


# Risk factors for stroke outcomes in adults

## Stroke in China

Rongli Fan, PhD<sup>a,\*</sup> , Jingjie Gu, BD<sup>a</sup>, Jingxin Zhang, BD<sup>c</sup>, Maiqiu Wang, PhD<sup>a</sup>, Zheng Chen, BD<sup>d</sup>, Fangshen Xu, BD<sup>d</sup>, Lei Zhang, PhD<sup>a,b</sup>

### Abstract

This study aimed to determine the possible risk factors for stroke outcomes based on prospective cohort study in China. A total of 146 stroke patients were recruited and divided into 2 groups, which assessed using the modified Rankin Scale (mRS), good outcomes (mRS  $\leq$  2) and poor outcomes group (mRS  $>$  2). Demographic, clinical, and laboratory characteristics of participants were obtained from the medical record. The multivariable logistic regression analysis was employed to assess the risk factors for stroke outcomes. Of 146 participants, 28 (19.18%) were presented with poor outcomes at day 90. As a result of multivariable logistic regression analysis, a significantly increased risk of stroke outcomes was found in patients with Barthel Index (BI) score (stroke (OR 1.50, 95% CI 1.21 ~ 1.85,  $P < .001$ ) and IS (OR 1.48, 95% CI 1.20 ~ 1.83,  $P < .001$ )).

**Abbreviations:** AIS = acute ischemic stroke, ALV = absolute lymphocyte value, AMC = absolute monocyte count, ANC = absolute neutrophil count, BAV = Basophil absolute value, BI = Barthel Index, CI = confidence interval, EAV = Eosinophil absolute value, GCP = good clinical practice, HDL = high-density lipoprotein, HDLC = high-density lipoprotein cholesterol, HS-CRP = high-sensitivity C-reactive protein, IS = ischemic stroke, LDLC = low-density lipoprotein cholesterol, mRS = modified Rankin Scale, NIHSS = National Institute of Health Stroke Scale, PC = platelet count, TC = total cholesterol.

**Keywords:** Barthel Index, modified Rankin scale, outcomes, risk factors, stroke

### 1. Introduction

Stroke, encompassing both ischemic and hemorrhagic forms, stands as the most prevalent neurological ailment and rank a leading cause of death and disability, making stroke prevention a global health priority.<sup>[1,2]</sup> Notably, China confronts an unparalleled stroke challenge, grappling with over 2 million fresh cases annually. This ailment is entwined with the highest disability-adjusted life-years toll among all afflictions within China.<sup>[3–5]</sup> In 2019, there were 3.94 million (95% uncertainty interval 3.43 ~ 4.58) new stroke cases in China.<sup>[6]</sup> Forecasts indicate that this burden will burgeon, fueled by population aging, a persistent prevalence of risk factors, and suboptimal management.<sup>[7–9]</sup> Despite enhancements in overall healthcare accessibility, specialized stroke care availability remains erratic nationwide.<sup>[10]</sup> Identifying risk factors linked to protracted recuperation following stroke could enhance our comprehension

of the convalescence process, potentially steering the quest for treatment targets and precursors predicting stroke outcomes.

Predicting functional outcomes in stroke presents a formidable challenge, largely owing to the intricate nature of the condition.<sup>[11]</sup> Consequently, we conducted a comprehensive examination of clinical peripheral blood samples extracted from stroke patients. Our objective was to uncover correlated risk factors linked to 90-day outcomes, as evaluated through the mRS. It is conceivable that certain among these factors could potentially serve as valuable tools for prognosticating functional recovery following a stroke. Furthermore, specific factors might emerge as potential targets for enhancing stroke outcomes.

Many studies have found the influence of factors such as age, gender, smoking, and alcohol consumption on stroke prognosis. A thorough examination of 39 research studies,

This research was funded by Zhejiang Province Key Research and Development Projects (2020C03071, 2021C03145), "Pioneer" and "Leading Goose" R&D Program of Zhejiang (2022C03043), and the key projects of major health science and technology plan of Zhejiang Province (WKJ-ZJ-2129).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The protocol was approved by the Ethics Committee of the Fourth Affiliated Hospital of Zhejiang University related to the protection of human research participants. Written informed consent was obtained from all participants or their proxy.

<sup>a</sup> Zhejiang Provincial Key Laboratory for Chemical & Biological Processing Technology of Farm Products, Department of Biological and Chemical Engineering, Zhejiang University of Science and Technology, Hangzhou, Zhejiang, China, <sup>b</sup> Department of Information and Electronic Engineering, Zhejiang University of Science and Technology, Hangzhou, Zhejiang, China, <sup>c</sup> Department of Neurology, The Fourth Affiliated Hospital, Zhejiang University School of Medicine, Yiwu, Zhejiang, China, <sup>d</sup> Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, The Fourth Affiliated Hospital, International

Institutes of Medicine, Zhejiang University School of Medicine, Yiwu, Zhejiang, China.

\*Correspondence: Rongli Fan, Zhejiang Provincial Key Laboratory for Chemical & Biological Processing Technology of Farm Products, Department of Biological and Chemical Engineering, Zhejiang University of Science and Technology, Hangzhou 310023, Zhejiang, China (e-mail: fanrongli@zust.edu.cn).

Copyright © 2023 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Fan R, Gu J, Zhang J, Wang M, Chen Z, Xu F, Zhang L. Risk factors for stroke outcomes in adults: Stroke in China. *Medicine* 2023;102:49(e36606).

Received: 29 August 2023 / Received in final form: 15 November 2023 / Accepted: 21 November 2023

<http://dx.doi.org/10.1097/MD.00000000000036606>

encompassing a collective participation of 359,783 individuals, unveiled a notable disparity in the prevalence of diabetes between ischemic strokes (IS) (33%, 95% CI ~ 28–38) and hemorrhagic strokes (26%, 95% CI ~ 19–33). Furthermore, the analysis established a clear association between both acute hyperglycemia and diabetes and adverse post-stroke outcomes, whether ischemic or hemorrhagic. These unfavorable consequences encompass a heightened mortality risk, compromised neurological and functional recovery, prolonged hospital stays, increased readmission rates, and an augmented likelihood of experiencing stroke recurrence.<sup>[12]</sup> Someeh et al<sup>[13]</sup> achieved the best model results using a neural network classification algorithm. Their findings indicated that smoking, low education, advanced age, lack of physical activity, and a history of diabetes were significant risk factors for stroke mortality. Comparatively, younger stroke survivors demonstrate slightly more pronounced advancements in their functional abilities than their older peers. Nonetheless, it crucial to recognize that factors such as initial admission scores hold a more decisive influence, and the pace of recovery may eventually align.<sup>[14]</sup> It worth highlighting that younger patients exhibit a higher likelihood of achieving mRS scores of 0 to 1 or 0 to 2 during follow-up assessments.<sup>[15,16]</sup> An investigation focused on the impact of stroke on women unveiled that post-stroke, females manifest a diminished quality of life in contrast to males. This divergence can be ascribed to variables including older age, instances of more severe stroke, existing dependency prior to the stroke event, and the existence of depression.<sup>[17]</sup> The female gender was associated with an unfavorable prognosis, emphasizing the potential need for intensified acute care measures to improve outcomes among women affected by strokes.<sup>[18,19]</sup> Positive results were noted among younger patients, whereas a less optimistic prognosis was linked to cases of cardioembolic strokes.<sup>[20]</sup> Tento et al<sup>[21]</sup> discovered that female patients over 60 years with hypertension, atrial fibrillation, and hemorrhagic stroke were more likely to progress from a good prognosis to a poor one in the first 3 years of follow-up. Active identification of controllable risk factors like smoking and lack of exercise could help reduce the risk of stroke and recurrence in patients with type 2 diabetes and hypertension. Samuthpongton et al<sup>[22]</sup> focused on IS in elderly individuals in Thailand, identifying atrial fibrillation as a risk factor associated with older age. Stroke patients over the aged of 75 years had higher mortality and poorer prognosis. A study found that all systolic blood pressure measures after alteplase were linked to poor prognosis in women with AIS aged  $\geq 60$  years. In men with AIS aged  $< 60$  years, only SBP at 24 hours after alteplase was related.<sup>[23]</sup> However, a study comparing risk factors and functional outcomes in stroke patients over 80 years old and younger stroke patients revealed that while older patients experienced more severe strokes, their post-stroke injuries were similar to those of younger patients, showed that stroke prognosis may have little correlation with age.<sup>[24]</sup> A gender study in Vietnam also found no differences in clinical outcomes between men and women 90 days after stroke.<sup>[25]</sup>

Furthermore, the presence of other comorbidities and specific clinical test indicators also exerts a discernible impact on stroke prognosis. Researchers discovered that within the population affected by an IS, the coexistence of chronic kidney disease displayed a connection with higher 1-month mRS scores.<sup>[26,27]</sup> Yang et al<sup>[28]</sup> suggested that early screening and treatment of liver fibrosis could reduce the risk of stroke in patients with non-valvular atrial fibrillation, especially in male patients. Furthermore, Chang et al<sup>[29]</sup> observed that patients with type 2 diabetes and/or hypertension had higher rates of new stroke and recurrence after 1 year of follow-up. Neutrophils, eosinophils, and neutrophil-to-lymphocyte ratio were independent factors for poor prognosis after mechanical thrombectomy in AIS patients.<sup>[30]</sup> High platelet count and high-sensitivity C-reactive protein (HS-CRP) were significantly associated with adverse

clinical outcomes.<sup>[31]</sup> High-density lipoprotein (HDL) was associated with mild cognitive impairment and dementia.<sup>[32,33]</sup> Wang et al<sup>[34]</sup> found a positive correlation between low plasma HDL and cognitive improvement 6 months later in AIS patients. The triglyceride to high-density lipoprotein cholesterol ratio showed a nonlinear relationship and threshold effect, with both low and high ratios associated with adverse outcomes in AIS patients.<sup>[35]</sup>

Our study was centered on analyzing pairs of risk factors to discern effective indicators for stroke prognosis. The primary aim was to unveil the composite profile of risk factors and the underlying mechanisms linked to strokes.

## 2. Methods

### 2.1. Standard protocol approvals, registrations, and patient consents

The study was undertaken in strict adherence to the ethical guidelines and received approval from the Ethics Committee of the Fourth Affiliated Hospital of Zhejiang University. The research protocol adhered to the “Measures for Ethical Review of Biomedical Research Involving Human Beings,” as well as the “International Ethical Guidelines for Health-Related Research Involving Human Beings” and the principles laid out in the Declaration of Helsinki. Additionally, the study complied with international ethical standards such as Good Clinical Practice (GCP) and International Conference on Harmonization – Good Clinical Practice, along with pertinent domestic laws and regulations. Rigorous patient screening was conducted in strict accordance with the study predefined inclusion and exclusion criteria.

### 2.2. Study subjects

We conducted a prospective cohort study, in a total of 146 stroke patients, admitted to the Fourth Affiliated Hospital of Zhejiang University (located in Zhejiang, China) from January 2020 to December 2023. Stroke was defined as the manifestation of acute neurological deficits persisting for over 24 hours, attributed to ischemic causes, with or without associated hemorrhagic brain damage, as evident from neuroimaging scans (cranial magnetic resonance imaging, with or without magnetic resonance angiography and magnetic resonance venography).

Inclusion criteria encompassed: patients admitted within 72 hours post onset of symptoms; patients diagnosed with acute stroke; age equal to or  $>18$  years.

Exclusion criteria encompassed: any preexisting psychiatric diagnoses such as schizophrenia and depression; prior history of other neurological disorders; inability to complete scale assessments due to aphasia; lack of mRS follow-up data; presence of severe medical conditions like myocardial infarction and end-stage renal failure.

### 2.3. Clinical and laboratory examination data collection

Peripheral venous blood samples were systematically collected from all patients upon their emergency admission and promptly dispatched to the hospital laboratory department. These samples underwent comprehensive testing, including assessments of blood routine, liver and kidney function, electrolyte levels, coagulation parameters, and various other pertinent indices.

Patients’ demographic characteristics and clinical data, encompassing factors such as age, gender, hypertension history, diabetes mellitus, coronary atherosclerotic heart disease, and prior incidents of cerebral infarction, White blood cell count, absolute monocyte count (AMC), LDLC, HDLC, absolute lymphocyte value (ALV), Basophil absolute value (BAV), Eosinophil absolute value (EAV), platelet count (PC), absolute neutrophil count (ANC), and total cholesterol (TC), were meticulously extracted from the electronic medical record system.

**2.4. Functional prognostic assessment and follow-up**

The prognostic parameters investigated within this study encompassed the functional outcomes of patients at either the 90-day mark post-onset or at the time of death. Evaluation of functional prognosis was conducted utilizing mRS, where a score falling within the range of 0 to 2 indicated a favorable functional prognosis, while a score of 3 to 6 suggested an unfavorable functional prognosis. Accordingly, patients who either survived within 90 days from disease onset or achieved an mRS score of 0 to 2 were classified under the category of favorable short-term prognosis. Conversely, those who experienced mortality within 90 days or attained an mRS score of 3 to 6 were categorized as having an unfavorable short-term prognosis.

**2.5. Data analysis**

Statistical analysis was conducted using Statistical Product and Service Solutions (SPSS, Version 23.0). Measurement data conforming to a normal distribution were presented as mean ± standard deviation, and comparisons between 2 means were carried out through the utilization of a 2 independent samples t-test. Non-normally distributed measurement data were represented as median (interquartile range) using the Mann–Whitney U test. Categorical data were subjected to analysis utilizing the chi-square test.

Variables that demonstrated a significance level of  $P < .05$  in the one-way analysis were subsequently included as independent variables within the binary logistic regression model. This step aimed to identify risk factors that exhibited differences between the groups with  $mRS > 2$  and those with  $mRS \leq 2$ .

**3. Results**

**3.1. Comparison of demographic and clinical data of stroke patients**

According to the mRS scores and corresponding symptoms in Table 1, we divided the 146 patients included in the study into groups. Table 2 provides an overview of the demographic and clinical characteristics of all enrolled patients. Among the cohort of 146 patients, 98 were male and 48 were female, with an average age of 63.53 years. Within this population, 28 cases (19.18%) were classified within the unfavorable outcomes group ( $mRS > 2$ ), while 118 cases (80.82%) were categorized

under the favorable outcomes group ( $mRS \leq 2$ ). A notable distinction was observed in the distribution of Age, BI National Institutes of Health Stroke Scale (NIHSS), Absolute lymphocyte value level, and Pulse, between the unfavorable outcomes group ( $mRS > 2$ ) and the favorable outcomes group ( $mRS \leq 2$ ) in all types of strokes. These differences demonstrated statistical significance ( $P < .05$ ). However, no noteworthy disparities were detected in the remaining clinical data ( $P > .05$ ).

**3.2. Regression analysis between good and poor outcomes in all type of stroke**

Variables that exhibited a significance level of  $P < .05$  in the univariate analysis were selected as independent variables, while the categorization of outcomes as good or poor (with “poor” denoted as 0 and “good” denoted as served as the dependent variable. Multivariate logistic regression analysis was conducted to ascertain independent risk factors for unfavorable outcomes, and the results demonstrated that BI emerged as a distinct independent risk factor for adverse outcomes (as indicated in Table 3).

**3.3. Comparison of demographic and clinical data of ischemic stroke patients**

In contrast to patients with favorable outcomes ( $mRS \leq 2$ ), those with unfavorable outcomes ( $mRS > 2$ ) exhibited several distinguishing characteristics. The former group comprised relatively younger individuals, a higher proportion of females, and a lower incidence of hypertension and diabetes. Notably, there were significant discrepancies in terms of Age, BI, NIHSS, and ALV between the 2 patient groups. Conversely, the remaining variables did not display a significant association with stroke outcomes, as detailed in Table 4.

**3.4. Logistic regression analysis in IS patients**

Within the framework of the multivariate analysis model, BI demonstrated a robust and independent association with an elevated risk of unfavorable outcomes during the IS phase (OR 1.48, 95% CI 1.20 ~ 1.83,  $P < .001$ ). Conversely, Age (OR 0.96, 95% CI 0.84 ~ 1.10,  $P = .58$ ), NIHSS at onset (OR 1.10, 95% CI 0.69 ~ 1.77,  $P = .69$ ), and ALV (compared to other stroke types: OR 0.86, 95% CI 0.06 ~ 12.37,  $P = .91$ ) did not exhibit an independent impact on outcomes during the IS phase, as detailed in Table 5.

**Table 1**  
**The modified Rankin Scale (mRS).**

Grade	Symptoms
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability: unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability: requiring some help, but able to walk without assistance
4	Moderately severe disability: unable to walk without assistance, unable to attend to needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

Patients are graded on the scale of 0 to 6.

\* The initial mRS was 0 to 5 and the 6th grade was added later. For outcome prediction in clinical trials, the mRS is usually dichotomized where good functional outcome is a score 0 to 2 and poor functional outcome 3 to 6.

**4. Discussion**

Precise evaluation of the prognosis for patients with acute stroke serves a dual purpose: it not only guides the selection of appropriate treatment strategies but also facilitates the implementation of targeted interventions. Accurate assessment of the prognosis of patients with acute stroke not only determines the choice of treatment options, but also helps to take targeted interventions.

BI is a common stroke detection item in clinical practice, and it is widely carried out in laboratory departments at all levels in my country. The BI scales was significant in our study, both in stroke (OR 1.50, 95% CI 1.21 ~ 1.85,  $P < .001$ ) and IS (OR 1.48, 95% CI 1.20 ~ 1.83,  $P < .001$ ). Many studies have reported the value of BI in stroke. Functional ability assessed by BI scores revealed that 60 points was a key score for steering assistance and independence, with scores above 40 associated with higher rates of patients being discharged home and shorter hospital stays.<sup>[36]</sup> Liu et al.<sup>[37]</sup> found the relationship of BI and its short form with the mRS in acute stroke patients. In a Rasch analysis of the modified

Table 2

Clinical characteristics and factors associated with outcomes compared between good and poor groups for stroke.

	Unit	Poor (mRS > 2)	Good (mRS ≤ 2)	Z/t/χ <sup>2</sup>	P value
Overall, n (%)		28 (19.18%)	118 (80.82%)		
Age, mean ± SD		72 ± 12.23	61.53 ± 12.18	4.078	0
Sex	Male, n (%)	21 (75.00%)	77 (65.25%)	0.974	.324
	Female, n (%)	7 (25.00%)	41 (34.75%)		
Hypertension, n (%)		22 (78.57%)	91 (77.12%)	0.027	.869
Diabetes mellitus, n (%)		9 (32.14%)	26 (22.03%)	1.269	.26
Stroke subtype	First-ever stroke, n (%)	16 (25.00%)	89 (75.42%)	0.552	.457
	Recurrent stroke, n (%)	7 (25.00%)	18 (15.25%)		
	Cerebral hemorrhage, n (%)	5 (17.86%)	11 (9.32%)		
BI, median (IQR)		60 (40)	100 (0)	-9.995	0
NHSS, median (IQR)		4 (7)	1.5 (2)	-3.908	0
WBCC, median (IQR)	×10 <sup>9</sup> /L	6.8 (4.9)	6.5 (2.83)	-0.52	.603
AMC, median (IQR)	×10 <sup>9</sup> /L	0.4 (0.28)	0.4 (0.1)	-0.751	.452
LDLC, mean ± SD	mmol/L	2.59 ± 0.95	2.52 ± 0.83	0.352	.727
Triglycerides, median (IQR)	mmol/L	1.28 (0.98)	1.32 (0.91)	-0.097	.923
HDLC, median (IQR)	mmol/L	1.19 (0.6)	1.09 (0.34)	-0.487	.626
ALV, median (IQR)	×10 <sup>9</sup> /L	1.15 (0.98)	1.65 (0.7)	-3.305	.001
Pulse, mean ± SD	beats/min	80.82 ± 15.24	75.77 ± 10.79	7.04	.009
BAV, median (IQR)	×10 <sup>9</sup> /L	0.03 (0.02)	0.03 (0.03)	-0.285	.776
EAV, median (IQR)	×10 <sup>9</sup> /L	0.09 (0.13)	0.1 (0.13)	-1.105	.269
Homocysteine, median (IQR)	μmol/L	15.45 (14.98)	13.2 (8.25)	-1.322	.186
PC, median (IQR)	×10 <sup>9</sup> /L	203.5 (73)	202.5 (70.75)	-0.057	.954
ANC, median (IQR)	×10 <sup>9</sup> /L	4.9 (4.45)	4.15 (2.6)	-1.248	.212
TC, mean ± SD	mmol/L	4.51 ± 1.23	4.42 ± 1.01	0.408	.684

AMC = absolute monocyte count, ANC = absolute neutrophil count, ALV = absolute lymphocyte value, BAV = Basophil absolute value, EAV = Eosinophil absolute value, HDLC = high-density lipoprotein cholesterol, LDLC = low-density lipoprotein cholesterol, PC = platelet count, TC = total cholesterol, WBCC = white blood cell count.

Table 3

Binary logistic regression analysis of risk factors for stroke.

	B	SE	Wald χ <sup>2</sup>	P values	Odds ratio (95% CI)
Pulse	-0.01	0.06	0.01	.91	0.99 (0.89 ~ 1.11)
Age	-0.04	0.07	0.33	.57	0.96 (0.84 ~ 1.10)
BI	0.40	0.11	13.48	.00	1.50 (1.21 ~ 1.85)
NHSS	0.11	0.25	0.19	.66	1.12 (0.68 ~ 1.84)
ALV	-0.16	1.36	0.01	.90	0.85 (0.06 ~ 12.30)

ALV = absolute lymphocyte value.

BI, researchers found that the modified BI had high reliability but a relatively bad matching degree between item difficulty and patient ability.<sup>[38]</sup> Li et al<sup>[39]</sup> concluded that early mobilization is associated with an increased BI and shorter hospital stay for patients. And the Greek Modified BI was deemed adequate for use in Greek stroke neurorehabilitation patients.<sup>[40]</sup> Therefore, BI score can be used as a risk factor for stroke prognosis.

In addition, in the one-way analysis of variance, this study found that age, NIHSS score, and ALV were highly significant for all stroke prognosis groups. There are also many reports on these 3 risk factors in previous studies.

Age is also a common risk factor for stroke prognosis. Age may reduced the regeneration ability of neurons and increased the difficulty of recovery by affecting the body physiological and metabolic processes. A study found the causes of childhood stroke are distinct from those in adults.<sup>[41]</sup> The rates of mortality and recurrence in arterial IS display notable distinctions between younger and older populations.<sup>[42]</sup> For instance, among young adults, the 1-year mortality rate for stroke stands at 4.5%, and the recurrence rate over the same period is 1.5%. In contrast, elderly individuals face more substantial figures, with 1-year mortality rates ranging from 15% to 35% and recurrence rates from 2% to 15%.<sup>[43,44]</sup> Furthermore, in terms of functional outcomes assessed by mRS, younger adults generally experience markedly better results than their older counterparts.<sup>[45]</sup> Nevertheless, a noteworthy proportion of young adult patients, approximately

11%, still encounter severe impairments (mRS 4 to 5), while 59% exhibit mild to moderate impairments (mRS 1 to 3). On a positive note, 30% of those affected achieve a complete recovery without residual symptoms (mRS 0).<sup>[45,46]</sup> Another acute stroke treatment and outcomes in the oldest old (90 years and older) at a tertiary care medical center in Germany found that acute stroke treatment is effective and safe in the oldest old.<sup>[47]</sup>

A higher NHSS score was an independent risk factor for stroke recurrence in patients with a history of stroke.<sup>[29]</sup> Lai et al<sup>[48]</sup> found that NIHSS can be used as a risk factor for 90-day prognosis in patients undergoing thrombectomy (EVT), and the 7-day NIHSS score is more accurate. While some studies found that both the Emergency Destination Stroke Field Assessment Scale and the Rapid Arterial Occlusion Assessment Scale were superior to the NIHSS for detecting large vessel occlusions in in-hospital remote stroke assessment.<sup>[49]</sup> And NIHSS is not enough for cognitive screening in acute stroke.<sup>[50]</sup> A clinical comparative analysis between expanded NIHSS and original NIHSS in posterior circulation IS found the e-NIHSS median was 2 points higher at baseline and 24 hours and was one point higher on discharge  $P < .001$ .<sup>[51]</sup>

Lymphocytes played an important role in stroke and were involved in inflammatory processes, immune responses, and neuroprotection. The mechanism of lymphocytes in stroke was complex, they might have had a positive impact on the repair of brain tissue, or might have aggravated brain damage by

**Table 4**  
**Clinical characteristics and factors associated with outcomes compared between and good and poor groups for ischemic stroke.**

	Unit	Poor (mRS > 2)	Good (mRS ≤ 2)	Z/t/χ <sup>2</sup>	P value
Overall, n (%)		23 (17.69%)	107 (82.31%)		
Age, mean ± SD		71.65 ± 12.42	62.03 ± 12.03	3.391	.002
Sex	Male, n (%)	18 (78.26%)	71 (66.36%)	1.243	.265
	Female, n (%)	5 (21.74%)	36 (33.64%)		
Hypertension, n (%)		20 (86.96%)	80 (74.77%)	1.585	.208
Diabetes mellitus, n (%)		9 (39.13%)	25 (23.36%)	2.436	.119
Stroke subtype	First-ever stroke, n (%)	16 (69.57%)	89 (83.18%)	1.467	.226
	Recurrent stroke, n (%)	7 (30.43%)	18 (16.82%)		
BI, median (IQR)		60 (40)	100 (0)	-9.094	0
NHISS, median (IQR)		4 (6)	1 (2)	-3.763	0
WBCC, median (IQR)	×10 <sup>9</sup> /L	6.7 (5.1)	6.5 (2.8)	-0.693	.489
AMC, median (IQR)	×10 <sup>9</sup> /L	0.4 (0.2)	0.4 (0.1)	-0.427	.669
LDLC, mean ± SD	mmol/L	2.69 ± 0.99	2.49 ± 0.83	0.948	.351
Triglycerides, median (IQR)	mmol/L	1.28 (0.95)	1.3 (0.91)	-0.448	.654
HDLC, mean ± SD	mmol/L	1.14 ± 0.34	1.13 ± 0.28	0.122	.904
ALV, mean ± SD	×10 <sup>9</sup> /L	1.25 ± 0.57	1.68 ± 0.53	-3.339	.002
Pulse, mean ± SD	beats/min	81.17 ± 14.32	75.68 ± 10.63	1.739	.093
BAV, median (IQR)	×10 <sup>9</sup> /L	0.03 (0.02)	0.03 (0.03)	-0.208	.836
EAV, median (IQR)	×10 <sup>9</sup> /L	0.08 (0.13)	0.1 (0.13)	-1.329	.184
Homocysteine, median (IQR)	μmol/L	18 (15.6)	13.5 (8.2)	-1.629	.103
PC, mean ± SD	×10 <sup>9</sup> /L	223.04 ± 74.13	208.29 ± 52.51	0.907	.373
ANC, median (IQR)	×10 <sup>9</sup> /L	5 (4.4)	4.1 (2.4)	-1.526	.127
TC, mean ± SD	mmol/L	4.6 ± 1.31	4.37 ± 1.02	0.766	.45

AMC = absolute monocyte count, ANC = absolute neutrophil count, ALV = absolute lymphocyte value, BAV = Basophil absolute value, EAV = Eosinophil absolute value, HDLC = high-density lipoprotein cholesterol, LDLC = low-density lipoprotein cholesterol, PC = platelet count, TC = total cholesterol, WBCC = white blood cell count.

**Table 5**  
**Binary logistic regression analysis of risk factors for ischemic stroke.**

	B	SE	Wald χ <sup>2</sup>	P values	Odds ratio (95% CI)
Age	-0.04	0.07	0.30	.58	0.96 (0.84 ~ 1.10)
BI	0.39	0.11	13.48	.00	1.48 (1.20 ~ 1.83)
NHISS	0.10	0.24	0.16	.69	1.10 (0.69 ~ 1.77)
ALV	-0.15	1.36	0.01	.91	0.86 (0.06 ~ 12.37)

ALV = absolute lymphocyte value.

triggering an excessive inflammatory response. Shichita et al<sup>[52]</sup> suggested that targeting the recruitment and activation of lymphocytes could be therapeutic in reducing inflammatory events after cerebral ischemia-reperfusion injury. Offner et al<sup>[53]</sup> discovered that the second immunosuppressive phase increased the risk of severe systemic infection and sepsis in stroke survivors. Yilmaz et al<sup>[54]</sup> identified CD4 + and CD8 + T lymphocytes as involved in experimental stroke-related inflammatory and thrombotic reactions, brain damage, and neurological deficits. Hurn et al<sup>[55]</sup> induced stroke in immunocompetent mice, revealing the destructive effects of T and B lymphocytes in the mouse brain and peripheral immune responses on early and progressive ischemic brain injury.

**5. Limitations**

Several limitations and shortcomings must be taken into account when interpreting the results and methods of this study. Firstly, the assessment of diverse biochemical levels is confined to a solitary fixed time point, failing to capture the dynamic fluctuations experienced by patients during their hospitalization. Secondly, the limited sample size restricts the comprehensive representation of stroke risk factors prevalent within the broader context of Chinese society. Consequently, future research endeavors should focus on conducting multi-center studies with larger sample sizes to more comprehensively explore and validate the risk factors associated with stroke prognosis.

**6. Conclusion**

In conclusion, this study underscores the pivotal role of the BI as a crucial determinant influencing, not only the short-term prognosis of stroke patients, but also as an independent risk factor impacting the short-term outcomes among individuals with both stroke (OR 1.50, 95% CI 1.21 ~ 1.85, P < .001) and IS (OR 1.48, 95% CI 1.20 ~ 1.83, P < .001). Consequently, the BI score assumes significant positive implications in the assessment of short-term prognoses for stroke patients. A higher BI score is more related to a poor prognosis of stroke. Therefore, early intervention and treatment should be carried out for stroke patients admitted with a higher BI score.

**Acknowledgments**

We would like to thank all the subjects for their participation in this study, and express our gratitude to Fang Jiajia team from Fourth Affiliated Hospital of Zhejiang University for their invaluable assistance in sample collection and provision of clinical data.

**Author contributions**

**Data curation:** Rongli Fan, Jingxin Zhang, Maiqiu Wang, Zheng Chen, Fangshen Xu, Lei Zhang.  
**Funding acquisition:** Rongli Fan, Maiqiu Wang, Lei Zhang.

**Investigation:** Jingjie Gu.

**Writing – original draft:** Jingjie Gu.

**Writing – review & editing:** Rongli Fan.

## References

- [1] Feigin VL, Mensah GA, Norrving B, et al. Atlas of the Global Burden of Stroke (1990-2013): the GBD 2013 study. *Neuroepidemiology*. 2015;45:230–6.
- [2] Pandian JD, Gall SL, Kate MP, et al. Prevention of stroke: a global perspective. *Lancet*. 2018;392:1269–78.
- [3] Wang Y-J, Li Z-X, Gu H-Q, et al. China Stroke Statistics: an update on the 2019 report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, the Chinese Stroke Association, National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Institute for Global Neuroscience and Stroke Collaborations. *Stroke Vasc Neurol*. 2022;7:415–50.
- [4] Xu J, Zhang X, Jin A, et al. Trends and risk factors associated with stroke recurrence in China, 2007-2018. *JAMA Netw Open*. 2022;5:e2216341.
- [5] Chen X, Liu L, Liu M, et al. Hypertensive retinopathy and the risk of stroke among hypertensive adults in China. *Invest Ophthalmol Vis Sci*. 2021;62:28.
- [6] Q M, R L, L W, et al. Temporal trend and attributable risk factors of stroke burden in China, 1990-2019: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 2021;6.
- [7] Feigin VL, Norrving B, Mensah GA. Global burden of stroke. *Circ Res*. 2017;120:439–48.
- [8] Feigin VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet*. 2014;383:245–54.
- [9] Wafa HA, Wolfe CDA, Emmett E, et al. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke*. 2020;51:2418–27.
- [10] Wu S, Wu B, Liu M, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol*. 2019;18:394–405.
- [11] Amini H, Knepp B, Rodriguez F, et al. Early peripheral blood gene expression associated with good and poor 90-day ischemic stroke outcomes. *J Neuroinflammation*. 2023;20:13.
- [12] Lau L-H, Lew J, Borschmann K, et al. Prevalence of diabetes and its effects on stroke outcomes: a meta-analysis and literature review. *J Diabetes Investig*. 2019;10:780–92.
- [13] Someeh N, Mirfeizi M, Asghari-Jafarabadi M, et al. Predicting mortality in brain stroke patients using neural networks: outcomes analysis in a longitudinal study. *Sci Rep*. 2023;13:18530.
- [14] Campo M, Togliola J, Jaywant A, et al. Young individuals with stroke in rehabilitation: a cohort study. *Int J Rehabil Res*. 2021;44:314–22.
- [15] Maaijwee NAMM, Rutten-Jacobs LCA, Schaapsmeeders P, et al. Ischaemic stroke in young adults: risk factors and long-term consequences. *Nat Rev Neurol*. 2014;10:315–25.
- [16] J P, D S, S M, et al. Functional outcome in young adult ischemic stroke: impact of lipoproteins. *Acta Neurol Scand*. 2013;127.
- [17] Thomas Q, Crespy V, Duloquin G, et al. Stroke in women: when gender matters. *Rev Neurol (Paris)*. 2021;177:881–9.
- [18] Wiszniewska M, Niewada M, Czlonkowska A. Sex differences in risk factor distribution, severity, and outcome of ischemic stroke. *Acta Clin Croat*. 2011;50:21–8.
- [19] Mirzaei H. Stroke in women: risk factors and clinical biomarkers. *J Cell Biochem*. 2017;118:4191–202.
- [20] Al-Hashel JY, Al-Sabah A-A, Ahmed SF, et al. Risk factors, subtypes, and outcome of ischemic stroke in Kuwait: a national study. *J Stroke Cerebrovasc Dis*. 2016;25:2145–52.
- [21] Tento T, Kume A, Kumaso S. Risk factors for stroke-related functional disability and mortality at Felege Hiwot Referral Hospital, Ethiopia. *BMC Neurol*. 2023;23:393.
- [22] Samuthpongton C, Jereerat T, Suwanwela NC. Stroke risk factors, subtypes and outcome in elderly Thai patients. *BMC Neurol*. 2021;21:322.
- [23] Liu B-J, Li J, Chen H-S. Age and sex affect the association of systolic blood pressure with clinical outcomes in thrombolysed stroke patient: a secondary analysis of the INTRECIIS study. *Front Neurol*. 2023;14:1273131.
- [24] Bentsen L, Christensen L, Christensen A, et al. Outcome and risk factors presented in old patients above 80 years of age versus younger patients after ischemic stroke. *J Stroke Cerebrovasc Dis*. 2014;23:1944–8.
- [25] Ton MD, Dao PV, Nguyen DT, et al. Sex disparity in stroke outcomes in a multicenter prospective stroke registry in Vietnam. *Int J Stroke*. 2023;18.
- [26] Roy J. Stroke outcome is associated with baseline renal function: a risk factor that matters! *Atherosclerosis*. 2018;269:258–9.
- [27] Kelly DM, Rothwell PM. Impact of multimorbidity on risk and outcome of stroke: Lessons from chronic kidney disease. *Int J Stroke*. 2021;16:758–70.
- [28] Yang L, Gao K, Shi R-J, et al. Fibrosis-4 index is closely associated with clinical outcomes in acute cardioembolic stroke patients with nonvalvular atrial fibrillation. *Intern Emerg Med*. 2023;18.
- [29] Chang W-W, Fei S-Z, Pan N, et al. Incident stroke and its influencing factors in patients with type 2 diabetes mellitus and/or hypertension: a prospective cohort study. *Front Cardiovasc Med*. 2022;9:770025.
- [30] Yu S, Huang Z-C, Wang H-S, et al. Eosinophil: a new circulating biomarker for risk of poor outcome in stroke patients undergoing mechanical thrombectomy. *Clin Interv Aging*. 2023;18:523–31.
- [31] Liu F, Yang P, Wang Y, et al. HS-CRP modifies the prognostic value of platelet count for clinical outcomes after ischemic stroke. *J Am Heart Assoc*. 2023;12:e030007.
- [32] Bonarek M, Barberger-Gateau P, Letenneur L, et al. Relationships between cholesterol, apolipoprotein E polymorphism and dementia: a cross-sectional analysis from the PAQUID study. *Neuroepidemiology*. 2000;19:141–8.
- [33] He Q, Li Q, Zhao J, et al. Relationship between plasma lipids and mild cognitive impairment in the elderly Chinese: a case-control study. *Lipids Health Dis*. 2016;15:146.
- [34] Wang R, Jiao Z, Wang A, et al. High-density lipoprotein cholesterol is associated with lowered cognitive recovery among acute ischemic stroke patients with mild cognitive impairment. *Acta Neurol Belg*. 2023.
- [35] Han Y, Huang Z, Zhou J, et al. Association between triglyceride-to-high density lipoprotein cholesterol ratio and three-month outcome in patients with acute ischemic stroke: a second analysis based on a prospective cohort study. *BMC Neurol*. 2022;22:263.
- [36] Cv G, Ls D, Nc P, et al. Stroke rehabilitation: analysis of repeated Barthel index measures. *Arch Phys Med Rehabil*. 1979;60.
- [37] F L, Rc T, J Z, et al. Relationship of Barthel Index and its Short Form with the Modified Rankin Scale in acute stroke patients. *J Stroke Cerebrovasc Dis*. 2020;29.
- [38] Yang H, Chen Y, Wang J, et al. Activities of daily living measurement after ischemic stroke: Rasch analysis of the modified Barthel Index. *Medicine (Baltim)*. 2021;100:e24926.
- [39] Li Z, Zhang X, Wang K, et al. Effects of early mobilization after acute stroke: a meta-analysis of randomized control trials. *J Stroke Cerebrovasc Dis*. 2018;27:1326–37.
- [40] Ferfeli S, Galanos A, Dontas IA, et al. Reliability and validity of the Greek adaptation of the modified Barthel Index in neurorehabilitation patients. *Eur J Phys Rehabil Med*. 2023.
- [41] Sporns PB, Fullerton HJ, Lee S, et al. Childhood stroke. *Nat Rev Dis Primers*. 2022;8:12.
- [42] Kittner SJ. Stroke in the young: coming of age. *Neurology*. 2002;59:6–7.
- [43] P A, Pc L, J L, et al. One-year risk of stroke after transient ischemic attack or minor stroke. *N Engl J Med*. 2016;374.
- [44] IST-3 collaborative group. Effect of thrombolysis with alteplase within 6 h of acute ischaemic stroke on long-term outcomes (the third International Stroke Trial [IST-3]): 18-month follow-up of a randomised controlled trial. *Lancet Neurol*. 2013;12:768–76.
- [45] Musolino R, La Spina P, Granata A, et al. Ischaemic stroke in young people: a prospective and long-term follow-up study. *Cerebrovasc Dis*. 2003;15:121–8.
- [46] Schöberl F, Ringleb PA, Wakili R, et al. Juvenile Stroke. *Dtsch Arztebl Int*. 2017;114:527–34.
- [47] Kauffmann J, Grün D, Yilmaz U, et al. Acute stroke treatment and outcome in the oldest old (90 years and older) at a tertiary care medical centre in Germany—a retrospective study showing safety and efficacy in this particular patient population. *BMC Geriatr*. 2021;21:611.
- [48] Lai Y, Jou E, Mofatteh M, et al. 7-Day National Institutes of Health Stroke Scale as a surrogate marker predicting ischemic stroke patients' outcome following endovascular therapy. *Transl Neurosci*. 2023;14:20220307.
- [49] English SW, Chhabra N, Hanus AE, et al. Prehospital stroke scales outperform National Institutes of Health Stroke Scale in predicting large vessel occlusion in a large academic telestroke network. *J Telemed Telecare*. 2023;1357633X231204066.

- [50] Abzhandadze T, Reinholdsson M, Stibrant Sunnerhagen K. NIHSS is not enough for cognitive screening in acute stroke: a cross-sectional, retrospective study. *Sci Rep.* 2020;10:534.
- [51] Roushdy T, Abdel Nasser A, Nasef A, et al. A clinical comparative analysis between expanded NIHSS and original NIHSS in posterior circulation ischemic stroke. *J Clin Neurosci.* 2023;114:77–80.
- [52] Shichita T, Sugiyama Y, Ooboshi H, et al. Pivotal role of cerebral interleukin-17-producing gammadeltaT cells in the delayed phase of ischemic brain injury. *Nat Med.* 2009;15:946–50.
- [53] Offner H, Vandenbark AA, Hurn PD. Effect of experimental stroke on peripheral immunity: CNS ischemia induces profound immunosuppression. *Neuroscience.* 2009;158:1098–111.
- [54] Yilmaz G, Arumugam TV, Stokes KY, et al. Role of T lymphocytes and interferon-gamma in ischemic stroke. *Circulation.* 2006;113:2105–12.
- [55] Hurn PD, Subramanian S, Parker SM, et al. T- and B-cell-deficient mice with experimental stroke have reduced lesion size and inflammation. *J Cereb Blood Flow Metab.* 2007;27:1798–805.