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The factors influencing the occurrence of post-ischemic stroke depression and its relationship with the burden score of cerebral small vessel disease

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Abstract. – OBJECTIVE: This study explored the determinants of post-stroke depression (PSD) in ischemic stroke (AIS) patients and its association with the burden score of cerebral small vessel disease (CSVD).

PATIENTS AND METHODS: We analyzed 374 AIS patients treated between January 2020 and January 2022. Patients were categorized into 90 with PSD and 284 without PSD, enabling an investigation into PSD risk factors and the CSVD-PSD relationship.

RESULTS: There was no significant difference in health factors between PSD and non-PSD patients ($p>0.05$). However, significant disparities were noted in age, gender, initial Barthel Index (BI), Mini-Mental State Examination (MMSE) score, plasma fibrinogen, homocysteine, red cell distribution width, National Institutes of Health Stroke Scale (NIHSS) score, and CSVD burden score ($p<0.05$). Regression analysis indicated that these variables were pivotal PSD predictors (OR>1, $p<0.05$). Surprisingly, a positive correlation with PSD occurrence was found for age, NIHSS score, plasma fibrinogen, homocysteine levels, red cell distribution width, CSVD burden score (r=0.565, 0.615, 0.482, 0.514, 0.572, 0.608, respectively; $p<0.05$). Meanwhile, the MMSE score and BI index were inversely related to PSD onset (r=-0.604, -0.590; $p<0.05$). The ROC curve analysis of the combination model based on MMSE, NIHSS and CSVD score revealed an AUC of 0.926 and Youden's index of 0.744.

CONCLUSIONS: Age, MMSE score, BI index, NIHSS score, plasma fibrinogen concentration, homocysteine level, red blood cell distribution width, and CSVD burden score are all major influencing factors in the occurrence of PSD. The combination model based on MMSE, NIHSS, and CSVD scores presented a valuable approach to predicting PSD.

Key Words:
Cerebral small vessel diseases, Burden score, Ischemic stroke, Depression.

Introduction

Cerebral small vessel disease (CSVD) refers to the development of lesions in the small blood vessels within the brain, affecting arterioles, capillaries, and venules, with diameters ranging from 30 to 800 micrometers[1,2]. The incidence of CSVD increases as individuals age, accompanied by a higher risk for cerebral vascular disease. CSVD can result in various abnormalities, including pathological, imaging, emotional, and behavioral changes[3].

Ischemic stroke (AIS), a subtype of cerebral vascular disease, is characterized by localized necrosis or softening of brain tissue due to impaired blood supply and ischemia-hypoxia. This condition is manifested through symptoms such as limb weakness, sensory impairment, visual disturbances, swallowing difficulties, cognitive decline, and mood alterations. AIS is associated with high mortality, disability rates, and recurrent episodes[4,5].

Post-stroke depression (PSD) is a prevalent emotional disorder observed among AIS patients and represents a common complication. It is characterized by depressive mood symptoms, including loss of interest in daily activities, decreased energy, insomnia, reduced appetite, and even suicidal thoughts. PSD is associated with an increased risk of stroke recurrence, higher stroke mortality rates, and poor functional prognosis[6,7]. Studies[8] suggest that approximately 31% of AIS patients experience PSD, regardless of the timeframe, and factors

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such as physical disability, cognitive impairment, stroke severity, gender, and lack of social support can contribute to its development.

Following the onset of PSD, patients frequently display reduced enthusiasm, compliance, and cooperation in their treatment, leading to medication non-compliance and a diminished belief in recovery. These factors can adversely affect the effectiveness of diagnosis and treatment in AIS patients. Therefore, early detection and intervention of PSD are crucial in determining the prognosis of AIS patients. Some clinical studies[9,10] have suggested a correlation between CSVD and PSD. In the literature, the association between PSD and specific subtypes of CSVD has been investigated. As patients can present with multiple CSVD conditions, the CSVD burden score provides a scoring method to assess its severity. Previous studies[11] have demonstrated the practicality and reliability of the CSVD burden score, which includes white matter hyperintensities (WMHs), subcortical lacunar infarcts (sLI), enlarged perivascular spaces (EPVS), and other subtypes. However, limited research exists on the relationship between the CSVD burden score and PSD. Given the clinical manifestations of PSD and its potential adverse effects, early detection and intervention of PSD are crucial. This study aims to investigate the connection between the CSVD burden score in AIS patients and the occurrence of PSD in order to establish an early detection and intervention method.

Patients and Methods

General Data

This study was approved by the Ethics Committee of the Taixing People's Hospital (No. LW2021007). All patients signed the informed consent form. Subjects for this clinical research were selected between January 2020 and January 2022 from 374 patients diagnosed and treated for acute AIS at our hospital. The patients were divided into two groups based on the presence or absence of PSD: 284 patients without PSD and 90 patients with PSD. Inclusion criteria: (1) complete clinical data; (2) approval of the study by The Hospital Pathology Committee; (3) adherence to the diagnostic criteria for CSVD stated in the "Expert Consensus on the Diagnosis and Treatment of Cerebral Small Vessel Disease in China 2021"[12] ; (4) age ≥18 years with full self-regulatory capacity; and (5) documented consent from the patient and their family, obtained by signing an informed consent form. Exclusion criteria: (1) pre-stroke diagnosis of depression, anxiety, or other psychiatric disorders; (2) severe systemic diseases combined with stroke; (3) impairment in consciousness, language, cognition, or other factors hindering completion of psychological assessments; (4) inability to undergo magnetic resonance imaging (MRI) detection; and (5) history of alcohol abuse or dependence.

Collection of Clinical Data

Clinical data were collected, including age, gender, history of hypertension, history of diabetes, history of dyslipidemia, smoking and alcohol use, coronary heart disease, systolic and diastolic blood pressure, body mass index, National Institutes of Health Stroke Scale (NIHSS) score, Mini-Mental State Examination (MMSE) score, baseline Barthel Index (BI), burden score of cerebral small vessel disease (CSVD), history of antiplatelet therapy, history of previous stroke, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, fasting blood glucose, homocysteine, high-sensitivity C-reactive protein, red blood cell distribution width, and lateralization of acute hemisphere infarction.

Follow-Up Assessment

A 3-month follow-up was conducted after the AIS event. During this period, all patients were assessed using the Hamilton Depression Rating Scale (HAMD) to evaluate depressive symptoms and the Cognitive Behavioral Assessment to assess cognitive function. Additionally, patients were assessed based on MMSE score and educational level standards for cognitive impairment.

Magnetic Resonance Imaging

Within 7 days of admission, patients underwent MRI using a 1.5T system. The imaging sequences included diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR), T2-weighted, T1-weighted, and susceptibility-weighted imaging (SWI). The Fazekas scoring criteria were applied to classify WMHs, extending to deep white matter irregularities or confluent deep WMHs around the ventricles.

Semiquantitative Scoring System

A Semiquantitative Scoring System was used, with a grade 3 assigned to 21-40 EPVS. In the presence of moderate to severe EPVS, or one cerebral microbleed (CMB), or sLI, each was scored as 1.

Statistical Analysis

Statistical analysis was performed using SPSS 21.0 software (IBM Corp., Armonk, NY, USA). Categorical data were expressed as [n (%)] and assessed using the Chi-square test. Continuous data were presented as mean ± standard deviation (SD) and compared *via* the *t*-test between groups. Variables that demonstrated significance in the univariate analysis were incorporated into a multivariate logistic regression model. The predictive model's accuracy was assessed by calculating the area under the receiver operating characteristic curve. Statistical differences were deemed significant at a level of $p<0.05$.

Results

Comparison of Age, Gender, and Vascular Risk Factors between Patients with PSD and Patients without PSD

There were notable differences in age and gender between patients with PSD and patients without PSD. Patients with PSD had a mean age of 61.15±9.76, while patients without PSD had a mean age of 63.63±10.18. These differences were statistically significant and established as independent risk factors ($p<0.05$). In terms of gender distribution, the percentage of females was higher in the group without PSD (53.33%) compared to the group with PSD (36.97%).

However, no significant differences were observed in the prevalence of various vascular risk factors, including hypertension (71.12% *vs.* 70.00%), diabetes (25.00% *vs.* 31.11%), hyperlipidemia (20.07% *vs.* 17.78%), smoking (34.51% *vs.* 32.22%), alcohol consumption (34.51% *vs.* 32.22%), and coronary heart disease (7.39% *vs.* 6.67%), between the two groups. Detailed information can be found in Table I.

Comparison of Laboratory Data between Patients with PSD and Patients without PSD

Clinical data analysis revealed no significant differences in various laboratory parameters between non-PSD patients and PSD patients. Systolic blood pressure (137.23±16.61 *vs.* 139.16±20.14), diastolic blood pressure (81.82±9.81 *vs.* 81.72±10.35), weight (25.13±3.11 *vs.* 25.36±3.25), history of antiplatelet therapy (13.38% *vs.* 15.56%), and previous stroke history (11.27% *vs.* 11.11%) did not show any statistically significant differences ($p>0.05$). However, there were significant differences in baseline BI (60.34±5.62 *vs.* 40.74±5.90), NIHSS score (10.32±2.10 *vs.* 11.48±3.65), MMSE score (24.68±2.16 *vs.* 20.15±2.05), and burden score of CSVD (1.96±0.45 *vs.* 3.50±0.38) between the two groups ($p<0.05$) (Table II).

Comparison of Lipid and Inflammatory Markers between Patients with and without PSD

In terms of lipid and inflammatory markers, there were no statistically significant differences between PSD patients and non-PSD patients in terms of total cholesterol (4.08±1.11 *vs.* 4.10±1.10), triglycerides (1.39±0.33 *vs.* 1.47±0.37), low-density lipoprotein (2.39±0.61 *vs.* 2.53±0.69), high-density lipoprotein (1.05±0.31 *vs.* 1.09±0.27), fasting blood glucose (5.55±1.82 *vs.* 5.45±1.86), and high-sensitivity C-reactive protein (4.09±1.63 *vs.* 4.32±1.51) ($p>0.05$). However, there were statistically significant differences between the groups in terms of homocysteine (14.16±3.02 *vs.* 18.89±4.39), plasma fibrinogen (4.65±1.02 *vs.* 6.60±1.14), and red blood cell distribution width (10.95±1.94 *vs.* 15.68±3.16) ($p<0.05$), as shown in Table III.

Analysis of Influencing Factors of Depression After Ischemic Stroke

The results of logistic regression analysis showed that age, MMSE score, BI index, NIHSS

Table I. Comparison of age, gender, and vascular risk factors.

Variables	Non-PSD (n=284)	PSD (n=90)	χ^2/t	*p*
Age (year)	61.15±9.76	63.63±10.18	2.079	0.038
Female (%)	105 (36.97)	48 (53.33)	7.5682	0.006
Vascular risk factors				
Hypertension (%)	202 (71.12)	63 (70.00)	0.766	0.445
Diabetes (%)	71 (25.00)	28 (31.11)	0.180	0.857
Hyperlipemia (%)	57 (20.07)	16 (17.78)	1.205	0.230
Smoke (%)	127 (44.72)	32 (35.53)	0.343	0.842
Drink (%)	98 (34.51)	29 (32.22)	0.189	0.910
Coronary heart disease (%)	21 (7.39)	6 (6.67)	0.136	0.713

Post-stroke depression (PSD).

Table II. Comparison of clinical data between patients with PSD and patients without PSD.

Clinical data	Non-PSD (n=284)	PSD (n=90)	χ^2/t	p
Systolic blood pressure (mmHg)	137.23±16.61	139.16±20.14	0.911	0.363
Diastolic blood pressure (mmHg)	81.82±9.81	81.72±10.35	0.075	0.940
Body Mass Index (kg/m²)	25.13±3.11	25.36±3.25	0.605	0.546
Barthel index (BI)	60.34±5.62	40.74±5.90	28.465	0.001
NIHSS score	10.32±2.10	11.48±3.65	3.749	0.001
MMSE score	24.68±2.16	20.15±2.05	17.547	0.001
CSVD score	1.96±0.45	3.50±0.38	29.315	0.001
History of antiplatelet therapy (%)	38 (13.38)	14 (15.56)	10.110	0.913
History of stroke (%)	32 (11.27)	10 (11.11)	0.364	0.716

Post-stroke depression (PSD), Barthel Index (BI), Mini-Mental State Examination (MMSE), National Institutes of Health Stroke Scale (NIHSS), cerebral small vessel disease (CSVD).

Table III. Comparison of laboratory data between patients with PSD and patients without PSD.

Laboratory data	Non-PSD (n=284)	PSD (n=90)	t	p
Total cholesterol (mmol/L)	4.08±1.11	4.10±1.10	0.149	0.881
Triglycerides (mmol/L)	1.39±0.33	1.47±0.37	1.945	0.053
Low-density lipoprotein (mmol/L)	2.39±0.61	2.53±0.69	1.837	0.067
High-density lipoprotein (mmol/L)	1.05±0.31	1.09±0.27	1.099	0.273
Fasting blood glucose (mmol/L)	5.55±1.82	5.45±1.86	0.452	0.652
Homocysteine (μmol/L)	14.16±3.02	18.89±4.39	11.506	0.001
Plasma fibrinogen (g/L)	4.65±1.02	6.60±1.14	11.353	0.001
Red blood cell distribution width (%)	10.95±1.94	15.68±3.16	17.062	0.002
High-sensitivity C-reactive protein (mg/L)	4.09±1.63	4.32±1.51	1.187	0.236

Post-stroke depression (PSD).

score, plasma fibrinogen concentration, homocysteine level, red blood cell distribution width, and CSVD burden score are the main influencing factors of PSD (OR>1, $p<0.05$), as shown in Table IV.

Correlation Analysis of Each Factor and the Occurrence of Depression After Ischemic Stroke

Correlation analysis revealed that age, NIHSS score, plasma fibrinogen concentration, homocysteine level, red blood cell distribution width, CSVD burden score, and the occurrence of post-stroke depression in ischemic stroke were positively correlated (r=0.565, 0.615, 0.482, 0.514, 0.572, 0.608, $p<0.05$). On the other hand, the MMSE score and BI index were negatively correlated with the occurrence of post-stroke depression (r=-0.604, -0.590, $p<0.05$), as shown in Table V.

ROC Curve of the Combination Model of MMSE, NIHSS and CSVD Score to Predict PSD

We included the indexes with |r|>0.6 and p-values (from correlation analysis and logistic regression analysis) <0.05 to develop a combined model for predicting post-stroke depression (PSD). The ROC curve analysis revealed an area under the curve (AUC) of 0.926 and Youden's index of 0.744 (Table VI and Figure 1). The sensitivity of the CSVD burden score in predicting PSD was 0.833, with a specificity of 0.883 (Table VI and Figure 1).

Discussion

AIS is caused by stenosis or occlusion of cerebral and vertebral arteries, resulting in inadequate blood supply to the brain and subsequent tissue necrosis[13]. Clinical symptoms of AIS typically include transient focal neurological dysfunction, limb numbness, weakness, sensory disorders, monocular haze, dizziness, diplopia, and ataxia[14,15]. Early detection of AIS injury is challenging, with cranial CT scans being commonly used to rule out cerebral hemorrhage. However, these scans often show no abnormalities in normal cases. After 24 hours of onset, MRI technology becomes more effective in diagnosing AIS.

Table IV. Factors influencing post-stroke depression in ischemic stroke.

Factors	β	S.E.	Wald	df	p	OR	95% CI
Age	1.001	0.332	9.104	1	0.003	2.720	1.420-5.209
MMSE score	0.650	0.286	5.175	1	0.023	1.915	1.094-3.351
BI score	0.549	0.209	6.892	1	0.009	1.732	1.149-2.610
NIHSS score	0.797	0.341	5.456	1	0.020	2.219	1.137-4.330
Plasma fibrinogen concentration	0.181	0.247	5.533	1	0.012	1.298	1.058-1.945
Homocysteine	1.416	0.268	27.969	1	<0.001	4.122	2.439-6.968
Red blood cell distribution width	1.356	0.255	10.266	1	0.020	1.186	1.014-1.882
CSVD burden score	1.152	0.179	41.234	1	<0.001	3.164	2.226-4.497

Barthel Index (BI), Mini-Mental State Examination (MMSE), National Institutes of Health Stroke Scale (NIHSS), cerebral small vessel disease (CSVD).

Digital subtraction angiography can provide valuable information about the location and nature of large artery lesions in the brain, highlighting the degree of arterial stenosis, occlusion, and distortion. Consequently, MRI is frequently utilized to detect AIS in patients[16,17].

CSVD is characterized by clinical and imaging abnormalities in the small arteries, arterioles, and capillaries of the brain. Although significant research efforts have been made to explore the pathogenesis, etiology, and clinical features of CSVD, it is still classified based on clinical manifestations and imaging features, with AIS being one subtype[18,19]. PSD is a unique form of depression that occurs as a result of physical illness in patients. PSD can lead to negative emotions, reduced compliance, and impaired coordination, resulting in patients not taking medication timely or as prescribed. This lack of adherence affects medication compliance, patient confidence in recovery, and ultimately, the clinical diagnosis and treatment of AIS patients[20,21]. Therefore, the early detection, prevention, and intervention of PSD are crucial to strengthen the prognosis of AIS patients.

The results of this study indicate that there is no statistically significant difference ($p>0.05$) in hypertension, diabetes, hyperlipidemia, smoking, alcohol consumption, coronary heart disease, systolic/diastolic blood pressure, body weight, cholesterol (total, triglycerides, low-density lipoprotein, high-density lipoprotein), fasting blood glucose, homocysteine, high-sensitivity C-reactive protein, lateralization of acute hemisphere infarction, and CMB between patients with and without PSD. However, significant differences ($p<0.05$) were observed in CSVD markers such as EPV, white matter lesions (WML), asymptomatic LI, CSVD category, age, and gender between patients with and without PSD. This suggests that factors like hypertension, diabetes, hyperlipidemia, smoking, alcohol consumption, and coronary heart disease, as well as indicators such as systolic blood

Table V. Comparison of age, gender, and vascular risk factors.

	Post-stroke depression	
Items	r	p
Age	0.565	0.016
MMSE score	-0.604	0.004
BI index	-0.590	0.007
NIHSS score	0.615	0.006
Plasma fibrinogen concentration	0.482	0.029
Homocysteine level	0.514	0.020
Red blood cell distribution width	0.572	0.012
CSVD burden score	0.608	0.001

Barthel Index (BI), Mini-Mental State Examination (MMSE), National Institutes of Health Stroke Scale (NIHSS), cerebral small vessel disease (CSVD).

Table VI. ROC curve for CSVD prediction of PSD.

Indexes	AUC	Standard error	Progressive significance	Youden's index	Sensitivity	Specificity	Progressive 95% confidence interval	
							Lower limit	Upper limit
CSVD	0.926	0.031	<0.001	0.744	0.833	0.883	0.782	0.941

Cerebral small vessel disease (CSVD).

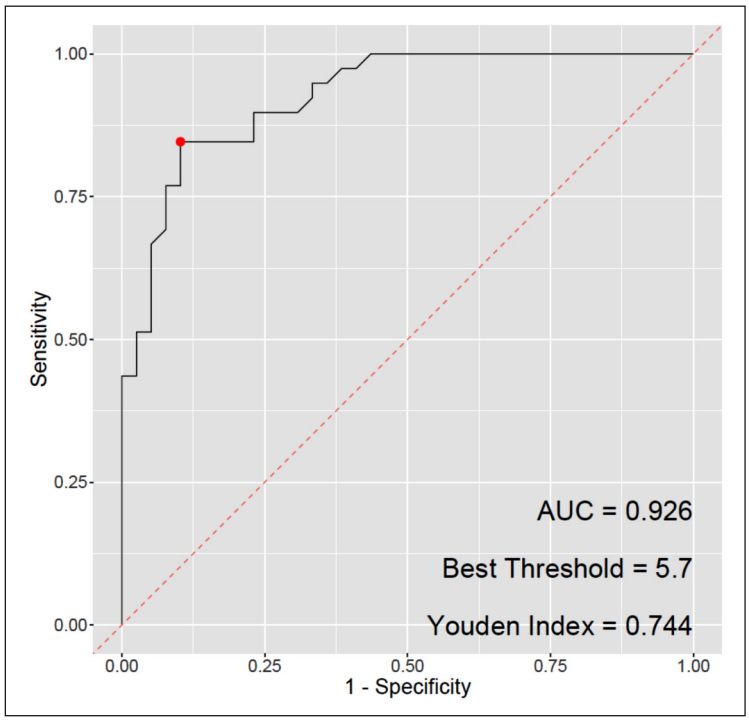

Figure 1. ROC curve of CSVD predicting PSD.

pressure, do not have a significant impact on the occurrence of PSD, as no abnormalities were observed in these parameters in either group.

On the other hand, age, MMSE score, BI index, NIHSS score, plasma fibrinogen concentration, homocysteine level, and red blood cell distribution width were identified as significant factors associated with post-stroke depression. Age, NIHSS score, plasma fibrinogen concentration, homocysteine level, red blood cell distribution width, and the occurrence of post-stroke depression in ischemic stroke were positively correlated ($p<0.05$). Conversely, the MMSE score and BI index were negatively correlated with the occurrence of post-stroke depression ($p<0.05$). Additionally, the CSVD burden score was found to be a major influencing factor for PSD, showing a positive correlation with its occurrence. Multiple mechanisms are believed to underlie the associations between CSVD and PSD. One such mechanism is the increased levels of monoamine oxidase in the aging brain, leading to a decrease in the concentrations of monoamine neurotransmitters such as serotonin (5-HT) and norepinephrine (NE), which can contribute to the development of PSD. Furthermore, the simultaneous effects of aging on the psychological and physiological aspects of elderly individuals result in decreased resilience to physical and emotional trauma, causing neuronal damage, changes in lifestyle, and factors related to family and social dynamics that can lead to the occurrence of depressive symptoms.

Females have been found to be more susceptible to the influence of psychological and social stressors compared to males. This increased susceptibility can lead to physiological and psychological imbalances, ultimately resulting in PSD when acute events occur in the brain with a strong increase in cerebral blood flow and overall neuronal development[22,23]. Moreover, moderate to severe cerebral atrophy can cause loss and shrinkage of brain tissue, which in turn affects emotional regulation and cognitive function. The occurrence of cerebral atrophy may disrupt neurotransmitter release, thereby impacting emotional stability and increasing the risk of PSD[24]. Stroke itself can cause damage to the brain's blood vessels, triggering the formation of blood clots. An elevated concentration of plasma fibrinogen, an important component in blood clot formation, may reflect changes in vascular damage and coagulation status. The presence of blood clots can potentially affect cerebral blood flow, subsequently influencing the function and metabolism of brain neurons, thus increasing the risk of PSD.

This study investigates the disparities in the severity of various CSVD markers between patients with and without PSD. WMHs are a common imaging indicator of CSVD. The white matter, which functions as a conduit for neural

signals and supports neuronal activity, is typically affected by WMHs[25-27]. WMHs are abnormal signal intensities in the white matter region and are generally caused by reduced cerebral blood flow or small vessel disease[28-30]. The presence of WMHs can reflect the extent of vascular damage and ischemic lesions in stroke patients. Studies in the literature have demonstrated a link between WMHs and the occurrence of PSD four months post-stroke, with the severity of WMHs independently associated with PSD. The existence of WMHs can lead to neural function impairment and abnormalities, thereby impacting the emotional and psychological state of patients. Additionally, WMHs may contribute to decreased cognitive function, reduced quality of life, and an increased risk of depressive symptoms following a stroke. It is possible that the formation of WMHs is linked to inflammation and alterations in neurotransmitters. Ischemic and reperfusion injury in brain tissue after a stroke triggers an inflammatory response that can affect neurotransmitters like serotonin and dopamine, potentially leading to emotional and psychological changes in patients and an increased likelihood of experiencing depressive symptoms.

Furthermore, sLI, which refer to asymptomatic lacunar infarctions, are associated with the incidence of PSD in the thalamus, basal ganglia, and deep white matter. By comparing key data between the two groups of patients, differences in the burden of moderate to severe WMHs, EPVS grade 2-4, sLI, and the overall CSVD score are evident, indicating variations in the data of the two groups[31].

The CSVD burden score offers several advantages. It provides a comprehensive assessment of the impact of CSVD on the brain, reducing the reliance on individual MRI features. Employing standardized visual rating definitions ensures the simplicity and practicality of the CSVD burden score, allowing for easy data comparison and combination. This score holds potential for baseline stratification and could serve as an alternative indicator for CSVD in prevention and treatment trials. We included the indexes with $|r|>0.6$ and p-values (from correlation analysis and logistic regression analysis)<0.05 to develop a combined model for predicting PSD. The ROC curve of the combination model of MMSE, NIHSS and CSVD score to predict PSD showed an AUC of 0.926 and Youden's index of 0.744. These suggested that the combination model presented a valuable approach to predicting PSD.

Conclusions

In conclusion, age, MMSE score, BI index, NIHSS score, plasma fibrinogen concentration, homocysteine level, red blood cell distribution width, and CSVD burden score are all major influencing factors for the occurrence of post-stroke depression. The combination model based on MMSE, NIHSS and CSVD score presented a valuable approach to predict PSD.

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Authors' Contributions
Qiaozhuan Li and Zhao Li conceived the manuscript's structure. Rujuan Zhou and Kepeng Zhao made the figures. Weixiang Wu reviewed it, and Zhengxiang Ji and Su Jiang edited it. All authors read and approved the final manuscript.

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Availability of Data and Materials
The datasets used and analyzed during the current study are available from the corresponding author, Qiaozhuan Li, on reasonable request.

Ethics Approval
This study was conducted in accordance with the ethical regulations of the Declaration of Helsinki. This study was approved by the Ethics Committee of the Taixing People's Hospital (No. LW2021007).

Conflict of Interest
The authors declare that they have no competing interests.

Informed Consent
All patients signed the informed consent form.

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References

1) Almhdawi KA, Alazrai A, Kanaan S, Shyyab AA, Oteir AO, Mansour ZM, Jaber H. Post-stroke depression, anxiety, and stress symptoms and their

associated factors: A cross-sectional study. Neuropsychol Rehabil 2021; 31: 1091-1104.

2) Arcadi FA, Corallo F, Torrisi M, Scarfi C, Lo Buono V, Formica C, Bramanti P, Marino S, Bonanno L, De Cola MC. Role of citicoline and choline in the treatment of post-stroke depression: an exploratory study. J Int Med Res 2021; 49: 3000605211055036.
3) Bi H, Wang M. Role of social support in poststroke depression: A meta-analysis. Front Psychiatry 2022; 13: 924277.
4) Chau JPC, Lo SHS, Zhao J, Choi KC, Lam SKY, Butt L, Thompson DR. Factors Associated with Post-Stroke Depression in Chinese Stroke Survivors. J Stroke Cerebrovasc Dis 2021; 30: 106076.
5) Chaudhary D, Friedenberg I, Sharma V, Sharma P, Abedi V, Zand R, Li J. Predictors of Post-Stroke Depression: A Retrospective Cohort Study. Brain Sci 2022; 12: 993.
6) Chen Y, Zou H, Peng M, Chen Y. Association between homocysteine levels in acute stroke and poststroke depression: A systematic review and meta-analysis. Brain Behav 2022; 12: e2626.
7) Dong L, Brown DL, Chervin RD, Case E, Morgenstern LB, Lisabeth LD. Pre-stroke sleep duration and post-stroke depression. Sleep Med 2021; 77: 325-329.
8) Feng RF, Ma R, Wang P, Ji X, Zhang ZX, Li MM, Jiao JW, Guo L. Efficacy of escitalopram for poststroke depression: a systematic review and meta-analysis. Sci Rep 2022; 12: 3304.
9) Frank D, Gruenbaum BF, Zlotnik A, Semyonov M, Frenkel A, Boyko M. Pathophysiology and Current Drug Treatments for Post-Stroke Depression: A Review. Int J Mol Sci 2022; 23: 15114.
10) Guo J, Wang J, Sun W, Liu X. The advances of post-stroke depression: 2021 update. J Neurol 2022; 269: 1236-1249.
11) Hang X, Li J, Zhang Y, Li Z, Zhang Y, Ye X, Tang Q, Sun W. Efficacy of frequently-used acupuncture methods for specific parts and conventional pharmaceutical interventions in treating post-stroke depression patients: A network meta-analysis. Complement Ther Clin Pract 2021; 45: 101471.
12) Hu J, Wang L, Fan K, Ren W, Wang Q, Ruan Y, Yuan C, Huang G, He J. The Association Between Systemic Inflammatory Markers and Post-Stroke Depression: A Prospective Stroke Cohort. Clin Interv Aging 2021; 16: 1231-1239.
13) Jaywant A, DelPonte L, Kanellopoulos D, O'Dell MW, Gunning FM. The Structural and Functional Neuroanatomy of Post-Stroke Depression and Executive Dysfunction: A Review of Neuroimaging Findings and Implications for Treatment. J Geriatr Psychiatry Neurol 2022; 35: 3-11.
14) Oestreich LKL, Wright P, O'Sullivan MJ. Hyperconnectivity and altered interactions of a nucleus accumbens network in post-stroke depression. Brain Commun 2022; 4: fcac281.
15) Pan C, Li G, Jing P, Chen G, Sun W, Miao J, Wang Y, Lan Y, Qiu X, Zhao X, Mei J, Huang S, Lian L, Wang H, Zhu Z, Zhu S. Structural disconnection-based prediction of poststroke depression. Transl Psychiatry 2022; 12: 461.
16) Pan C, Li G, Sun W, Miao J, Wang Y, Lan Y, Qiu X, Zhao X, Wang H, Zhu Z, Zhu S. Psychopathological network for early-onset post-stroke depression symptoms. BMC Psychiatry 2023; 23: 114.
17) Petrea RE, O'Donnell A, Beiser AS, Habes M, Aparicio H, DeCarli C, Seshadri S, Romero JR. Mid to Late Life Hypertension Trends and Cerebral Small Vessel Disease in the Framingham Heart Study. Hypertension 2020; 76: 707-714.
18) Ryu YH, Kim SY, Kim TU, Lee SJ, Park SJ, Jung HY, Hyun JK. Prediction of Poststroke Depression Based on the Outcomes of Machine Learning Algorithms. J Clin Med 2022; 11: 2264.
19) Sarkar A, Sarmah D, Datta A, Kaur H, Jagtap P, Raut S, Shah B, Singh U, Baidya F, Bohra M, Kalia K, Borah A, Wang X, Dave KR, Yavagal DR, Bhattacharya P. Post-stroke depression: Chaos to exposition. Brain Res Bull 2021; 168: 74-88.
20) Stahl B, Millrose S, Denzler P, Lucchese G, Jacobi F, Floel A. Intensive Social Interaction for Treatment of Poststroke Depression in Subacute Aphasia: The CONNECT Trial. Stroke 2022; 53: 3530-3537.
21) Volz M, Ladwig S, Werheid K. Gender differences in post-stroke depression: A longitudinal analysis of prevalence, persistence and predictive value of known risk factors. Neuropsychol Rehabil 2021; 31: 1-17.
22) Wang X, Cai W, Wang Y, Huang S, Zhang Q, Wang F. Is Electroacupuncture an Effective and Safe Treatment for Poststroke Depression? An Updated Systematic Review and Meta-Analysis. Biomed Res Int 2021; 2021: 8661162.
23) Wijeratne T, Sales C. Understanding Why Post-Stroke Depression May Be the Norm Rather Than the Exception: The Anatomical and Neuroinflammatory Correlates of Post-Stroke Depression. J Clin Med 2021; 10: 1674.
24) Wijeratne T, Sales C, Wijeratne C. A Narrative Review on the Non-Pharmacologic Interventions in Post-Stroke Depression. Psychol Res Behav Manag 2022; 15: 1689-1706.
25) Woranush W, Moskopp ML, Sedghi A, Stuckart I, Noll T, Barlinn K, Siepmann T. Preventive Approaches for Post-Stroke Depression: Where Do We Stand? A Systematic Review. Neuropsychiatr Dis Treat 2021; 17: 3359-3377.
26) Wu T, Yue T, Yang P, Jia Y. Notable efficacy of Shugan Jieyu capsule in treating adult with post-stroke depression: A PRISMA-compliant meta-analysis of randomized controlled trials. J Ethnopharmacol 2022; 294: 115367.
27) Zhang J, Song Z, Gui C, Jiang G, Cheng W, You W, Wang Z, Chen G. Treatments to post-stroke depression, which is more effective to HAMD improvement? A network meta-analysis. Front Pharmacol 2022; 13: 1035895.
28) Xia W, Xu Y, Gong Y, Cheng X, Yu T, Yu G. Microglia Involves in the Immune Inflammatory

Response of Poststroke Depression: A Review of Evidence. Oxid Med Cell Longev 2022; 2022: 2049371.

29) Yang L, Zhao Q, Liu H, Zhu X, Wang K, Man J. Family Functioning Mediates the Relationship Between Activities of Daily Living and Poststroke Depression. Nurs Res 2021; 70: 51-57.

30) Yue Y, You L, Zhao F, Zhang K, Shi Y, Tang H, Lu J, Li S, Cao J, Geng D, Wu A, Yuan Y. Common susceptibility variants of KDR and IGF-1R are associated with poststroke depression in the Chinese population. Gen Psychiatr 2023; 36: e100928.

31) Zhang X, Tang Y, Xie Y, Ding C, Xiao J, Jiang X, Shan H, Lin Y, Li C, Hu D, Li T, Sheng L. Total magnetic resonance imaging burden of cerebral small-vessel disease is associated with poststroke depression in patients with acute lacunar stroke. Eur J Neurol 2017; 24: 374-380.