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ARTICLE

Application Value of a Machine Learning Model in Predicting Mild Depression Associated with Migraine without Aura

Sheng-wei Cui[1], Pei Pei[1,*], Wen-ming Yang[1,2,3,*]

[1]Department of Neurology, The First Affiliated Hospital of Anhui University of Traditional Chinese Medicine, Hefei, Anhui, China
[2]Center for Xin'An Medicine and Modernization of Traditional Chinese Medicine, Institute of Health and Medicine, Hefei Comprehensive National Science Center, Hefei, Anhui, China
[3]Key Laboratory of Xin'An Medicine, Ministry of Education, Hefei, Anhui, China
*Correspondence: pobingpei@163.com (Pei Pei); 18019981683@163.com (Wen-ming Yang)

Abstract

Aims/Background To investigate the application value of a machine learning model in predicting mild depression associated with migraine without aura (MwoA).

Methods 178 patients with MwoA admitted to the Department of Neurology of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine from March 2022 to March 2024 were selected as subjects. According to their inpatient medical records, 38 patients were selected as the validation group by random number method, and the remaining 140 patients were included in the modelling group. According to the diagnosis results, the patients in the modelling group and validation group were further divided into a MwoA with mild depression group and a MwoA without mild depression group.

Results The results of univariate analysis and Multivariate logistic regression analysis showed that gender, course of disease, attack frequency, headache duration, Migraine Disability Assessment Questionnaire (MIDAS), and Headache Impact Test-6 (HIT-6) score were independent influencing factors for mild depression in MwoA patients ($p < 0.05$). The receiver operating characteristic (ROC) analysis results showed that the area under the curve of the established prediction model for MwoA patients with mild depression in the modelling group and the validation group was 0.982 and 0.901, respectively, the sensitivity was 0.978 and 0.857, respectively, and the specificity was 0.892 and 0.929, respectively.

Conclusion Gender, course of disease, seizure frequency, headache duration, MIDAS score, and HIT-6 score are independent influencing factors for mild depression in patients with MwoA. The model displays good performance for the prediction of mild depression in patients with MwoA.

Key words: machine learning; migraine without aura; mild depression; decision curve; receiver operating characteristic curve

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Introduction

Migraine is a common paroxysmal nervous system disease with unilateral pulsatile headache accompanied by symptoms such as nausea, vomiting, paraesthesia, and photophobia. The incidence of the disease in the normal population is 11.6%, and it is higher in women than men (Bjornsdottir et al, 2023; Verhagen et al, 2023). According to the presentation, migraine can be divided into two types: migraine without aura (MwoA) and migraine with aura. Migraine without aura is more common and can progress to chronic migraine for patients with recurrent

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MwoA attacks, leading to cognitive impairment and mood changes (Fraser et al, 2019; Olesen, 2022). Depression is the most common comorbid type of MwoA. The incidence of depression in MwoA patients is 2–4 times that of healthy people (Xu et al, 2020). In clinical practice, comorbid depression in MwoA patients is often ignored and has a low diagnostic rate, which not only significantly increases the treatment burden of patients but also adversely affects their prognosis. However, its pathophysiological mechanism is not fully clear, and there is still a lack of effective drug or non-drug interventions in clinical practice (O'Hare et al, 2021; Russo et al, 2019) for the treatment of patients with MwoA comorbid depression. Therefore, it is important to develop appropriate methods for the prediction of depression, in order to make a timely and accurate diagnosis. At present, there are epidemiological surveys on MwoA comorbid depression both in this country and abroad (Harriott et al, 2019; Karsan et al, 2023; Major et al, 2020), but there are certain differences between studies regarding its risk factors. In addition, some small sample studies can only identify some of the influencing factors related to MwoA comorbid depression, and it is difficult to quantify the relative influence of those factors. In recent years, diversified biostatistical modelling schemes based on machine learning have provided effective assistance for the accurate identification of comorbid depression in clinical practice (Puac-Polanco et al, 2023; Sajjadian et al, 2021; Ziobrowski et al, 2023). This study analyzed the influencing factors of MwoA comorbid depression based on single-centre retrospective data and established a prediction model to provide valuable insights into the screening, diagnosis, and management of such patients, ultimately improving the management of patients and their prognosis.

Methods

Research Subjects

MwoA patients admitted to the Department of Neurology of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine from March 2022 to March 2024 were selected as subjects. Inclusion criteria: ① The MwoA diagnostic criteria in the International Classification of Headaches, Third Edition (ICHD, III) were met (van de Berg et al, 2021). ② Aged 18–70. ③ The course of the disease was more than 2 weeks. ④ Normal cognitive function and hearing. ⑤ Relevant clinical data were complete. Exclusion criteria: ① Patients with malignant tumours and severe organ function impairment. ② Patients with immune system diseases or other types of migraine. ③ Patients with moderate or severe depression. For 178 patients meeting the above conditions, 38 patients were selected as the validation group and the remaining 140 patients were included in the modelling group by random number method according to their hospitalization medical records. All patients were evaluated using the diagnostic criteria for depression in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) in the United States (First et al, 1995). Patients' degree of depression was assessed according to the Hamilton Depression Rating Scale (24-item versions) (Zheng et al, 1988). The diagnostic criteria for mild depression were: typical symptoms of depression, but not very serious, and the whole period of depression continued for at least 2

weeks (Hamilton Depression Rating Scale (HAMD)-24 score, 0–7). Patients in the modelling group and validation group were further divided into MwoA with mild depression and MwoA without mild depression groups. This study adhered to the "Declaration of Helsinki" and was approved by the Medical Ethics Committee of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine (Approval numbers: 2024MCZQ13).

Data Collection

Information such as gender, age, education level, combined vomiting, photophobia, phonophobia, course of disease, seizure frequency, and duration of headache was collected from the electronic medical record system and self-designed questionnaire. The Visual Analogue Scale (VAS) score was used to assess the degree of headache in patients, including mild headache (VAS score, 1–3), moderate headache (VAS score, 4–6), and severe headache (VAS score, 7–9). The severity of the disease in migraine patients was assessed using Migraine Disability Assessment Questionnaire (MIDAS) and Headache Impact Test-6 (HIT-6).

Statistical Analysis

The collected experimental data were analyzed using SPSS27.0 (IBM Corp, Armonk, NY, USA) and Matlab R2021a (MathWorks, Natick, MA, USA). Normally distributed data, based on analysis of histograms, were expressed as $\bar{X} \pm S$, and the independent samples *t*-test was used for comparison. Categorical data were expressed as the number of cases or rate, and the χ^2 test was used for comparison. Univariate and multivariate methods were used to analyze MwoA patients, and a prediction model was established based on the results of the logistic regression analysis. The receiver operating characteristic (ROC) curve and calibration curve were used to evaluate the predictive value of the model for mild depression in MwoA patients, the decision curve was used to evaluate the clinical benefit of the model, and $p < 0.05$ was considered statistically significant.

Results

Comparison of General Data between the Two Groups

There were no statistically significant differences in the demographic and clinical measurements between the modelling group and the validation group ($p > 0.05$), indicating that they were comparable (Table 1).

Univariate Analysis of the Risk Factors for Mild Depression in MwoA Patients

The results of univariate analysis showed that there were statistically significant differences in gender, course of disease, seizure frequency, duration of headache, MIDAS score, and HIT-6 score between the MwoA group with mild depression and the MwoA group without mild depression ($p < 0.05$); there was no statistically significant difference in age, education level, vomiting, photophobia, or phonophobia between the two groups ($p > 0.05$), as shown in Table 2.

Table 1. Comparison of general characteristics between the two groups.

Factor	Category	Modelling group (n = 140)	Validation group (n = 38)	t/χ^2	*p*-value
Sex	Male	69	20	0.134	0.715
	Female	71	18		
Age	≥60 y	38	16	3.166	0.075
	<60 y	102	22		
Education level	Primary school and below	37	12	0.546	0.761
	Middle/High school	59	16		
	Junior college or above	44	10		
Concurrent vomiting (yes/no)		105/35	30/8	0.254	0.614
Photophobia (yes/no)		91/49	26/12	0.155	0.694
Voice fear (yes/no)		85/55	22/16	0.099	0.753
Course of disease (years)		8.75 ± 3.66	8.57 ± 3.45	0.272	0.786
Degree of pain	Mild headache	40	10	0.530	0.767
	Moderate headache	50	16		
	Severe headache	50	12		
Seizure frequency (times/month)		2.44 ± 0.48	2.53 ± 0.51	1.011	0.313
Duration of headache (h)		20.18 ± 7.03	19.88 ± 6.68	0.236	0.814
MIDAS score (points)		6.85 ± 2.55	6.68 ± 2.76	0.358	0.721
HIT-6 (points)		62.86 ± 8.53	60.18 ± 7.99	1.740	0.084

MIDAS, Migraine Disability Assessment Questionnaire; HIT-6, Headache Impact Test-6.

Table 2. Univariate analysis of the influencing factors for mild depression in MwoA patients.

Factor	Category	MwoA not combined with mild depression group (n = 31)	MwoA with mild depression (n = 109)	t/χ^2	*p*-value
Sex	Male	10	59	4.619	0.032
	Female	21	50		
Age	≥60 y	8	30	0.036	0.850
	<60 y	23	79		
Education level	Primary school and below	6	31	1.131	0.568
	Middle/High school	15	44		
	Junior college or above	10	34		
Vomiting (yes/no)		22/9	83/26	0.345	0.557
Photophobia (yes/no)		16/15	75/34	3.137	0.077
Voice fear (yes/no)		15/16	70/39	2.537	0.112
Course of disease (years)		7.30 ± 2.38	9.96 ± 3.53	4.889	<0.001
Degree of pain	Mild headache	10	30	0.323	0.851
	Moderate headache	11	39		
	Severe headache	10	40		
Seizure frequency (times/month)		2.15 ± 0.39	2.75 ± 0.53	6.946	<0.001
Duration of headache (h)		16.55 ± 6.79	23.83 ± 8.75	4.926	<0.001
MIDAS score (points)		6.16 ± 2.40	7.53 ± 2.75	2.714	0.008
HIT-6 (points)		60.18 ± 7.95	65.86 ± 8.36	3.470	<0.001

MwoA, migraine without aura.

Table 3. Assignment table.

Variable	Assignment method
Sex	Male = 0, Female = 1
Course of disease	Enter the model with actual values
Seizure frequency	Enter the model with actual values
Duration of headache	Enter the model with actual values
MIDAS score	Enter the model with actual values
HIT-6 score	Enter the model with actual values

Table 4. Multivariate logistic regression analysis of the influencing factors for MwoA with mild depression.

Risk factors	β value	SE value	Ward value	OR value	95% CI	p-value
Sex	0.304	0.136	4.990	1.355	1.037–1.769	0.044
Course of disease	0.606	0.166	13.349	1.834	1.325–2.539	<0.001
Seizure frequency	1.017	0.198	26.384	2.765	1.876–4.076	<0.001
Duration of headache	0.564	0.170	11.014	1.758	1.260–2.453	<0.001
MIDAS score	0.459	0.150	9.766	1.598	1.191–2.144	0.002
HIT-6 score	0.597	0.173	11.894	1.816	1.294–2.549	<0.001

CI, Confidence Interval; OR, Odds Ratio; SE, Standard Error.

Multivariate Logistic Regression Analysis of the Influencing Factors for MwoA with Mild Depression

A logistic regression analysis model was established with the presence or absence of concurrent mild depression as the dependent variable and the statistically significant indicators in the univariate analysis as independent variables. Stepwise regression was used to screen for statistically significant influencing factors, with an inclusion criterion of $p < 0.05$. Using statistically significant variables from the multivariate analysis, a logistic regression model was built based on the training set and evaluated using the test set. The results of multivariate logistic regression analysis showed that gender, course of disease, attack frequency, headache duration, MIDAS score, and HIT-6 score were independent influencing factors for mild depression in MwoA patients ($p < 0.05$), as shown in Tables 3,4.

Establishment and Evaluation of Prediction Model

This study established a nomogram model based on the results of the logistic regression analysis. The ROC analysis results showed that the area under the curve of the established prediction model for MwoA with mild depression in the modelling group and the validation group was 0.982 and 0.901, respectively, the sensitivity was 0.978 and 0.857, respectively, and the specificity was 0.892 and 0.929, respectively, demonstrating that the model had good predictive power. The analysis results of the calibration curve and validation curve showed that the prediction of mild depression in MwoA patients was consistent with its actual occurrence, as shown in Table 5 and Figs. 1,2,3.

Table 5. The predictive value for MwoA combined with mild depression in the modelling group and validation group by ROC evaluation prediction model.

Indicator	Area under the curve (AUC)	Sensitivity (%)	Specificity (%)	Accuracy
Modelling group	0.982	0.978	0.892	0.985
Validation group	0.901	0.857	0.929	0.896

ROC, receiver operating characteristic.

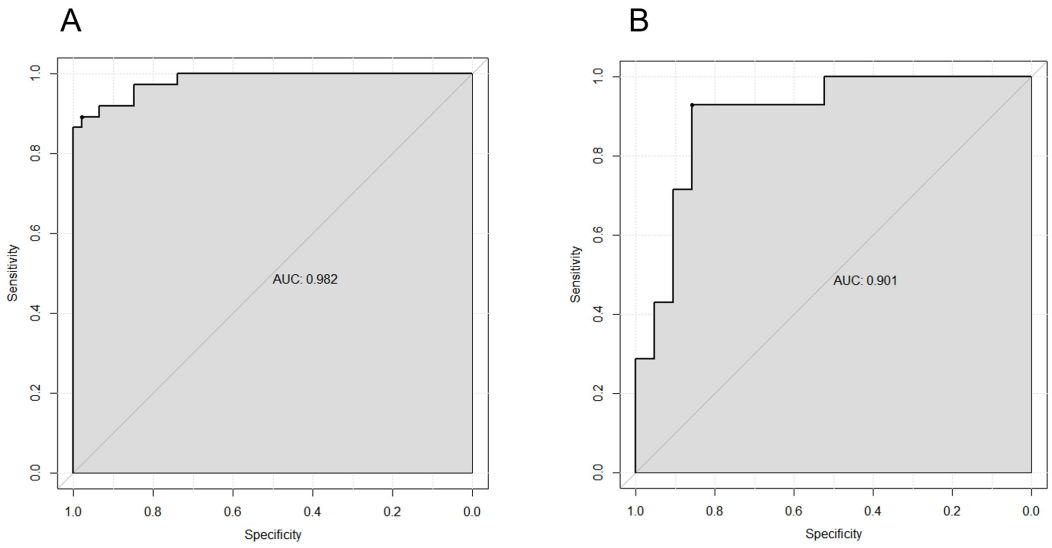

Fig. 1. Predictive value for MwoA combined with mild depression in the modelling group (A) and validation group (B) of the prediction model.

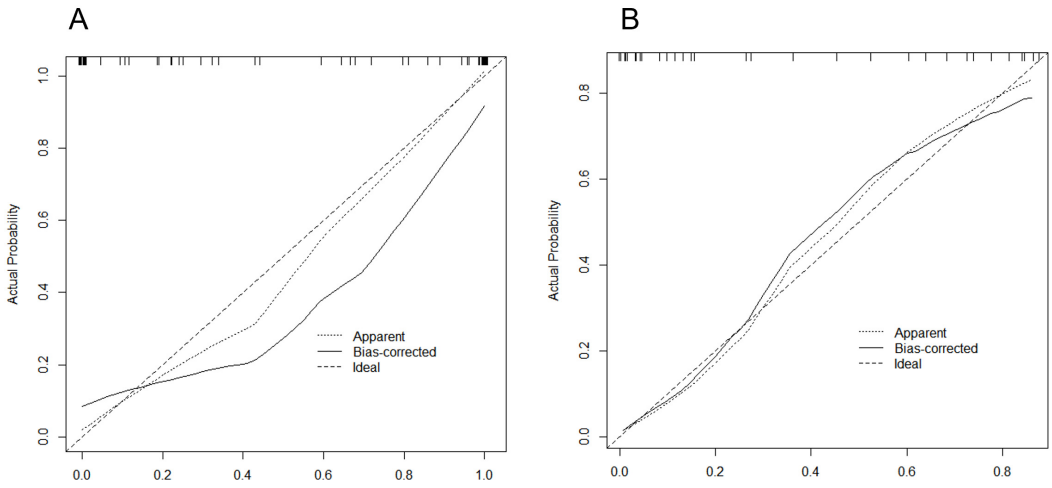

Fig. 2. Calibration curves of the modelling (A) and validation groups (B) for prediction models.

Discussion

Depression is the most common comorbidity of MwoA, which not only significantly increases patients' medical expenses and reduces their treatment efficacy, but also results in a considerable number of MwoA patients who develop lifelong depressive disorder with persistent adverse effects on their quality of life. In terms

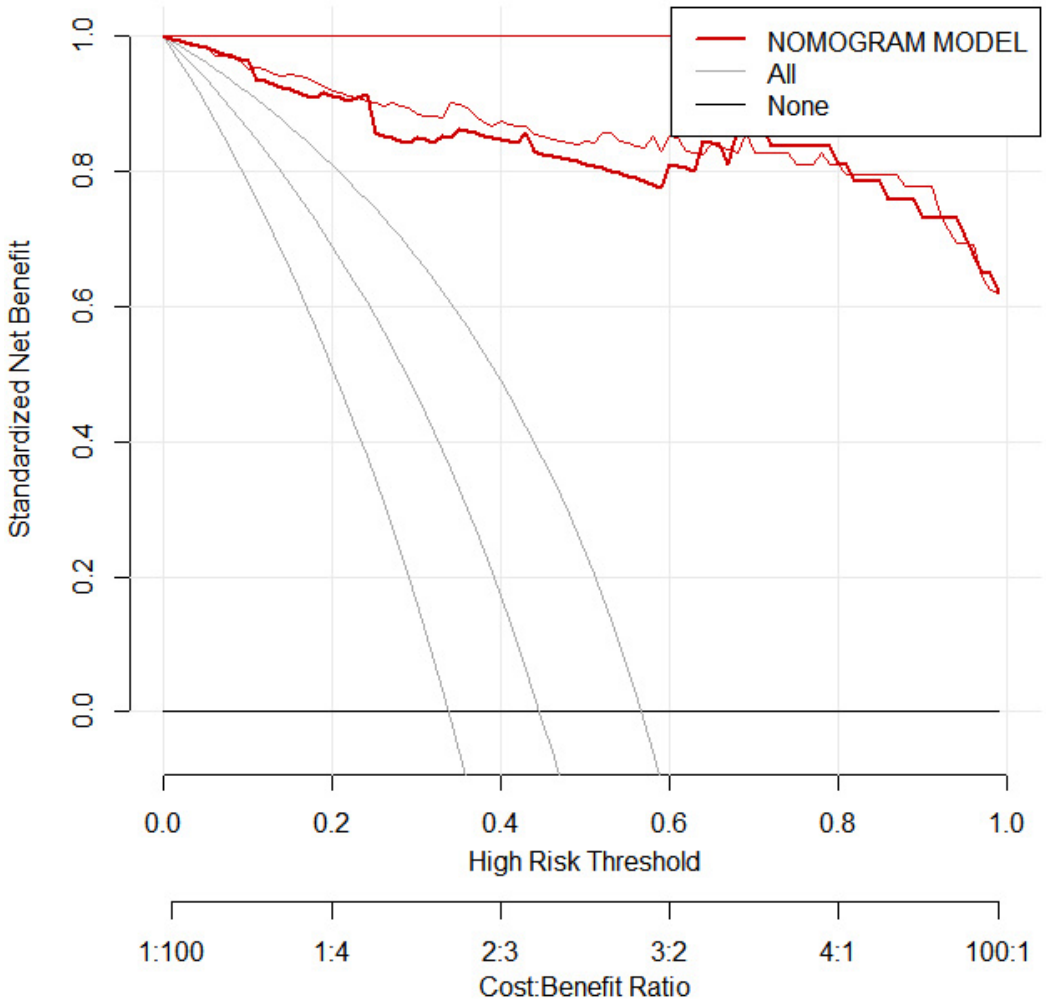

Fig. 3. Predictive model decision curves.

of comorbidity prevalence, there is considerable variation among different studies in the reported incidence of MwoA combined with depression due to differences in included cohorts and assessment methods. In this study, there were 140 patients in the modelling group, 109 of whom had mild depression, with an overall incidence of 77.86%, slightly higher than that reported by studies in other countries (Desouky et al, 2019; O'Hare et al, 2021). The reason may be related to the fact that most of the subjects enrolled in this study were those with longer course of disease. Results of imaging studies (Lv et al, 2023; Morais et al, 2023) show that the left medial prefrontal cortex of patients with MwoA or depression has similar developmental characteristics, and many brain regions have similar spontaneous activities in the resting state, which are significantly related to the clinical characteristics of patients. In addition, mechanistic studies have also found that neurotransmitter abnormalities may lead to the co-occurrence of MwoA and depression, including those involving the production, secretion, and release of internal neurotransmitters such as 5-hydroxytryptamine, dopamine, y-aminobutyric acid, and norepinephrine (Georgescu et al, 2019; Harriott et al, 2019; Kudo et al, 2023; Scutelnic et al, 2023; Takizawa et al, 2020), all of which may lead to changes in the state of brain systems,

contributing to the occurrence of MwoA or depression. Thus, for MwoA patients, it is of great clinical importance to intervene as soon as possible in order to improve their prognosis.

The results of univariate analysis showed that there were statistically significant differences in gender, course of disease, seizure frequency, headache duration, MIDAS score, and HIT-6 score between the MwoA with mild depression group and the MwoA without mild depression group ($p < 0.05$). The results of multivariate logistic regression analysis showed that gender, course of disease, seizure frequency, headache duration, MIDAS score, and HIT-6 score were independent influencing factors for MwoA patients with mild depression. Previous studies have consistently found that the incidence of comorbid depression in women was slightly higher than that in men due to differences in physiological, emotional, and hormonal factors (Morais et al, 2023; Viudez-Martínez et al, 2024), which is consistent with the results of this study. The course of disease, attack frequency, headache duration, MIDAS score, and HIT-6 score reflect the patient's disease state. The more severe the disease is, the greater the impact on quality of life, and the higher the probability of depressive comorbidity (Suryavanshi et al, 2024). In addition, previous studies have found that whenever premonitory symptoms of MwoA patients occurred, they always had adverse psychological effects, because the occurrence of premonitory symptoms indicated that MwoA was about to occur, and the patients became nervous and agitated, worrying that headache would affect their life and ability to study. When headache attacks after the end of premonitory symptoms, the physiological headache is also unbearable to patients, and the combination of psychological and physical shocks may be the reason for severe depression (Mastria et al, 2023; Pelzer et al, 2023). The ability to control emotions and relax one's mood is the most important obstacle in the mental aspect of migraine. When aura symptoms occur, how to alleviate these negative effects through correct and effective treatment and positive psychological suggestions deserves further exploration.

In this study, a prediction model for MwoA patients with depression was established based on the results of logistic regression analysis. The ROC analysis results showed that the established prediction model had good predictive power for MwoA patients with mild depression in the modelling group and the validation group. The results of calibration curve and validation curve analysis showed that the prediction of mild depression in MwoA patients was consistent with its actual occurrence. Compared with prediction using a single index and disease score in previous studies (Kanner, 2022; Major et al, 2020), the score used in the present study is more suitable for predicting MwoA with mild depression in China, and its quantitative results provide critical guidance for interventions by clinical medical staff.

Conclusion

In conclusion, the results of this study show that gender, course of disease, attack frequency, headache duration, MIDAS score, and HIT-6 score are independent influencing factors for mild depression in MwoA patients, and the prediction model

established based on these factors has good application potential to predict mild depression in patients. As a single-center study, this study has certain shortcomings. ① The sample size included in this study needs to be further increased. ② In this study, the MwoA was assessed using subjective assessment scales. ③ Serological indicators, computed tomography (CT), Magnetic Resonance Imaging (MRI), and other imaging examination parameters were not included in this study. Future studies should expand the sample size and increase the number of study variables, in order to optimize the existing model, and to improve the predictive ability of the model for MwoA with mild depression, thus improving patient prognosis.

Key Points

- To investigate the application value of a machine learning model in predicting mild depression associated with migraine without aura (MwoA).
- Gender, course of disease, seizure frequency, headache duration, MIDAS score, and HIT-6 score are independent influencing factors for mild depression in patients with MwoA.
- ROC analysis results showed that the area under the curve of the established prediction model for MwoA patients with mild depression in the modelling group and the validation group was 0.982 and 0.901, respectively, the sensitivity was 0.978 and 0.857.
- The model displays good performance for the prediction of mild depression in patients with MwoA.

Availability of Data and Materials

All data included in this study are available upon request by contact with the corresponding authors.

Author Contributions

SC designed the research study. SC and PP performed the research. WY provided help and advice on funding, administration, and supervision. WY analyzed and interpreted the data. SC drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study adhered to the "Declaration of Helsinki" and was approved by the Medical Ethics Committee of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine (Approval numbers: 2024MCZQ13). Informed consent was waived by the Medical Ethics Committee of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine.

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Conflict of Interest

The authors declare no conflict of interest.

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