High Risk Factors and Preventive Measures of Bipolar Disorder After Ischemic Stroke

ABSTRACT

Background: Bipolar disorder (BD) is a recurrent chronic disease. There are few Chinese studies to explore the BD after ischemic stroke. This study aimed to analyze the high risk factors of BD after ischemic stroke and investigate prevention strategies.

Methods: 197 patients with ischemic stroke in our hospital from March 2020 to March 2022 were selected as research subjects. The demographic information, clinical data, and scores of Mood Disorder Questionnaire (MDQ) and Activity of Daily Living Scale (ADL) in patients were retrospectively analyzed to count the incidence of BD in patients. Binary logistic regression analysis was used to analyze the influencing factors for BD after ischemic stroke, and preventive measures were discussed based on study results.

Results: The incidence of BD in patients with ischemic stroke was 45.18% (89/197), and the median and quartile in the first part of MDQ score was 6.00 (5.00,10.00) points. The subjects were divided into BD group (n = 89) and non-BD group (n = 108) based on the presence of BD in patients with ischemic stroke. Education background (OR = 0.485), lesions involving the frontal or temporal lobes (OR = 2.724), sleep disorders (OR = 2.246), and daily living ability (OR = 3.108) were influencing factors for BD after ischemic stroke ($P < .05$).

Conclusion: The risk of BD after ischemic stroke is high. Based on the above research results, clinical attention should be paid to knowledge popularization, lesion examination, and the improvement of sleep quality and daily living ability, to prevent the occurrence of BD and improve the prognosis.

Keywords: Ischemic stroke, bipolar disorder, risk factors, preventive measures

Introduction

The Global Burden of Diseases, Injuries, and Risk Factors Study[1] in 2019 has shown that mental disorders such as depression, anxiety, and bipolar disorder (BD) are still one of the causes of top 10 burdens in the world. BD is a severe psychosocial disorder,[2] which is characterized by pathological changes of emotions and recurrent mania, hypomania, depression, and mixed symptoms.[3] The disease includes 2 types, type I (defined as the presence of syndrome and a manic episode) and type II (defined as the presence of a syndrome, mild manic episode, and severe depressive episode).[4] Clinical evidence has shown that BD is one of the most representative mental disorders among suicidal patients, with 30%-50% of patients attempting suicide, and the suicide rate of BD patients is about 20-30 times higher than that of the general population.[5-7] Thus, BD poses a great threat to the life safety of people. Exploring the influencing factors of BD is helpful to improve clinical preventive measures and reduce the suicide rate of patients.

There is a potential link between mental illness and stroke. Stroke leads to early death and physical and mental illnesses.[8] Ischemic stroke is one of the leading reasons for death and disability worldwide, resulting in severe neurological impairment, which is mainly caused by the interruption of cerebral blood flow.[9-11] Because BD is a multi-system disease that affects cardiovascular status and immune function, this mental illness may aggravate the condition of patients with ischemic stroke. Martinez-Aran Anabel et al.[12] have pointed out that one of

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the most popular areas of research on BD is the neurocognitive disorders and its causes and consequences, as well as the development of new treatment strategies to manage or prevent such defects.

One report states that the risk of mental disorders after stroke is much higher.[13] Therefore, it is necessary to strengthen the identification and management of mental disorders and sleep disorders after stroke.[14] The clinical treatment and nursing mainly focus on the basic treatment and nursing of ischemic stroke,[15] and lack experience and countermeasures for the prevention of patients with mental illness and stroke. This study investigated and analyzed the incidence and risk factors of BD in patients with ischemic stroke, aiming to strengthen the preventive measures of BD in patients with ischemic stroke, and reduce the burden of mental disorders.

Material and Methods

Research Design

The research subjects were 197 patients with ischemic stroke in our hospital from March 2020 to March 2022. Inclusion criteria: (1) patients were diagnosed with ischemic stroke by craniocerebral CT or MRI and were in the recovery period with stable vital signs. (2) Patients with education at the level of junior high school and above could cooperate to complete the questionnaire or scale. (3) Patients had complete clinical data. (4) BD screening showed negative at the time of diagnosis, and patients did not have a family history of BD. Exclusion criteria: (1) The condition of the patients was unstable or worsened after treatment. (2) Patients had a history of mental illness or medical history. (3) Patients had malignant tumor diseases.

This study was approved by the Ethical Committee of the First Affiliated Hospital with Nanjing Medical University (Approval No: 2022-SR-341; Approval Date: June 7, 2022). Since this study is retrospective, it is not necessary to obtain the informed consent of patients.

Diagnosis of BD. In BD screening, the diagnosis for positive patients was made by 3 senior associate directors and above in the hospital according to the relevant standards of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).[16]

Two researchers with professional training experience were arranged to collect the demographic data and clinical information of patients through the medical record system. Logistic regression analysis was made to identify high-risk factors and explore preventive measures. The technical route of this study is shown in Figure 1.

MAIN POINTS

- The risk of BD after ischemic stroke is higher, with an incidence of 45.18%.
- Low education, lesions involving the frontal or temporal lobes, and sleep or daily living ability disorders are high risk factors for BD after an ischemic stroke.
- Clinical attention should be paid to patients with high-risk factors and changes in their mental state, and corresponding intervention measures should be taken as soon as possible.
- The preventive measures of BD in the majority of patients with ischemic stroke are improving the awareness of mental illness knowledge in patients, strengthening the examination of lesion range, improving their sleep quality and daily living ability, and taking into account the physical and mental health of patients.

Data Collection from Patients

General demographic characteristics and clinical data included age, body mass index, gender, smoking, marital status, education level, medical insurance, course of disease, location of disease, therapeutic methods (thrombolysis and defibrase), whether the lesion involved the frontal lobe or temporal lobe, complications (hypertension, hyperlipidemia, and diabetes mellitus), family history of stroke, and sleep disorders (difficulty in falling asleep, difficulty in deep sleep, or too much sleep).

Mood Disorder Questionnaire (MDQ)[17] consisted of 3 parts. The first part contained 13 items related to mania or hypomania symptoms, with a score of 1 point for "yes" and 0 point for "no". The second part was whether several of the above symptoms coexisted at the same time period, and the third part was the degree of functional impairment caused by the above symptoms. Positive of BD was to meet the following conditions. The score of first part was ≥ 7 points, the answer of second part was "yes", and the severity in the third part reached "moderate" or "serious problem".

The Activity of Daily Living Scale (ADL)[18] scale was divided into the Physical Self-Maintenance Scale (6 items) and the Instrumental Activities of Daily Living Scale (8 items), with a total of 14 items and a total score of 56 points. Each item was scored on 4 levels (1 point, doing by oneself; 2 points, doing by oneself with difficulties; 3 points, needing someone's help; and 4 points, no way to do). Scoring criteria were as follows. Total score ≥ 22 points, or 2 and more items ≥ 3 points indicated overt functional impairment.

Statistical Analysis

After collecting the sample data, all the data were imported into the statistical professional software Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM SPSS Corp.; Armonk, NY, USA) for processing and analysis. The enumeration data were detected by χ^2 test and indicated by [n (%)]. The measurement data that did not meet the normal distribution were detected by the Mann–Whitney U-test, indicated by M (P_{25}, P_{75}). High-risk factors were analyzed by binary logistic regression analysis. $P < .05$ indicated that the difference was statistically significant. The image drawing software used were GraphPad Prism 7 (GraphPad Software, San Diego, CA, USA), and Microsoft Office Word 2006 (Microsoft Corporation, Redmond, WA, USA).

Results

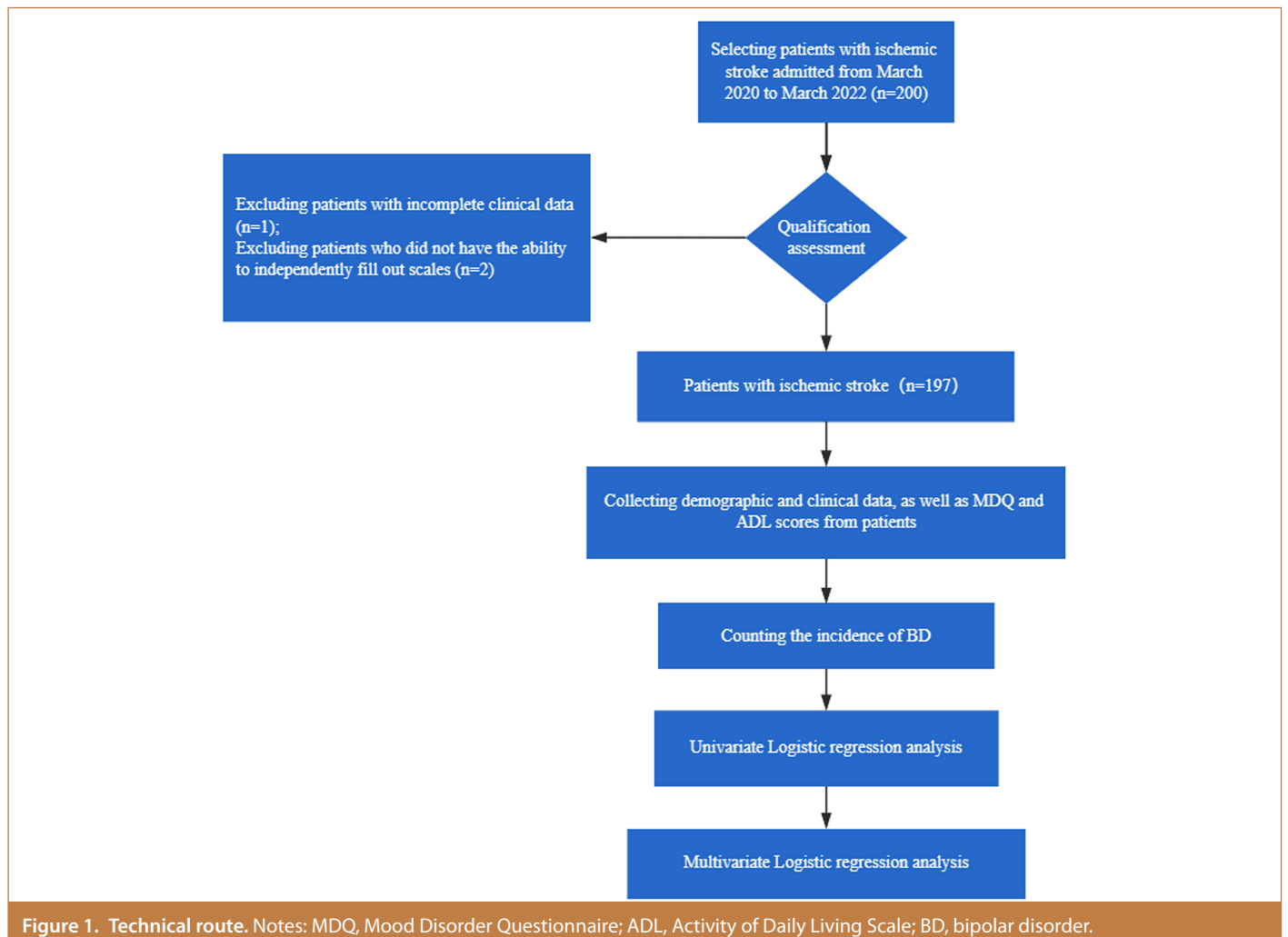### General Demographic Characteristics and Clinical Data

The general demographic characteristics and clinical data of 197 patients with ischemic stroke were shown in Table 1.

Conditions and Grouping of Patients with Ischemic Stroke and BD

Among the 197 patients with ischemic stroke, a total of 89 patients had BD, with an incidence of 45.18%. The median in the first part of the MDQ score was 6.00 (5.00, 10.00) points. The research subjects were divided into BD group (n = 89) and non-BD group (n = 108) based on the presence of BD in patients with ischemic stroke.

Univariate Regression Analysis

Education level, lesions involving the frontal lobe or temporal lobe, hyperlipidemia, sleep disorders, and daily living ability (ADL score) may be high-risk factors for BD after an ischemic stroke ($P < .05$), as detailed in Table 2 and Figure 2.

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Figure 1. Technical route. Notes: MDQ, Mood Disorder Questionnaire; ADL, Activity of Daily Living Scale; BD, bipolar disorder.

Multivariate Regression Analysis

Low education (OR = 0.485), lesions involving the frontal or temporal lobes (OR = 2.724), sleep disorders (OR = 2.246), and poor daily living ability (OR = 3.108) were high-risk factors for BD after an ischemic stroke ($P < .05$), while hyperlipidemia was not a high-risk factor ($P > .05$). See details in Table 3.

Discussion

A Chinese burden study of stroke has shown that the age-standardized morbidity and mortality have decreased since 1990, but the burden of diseases remains high.[19] Some scholars consider that emotional disorders have the greatest impact on the survival and quality of life of patients among the stroke-related injuries.[20] However, clinical practice often focuses more on the treatment and recovery of physical dysfunction such as limb and swallowing in stroke patients, with relatively low emphasis on emotional and mental aspects of patients. Therefore, this study counted the incidence of BD after ischemic stroke. The results showed that 89 patients had BD among the 197 patients with ischemic stroke, with an incidence of 45.18%, and the patients generally had typical manic episodes alternating with low mood, retardation of thinking, and pessimism.

Based on the general demographic characteristics and clinical data of patients, this study conducted a preliminary analysis on the high-risk factors for BD after an ischemic stroke. The data showed that education level, lesions involving the frontal or temporal lobes, sleep disorders, and daily living ability were high-risk factors for BD after an ischemic stroke. One clinical study has shown that whole-brain cortical atrophy and reduced education level can be used as rapid indicators of early cognitive impairment in patients with a transient ischemic attack and acute mild ischemic stroke, and medial temporal lobe atrophy also seems to be related to mental processing speed in such patients.[21] This is similar to the results of this study. BD is a mental illness that involves emotional, cognitive, and behavioral changes.[22] In the functional area of the brain, the function of the frontal cortex is related to emotion, cognition, and behavior management, and the temporal lobe is associated with language comprehension, memory, and mental activity. Lesions involving the frontal or temporal lobes of patients can cause the blocked synthesis of 5-hydroxytryptamine, thereby affecting the ability of nerve cells or synapses to synthesize dopamine, so such patients have a higher risk of BD after ischemic stroke.[23-25]

Sleep disorder is also a risk factor for BD after ischemic stroke. Insomnia affects 20%-56% of stroke patients, usually occurring in the

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Table 1. General Demographic Characteristics and Clinical Data

Projects	(n = 197)
Age [years old, M (P$_{25}$, P$_{75}$)]	62.00 (54.20, 70.00)
Body mass index [kg/m², M (P$_{25}$, P$_{75}$)]	24.58 (23.18, 25.72)
Gender [n (%)]	
Male	117 (59.39)
Female	80 (40.61)
Smoking [n (%)]	
Yes	71 (36.04)
No	126 (63.96)
Marital status [n (%)]	
Married	161 (81.73)
Unmarried	18 (9.14)
Divorced/widowed	18 (9.14)
Education level [n (%)]	
Junior high school	81 (41.12)
Senior high school/technical secondary school	91 (46.19)
Undergraduate/junior college	22 (11.17)
Postgraduate and above	3 (1.52)
Medical insurance [n (%)]	
Yes	148 (75.13)
No	49 (24.87)
Sites of disease [n (%)]	
Left hemisphere	101 (51.27)
Right hemisphere	96 (48.73)
Thrombolytic therapy [n (%)]	
Yes	34 (17.26)
No	163 (82.74)
Fibrinolytic therapy [n (%)]	
Yes	51 (25.89)
No	146 (74.11)
Lesions involving the frontal lobe or temporal lobe [n (%)]	
Yes	81 (41.12)
No	116 (58.88)
Hypertension [n (%)]	
Yes	152 (77.16)
No	45 (22.84)
Hyperlipidemia [n (%)]	
Yes	40 (20.30)
No	157 (79.70)
Diabetes [n (%)]	
Yes	38 (19.29)
No	159 (80.71)
Family history of stroke [n (%)]	
Yes	50 (25.38)
No	147 (74.62)
Sleep disorders [n (%)]	
Yes	77 (39.09)
No	120 (60.91)
ADL score [points, M (P$_{25}$, P$_{75}$)]	19.00 (16.00, 21.00)
Daily living activity [n (%)]	
Normal condition	160 (81.22)
Obstacles[a]	37 (18.78)

ADL, Activity of Daily Living Scale.
[a]Obstacles indicated that ADL score was ≥22 points

acute phase, which may be related to the location of the disease. The incidence of insomnia in patients with right hemisphere, thalamus, or brainstem stroke is higher.[26] However, the results of this study showed that the location of the disease was not a high-risk factor for BD after ischemic stroke. The reason may be that lesions of patients with left hemisphere brain injury mostly involve the frontal lobe, and such patients also have a high risk of BD. This indicates the difference between the location of the disease and the influence mechanism of BD after ischemic stroke. In clinical practice, patients with disorders of daily living ability often have neurological deficits, and the risk of emotional disorders also increases in patients with severe neurological deficits through biogenic amines and cytokine pathways. In addition, one report states that atopic-related immune disorders can explain the correlation between BD and ischemic stroke,[27] which should be further elaborated in future studies.

Based on the above results, this study further explored the preventive measures of BD after ischemic stroke in the following 2 aspects.

Firstly, the high-risk group of BD after ischemic stroke was determined based on the results of high-risk factors. Examination of the mental state in patients was strengthened to find potential patients with BD. Medical staff should guide patients to face the disease correctly and take early comprehensive management interventions in basic medical and psychiatric treatment[28] to avoid further development of the disease. The underlying mechanism between severe mental illness and the development or worse outcome of cardiovascular disease may be related to poor treatment compliance of patients.[29] Therefore, medical staff need to strengthen communication with the family members of patients clinically and complete the cooperation between hospitals and families to improve the compliance of patients. A study has shown that the improvement of health literacy is directly and indirectly related to the less likelihood of people's mental health problems through family health.[30] Thus, mental health interventions should be taken at the individual and family levels of patients to achieve ideal prevention and treatment effects of BD through good family support.

Secondly, targeted preventive measures were carried out based on the analysis of high-risk factors of BD after an ischemic stroke. (1) Medical staff actively popularized knowledge related to ischemic stroke, mental illness, and BD by plain language, especially for those with low education, and utilized videos and images to enhance the cognition of patients. (2) Medical staff strengthened the examination of the lesion range of patients, especially the frontal and temporal lobes. Once the lesions involving the frontal or temporal lobes were found, medical staff should arrange BD scale screening for patients and implement respiratory training relaxation, music transfer therapy, and mindfulness training therapy to help patients eliminate negative emotions. (3) Medical staff provided patients with a quiet environment. Patients were informed of foot soaking and massage before going to bed to ensure good sleep quality. Necessary treatment measures were taken for patients with sleep disorders, including medication and transcranial magnetic stimulation therapy. (4) Medical staff emphasized the cultivation of daily living abilities in patients. The family members of patients with severe neurological deficits should be advised to keep patient and care for the daily life of patients. Patients were helped with rehabilitation exercises such as cultivating self-care abilities to integrate into normal life and enhance the sense of happiness.

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Table 2. Univariate Regression Analysis of bipolar disorder After Ischemic Stroke

Factors	B	Wald	P	OR	95% CI
Age	0.016	0.015	.283	1.017	0.986-1.048
Body mass index	0.120	0.088	.171	1.128	0.949-1.340
Gender	0.413	0.292	.158	1.511	0.852-2.679
Smoking	0.171	0.298	.566	1.186	0.662-2.127
Marital status	0.139	0.231	.547	1.149	0.731-1.807
Education level	−0.740	0.223	.001	0.477	0.309-0.738
Medical insurance	−0.094	0.331	.775	0.910	0.476-1.739
Location of disease	0.298	0.287	.299	1.347	0.768-2.365
Thrombolytic therapy	−0.052	0.380	.891	0.950	0.451-1.998
Fibrinolytic therapy	−0.111	0.328	.894	0.894	0.470-1.701
Lesions involving the frontal lobe or temporal lobe	1.158	0.301	<.001	3.184	1.764-5.750
Hypertension	0.641	0.355	.072	1.897	0.945-3.808
Hyperlipidemia	0.753	0.361	.037	2.123	1.046-4.309
Diabetes mellitus	0.240	0.362	.507	1.271	0.626-2.583
Family history of stroke	0.260	0.328	.428	1.297	0.682-2.467
Sleep disorders	0.977	0.300	.001	2.657	1.475-4.788
Daily living ability	1.139	0.386	.003	3.125	1.465-6.665
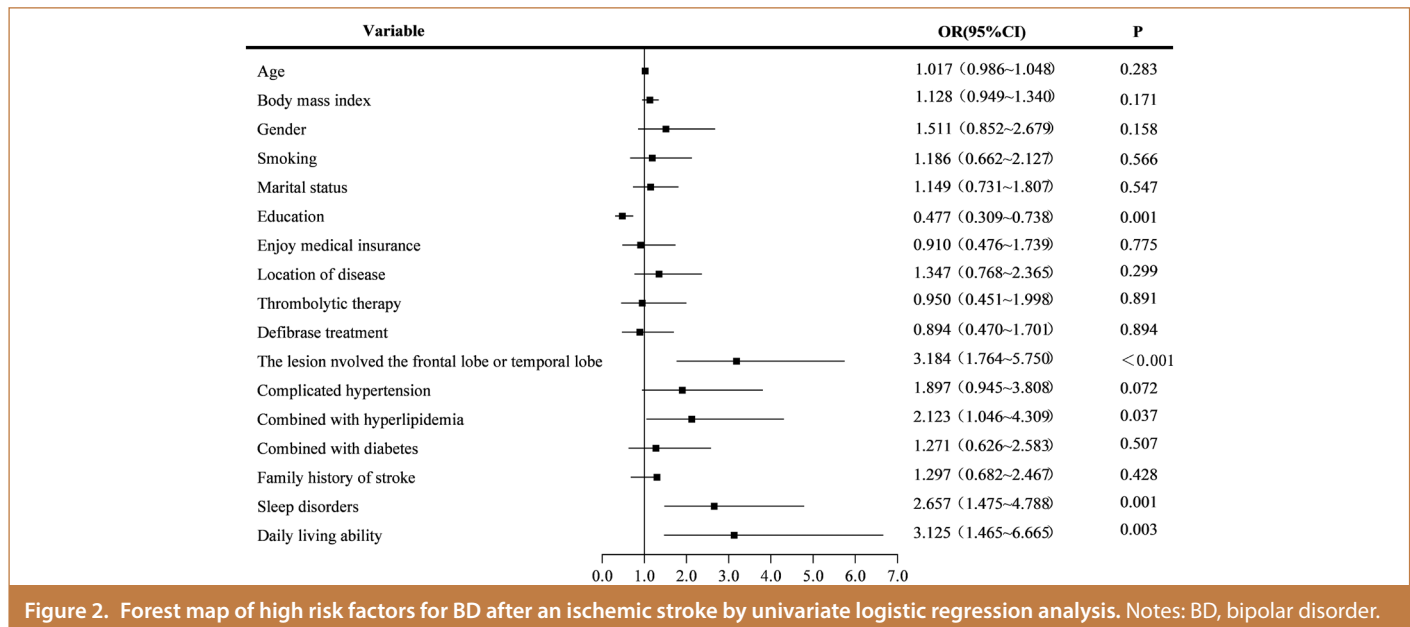
Figure 2. Forest map of high risk factors for BD after an ischemic stroke by univariate logistic regression analysis. Notes: BD, bipolar disorder.

Table 3. Multivariate Regression Analysis of bipolar disorder After Ischemic Stroke

Factors	B	SE	Wald	P	OR	95% CI Lower Limit	Upper Limit
Education level	−0.723	0.239	9.119	.003	0.485	0.304	0.776
Lesions involving frontal or temporal lobes	1.002	0.325	9.501	.002	2.724	1.440	5.151
Hyperlipidemia	0.689	0.404	2.914	.088	1.992	0.903	4.395
Sleep disorders	0.809	0.327	6.109	.013	2.246	1.182	4.267
Daily living ability	1.134	0.424	7.142	.008	3.108	1.353	7.138

However, due to various factors such as research methods, inclusion criteria, and samples, this study only selects patients with junior high school education or above retrospectively from our hospital's information system to ensure the effectiveness of the scale. Therefore, the incidence, high-risk factors, and the applicability of countermeasures obtained from this study are limited. In the future, the sample range

will be expanded, and multi-center research for in-depth discussion will be carried out, in order to provide more effective data reference for clinical practice.

The risk of BD after ischemic stroke is higher, and the high-risk factors include low education, lesions involving the frontal or temporal

lobes, sleep disorders, and disorders of daily living ability. Thus, clinical attention should be paid to the above factors. In order to prevent the occurrence of BD and improve the prognosis, knowledge popularization and lesion examination should be strengthened, and the sleep quality and daily living ability of patients should be improved.

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