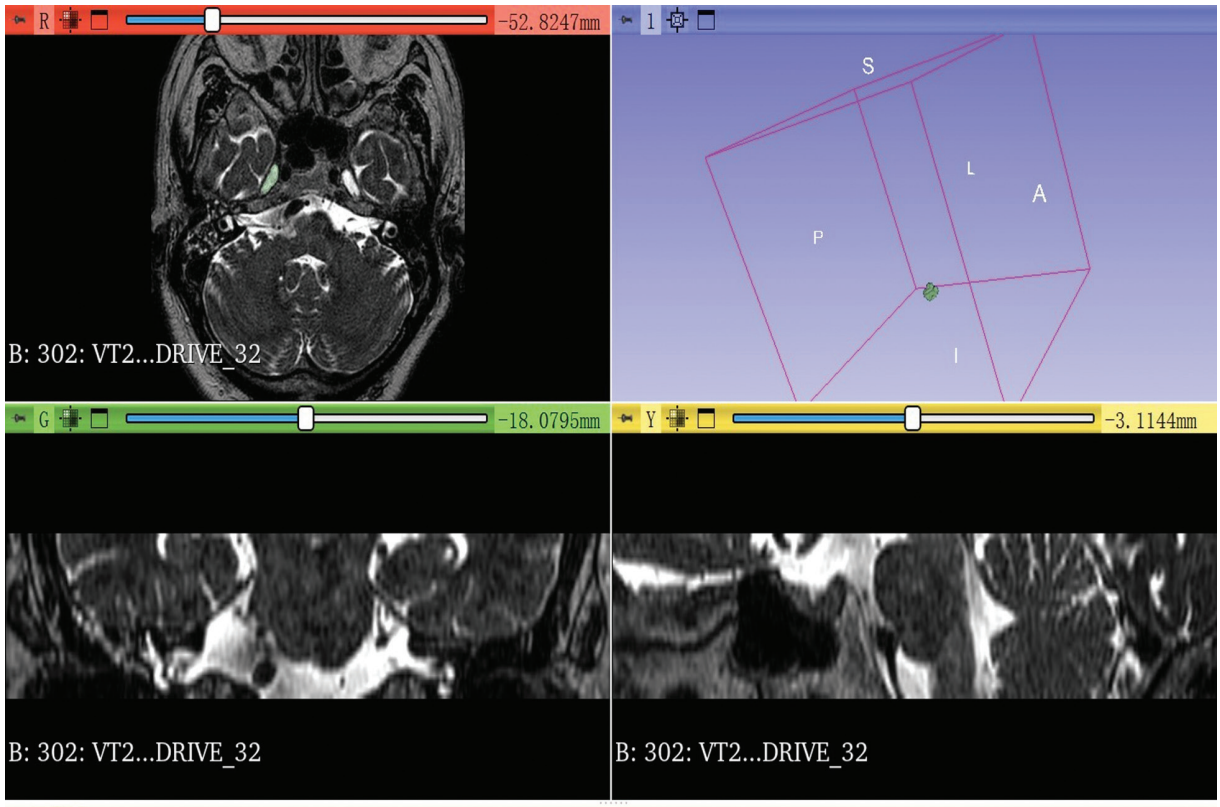
Procedures for PMC Treatment

All patients were in the supine position with the head slightly tilted back after successful general anesthesia. The needles were punctured into the oval foramen under fluoroscopic guidance by C-arm or digital subtraction angiography guidance following 2 projections. One was an anterior-posterior projection of the puncture path between a puncture point and the pupil of the affected side, and the other was a lateral projection between a puncture point and the affected anterior external auditory canal (11).

After the air was evacuated from the balloon, the balloon was placed into the MC. Subsequently, the balloon was slowly filled with an iohexol contrast agent. After we obtained a lateral view of the skull, the standard pear-shaped balloon was formed (Fig. 2), and continuous compression was applied. After compression, the contrast agent was drained out of the balloon and the catheter with the balloon was withdrawn. The puncture site was covered with a bandage. Following anesthesia recovery and extubation, patients were transferred to the general ward. The contrast agent dosage and compression time were recorded. No patient experienced severe postoperative complications.

Follow-Up Evaluation

Patients' postoperative pain was assessed on the BNI-P scale. Follow-up visits were conducted and documented at POD1 and POD7.



	A	B	C	D
1	Segment	Number of voxels [voxels]	Volume [mm3] (1)	Volume [cm3] (1)
2	Segment_1	14215	335.523	0.335523

Fig. 1. *The reconstruction and volume of MC.*

Statistical Analysis

The basic characteristics and regression analysis were processed by the statistical software program SAS 9.4. Differences were considered statistically significant at $P < 0.05$. Continuous variables are presented as mean ± standard deviation, while categorical data are shown as frequencies (percentages). Spearman's correlation analysis was used to analyze correlations.

The construction and validation of the decision tree model were conducted via RStudio version 2023.06.2 + 561 (Posit), a robust open-source tool widely used for statistical analysis and data modeling. The decision tree model was built using the rpart package in R.

We evaluated the model's performance using ROC (receiver operating characteristic) curves, which were generated using the multiclass.roc function from the pROC package and calculated the area under the curve (AUC) for each category.

Results

Baseline of clinical characteristics: A total of 118 patients who underwent PMC were recruited. The demographic information and clinical characteristics of all patients are shown in Table 1. We observed a total effectiveness of 97.46% (115/118) and a failure rate of 2.54% (3/118) for the PMC procedure.

The full logistic regression model indicated that no factors were statistically significant with the dependent variable of "BNI_1" from Table 2.

The full logistic regression model indicated that no factors were statistically significant with the dependent variable of "BNI_7" from Table 3.

Fig. 2. *A pear-shaped balloon.*

The linear regression analysis indicated a linear relationship between the dosage of iohexol used and the MC size and BNI_1. The linear relationship of iohexol dose, MC size, and BNI_1 is statistically significant (Table 4). The adjusted R^2 is 0.12. The linear regression model could be applied to surgeons' considerations of the iohexol dosage to use before performing PMC. Further validation is needed for this generalization.

ROC curve analysis was performed on this mathematical model. Initially, we preprocessed the data to categorize the dosage of intraoperative iohexol into distinct groups. The following classification rules were applied to determine which level of dosage to sort into which group:

- Iohexol_dosage < 0.6: Classified as "< 0.6";
- 0.6 ≤ Iohexol_dosage < 0.8: Classified as "≥ 0.6 and < 0.8";
- Iohexol_dosage ≥ 0.8: Classified as "≥ 0.8".

To ensure the reliability and predictive power of our model, we divided the dataset into a training set and a validation set. The training set, which comprised 80 patients (70% of the total sample), was used for model training and parameter tuning. The validation set comprised 35 patients (30% of the total sample) and was used for assessing the model's performance and generalizability.

Table 1. *Basic characteristics of patients (n = 118).*

Characteristics	Value*
No. of patients (n)	118
Age (years)	72.07 ± 7.10
Gender (Male/Female)	34 (28.81%)/84 (71.19%)
Pre_DBP (mmHg)	83.86 ± 10.67
Pre_SBP (mmHg)	138.91 ± 17.78
Pre_BNI (V/I)	118 (100%)/0(0%)
BNI_1 (V/I)	3 (2.54%)/115 (97.46%)
BNI_7 (V/I)	3 (2.54%)/115 (97.46%)
Compress_time (min)	2.79 ± 0.70
Iohexol_dosage (mL)	0.71 ± 0.17
MC_volume (mm3)	379.32 ± 136.98
Ratio	2.08 ± 0.88
DM_history (Y/N)	17 (14.41%)/101 (85.59%)
Hypertension_level (I level/II level/III level/unrecorded level)	12 (10.17%)/32 (27.12%)/14 (11.86%)/ 60(50.85%)
Stroke_history (Y/N)	8 (6.78%)/110 (93.22%)
PTN (Y/N)	118 (100%)/0 (0%)
RTN (Y/N)	35 (29.66%)/83 (70.34%)
Preoperative_pain_site (Left/Right)	51 (43.22%)/67 (56.78%)
Postoperative_pain_site (Left/Right/No)	2 (1.69%)/1 (0.85%)/115 (97.46%)
Pain_tri (singular/binary/triple)	(38.98%)/58 (49.15%)/14 (11.86%)

* Continuous variables are presented as mean ± standard deviation, while categorical data are shown as frequencies (percentages).
Ratio = value of iohexol_dosage (mL) /value of MC_volume(cm^3).
Abbreviations: DBP: diastolic blood pressure; SBP: systolic blood pressure; Pre_BNI: preoperative BNI-P score; BNI_1: BNI-P score at the postoperative day 1; BNI_7: BNI-P score at the postoperative day 7; V/I:BNI-P score=V/ BNI-P score=I; DM: diabetes mellitus; PTN: primary trigeminal neuralgia; RTN: recurrent trigeminal neuralgia; Y/N: Yes/No; Pain_tri: number of branches of trigeminal neuralgia

The decision tree model was developed to identify key features and factors influencing the classification of the iohexol dosage. The construction of the decision tree involved the following steps:

- Initialization at the root node: Starting with the root node that contained all the data;
- Recursive data splitting: Through the use of optimal splitting criteria (such as Gini index or information gain), the dataset was recursively split into multiple subsets until stopping conditions were met (e.g., maximum tree depth or minimum node size);
- Formation of leaf nodes: When further splitting was neither possible nor beneficial, the process

stopped, and each leaf node represented a final classification.

The resulting tree structure provided a clear and interpretable representation of how different patient characteristics related to the iohexol dosage classifications, summarized in Fig. 3.

The multi-class area under the curve (AUC) equals to 0.6597 for those 3 iohexol dosage levels (< 0.6, 0.6-0.8 and ≥ 0.8), over 0.5 and close to 1.0, indicating a good accuracy for the model. The result of sensitivity and specificity is shown in Fig. 4.

Discussion

TN is a common type of pain in the head and face characterized as paroxysmal stabbing pain provoked by stimuli (12). The condition severely affects patients' ordinary lives. Microvacular decompression (MVD) is a usually direct and complex therapy for treating TN that can precisely solve the arterial compression and effectively relieve the pain symptoms involved (13). However, the procedure can lead to severe complications (14) like cerebrospinal fluid leakage, brain stem infarction, and even death. Many senile patients are not eligible for MVD because they cannot tolerate surgeries that may cause major trauma and severe complications (15,16). As a minimally invasive treatment for TN, PMC is known to be safe and effective for elderly patients with underlying diseases (17). Therefore, these patients need PMC not only for its minimally invasive nature but also its immediate pain relief, low recurrence rate, and small number of complications (18). More importantly, PMC operations can be repeated (19) if TN recurs. Other therapeutic methods, including percutaneous glycerol rhizolysis and percutaneous radiofrequency treatments, have lower rates of effective pain relief (20).

PMC is a reliable method of treating TN, and the key to the success of the procedure lies in its effective compression of the Gasserian ganglion. The common cure ratio is 91%-92% (21,22). Though a pear-shaped balloon is a sign of surgical success and an important factor affecting the prognosis, the sight of a piriform balloon alone does not guarantee that the compression will be successful. The effectiveness of the treatment still relies on the subjective expertise of the clinicians (23). Surgeons with more expertise can master subjective judgment more effectively and thereby reduce the failure rate of the treatment. Even though all balloons achieved the optimal pyriform in this study, the rate of effective treatment by surgeons with less operational experience in Tongling People's Hospital from September 2022 to March 2024 was 86.67% (13/15). In Nanjing Drum Tower Hospital, from January 2023 to October 2023, surgeons with more experience achieved a success rate of 99.03% (102/103). As can be seen, a pyriform balloon is not in and of itself an accurate indication of a successful treatment. Currently, there is no effectively objective criterion for reducing the uncertainty associated with subjective experience and judgment.

The aim of this study was to discover a standardized and objective procedure for eliminating the experience gap. As seen in Tables 2 and 3, no significant relationship was found between pain relief and age, gender, underlying diseases, or MC size. Therefore,

Table 2. *Logistic regression of BNI_1 with factors.*

Parameters	Estimate	SD	Wald	*P* value
Intercept	22.277	660372	0	1
Preoperative_pain_site	3.58E-11	66.4796	0	1
Pain_tri	3.14E-11	50.6543	0	1
Age	7.27E-12	4.8328	0	1
Sex	8.69E-12	73.9125	0	1
Hypertension_level	-2.61E-11	30.8029	0	1
DM_history	3.01E-11	92.494	0	1
MC_volume	-1.41E-12	0.36	0	1
Ratio	-5.16E-11	50.4399	0	1
BNI_7	-10.5899	660372	0	1

Table 3. *Logistic regression on BNI_7 with factors.*

Parameters	Estimate	SD	Wald	*P* value
Intercept	22.277	660372	0	1
Preoperative_pain_site	3.58E-11	66.4796	0	1
Pain_tri	3.14E-11	50.6543	0	1
Age	7.27E-12	4.8328	0	1
Sex	8.69E-12	73.9125	0	1
Hypertension_level	-2.61E-11	30.8029	0	1
DM_history	3.01E-11	92.494	0	1
MC_volume	-1.41E-12	0.36	0	1
Ratio	-5.16E-11	50.4399	0	1

Table 4. *Linear regression on iohexol_dosage with MC volume and BNI_1.*

Parameters	Estimate	SD	t	*P* value
Intercept	0.54336	0.04806	11.3	< 0.0001
MC_volume	0.00060286	0.00012785	4.72	< 0.0001
BNI_1	-0.05654	0.0277	-2.04	0.0435

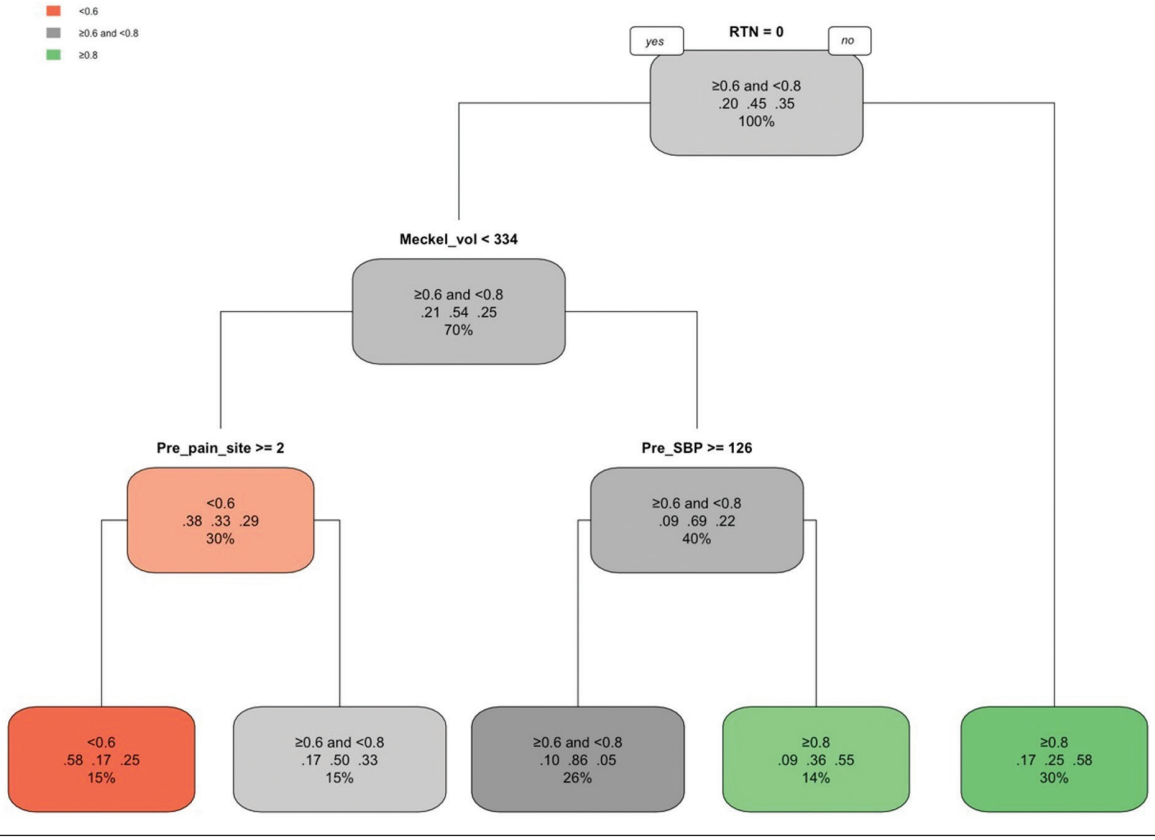


Fig. 3. *The decision tree model.*
Note: The following 4 variables included in the model: RTN, MC_volume (expressed as Mechel_vol), Preoperative_pain_site (expressed as Pre_pain_site), and Pre_SBP. Line 1 stands for the iohexol_dosage group; Line 2 stands for the probability of the observation in each dosage group; Line 3 stands for the proportion of the sample size.

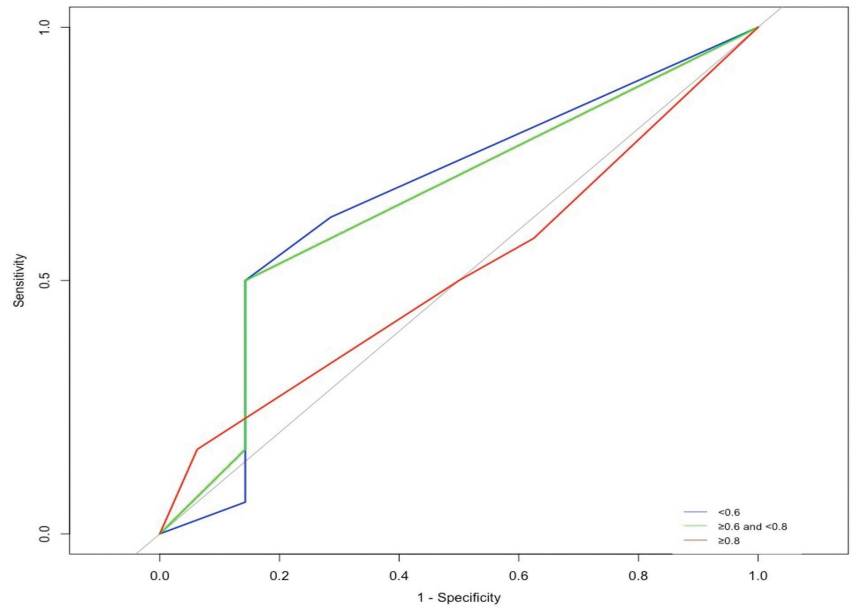


Fig. 4. *The sensitivity and specificity of the ROC curve.*

it is not possible to judge the effectiveness of a PMC procedure by the size of the MC. Similarly, there is no correlation between compression time and operation success. A longer duration of compression does not improve the rate of pain relief but rather increases the rate of complications (24).

As shown in Table 4, iohexol dosage has a correlation with MC size and BNI_1. The linear correlation between iohexol dosage and MC size is positive, whereas the correlation between iohexol dosage and BNI_1 is negative. A standardized mathematical model was constructed to predict the relationship of iohexol dosage, MC size, and BNI_1. The prediction formula is as follows: iohexol dosage = 0.54336 + 0.00060286 x MC Volume -0.05654 x BNI_1. When BNI_1 = 1, meaning complete pain relief, the formula can be reduced to iohexol dosage = 0.54336 + 0.00060286 x MC volume - 0.05654, which becomes a simple linear positive correlation equation. The equation is easy to master and can assist surgeons in calculating the iohexol dosage to use and judging the extent of pain relief.

From the analysis of the ROC curve, it can be shown that the multi-class area under the curve (AUC) equals 0.6597, demonstrating a good accuracy for the model.

It is worth noting why experienced physicians can achieve a higher pain relief rate even if all surgeons can obtain the optimal pyriform for balloons during compression. The answer may lie in the anatomy of the MC structure. The MC is formed by continuous dura mater, not a bony cave (25). Therefore, during the compression process, the shape of the MC can change as the balloon expands, which may lead to changes in the volume of the MC. Thus, the regular volume of iohexol dosage associated with optimal pyriform compression does not always mean complete compression. As a result, the success of the operation still depends on the experience and tactile feeling of the surgeons involved. In this study, the prediction formula is effectively able to reduce the failure that accompanies subjective inexperience and help physicians achieve objective judgment of optimal balloon compression.

In this study, the volume of each patient's MC was calculated by 3D Slicer software (Brigham and Women's Hospital), and the 3-dimensional shape of the MC and its surrounding structure was intuitively observed by this software preoperatively. Intraoperatively, surgeons can compare the 3D structure of the MC and its 2D shape by contrast-enhanced images. By this method, surgeons can obtain judge the effectiveness of balloon compression more directly and objectively.

Limitations

The study was retrospective, so it could not analyze the iohexol dosage and MC size during an operation to validate the accuracy of the model. Additionally, the duration of the follow-up was only 7 days; and the sample size was relatively small. All those limitations might have contributed to bias in the final results.

A prospective study with a long follow-up duration and a larger sample size should be performed to further investigate the accuracy of the model.

Conclusions

Based on the available evidence, PMC is an effective and minimally invasive method of pain relief for elder patients suffering from TN. Preoperative measurement of MC size and iohexol dosage calculation are simple, effective, and convenient steps that surgeons can take to improve their chances of achieving successful operations that give patients complete pain relief.

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