Article

Logistic Regression Analysis-Based Study of Risk Factors and Assessment Model of Non-Acute-Phase Post-Stroke Depression

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Abstract

Background: This work aimed to investigate the risk factors for post-stroke depression (PSD) during the non-acute phase of stroke, and to construct and validate a risk assessment model for PSD using logistic regression analysis, thereby providing a basis for early clinical screening and intervention.

Methods: A total of 900 stroke patients admitted to our hospital from April 2021 to April 2023 were enrolled in a prospective cohort study. After 6 months of follow-up, patients were divided into a PSD group (n = 485) and a non-PSD group (n = 415) based on the 17-item Hamilton Depression Rating Scale (HAMD-17) scores and diagnostic criteria. Data on demographics, disease characteristics, lifestyle factors, biochemical indicators, and scale scores were collected. Independent influencing factors were identified using univariate and multivariate logistic regression analyses. A risk prediction model was then constructed and validated using the receiver operating characteristic (ROC) curve.

Results: Multivariate logistic regression analysis showed that sex, parietal lobe lesions, alcohol consumption, smoking, hypertension, family support, National Institutes of Health Stroke Scale (NIHSS) score, Mini-Mental State Examination (MMSE) score, Social Support Rating Scale (SSRS) score, and Barthel Index (BI) were independent influencing factors for depression in non-acute stroke patients (all $p < 0.05$). The optimal cut-off value of the model was 18.12 points, and the area under the ROC curve (AUC) was 0.91 ($p = 0.001$), indicating good predictive performance.

Conclusions: This study successfully constructed a risk assessment model with excellent predictive performance for PSD during the non-acute phase of stroke. The model can be used to assess PSD symptoms and screen high-risk populations, providing a reference for early clinical intervention.

Keywords

non-acute stroke; depression; risk factors; patient prognosis; Logistic regression; assessment model

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Introduction

Stroke is a common neurological disorder typically accompanied by acute-phase neurological damage and functional impairment [1]. Post-stroke depression (PSD) refers to an emotional and psychological disorder that occurs after a stroke. It is characterized by sustained loss of interest in life, feelings of sadness, self-denial, sleep disturbances, decreased appetite, and potentially accompanied by anxiety, among other symptoms. PSD is a prevalent complication during the stroke recovery process. Its occurrence not only significantly reduces the quality of life for patients but may also impede the rehabilitation process, exerting a profound impact on the recovery and social integration of patients [2,3].

The etiology of PSD is complex and remains not fully understood. It may be related to pathophysiological changes induced by brain injury, or it may result from significant alterations in life circumstances due to post-stroke functional decline, thereby leading to adverse psychological effects [4]. Stroke itself is a major risk factor for PSD, but other factors may also increase the risk of its occurrence. A systematic review and meta-analysis further found [5] that baseline cognitive impairment was the strongest risk factor for predicting post-stroke cognitive impairment (PSCI) and post-stroke dementia. Additionally, modifiable risk factors included diabetes mellitus, atrial fibrillation, and markers of cerebral small vessel disease (e.g., moderate-to-severe white matter hyperintensities, increased severity of white matter hyperintensities, and more than three lacunar infarcts). Other risk factors independent of age and stroke severity included lower educational level, prior stroke history, left hemisphere stroke, brain atrophy, and poorer baseline functional status. Of note, the strength of the associations between these risk factors and PSD has diminished in studies published in recent years, although attention should still be paid to the impact of inter-study heterogeneity and publication bias. The pathological mechanisms of PSD are complex, involving dysfunction of the monoaminergic system, dysregulation of the glutamatergic system, abnormalities in the gut-brain axis, and neuroinflammation. However, the exact mechanisms remain not fully understood [6].

Logistic regression modeling can also provide insight into the extent to which independent variables influence the probability of events. In the medical field, it can be employed for predicting disease occurrence, assessing drug efficacy, or evaluating patient outcomes [7]. Investigating the risk factors for PSD is of paramount importance for early identification, intervention in depressive symptoms, and enhancing the rehabilitation process for patients. At present, logistic regression analyses of risk factors for PSD have identified multiple factors that may influence the occurrence of PSD. A retrospective cohort study of PSD during the 3-month subacute phase in acute ischemic stroke survivors indicated a bidirectional relationship between the severity of neurological deficits, quantified by the National Institutes of Health Stroke Scale (NIHSS) scale, and the course of depressive symptoms after stroke [8]. Elevated baseline depression scores and prolonged hospital stay both independently increased the risk of persistent PSD at 3 months post-stroke; conversely, patients with milder neurological deficits at discharge were more likely to experience remission of depressive symptoms during the subacute phase. The study also emphasized that environmental clinical indicators, such as hospital stay length, are underrecognized prognostic factors in PSD and warrant greater attention in clinical screening and intervention. Another case-control study of 103 stroke patients found [9] that inflammation-related factors also participate in the pathogenesis of PSD: multiple polymorphisms of the *C-reactive protein (CRP)* gene (rs2794520, rs1205, rs3091244) were significantly associated with early-onset PSD, and decreased splenic Computed Tomography (CT) values based on specific CRP genotypes, as well as reduced peripheral blood monocyte counts, were also independent risk factors for PSD. These results suggest that, in addition to the degree of neurological deficit, genetic background, immune-inflammatory responses, and sociocultural factors may together constitute a risk prediction system for PSD. Some scholars have emphasized the significance of long-term tracking of PSD because depressive symptoms may manifest at different time points following stroke [10]. Logistic regression can be utilized to analyze risk factors at various time points. Logistic regression analysis has yielded valuable insights into investigating risk factors for PSD after stroke. Most existing studies have focused on PSD in the acute phase, while research on the pathogenesis and risk prediction models for non-acute-phase PSD remains limited. Early identification and prediction of non-acute-phase PSD risk can provide a basis for early clinical intervention, reduce the incidence of PSD, and improve patients' psychological status and rehabilitation outcomes.

In this study, the risk factors for PSD in non-acute stroke patients were assessed using a Logistic regression model, and a predictive model was constructed based on these risk factors to determine whether depressive symptoms might be experienced by the patients. The goal was to provide guidance for the assessment of PSD risk, with the ultimate aim of optimizing preventive strategies for PSD and encouraging active participation of patients in compre-

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hensive rehabilitation treatment, thereby reducing the duration of the rehabilitation process.

Materials and Methods

Study Subjects

The study selected 900 stroke patients who were admitted to Jieyang People's Hospital, Guangdong Province, for inpatient treatment from April 2021 to April 2023 as the research subjects. The clinical data of the patients will be prospectively collected. Among the 900 patients, there were 587 males and 313 females, with ages ranging from 18 to 78 years and a mean age of (53.16 ± 12.97) years. Based on the 17-item Hamilton Depression Rating Scale (HAMD-17) score, a cutoff value of ≥8 was used as the positive threshold for depression [11,12]. Combined with the diagnostic criteria for PSD, the patients were divided into a PSD group (485 cases) and a non-PSD group (415 cases).

Inclusion criteria: (i) Patients with intracerebral hemorrhage or ischemic stroke confirmed by cranial CT or Magnetic Resonance Imaging (MRI); the diagnostic criteria for depressive disorders based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [13] were used only for subgroup classification at the 6-month follow-up, rather than as a mandatory requirement at enrollment. The diagnostic criteria for depressive disorder due to another medical condition are as follows: prominent and persistent depressed mood, or markedly diminished interest or pleasure in almost all activities; symptoms persisting for at least 2 weeks; evidence that the disorder is the direct pathophysiological consequence of stroke; symptoms that are not better explained by another mental disorder and do not occur exclusively during delirium; and symptoms that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. (ii) patients aged over 18 years; (iii) onset of stroke occurred within one week; (iv) patients had clear consciousness upon admission, with stable medical conditions and independent comprehension of others' language and behavior.

Exclusion criteria: (i) patients with concomitant significant organ diseases; (ii) patients with a history of psychiatric disorders; (iii) patients with severe heart, liver, or kidney dysfunction.

In this study, the disease course was staged according to the international unified stroke staging criteria issued by the Stroke Recovery and Rehabilitation Roundtable (SRRR) [14], with the staging definitions based on the following considerations. (1) Clinical staging criteria: stroke hyperacute phase (0–24 hours) and acute phase (1–7 days), during which the core priorities are stabilizing vital signs and preventing complications; early subacute phase (7 days to 3 months postonset) and late subacute phase (3–6 months), which represent the peak period of neuroplasticity, with the emphasis on early initiation of rehabilitation interventions; and chronic phase (>6 months postonset). The enrolled patients in this study were hospitalized predominantly during the acute phase (within one week of onset). (2) Alignment with research purpose: this study aimed to investigate risk factors for depression in the nonacute phase of stroke and selected the 6month postonset followup time point, which falls within the late subacute phase. This time point is beyond the acute emergency treatment phase and precisely covers the critical period of high depression incidence during stroke rehabilitation, thereby conforming to the nonacute research positioning. (3) Academic uniformity: this staging scheme is consistent with the mainstream international stroke staging system established by the SRRR consensus, where the nonacute phase corresponds to the entire period from 7 days postonset onward. This ensures comparability of the study results with similar literature and facilitates adaptation to clinical practice.

Study Methodologies

A comprehensive analysis of various factors, including sex, age, educational level, stroke location, family support, degree of neurological impairment, and social support, was conducted for all patients included in the study. Univariate analysis using logistic regression was carried out on factors exhibiting marked differences to ultimately identify the risk factors influencing depression in PSD patients. The patients were followed up for six months through inpatient or outpatient visits; all variables were assessed at admission and at 2 weeks, 1 month, 3 months, and 6 months after stroke onset. PSD outcome was determined at the 6-month assessment based on PSD diagnostic criteria and depression rating scales.

Screening of Relevant Influencing Factors for PSD

Based on a literature review and clinical experience, the potential influencing factors included in this study encompass the following five categories, and all variables were collected at admission or during follow-up.

(1) Sociodemographic factors: Age, sex, and educational level (categorized as primary school or below, junior high school, high school/technical secondary school, and

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college or above).

(2) Disease-related factors: Stroke type (ischemic/hemorrhagic), lesion location (basal ganglia, frontal lobe, parietal lobe, temporal lobe, and occipital lobe; all dichotomized as yes/no), history of hypertension (yes/no), history of diabetes (yes/no), severity of neurological deficit at admission (NIHSS score, continuous variable), and cognitive function (Mini-Mental State Examination (MMSE) score, continuous variable).

(3) Lifestyle factors: Smoking history and drinking history. For the convenience of clinical statistical analysis, both variables were dichotomized as "yes/no". Specifically, smoking history was defined as "smoking at least one cigarette per day for more than 6 months"; drinking history was defined as "consuming alcohol at least once per week for more than 6 months".

(4) Biochemical indicators: Fasting venous blood was collected on the morning of the day after admission to measure laboratory parameters, including brain-derived neurotrophic factor (BDNF) and platelet-to-lymphocyte ratio (PLR).

(5) Psychosocial factors and functional status: Family care (measured by the family Adaptation, Partnership, Growth, Affection, and Resolve (APGAR) index, categorized as well-functioning or dysfunctional with a cutoff of 7 points), social support level (Social Support Rating Scale (SSRS) score, continuous variable), and activities of daily living (Barthel Index (BI), continuous variable).

Observation Indicators and Effectiveness Evaluation Standards

(1) The severity of neurological impairment was assessed using the NIHSS [15]. The grading criteria were as follows: a score of 0 indicated normal neurological function, scores from 1 to 4 denoted mild stroke, scores from 5 to 15 represented moderate stroke, and scores exceeding 16 indicated severe stroke.

(2) The HAMD-17 was adopted to assess the degree of depression in patients [11]. The scoring criteria were as follows: ① The scale covered 17 core symptoms, including depressive mood, guilt, and suicidal ideation, and adopted a graded scoring system of 0–2 points or 0–4 points for each item. The total score ranged from 0 to 52 points, with a higher score indicating more severe depressive symptoms. ② Screening threshold: a total score of $\geq$8 points was set as the positive criterion for depressive symptoms. This point has been detailed in section "Study Subjects".

(3) The level of cognitive impairment was assessed using the MMSE [16]. The scoring criteria were as follows: ① The score range was 0–30 points, covering multiple cognitive domains such as orientation, memory, attention, calculation ability, and language function; ② Scoring principle: higher scores indicated better cognitive function while lower scores indicated more severe cognitive impairment, which was consistent with the general evaluation norms of the MMSE scale.

(4) The SSRS (Chinese version) [17] was used to evaluate the degree of social support for patients. The scoring rules were as follows: ① The scale consisted of 10 items, covering three dimensions including objective support, subjective support, and the utilization degree of support; ② Items 1–4 and 8–10 were single-choice questions, scored 1–4 points according to the options selected; Item 5 was scored 1–4 points based on the degree of family support (from no support to complete support); Items 6–7 were multiple-choice questions, with "no source" scored 0 point and 1 point awarded for each selected support source; ③ Total score calculation: the sum of objective support score (total scores of Items 2, 6, and 7), subjective support score (total scores of Items 1, 3, 4, and 5), and support utilization score (total scores of Items 8, 9, and 10). The total score range was 12–66 points, with higher scores indicating higher levels of social support.

(5) Daily living abilities were assessed using the BI [18]. The original scoring criteria of this scale were as follows: ① It included 10 core items such as feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, transferring between bed and chair, walking on flat ground, and climbing stairs; ② Itemized scoring: each item was assigned 0–15 points according to the ability of independent completion. For example, feeding was scored 10 points (completely independent), 5 points (partially assisted), and 0 points (completely dependent); transferring between bed and chair was scored 15 points (completely independent), 10 points (minimally assisted), 5 points (maximally assisted), and 0 points (completely dependent); ③ Total score and classification: the total score (0–100 points) was the sum of scores of all items Higher scores indicated stronger activities of daily living ability.

(6) The Family APGAR Index Questionnaire (Chinese version) [19] was applied to evaluate the level of family care for patients. This scale was compiled by Smilkstein [20] in 1978. It consisted of 5 items, covering 5 dimensions, including family adaptability, cooperation, maturity, affection, and intimacy. The scoring rules were as follows: ① Each item was rated using a 3-point Likert scale, with "rarely" scored 0 point, "sometimes" scored 1 point, and

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"often" scored 2 points; ② Total score calculation: the total score was the sum of scores of the 5 items, ranging from 0–10 points; ③ Classification criteria: scores of 0–3 points indicated severe family dysfunction, scores of 4–6 points indicated moderate family dysfunction, A score of 7–10 indicates good family function; this study used a cutoff of 7 for grouping. Higher scores indicated more adequate family care obtained by patients [21].

For subjective questions, patients provided individual responses, while objective questions were answered by caregivers. Scores for patients' abilities in daily living, severity of fatigue, sleep quality, and social support index were collected, and interviews were conducted jointly by two trained members of the research team.

Statistical Methodologies

Statistical analyses were performed using SPSS 23.0 (IBM Corp., Chicago, IL, USA). Normality tests were conducted first. Normally distributed continuous data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and comparisons between two groups were performed using the independent samples *t*-test. Non-normally distributed continuous data were expressed as median (interquartile range) [M (P25, P75)], and comparisons between two groups were performed using the Mann-Whitney U test. Categorical data were expressed as the number of cases (percentage), and comparisons between groups were performed using the chi-square (χ^2) test. Pairwise comparisons among multiple groups were performed using the Bonferroni correction. Collinearity diagnostics were performed before model building, and interaction terms such as sex × smoking were included in the analysis. With PSD occurrence as the dependent variable (coded as: occurrence = 1, non-occurrence = 0), variables with $p < 0.05$ in the univariate analysis were entered as independent variables to construct a multivariate logistic regression model. This model was used to evaluate the linear effects of each influencing factor on the log odds of PSD occurrence, and its standard functional form is presented as Formula (Eqn. 1).

$$Logit(p) = \ln\left(\frac{p}{1-p}\right) = \alpha_0 + \alpha_1 X_1 + \alpha_2 X_2 + \ldots + \alpha_n X_n \quad (1)$$

Among them, *p* represents the predicted probability of PSD occurrence, α_0 is the constant term, and α_1, ..., α_n are the partial regression coefficients of the respective covariates X_1, ..., X_n [22]. After calculating the Logit(*p*) value using this formula, the predicted probability of an individual developing PSD can be obtained through the logistic transformation ($p = 1/(1 + e^{-Logit(p)})$). The Logistic *p* regression model was employed to calculate the individual's probability (*p*) of the event happening. Model evaluation was performed by utilizing diagnostic tests and receiver operating characteristic (ROC) curves to determine the assessment threshold. The Youden Index, found in diagnostic tests, was used to determine the optimal threshold, and the area under the ROC curve (AUC) clarified the accuracy of the threshold assessment results. An AUC in the range of 0.5 to 0.7 suggested a lower diagnostic value for the evaluated parameter. An AUC of 0.5 indicates no diagnostic discrimination ability; the closer the value is to 1, the higher the diagnostic accuracy, with 1 representing ideal perfect discrimination [23]. A significance level of $p < 0.05$ denoted a statistically significant difference.

Results

Basic Information of the Research Object

The demographic characteristics of patients are shown in Table 1. A total of 900 patients were enrolled, including 485 in the PSD group and 415 in the non-PSD group. No statistically significant differences were observed between the two groups in terms of age, body mass index (BMI), heart rate, follow-up duration, pain score, lipid parameters (total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL)), high-sensitivity C-reactive protein (hs-CRP), homocysteine (Hcy), serum amyloid A, thyroid-stimulating hormone (TSH), or neutrophil-to-lymphocyte ratio (NLR) (all $p > 0.05$). However, significant differences were found between the two groups in sex distribution, BDNF levels, and PLR (all $p < 0.05$): the PSD group had a higher proportion of females (246 vs. 124, $p = 0.030$), significantly lower BDNF levels (5.83 ± 3.59 vs. 6.02 ± 3.72, $p = 0.007$), and significantly higher PLR levels (176.45 ± 32.43 vs. 169.38 ± 28.76, $p = 0.006$) compared with the non-PSD group.

Statistical Results of Basic Characteristics

Compared with the non-PSD group, the PSD group had significantly higher proportions of parietal lobe lesions, smoking, alcohol consumption, diabetes, hypertension, and family dysfunction (all $p < 0.05$). There were no significant differences between the two groups in stroke type, other lesion locations, or education level ($p > 0.05$) (See Table 2).

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Table 1. Sociodemographic characteristics of patients.

Indicator	PSD group (n = 485)	Non-PSD group (n = 415)	χ^2/t	p value
Age (years)	61.7 ± 4.9	59.1 ± 5.7	0.972	0.331
Gender (male/female)	239/246	291/124	4.765	0.030
BMI (kg/m^2)	24.6 ± 1.8	24.7 ± 2.2	2.283	0.376
Heart rate (beats/min)	89.8 ± 1.8	88.7 ± 2.1	1.087	0.895
Follow-up time (d)	265.3 ± 121.6	237.65 ± 118.67	3.102	0.704
Pain rating (points)	1.92 ± 1.43	1.95 ± 1.83	1.045	0.211
TC (mmol/L)	3.86 ± 0.87	3.72 ± 0.73	2.871	0.308
TG (mmol/L)	1.64 ± 0.83	1.62 ± 0.76	2.231	0.217
HDL (mmol/L)	1.08 ± 0.67	1.05 ± 0.57	0.917	0.132
LDL (mmol/L)	2.23 ± 0.86	2.31 ± 0.69	0.721	0.132
hs-CRP (mg/L)	5.98 ± 6.18	4.87 ± 6.84	2.654	0.367
Hcy (μmol/L)	16.87 ± 4.32	15.98 ± 3.97	3.408	0.145
BDNF (ng/mL)	5.83 ± 3.59	6.02 ± 3.72	2.063	0.007
Serum amyloid protein A (mg/L)	24.56 ± 16.72	23.97 ± 15.83	4.781	0.182
TSH (IU/L)	1.45 ± 0.67	1.56 ± 0.83	1.091	0.143
NLR	2.13 ± 1.34	2.08 ± 1.03	1.453	0.254
PLR	176.45 ± 32.43	169.38 ± 28.76	1.308	0.006

BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; Hcy, homocysteine; TSH, thyroid-stimulating hormone; NLR, neutrophil-to-lymphocyte ratio; PSD, post-stroke depression; BDNF, brain-derived neurotrophic factor; PLR, platelet-to-lymphocyte ratio.

Comparison of Ratings Between Two Groups

In the PSD group (n = 485), the NIHSS score was 11.04 ± 2.91, the HAMD-17 score was 17.41 ± 3.84, the MMSE score was 18.46 ± 2.76, the SSRS score was 28.46 ± 6.95, and the BI score was 38.04 ± 17.65. In the non-PSD group, the NIHSS score was 5.24 ± 2.75, the HAMD-17 score was 5.28 ± 1.86, the MMSE score was 23.61 ± 2.56, the SSRS score was 37.65 ± 6.75, and the Barthel score was 62.41 ± 18.05. The differences in all scale scores between the two groups were statistically significant (all $p < 0.05$) (Fig. 1).

Model Construction Evaluation

In this study, indicators with a p-value <0.05 in univariate analysis were included in the logistic regression, and a stepwise regression method was used to construct the model. The variable assignment is shown in Table 3.

Evaluation of Model Construction

A logistic regression analysis was performed with the presence of depressive symptoms as the dependent variable and sex, parietal lobe lesions, alcohol consumption, smoking, hypertension, family support, NIHSS, MMSE, SSRS, and Barthel scores as independent variables. The results showed that all of the above variables were significantly associated with the risk of depression in patients ($p < 0.05$). Univariate analysis showed that the differences between groups in BDNF and PLR were statistically significant ($p < 0.05$). However, after collinearity diagnostics and stepwise screening, these two biomarkers were excluded from the final multivariate logistic regression. BDNF and PLR indirectly affect PSD through pathways involving inflammatory responses and cerebral neural repair, and their predictive effects are mediated by core variables included in the model, such as neurological impairment, cognitive function, and activities of daily living. Therefore, after adjustment for confounding factors, they did not exert independent predictive value.

Based on the β coefficients presented in Table 4, the assessment model formula is as follows:

Logit (p) = 9.01 – 0.328 × sex + 0.167 × parietal lobe lesion + 0.337 × alcohol consumption + 0.327 × smoking + 0.656 × hypertension – 0.416 × family care – 0.189 × MMSE – 0.215 × SSRS – 0.342 × Barthel + 0.026 × NIHSS.

Univariate analysis showed higher proportions of alcohol consumption and smoking in the non-PSD group, whereas after adjusting for confounders in the multivariate

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Table 2. Basic patient characteristics.

Indicator	PSD group (n = 485)	Non-PSD group (n = 415)	χ^2	*p* value
Type of stroke			2.674	0.102
Hemorrhagic	189 (38.97%)	197 (47.47%)		
Ischemic	296 (61.03%)	218 (52.53%)		
Basal ganglia lesions			3.512	0.061
No	339 (69.90%)	361 (86.99%)		
Yes	146 (30.10%)	54 (13.01%)		
Frontal lobe lesions			3.621	0.058
No	346 (71.34%)	352 (84.82%)		
Yes	139 (28.66%)	62 (14.94%)		
Parietal lobe lesion			5.317	0.021
No	371 (76.49%)	326 (78.55%)		
Yes	114 (23.51%)	89 (21.45%)		
Temporal lobe lesions			1.527	0.217
No	438 (90.31%)	386 (93.01%)		
Yes	47 (9.69%)	29 (6.99%)		
Occipital lobe lesions			2.886	0.089
No	422 (87.01%)	382 (92.05%)		
Yes	63 (12.99%)	33 (7.95%)		
Smoking history			4.462	0.035
No	246 (50.72%)	199 (47.95%)		
Yes	239 (49.28%)	216 (52.05%)		
Drinking history			11.526	<0.001
No	267 (55.05%)	134 (32.29%)		
Yes	218 (44.95%)	281 (67.71%)		
Education level			3.974	0.115
Primary school or below	62 (12.78%)	45 (10.84%)		
Junior high school	69 (14.23%)	44 (10.60%)		
Senior high school/technical secondary school	223 (45.98%)	237 (57.11%)		
College or above	131 (27.01%)	89 (21.45%)		
Diabetes			4.651	0.032
No	208 (42.89%)	226 (54.46%)		
Yes	277 (57.11%)	189 (45.54%)		
Family care level			10.247	<0.001
≥7 points	207 (42.68%)	192 (46.27%)		
<7 points	278 (57.32%)	223 (53.73%)		
Hypertension			5.628	0.018
No	198 (40.82%)	164 (39.52%)		
Yes	287 (59.18%)	251 (60.48%)		

PSD, post-stroke depression.

analysis, both became risk factors, suggesting a confounding effect. Higher NIHSS scores were associated with an increased risk of PSD; higher MMSE, SSRS, and Barthel index scores were associated with a lower risk of PSD.

Determination of Evaluation Threshold for PSD Hazard Assessment Model

This study used the ROC curve combined with continuous interpolation fitting via the Youden index to determine the optimal cutoff value of the model. Table 5 only presents discrete threshold nodes selected by interval sampling and does not cover all continuous model scores. The optimal cutoff value of 18.12 was obtained through full-sample continuous ROC curve interpolation and does not appear among the discrete thresholds listed in Table 5. Due to discrete data sampling and confounding factors in indi-

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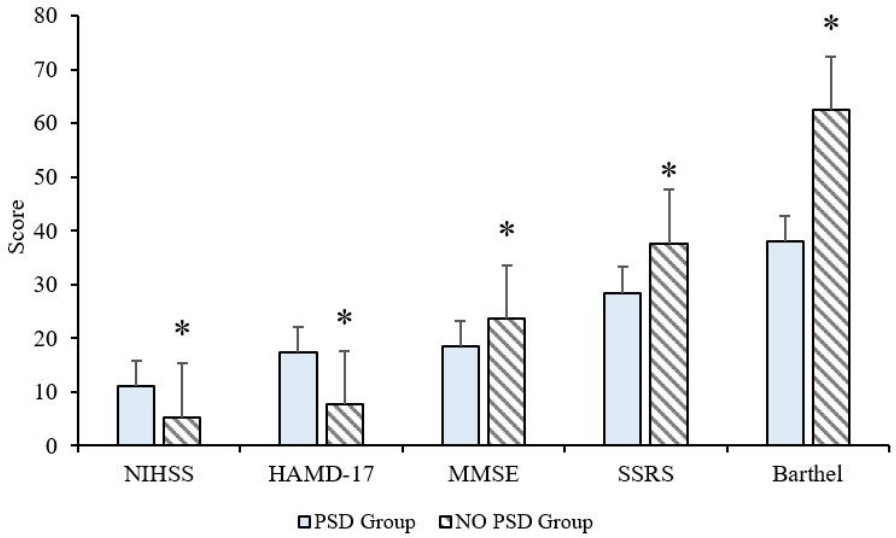


Fig. 1. Comparison of scores between two groups. NIHSS, National Institutes of Health Stroke Scale; HAMD-17, 17-item Hamilton Depression Rating Scale; MMSE, Mini-Mental State Examination; SSRS, Social Support Rating Scale; PSD, post-stroke depression. *$p < 0.05$ between non-PSD and PSD groups.

Table 3. Assignment of influencing factors.

Variables	Assignment	
Depression	No = 0	Yes = 1
Gender	Female = 0	Male = 1
Parietal lobe lesion	No = 0	Yes = 1
Drinking	No = 0	Yes = 1
Smoking	No = 0	Yes = 1
Hypertension	No = 0	Yes = 1
Family care	<7 points = 0	≥7 points = 1
Diabetes	No = 0	Yes = 1
NIHSS	Numerical variable	
MMSE	Numerical variable	
SSRS	Numerical variable	
Barthel	Numerical variable	

NIHSS, National Institutes of Health Stroke Scale; MMSE, Mini-Mental State Examination; SSRS, Social Support Rating Scale.

vidual cases, the sensitivity and 1 – specificity values corresponding to adjacent thresholds in Table 5 show minor fluctuations and do not exhibit a strictly monotonic decreasing pattern, which is a normal phenomenon in discretely sampled data. The overall trend is consistent with the inherent characteristics of the ROC curve: as the cutoff value increases, both sensitivity and 1 – specificity generally show a gradual decreasing trend.

All 900 study subjects were entered into the logistic regression equation to calculate model scores. Based on the maximum and minimum observed scores among all subjects, the total model score range was determined to be 8.05–27.51. In Table 5, the values of 8.05 and 27.51 merely represent the extreme scores that happened to be selected during the sampling process; the total score range of the model should not be defined solely based on the discrete sampling nodes in this table. Through continuous curve interpolation, the optimal cutoff value of the model was 18.12, with a corresponding sensitivity of approximately 0.76 and specificity of approximately 0.72. The clinical decision rule was defined as follows: a model score ≥18.12 indicates a high-risk population for post-stroke non-acute depression.

AUC

The ROC curve was plotted to evaluate the predictive performance of the model (Fig. 2). The AUC value of the model was 0.91, with a 95% CI of 0.88–0.94, indicating a reasonable interval range.

Discussion

This study focused on risk factors for PSD in the non-acute phase of stroke, successfully constructed a predictive model, and identified an optimal cutoff value of 18.12, with an AUC of 0.91, indicating that the model has excellent clinical predictive performance and can be used for early screening of high-risk populations. Whether a stroke patient develops PSD is influenced by numerous factors,

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Table 4. Logistic regression analysis results of PSD influencing factors.

Variables	β	SE	Wald	OR	95% confidence interval (CI)	p
Sex	–0.328	0.105	9.762	0.72	0.581~0.892	0.003
Parietal lobe lesion	0.167	0.084	3.952	1.182	1.009~1.385	0.009
Drinking	0.337	0.126	7.183	1.401	1.102~1.782	0.002
Smoking	0.327	0.121	7.256	1.386	1.103~1.743	0.012
Hypertension	0.656	0.218	9.035	1.93	1.274~2.928	0.022
Family care	–0.416	0.067	38.552	0.659	0.512~0.848	0.001
MMSE	–0.189	0.063	8.972	0.826	0.735~0.928	0.001
SSRS	–0.215	0.078	7.638	0.806	0.692~0.939	0.012
Barthel	–0.342	0.112	9.271	0.709	0.568~0.885	0.002
NIHSS	0.026	0.008	10.563	1.026	1.011~1.042	0.001
Constant	9.01	1.872	23.514	—	—	<0.001

NIHSS, National Institutes of Health Stroke Scale; MMSE, Mini-Mental State Examination; SSRS, Social Support Rating Scale; SE, standard error; OR, odds ratio.

Table 5. Sensitivity and specificity results under various evaluation thresholds.

Threshold	Sensitivity	1 – specificity	Threshold	Sensitivity	1 – specificity
8.05	1	1	17.78	0.81	0.33
9.17	1	0.99	18.53	0.72	0.23
9.58	1	0.97	18.89	0.65	0.18
10.02	1	0.95	19.25	0.62	0.15
10.56	1	0.94	19.96	0.58	0.12
11.09	1	0.92	20.05	0.54	0.08
11.58	1	0.91	20.36	0.53	0.07
12.08	1	0.87	21.67	0.5	0.06
12.61	1	0.86	22.87	0.48	0.05
12.78	1	0.85	23.13	0.47	0.05
12.98	1	0.83	24.49	0.46	0.04
13.04	1	0.83	24.78	0.38	0.04
14.17	0.99	0.81	25.03	0.32	0.03
14.34	0.99	0.79	25.89	0.29	0.03
14.68	0.98	0.74	26.04	0.28	0.02
14.95	0.97	0.68	26.17	0.18	0.02
15.01	0.96	0.58	26.26	0.14	0.01
15.36	0.94	0.57	26.32	0.08	0.01
16.08	0.89	0.53	26.89	0.04	0
17.02	0.85	0.47	27.51	0	0

The data in this table represent discrete threshold values obtained by interval sampling, intended solely to illustrate the trend of the indicators. The optimal cutoff value of 18.12 was derived by interpolation from the continuous ROC curve and is not included among the discrete points in this table. Due to discrete sampling, the local indicators are not strictly monotonically decreasing; however, the overall trend follows the rule that as the threshold increases, both sensitivity and 1 – specificity gradually decrease.

as depression is a multifactorial condition, and each individual's experience with the illness can vary significantly. There are many contributing factors. However, assessing the risk of PSD in patients requires a clear understanding of the primary factors influencing PSD.

This study showed that female sex, parietal lobe lesions, alcohol consumption, smoking, hypertension, and high NIHSS score were independent risk factors for PSD, whereas good family support and high MMSE, SSRS, and Barthel scores were protective factors. Unlike most studies focusing on the acute phase, this study targeted the non-

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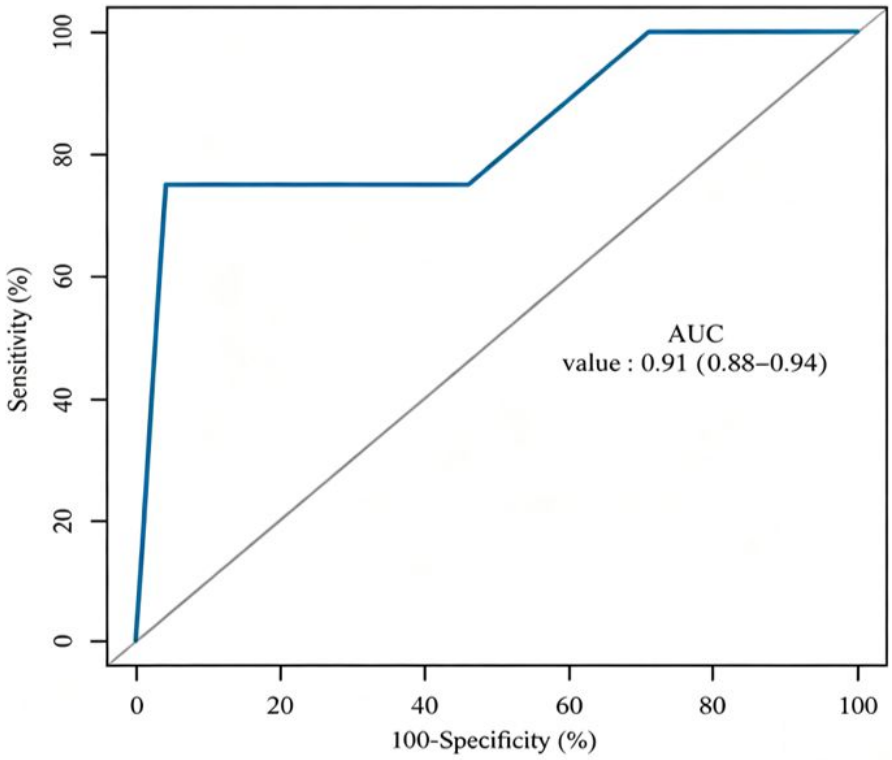


Fig. 2. Area under ROC curve (AUC).

acute phase population and identified specific risk factors during the critical rehabilitation period, thereby filling a gap in existing research. Univariate comparison showed significant differences in BDNF and PLR between the groups, yet neither of these two indicators was included in the multivariate regression model. These two biomarkers indirectly participate in the pathogenesis of PSD through the regulation of inflammation and neuroplasticity, and their effects are fully mediated by concomitant predictors such as the NIHSS, MMSE, and Barthel index, leading to a loss of independent predictive ability after multivariate adjustment. In addition, a phenomenon observed in this study is that in univariate analysis, smoking and alcohol consumption were more prevalent in the non-PSD group, but after multivariate adjustment, both became independent risk factors. This inconsistency can be explained by confounding bias. Univariate analysis does not exclude interference from factors such as neurological impairment, family support, cognitive function, and underlying diseases. Some patients with a history of smoking or alcohol consumption may have milder neurological deficits or better family support, which erroneously reduces the observed risk in univariate analysis. After adjusting for all confounding factors, the true independent adverse effects of smoking and alcohol consumption on mood regulation and brain function were revealed, confirming them as genuine risk factors for PSD. Therefore, multivariate logistic regression results are more reliable for identifying independent influencing factors. A resting-state functional magnetic resonance imaging study of patients with PSD following temporal lobe lesions indicated [24] that abnormal functional connectivity between the amygdala and the cerebral cortex is closely associated with depressive mood. The study found that in depressed patients, connectivity between the left amygdala and the bilateral precuneus, as well as the right orbitofrontal cortex, was enhanced, while connectivity with the right putamen was reduced; connectivity between the right amygdala and the right temporal pole, the right gyrus rectus, and the left orbitofrontal cortex was enhanced, while connectivity with the right primary somatosensory cortex was reduced. Furthermore, the functional connectivity strength between the amygdala and the right orbitofrontal cortex, right insula, and right cingulate gyrus was significantly correlated with HAMD-17 scores, suggesting that dysfunction of the prefrontal-limbic-striatal circuit may be involved in the pathogenesis of PSD. Another study based on a Spanish national health survey pointed out [25] that lifestyle is closely related to the prevalence of depression. Sedentary behavior is the most common adverse lifestyle factor, followed by unhealthy diet, smoking, and high-risk alcohol consumption. Compared with individuals with no adverse lifestyle factors (depression prevalence 2.5%), those with at

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least one adverse lifestyle factor had a significantly higher prevalence of depression (≥5.2%). Among these, physical inactivity (odd ratio (OR) = 1.6) and smoking (OR = 1.3) increased the risk of depression, whereas high-risk wine drinkers had a lower likelihood of depression (OR = 0.26). A study based on self-determination theory noted [26] that the impact of social relationships on the well-being of depressed individuals depends on whether the relational partner satisfies or frustrates the individual's basic psychological needs. Integrating the buffering effect model and the main effect model of social support, the study proposed that depressed individuals' own negative cognitive styles and stress generation tendencies affect their perception of the relational partner's need responsiveness, thereby modulating the influence of social relationships on depressive outcomes. A systematic review of risk prediction models for PSD pointed out [27] that the degree of neurological impairment represented by an elevated NIHSS score is one of the most frequently included predictors in models. It may increase the risk of PSD by reducing patients' confidence in rehabilitation and their ability to perform daily functional activities. Consistent with the above findings, BDNF and PLR showed significant differences between the two groups in univariate testing but were excluded from the final predictive model. Their biological effects on PSD are mediated by measures of neurological deficits, cognitive status, and daily functioning included in the model, with no independent predictive role after adjustment for confounders. Another study based on the South London Stroke Register with long-term follow-up indicated [28] that patients with depressive symptoms at three months post-stroke (accounting for 35.6%) had an increased risk of death during the 10-year follow-up period (adjusted hazard ratio (aHR) = 1.18) and were significantly associated with impaired activities of daily living (adjusted odds ratio (aOR) = 2.94) and reduced quality of life. The study also found that patients who recovered from depression within one year had significantly lower risks of stroke recurrence and functional impairment, as well as significantly improved quality of life. In contrast, patients who remained depressed at one or five years post-stroke had a persistently elevated risk of adverse outcomes.

In summary, compared with similar studies, this study not only confirmed female sex and neurological impairment as risk factors for PSD but also, for the first time, constructed a quantitative predictive model for the non-acute phase, which is superior to previous studies that only performed risk factor analysis, providing a directly applicable assessment tool for clinical practice. In clinical intervention, it is recommended to apply the predictive model to female patients with parietal lobe injury and a history of smoking or alcohol use, as well as female patients with elevated NIHSS scores. Furthermore, for high-risk individuals with a score ≥18.12, early initiation of cognitive behavioral therapy and social support interventions is recommended. In addition, strengthening family care guidance and improving daily activity training can effectively reduce the incidence of non-acute phase PSD.

This study revealed that the mean scores of non-PSD patients were significantly lower than those of PSD patients, and a multifactorial analysis demonstrates that a higher NIHSS score is associated with an increased risk of PSD development. The limitations of this study include that it was a single-center study, and the model was only internally validated. Future multicenter external validation is needed to improve the generalizability of the model. Although this study adopted a prospective design, the characteristics of lost-to-follow-up cases were not systematically analyzed, which may introduce some loss-to-follow-up bias. Additionally, the exclusion of patients with cognitive or communication impairments may lead to selection bias. Future studies should expand the study population and improve bias control to further validate and optimize the model. In a study by Wang *et al*. [29] (2016), multivariate logistic regression analysis indicated a correlation between insomnia and the extent of neurological impairment with PSD. This study also emphasized that neurological impairment was a notable factor in depression among PSD patients. Shi *et al*. [30] (2015) reported that approximately one-third of first-time mild ischemic stroke patients may experience depression in the first year post-stroke. Factors such as being female, smoking, mild global cognitive impairment, and stroke recurrence predict early or late-onset PSD in mild ischemic stroke patients. According to a study by Wang *et al*. [31] (2017), the prevalence of PSD was higher among female patients. The risk factors for PSD in the acute and chronic phases of stroke differ. In the acute phase of stroke, being female is an independent risk factor for PSD. Smoking, frontal lobe lesions, and living alone are predictive factors for PSD in the chronic phase of stroke. The NIHSS score is a risk factor for PSD in both the acute and chronic phases. As indicated by Meng *et al*. [32] (2017), identifying higher NIHSS scores, higher HAMD-17 scores, lower dopamine levels, lower serotonin levels, higher tumor necrosis factor-alpha levels, and lower levels of nerve growth factor may assist clinical practitioners in recognizing and treating depression in post-stroke patients. Yang *et al*. [33] (2019) suggested that a decreased adiponectin level may be associated with PSD in patients following acute ischemic stroke. Xu *et al*. [34] (2018) indicated that reduced BDNF levels may serve as a predictor for the development of depression in patients after acute ischemic stroke, with markedly lower serum BDNF concen-

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trations in stroke patients at an early stage who are prone to PSD. Han *et al*. [35] (2020) stated that the correlation between BDNF and motor functional outcomes in PSD is minimal, with no considerable association with post-stroke anxiety in motor functional outcomes. Luo *et al*. [36] (2019) reported that serum BDNF levels were associated with fractional anisotropy. In this study, an observable difference in BDNF levels between PSD and non-PSD patients was observed. This highlights the crucial role of BDNF in neuroplasticity and neurogenesis following both ischemic and non-ischemic brain injuries. This study has several limitations: it was a single-center study, and the model underwent only internal validation without external cohort validation. Patients with severe cognitive or communication impairments were excluded, which may introduce selection bias and limit the generalizability of the findings. Future multicenter, large-sample external validation is needed to further optimize the model and enhance its generalizability and clinical utility.

Conclusions

Through a prospective cohort design, this study successfully constructed and validated a risk assessment model for PSD during the non-acute phase, demonstrating good predictive performance and clinical application value. Parietal lobe lesions, female sex, alcohol consumption, smoking, hypertension, and high NIHSS score were independent risk factors for non-acute phase PSD, whereas adequate family support, high MMSE score, high SSRS score, and high Barthel index were protective factors. The clinical application scenario of this study is as follows: the model is suitable for patients who are conscious and within 1 to 6 months after stroke onset, enabling rapid screening of high-risk populations for PSD and guiding early psychological and rehabilitation interventions.

Availability of Data and Materials

The datasets used and/or analysed during the current study were available from the corresponding author on reasonable request.

Author Contributions

MX conceived and designed the study, revised the full manuscript, and takes overall accountability for all aspects of this work; MYC and QSH were responsible for patient enrollment and original clinical data collection; KSL took part in study design and stroke case screening; MHC performed subject eligibility assessment and baseline data sorting; SSC and BBL collected laboratory biochemical indicators and completed preliminary data checking; XWL and CHX conducted literature search and linguistic revision of the manuscript; ZYH and ZL assisted in statistical analysis and result interpretation. All authors participated in critical revision of the manuscript, read and approved the final version to be published, and agreed to be accountable for all aspects of the work to ensure that any questions related to the accuracy or integrity of any part of the article are properly investigated and resolved.

Ethics Approval and Consent to Participate

This study was performed in strict accordance with the World Medical Association Declaration of Helsinki. The research protocol has been approved by the Ethics Committee of Jieyang People's Hospital (Approval No.: [2021-004-02-IIT]). Written informed consent was obtained from all participants and their legal guardians prior to enrollment.

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Conflict of Interest

The authors declare no conflict of interest.

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