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Original Contribution

Predicting postoperative delirium after microvascular decompression surgery with machine learning

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ABSTRACT

Objective: The aim of this study was to predict early delirium after microvascular decompression using machine learning.
Design: Retrospective cohort study.
Setting: Second Hospital of Lanzhou University.
Patients: This study involved 912 patients with primary cranial nerve disease who had undergone microvascular decompression surgery between July 2007 and June 2018.
Interventions: None.
Measurements: We collected data on preoperative, intraoperative, and postoperative variables. Statistical analysis was conducted in R, and the model was constructed with python. The machine learning model was run using the following models: decision tree, logistic regression, random forest, gbm, and GBDT models.
Results: 912 patients were enrolled in this study, 221 of which (24.2%) had postoperative delirium. The machine learning Gbm algorithm finds that the first five factors accounting for the weight of postoperative delirium are CBZ use duration, hgb, serum CBZ level measured 24 h before surgery, preoperative CBZ dose, and BUN. Through machine learning five algorithms to build prediction models, we found the following values for the training group: Logistic algorithm (AUC value = 0.925, accuracy = 0.900); Forest algorithm (AUC value = 0.994, accuracy = 0.948); GradientBoosting algorithm (AUC value = 0.994, accuracy = 0.970) and DecisionTree algorithm (aucvalue = 0.902, accuracy = 0.861); Gbm algorithm (AUC value = 0.979, accuracy = 0.944). The test group had the following values: Logistic algorithm (aucvalue = 0.920, accuracy = 0.901); DecisionTree algorithm (aucvalue = 0.888, accuracy = 0.883); Forest algorithm (aucvalue = 0.963, accuracy = 0.909); GradientBoostingc algorithm (aucvalue = 0.962, accuracy = 0.923); Gbm algorithm (AUC value = 0.956, accuracy = 0.920).
Conclusion: Machine learning algorithms predict the occurrence of delirium after microvascular decompression with an accuracy rate of 96.7%. And the major risk factors for the development of post-cardiac delirium are carbamazepine, hgb, and BUN.

1. Introduction

Microvascular decompression (MVD) is a common neurosurgical treatment option for patients with primary cranial nerve disease, including trigeminal neuralgia, facial spasm, and glossopharyngeal pain, and various forms of neurovascular compression [1]. However, delirium is a common complication after MVD surgery, with a reported incidence of 14.9%–27.3% [2]. Postoperative delirium is an acute, but transient, organic brain syndrome characterized by disturbed attention span and altered levels of consciousness [3]. Delirium following surgery is deleterious to patient prognosis. This can increase time in the ICU, incidence of complications, hospital stays, hospital costs, and probability of further convalescence after surgery [4] [5]. Similarly, delirium after MVD surgery tends to prolong hospital stays and increase medical costs, as well as morbidity and mortality [6]. Therefore, an in-depth understanding of risk factors and populations at risk for postoperative delirium (PODE) is needed to identify high-risk patients and possible therapeutic interventions.

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Machine learning is an interdisciplinary field. It refers to using computer simulation of an act to realize human learning. Because of its advantages such as efficiency, accuracy and universality, increasing attention has been paid to the application of artificial neural networks and emerging deep learning across various fields of society [7]. The combination of machine learning and medicine has become a hot spot, and has achieved fruitful results in just a few years, among which computer-aided diagnosis is most prominent [8] [9]. Oh et al. used the support vector machine classifier in machine learning to predict the occurrence of delirium in ICU patients [10]. Similarly, Corradi et al. [11] used the random classifier in machine learning to predict the occurrence of delirium in hospitalized patients. In this study, the area generated under the receiver operating characteristic curve (ROC AUC) was 0.909. Additionally, based on information from 302 patients, Bello et al. [12] used deep learning to construct survival prognosis for cardiac patients.

At present, there is no existing research on machine learning models and delirium after MVD surgery. We hope our findings will indicate possible clinical interventions to minimize the risk of PODE in these patients.

2. Methods

The present study has been approved by the Medical Ethics Committee at the Second Hospital of Lanzhou University (2018A-005). It has been conducted in accordance with the principles of the Declaration of Helsinki. The Ethics Committee has waived the requirement for personal informed consent, as it is a retrospective study of electronic medical records.

2.1. Patients

This retrospective study involved patients with primary cranial nerve disease who had undergone MVD surgery between July 2007 and June 2018. None of these patients had any abnormalities in preoperative imaging, such as multiple sclerosis, vascular malformation, or tumors. In addition, no patients had psychiatric histories. All patients had undergone MVD using the same surgical technique, performed by the same senior neurosurgeon, under the same anesthesia.

2.2. Diagnostic criteria for PODE

For all patients, the delirium observation screening score was calculated 3 times a day, from the second to the fifth postoperative day [13]. For patients with a score of 3 or more, a psychiatrist was asked to confirm the PODE diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM V, 2013) [14]. Patients who did not experience delirium within the first 5 days after surgery were included in the non-PODE group.

2.3. Data collection

We collected data on preoperative, intraoperative, and postoperative variables. Preoperative variables were age, sex, body mass index, smoking (smoking within 3 months prior to surgery), alcohol use (alcohol use within 3 months prior to surgery), heart disease (coronary artery disease, myocardial infarction, and unstable angina), hypertension (blood pressure > 140/90 mmHg), diabetes mellitus, and cerebrovascular disease. Intraoperative variables were mean operative time, affected vessels, and mean blood loss. Postoperative variables were intensive care unit (ICU) length of stay and fever (temperature > 38 °C).

We also recorded the following postoperative laboratory data measured within 3 days after surgery: hemoglobin, white blood cell count, serum sodium, serum potassium, blood urea nitrogen (BUN), and creatinine. In addition, we collected the following details on carbamazepine (CBZ) treatment: history of preoperative CBZ treatment, preoperative CBZ dose, mean CBZ use time, and serum CBZ level before surgery and 24 h after surgery.

Table 1
Baseline data.

Delirium	No	Yes	P-value
N	691	221	
Age (years)	59.2 ± 10.2	61.0 ± 11.7	0.072
BMI (kg/m^2)	25.2 ± 2.6	25.3 ± 2.7	0.470
Mean operative time (min)	155.1 ± 12.9	156.1 ± 13.9	0.549
Mean blood loss (mL)	331.4 ± 30.7	328.7 ± 32.1	0.334
HGB (g/L)	100.1 ± 4.4	100.7 ± 4.8	0.117
WBC (×109/L)	10.7 ± 2.2	10.9 ± 2.0	0.275
Serum Na (mmol/L)	136.96 ± 24.4	136.95 ± 22.5	0.293
BUN (mmol/L)	4.0 ± 0.4	4.0 ± 0.3	0.859
CREA (μmol/L)	80.3 ± 28.5	81.5 ± 2.6	< 0.001
Duration of CBZ use (years)	4.9 ± 0.6	6.0 ± 0.8	< 0.001
Preoperative CBZ (μg/mL)	5.3 ± 1.1	6.1 ± 1.2	< 0.001
Postoperative CBZ (μg/mL)	1.4 ± 0.2	1.4 ± 0.2	0.325
Gender			< 0.001
Female	461 (66.7%)	97 (43.9%)	
Male	230 (33.3%)	124 (56.1%)	
Smoking (n, %)			0.862
No	556 (80.5%)	179 (81.0%)	
Yes	135 (19.5%)	42 (19.0%)	
Alcohol use (n, %)			0.502
No	591 (85.5%)	193 (87.3%)	
Yes	100 (14.5%)	28 (12.7%)	
Cardiac disease (n %)			< 0.001
No	628 (90.9%)	181 (81.9%)	
Yes	63 (9.1%)	40 (18.1%)	
Hypertension (n, %)			< 0.001
No	581 (84.1%)	155 (70.1%)	
Yes	110 (15.9%)	66 (29.9%)	
Diabetes mellitus (n, %)			0.019
No	563 (81.5%)	164 (74.2%)	
Yes	128 (18.5%)	57 (25.8%)	
Cerebrovascular disease (n, %)			0.006
No	510 (73.8%)	142 (64.3%)	
Yes	181 (26.2%)	79 (35.7%)	
ICU stay (days)			0.210
1	32 (4.6%)	19 (8.6%)	
2	189 (27.4%)	62 (28.1%)	
3	239 (34.6%)	68 (30.8%)	
4	181 (26.2%)	54 (24.4%)	
5	50 (7.2%)	18 (8.1%)	
Temperature > 38 °C (n, %)			0.981
No	607 (87.8%)	194 (87.8%)	
Yes	84 (12.2%)	27 (12.2%)	
Sleep disturbance (n, %)			< 0.001
No	658 (95.2%)	175 (79.2%)	
Yes	33 (4.8%)	46 (20.8%)	
Mount Fuji sign (n, %)			< 0.001
No	628 (90.9%)	164 (74.2%)	
Yes	63 (9.1%)	57 (25.8%)	
Preoperative CBZ dose (mg)			< 0.001
400	1 (0.1%)	0 (0.0%)	
500	75 (10.9%)	1 (0.5%)	
550	217 (31.4%)	13 (5.9%)	
600	169 (24.5%)	5 (2.3%)	
650	136 (19.7%)	46 (20.8%)	
700	52 (7.5%)	61 (27.6%)	
750	40 (5.8%)	55 (24.9%)	
800	1 (0.1%)	40 (18.1%)	
Preoperative CBZ therapy (n, %)			0.006
No	185 (26.8%)	39 (17.6%)	
Yes	506 (73.2%)	182 (82.4%)	

Note: BMI, body-mass index;ICU, intensive care unit; HGB, hemoglobin; WBC, white blood cell count; BUN, blood urea nitrogen; CREA, creatinine.

2.4. Statistical analysis

R version 3.4.3. (R Development Core Team, Vienna, Austria) was used for our analysis. The statistics were carried out with Anaconda.

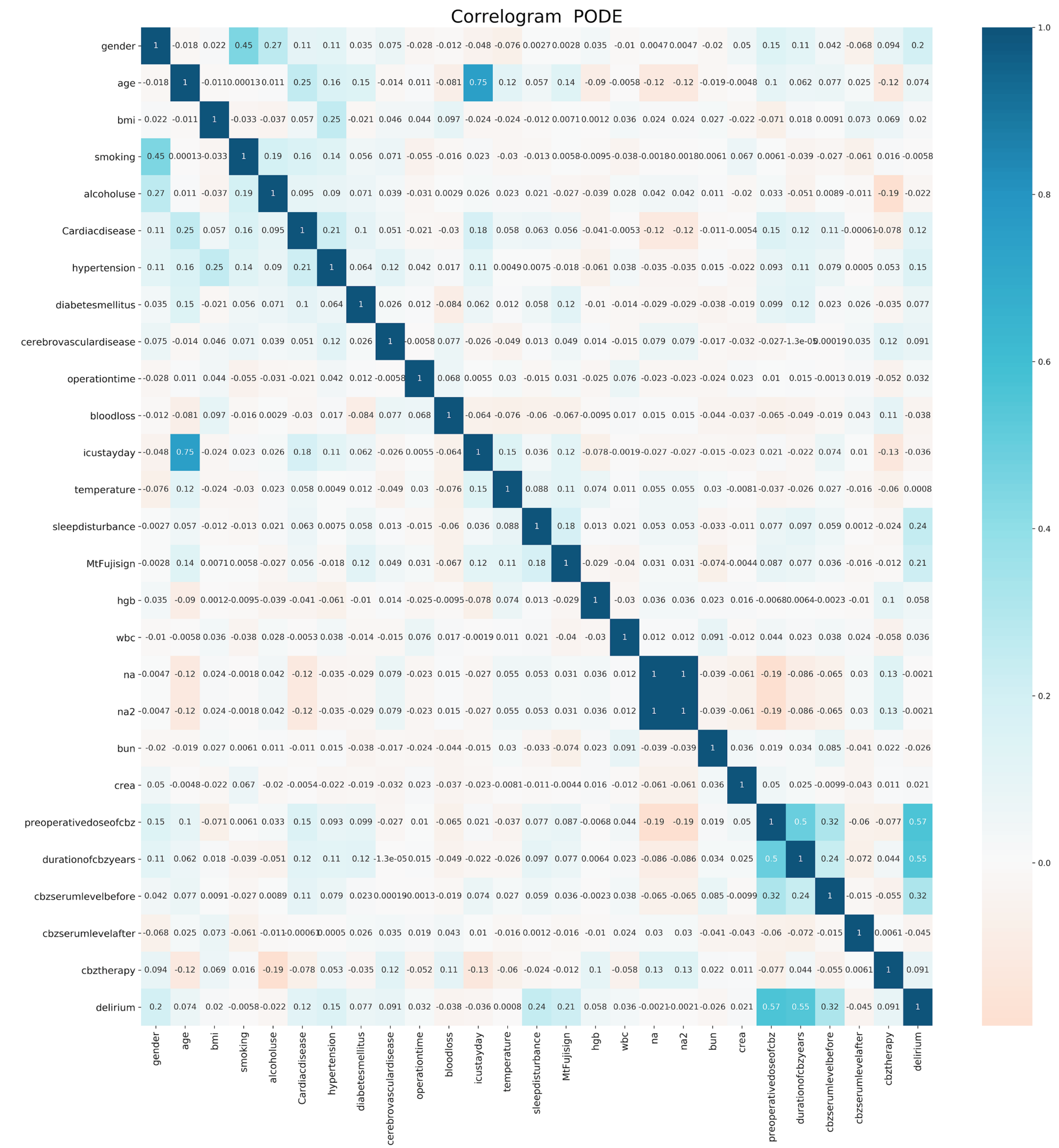

Fig. 1. Correlation between variables.

Statistics and descriptions were done in Python. Among the total samples and with the randomized method, 70% were divided into training groups for development, and 30% were divided into test groups for verification. The accuracy rate of the event occurrence is distinguished by the model's optimal segment. The area value under the ROC curve is between 1.0 and 0.5. It is less accurate when AUC falls between 0.5–0.7. It maintains accuracy when AUC falls between 0.7 and 0.9. When the missing value is classified into two categories, multiple digits are used. Meanwhile, multiple interpolation is used for continuous variables. Accuracy, precision, recall rate and specificity are reported at the operating point that maximizes common performance indicators. "Fuzzy measure"(f1_score) is a weighted harmonic means of precision and recall. MSE is the mean square deviation. The programming analysis code used in this study is shown in Appendix code 1.

3. Results

A total of 912 patients were enrolled in the study, and 221 patients

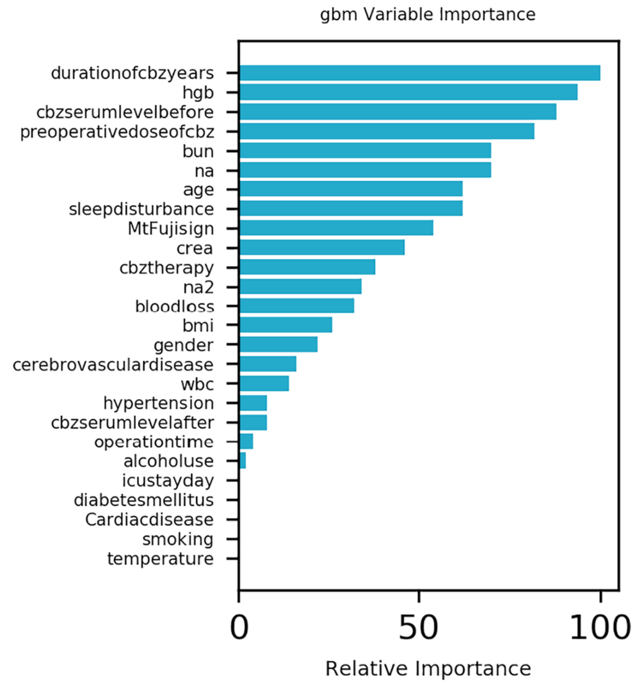

Fig. 2. Variable importance of features included in machine learning algorithm for prediction of PODE
Note:gbm: LightGBM.

Table 2
Forecast results for training group.

	Accuracy	Precision	Recall	f1_score	auc
Logistic	0.900	0.876	0.684	0.768	0.925
DecisionTree	0.861	0.817	0.548	0.656	0.902
forest	0.948	0.984	0.800	0.883	0.994
GradientBoosting	0.970	0.972	0.903	0.936	0.994
gbm	0.944	0.934	0.826	0.877	0.979

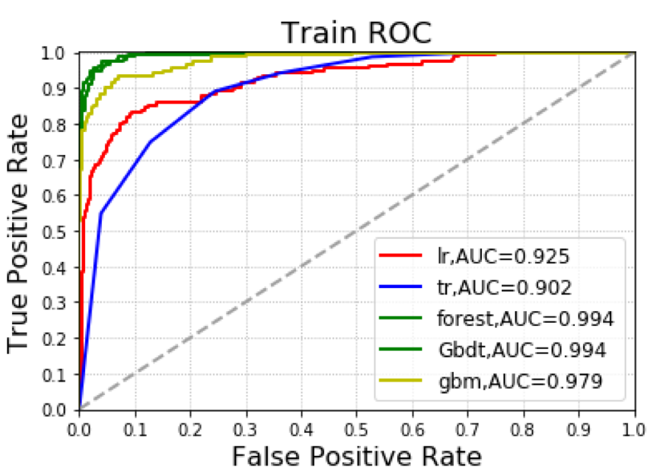

Fig. 3. Different machine learning algorithms predict the PODE in the training group.

(24.2%) experienced postoperative delirium. There was a significant difference in CRE and Preemptive CBZ between the two groups ($P < 0.001$), while there was no significant difference in sex, operating time, or BMI between the two groups ($P > 0.05$) (Table 1).

The correlation analysis showed a significant positive correlation between Preemptive CBZ dose and CBZ use duration and postoperative delirium. In addition, the gbm algorithm in the machine learning resulted in the first 5 factors contributing to the postoperative delirium weight: CBZ use duration, hgb, serum CBZ level measured 24 h before surgery, Preoperative CBZ dose, and BUN (Figs. 1 and 2). At the same time, we verified the weight ranking of features in the other three algorithms, and also supported CBZ and BUN as important influencing factors for postoperative delirium after MVD. (Supplementary Figs. 1, 2 and 3).

Table 3
Forecast results for testing group.

	Accuracy	Precision	Recall	f1_score	auc
Logistic	0.901	0.842	0.727	0.780	0.920
DecisionTree	0.883	0.854	0.621	0.719	0.888
forest	0.909	0.887	0.712	0.790	0.963
GradientBoosting	0.923	0.881	0.788	0.832	0.962
gbm	0.920	0.879	0.773	0.823	0.956

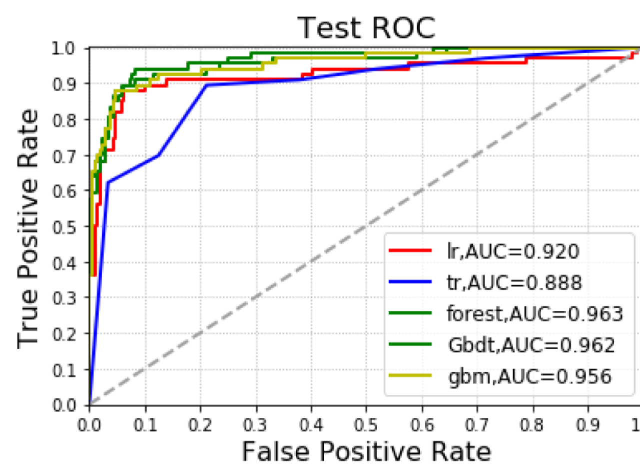

Fig. 4. Different machine learning algorithms predict the results of death in the test group.

By machine learning five algorithms to build prediction models, we found the following values in the training group, Logistic algorithm (AUC value = 0.925, accuracy = 0.900, precision = 0.876, recall = 0.684, f1_score = 0.768); Forest algorithm (AUC value = 0.994, accuracy = 0.948, precision = 0.984, recall = 0.800, f1_score = 0.883); GradientBoosting algorithm (aucvalue = 0.994, accuracy = 0.970, precision = 0.972, recall = 0.903, f1_score = 0.936) and DecisionTree algorithm (aucvalue = 0.902, accuracy = 0.861, precision = 0.817, recall = 0.548, f1_score = 0.656); Gbm algorithm (aucvalue = 0.979, accuracy = 0.944, precision = 0.934, recall = 0.826, f1_score = 0.877) (Table 2 and Fig. 3).

For the test group, Logistic algorithm, we found the following values (AUC value = 0.920, accuracy = 0.901, precision = 0.842, recall = 0.727, f1_score = 0.780); DecisionTree algorithm (aucvalue = 0.888, accuracy = 0.883, precision = 0.854, recall = 0.621, f1_score = 0.719); Forest algorithm (aucvalue = 0.963, accuracy = 0.909, precision = 0.887, recall = 0.712, f1_score = 0.790); GradientBoostingc algorithm (aucvalue = 0.962, accuracy = 0.923, precision = 0.881, recall = 0.788, f1_score = 0.832); Gbm algorithm (aucvalue = 0.956, accuracy = 0.920, precision = 0.897, recall = 0.773, f1_score = 0.823) (Table 3 and Fig. 4).

4. Discussion

PODE's pathological changes remain unclear. The PODE treatment effect is not ideal. Additionally, the combination of non-drug therapy and drug therapy is more important than treatment. The intervention of risk factors can reduce delirium occurrence and shorten delirium time [15] . Various evaluation methods suggest that the incidence of delirium in adults ranges from 6% to 56% [16]. The results of this study showed that 24.2% of the patients developed postoperative delirium, consistent with the present study. The prediction model is established by 5 machine learning algorithms. It is found that the prediction model can be established by all 5 algorithms in this study. Among them, the accuracy of the GradientBoosting algorithm is up to 96.7%, and the accuracy of the DecisionTree algorithm is at least 86.1%. In the gbm algorithm, we found that CBZ use duration, hgb, preemptive CBZ dose, and BUN accounted for a significant proportion of the data regarding the occurrence of delirium.

Several studies [17,18] have shown that age and sex are independent risk factors for postoperative delirium. Old age and low body mass index (BMI) levels have also been shown to be risk factors for postoperative delirium [19] . In addition, the primary inflammatory response in humans can cause nerve inflammation and increase the risk of PODE [20]. Mu et al. [21] have found that operation time is an important factor in the occurrence of delirium; the longer the operation, the more complicated the operation, the higher the anesthesia dosage, and the higher the operation time (by 1 h intervals), the higher the incidence of delirium by 36%. In older men, cognitive function and immunity are poor, and they are more likely to experience negative mood due to surgical wounds, unfamiliar environments, and medical instruments associated with MVD [22] . These findings are also supported by the results of this study.

Electrolyte disturbances are also related to postoperative delirium. Studies[19]have shown that BUN levels > 14.9 mg/dL 3 days after surgery are independent risk factors for postoperative delirium in elderly patients undergoing total hip arthroplasty. Meanwhile, studies [23] have also shown that high intraoperative blood loss, low preoperative serum Na concentration and high body temperature are important risk factors for postoperative delirium after spinal surgery. In addition, low preoperative Hgb levels may increase postoperative delirium in older men [24]. Our results are similar to these findings.

At present, CBZ is used to treat primary cranial nerve disorders [25]. CBZ is an inhibitor of the neuronal membrane sodium channel and hinders the discharge of high frequency neurons [26]. The results of this study found a significant positive association between carbamazepine and postoperative delirium, as well as an important weight for the postoperative delirium.

Accurate monitoring of the depth of deep anesthesia is crucial to the health of patients during and after surgery. Machine learning classification processor can accurately estimate the depth of anesthesia [27,28]. Moreover, the multi-modal head-mounted system can accurately monitor EEG in real time [29]. However, there is no machine learning study on postoperative delirium of MVD patients. Our research results can provide some reference for the prognosis of such patients and related personnel.

Despite this study's positive results, it has some limitations. First, this is a retrospective study, so some information that may affect PODE incidence may be either unavailable or incomplete, such as cognitive function, antipsychotic use, or functional status prior to admission. Furthermore, information from genomics has yet to be adopted, which may be detrimental to mechanistic studies. Also, because all patients underwent MVD using the same surgical technique performed by the same senior neurosurgeon, this may have limited the generalizability of the model to patients of other surgeons. And the same senior neurosurgeon is a major limitation of this study, because it severely limits the generalizability of the model to patients of any other surgeon. Thus, multi-center, prospective, and combo-gene multi-cohort studies are needed in the future.

In summary, the major risk factors for the development of postcardiac delirium are carbamazepine, hgb, and BUN. Machine learning algorithms can be established to predict the occurrence of postoperative delirium after microvascular decompression.

CRediT authorship contribution statement

Ying Wang:Conceptualization, Methodology, Software, Data curation, Writing - original draft, Visualization, Investigation, Writing - review & editing.**Lei Lei**:Conceptualization, Methodology, Software, Data curation, Writing - original draft, Writing - review & editing.**Muhuo Ji**:Conceptualization, Methodology, Software, Writing - review & editing.**Jianhua Tong**:Conceptualization, Methodology, Software, Writing - review & editing.**Cheng-Mao Zhou**:Conceptualization, Methodology, Software, Data curation, Writing - original draft, Visualization, Investigation, Supervision, Software, Validation, Writing - review & editing.**Jian-Jun Yang**:Conceptualization, Methodology, Software, Data curation, Writing - original draft, Visualization, Investigation, Supervision, Software, Validation, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinane.2020.109896.

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