Clinical Investigation

Analysis of Clinical Symptoms and Risk Factors Related to Functional Prognosis in Patients With Cardiogenic Stroke

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Abstract

Background: Cardiogenic stroke is associated with substantial morbidity and mortality, necessitating a better understanding of its clinical characteristics for improved patient outcomes. This study aimed to identify clinical characteristics influencing short-term functional prognosis in patients with cardiogenic stroke.

Methods: The study prospectively enrolled 212 patients with cardiogenic stroke, collecting their clinical data and laboratory results. The modified Rankin Scale score at 90 days was used to define functional prognosis, with patients having a good prognosis (modified Rankin Scale \leq 2; n = 164) or poor prognosis (modified Rankin Scale \geq 3; n = 48).

Results: The poor prognosis group had higher rates of total anterior circulation infarcts (12.5% vs 0.0%; P < .001) and posterior circulation infarction (50.0% vs 38.4%; P < .001) compared with the good prognosis group. Lesion characteristics differed significantly, with the poor prognosis group exhibiting more large-area lesions (39.6% vs 18.9%; P < .001) and multiple confluent lesions (56.3% vs 24.4%; P < .001). Admission-based National Institute of Health Stroke Scale scores were higher in the poor prognosis group (median [IQR], 12 [8-18] vs 5 [4-7]; P < .001), correlating with worse outcomes. The admission National Institute of Health Stroke Scale score predicted patients' 90-day prognosis with good accuracy (area under the curve, 0.937 [95% CI, 0.895-0.965]; P < .001), with a threshold of 7 yielding 85.42% sensitivity and 85.37% specificity.

Conclusion: Higher admission National Institute of Health Stroke Scale scores were significantly associated with poor functional prognosis at 90 days, highlighting the importance of early National Institute of Health Stroke Scale-based assessment for improved outcomes.

Keywords: Prognosis; clinical manifestation; risk factors

Introduction

ardiogenic stroke is a prevalent and severe cerebrovascular disease that has garnered substantial attention because of its epidemiological characteristics and associated risks.¹ Recent research data indicate a global increase in the incidence and disability rate of cardiogenic stroke.² Each year, millions of people worldwide suffer death or disability as a result of cardiogenic stroke, imposing substantial burdens on individuals, families, and societies.³ Extensive research has been conducted in recent years to investigate the treatment and prognostic factors of cardiogenic stroke, aiming to enhance patient outcomes and improve their quality of life. Clinical trials and systematic reviews have demonstrated that early reperfusion therapies, such as thrombolysis and mechanical thrombectomy, significantly improve the prognosis of patients with cardiogenic stroke.⁴ In addition, antiplatelet therapy and anticoagulation are widely employed for secondary prevention in these patients.⁵ Despite these advancements, many patients still experience poor prognosis following treatment, highlighting the need for further

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exploration and identification of additional prognostic factors.⁶

Recent research progress suggests that the prognosis of cardiogenic stroke is influenced not only by clinical characteristics but also by factors such as inflammatory response, endocrine disorders, and blood biochemical markers.7 For instance, recent studies have identified the significant roles of inflammatory markers, including C-reactive protein and leukocyte count, in the occurrence and prognosis of cardiogenic stroke.8 Cardiovascular risk factors, such as high cholesterol levels, hypertension, diabetes, and obesity, are additionally recognized as important determinants of poor prognosis in cardiogenic stroke.^{9,10} Despite some existing research on the epidemiology and prognostic factors of cardiogenic stroke, several unresolved issues and knowledge gaps persist. Current studies often rely on small observational methods and lack large-scale, multicenter, randomized controlled trials. Data on the association between laboratory examination markers and prognosis in cardiogenic stroke are furthermore relatively limited. Comprehensive, in-depth research is therefore necessary to further elucidate the epidemiologic characteristics, risk factors, and prognostic factors of cardiogenic stroke.

Building upon the background and knowledge gaps previously mentioned in this section, this study aims to comprehensively evaluate the clinical characteristics, laboratory examination markers, and prognostic factors in patients with cardiogenic stroke and explore their interrelationships. By integrating the latest research progress and evidence, the study sought to provide more precise insights into the pathogenesis, risk factors, and prognostic impact of cardiogenic stroke, thereby offering reliable scientific evidence for clinical decision-making. The findings of this study are expected to provide new perspectives and strategies for early intervention, individualized treatment, and rehabilitation of patients with cardiogenic stroke, ultimately leading to improved prognosis and enhanced quality of life.

Patients and Methods

This study was approved by the ethics committee of Beijing Anzhen Hospital, Capital Medical University (Ethics study No. 2023161x). It was a prospective study, and all participants' information was protected, with informed consent obtained upon enrollment. The study did not involve personal privacy or commercial interests,

Key Points

- Patients with cardiogenic stroke presenting with single large-area lesions and multiple confluent lesions had a poorer short-term functional prognosis than patients with single small-area lesions.
- Higher NIHSS scores at hospital admission were closely associated with worse functional prognosis in patients with cardiogenic stroke.
- Total anterior circulation infarcts and posterior circulation infarction were significantly linked to poor prognosis, highlighting the importance of identifying underlying etiologies in prognostic assessment.
- The study's findings provide new perspectives for individualized treatment strategies based on clinical characteristics and NIHSS scores at admission.
- Further investigation is warranted to deepen clinical understanding of cardiogenic stroke pathogenesis and prognostic factors and to facilitate more effective clinical decision-making and interventions.

Abbreviations

CT, computed tomography
mRS, modified Rankin Scale
NIHSS, National Institute Health Stroke Scale
OCSP, Oxfordshire Community Stroke Project
TOAST, Trial of ORG 10172 in Acute Stroke Treatment

and all research protocols and procedures were conducted in accordance with the Helsinki Declaration.

The study was conducted on consecutively screened patients with cardiogenic stroke who were treated in the hospital's neurology department between January 2022 and June 2023. The inclusion criteria were as follows: (1) Patients were adults, aged at least 18 years; (2) computed tomography (CT) or magnetic resonance imaging confirmed new-onset ischemic stroke; (3) time from symptom onset to hospital admission was less than 4.5 hours; and (4) a cardiogenic stroke had been diagnosed according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification.¹¹ Cardiogenic stroke was defined as the presence of cortical or cerebellar dysfunction. The diagnosis was made when there was no evidence to suggest an alternative embolic source and the patient met high-risk or medium-risk criteria for cardiogenic embolism. The exclusion criteria were as follows: (1) The patient had a history of hematologic disorders, (2) the patient had severe hepatic or kidney dysfunction, (3) the patient had concomitant severe infection, (4) the patient was unwilling to comply with follow-up, and (5)

intracerebral hemorrhage was present upon admission. The evaluation included comprehensive assessments through transesophageal echocardiography, transthoracic echocardiography, electrocardiography, and other relevant clinical data. Brain magnetic resonance imaging and cerebrovascular imaging, including CT angiography, magnetic resonance angiography, and digital subtraction angiography, were performed. The National Institute Health Stroke Scale (NIHSS) scores at admission and discharge as well as the modified Rankin Scale (mRS) scores at the third month after symptom onset were recorded for all eligible patients. The end point of the study was the functional outcome assessed by the mRS score in the third month after symptom onset.¹²

The study aimed to evaluate the functional outcomes at 3 months after onset and employed the mRS as a modified version for assessment. Based on mRS score, patients were categorized into having no disability (mRS, 0-1), mild disability (mRS, 2-3), severe disability (mRS, 4-5), or having died (mRS, 6), with an mRS score greater than 3 indicating poor prognosis.13 The mRS score at 90 days was used to define functional prognosis, with patients having a good prognosis (mRS \leq 2) or a poor prognosis (mRS \geq 3). Experienced neurologists assessed the mRS score of patients during telephone interviews or clinic visits without knowledge of the study objectives. Computed tomography angiography was used to assess cerebral artery stenosis within 24 hours after stroke onset. Two experienced neuroimaging specialists analyzed all CT angiographic data and resolved any discrepancies through collective discussion. The CT angiography was performed using the Revolution CT scanner (GE Healthcare), and the data analysis was conducted using GE Advantage Workstation 4.7 software (GE Healthcare).

Before enrollment, patients underwent CT scans to assist in refining their clinical classification. Two neurologists independently examined the patients and assigned them to 1 of the 4 Oxfordshire Community Stroke Project (OCSP) categories. The examiners recorded the patients' medical history, performed physical examinations, and evaluated the CT scans. In cases of disagreement between the examiners, a third reviewer independently classified the patients. For patients undergoing thrombolysis, a clinical OCSP grading was performed before treatment, which included categories for partial anterior circulation infarction, total anterior circulation infarction, and lacunar infarction. Further classification was performed based on lesion characteristics, dividing patients

with cardiogenic stroke into 3 groups: (1) single largearea lesion, (2) single small-area lesion, and (3) multiple and confluent lesions.

Standard laboratory examination methods were employed in this study to assess the biochemical parameters, coagulation function, and immune system status of patients with cardiogenic stroke. Blood samples were obtained through venipuncture, adhering to strict aseptic techniques and safety regulations to ensure sample purity and prevent contamination. Automated biochemical analyzers were then used to measure the blood biochemical parameters. These analyzers provide rapid and accurate measurements of complete blood count, liver function, kidney function, lipid profiles, blood glucose, and other parameters. The operation guidelines provided by the manufacturers were followed to ensure measurement accuracy and reliability. For coagulation function evaluation, standard coagulation analyzers were used to determine the international normalized ratio and other relevant indices. These instruments automate the analysis of the coagulation function and provide reliable results. Finally, specific immunological analysis methods were employed for immune testing. For example, an enzyme-linked immunosorbent assay was used to measure the level of high-sensitivity C-reactive protein, a hematology analyzer was used for white blood cell count and classification, and a platelet counter was used to measure platelet count. These methods have been validated and standardized to provide accurate immunological measurements. Throughout the laboratory examination process, strict quality control procedures were followed, including the use of quality control samples for calibration and validation. Regular equipment maintenance and calibration were performed to ensure measurement reliability and consistency.

Statistical Analysis

The Shapiro-Wilk test was used to assess the normalcy of continuous variables. Normally distributed quantitative data are presented as mean (SD) values, and the t test was used for between-group comparisons. Nonnormally distributed quantitative data are presented as median (IQR) values. The Mann-Whitney U test was used to compare non-normally distributed quantitative data between groups. Qualitative data are presented as frequencies. The χ^2 test was used for qualitative data. Logistic regression analysis was performed to evaluate factors influencing prognosis, and results are presented as odds ratios with 95% CIs. All statistical results were considered significant at a 2-tailed P < .05. Statistical

analysis was conducted using SPSS Statistics, version 23.0, software (IBM Corp). Receiver operating characteristic curves were used to assess the predictive ability of risk factors for poor prognosis, with an area under the curve of more than 0.8 indicating good predictive ability. Variables with potential associations (typically $P \le .2$ in univariate analysis), including white blood cell count, dimerized plasmin fragment D values, dyslipidemia, smoking status, alcohol use, length of stay, peripheral artery disease, lymphocytes, OCSP classifications, lesion characteristics, stroke or transient ischemic attack, and coronary artery disease, were considered confounders for inclusion in the multivariate analysis. Patients' NIHSS scores at discharge were excluded from the model because of the inclusion of NIHSS scores at admission, which better represent initial stroke severity and avoid redundancy. Modified Rankin Scale scores at admission and discharge were similarly excluded as they serve as outcome measures, not predictors. This approach was chosen to avoid circular reasoning and ensure the robustness and clarity of the model. The therapeutic strategy was also excluded as it was closely tied to initial assessments like NIHSS score at admission, which could introduce multicollinearity. Including treatment variables could moreover obscure the independent effects of the baseline clinical factors of the study. The goal was to ensure that potentially important factors were not overlooked and to explore their independent contributions to the outcome of interest in the multivariate model.

Results

A total of 283 consecutive patients fulfilling the inclusion criteria were screened for their eligibility, and 71 of these patients were excluded based on predefined exclusion criteria (Fig. 1). A total of 212 patients with cardiogenic stroke were included in this study, with a mean (SD) age of 65.73 (12.41) years. Among them, 132 were men (62.3%) with a mean (SD) age of 63.45 (11.75) years, and 80 were women (37.7%) with a mean (SD) age of 69.50 (12.63) years. The top 3 etiologies of cardiogenic stroke among all the patients were atrial

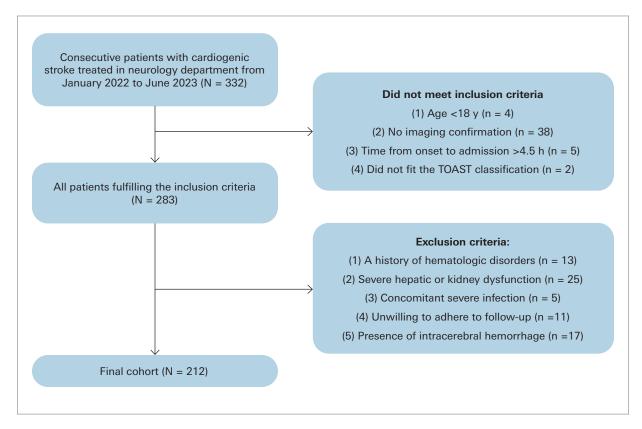


Fig. 1 Flow diagram shows patient selection.

TOAST, Trial of ORG 10172 in Acute Stroke Treatment

arrhythmia (131 cases [61.8%]), left atrial thrombus (26 cases [12.3%]), and patent foramen ovale (21 cases [9.9%]). Risk factors included a history of hypertension (184 patients), smoking (94 patients), diabetes (175 patients), hyperlipidemia (187 patients), previous stroke (88 patients), and coronary heart disease (92 patients). All 212 patients completed the 90-day follow-up, and there were no missing data in the study's dataset. Based on their mRS scores at the 90-day follow-up, patients were divided into a good prognosis group (mRS \leq 2; n = 164) and a poor prognosis group (mRS \geq 3; n = 48). There were no significant differences between the 2 groups in terms of age, sex, body mass index, etiology, risk factors, medication status, or coagulation score distribution (P > .05). According to the OCSP classifi-

cation, patients in the poor prognosis group were more likely to have total anterior circulation infarcts (12.5% vs 0.0%) and posterior circulation infarction (50.0% vs 38.4%), but they had a lower prevalence of partial anterior circulation infarction (37.5% vs 55.5%; overall P < .001). In terms of lesion characteristics, the poor prognosis group had a higher proportion of large-area lesions (39.6% vs 18.9%) and multiple confluent lesions (56.3% vs 24.4%) while the good prognosis group was primarily characterized by small-area lesions (56.7% vs 4.2%; overall P < .001).

As shown in Table I, there was no significant difference in the length of hospital stay between the 2 groups (P = .19). Compared with the good prognosis group, however, the poor prognosis group had higher NIHSS

TABLE I. Patients' Clinical Characteristics, Through 90-Day Prognosis (N = 212)^a

Variable	Good prognosis group (n = 164)	Poor prognosic aroun /n = 40\	Dyalua
Age, median (IQR), y	66 (59-75)	65 (56-77)	.67
	00 (33-73)	00 (00-77)	
Sex, No. (%)	400 (00 0)	00 (00 5)	.97
Male	102 (62.2)	30 (62.5)	
Female	62 (37.8)	18 (37.5)	
Body mass index, No. (%)	25.8 (3.5)	25.5 (2.4)	.47
Hypertension, No. (%)	140 (85.4)	44 (91.7)	.26
Systolic blood pressure, No. (%), mm Hg	133.9 (17.4)	130.5 (18.5)	.25
Diastolic blood pressure, No. (%), mm Hg	76.9 (11.9)	74.5 (12.3)	.23
Etiology of cardiogenic stroke, No. (%)			.79
Abnormal atrial rhythm	105 (64.0)	26 (54.2)	
Left atrial thrombus	19 (11.6)	7 (14.6)	
Patent foramen ovale	15 (9.1)	6 (12.5)	
Heart valve-related disease	11 (6.7)	4 (8.3)	
Atrial septal aneurysm	3 (1.8)	2 (4.2)	
Cardiac tumor	7 (4.3)	2 (4.2)	
Pulmonary arteriovenous fistula	2 (1.2)	1 (2.1)	
Mitral valvular prolapse	2 (1.2)	0 (0)	
Complications, No. (%)			
Diabetes	133 (81.1)	42 (87.5)	.30
Stroke or transient ischemic attack	73 (44.5)	15 (31.3)	.10
Coronary artery disease	76 (46.3)	16 (33.3)	.14
Peripheral artery disease	8 (4.9)	0 (0.0)	.20
Congestive heart failure	23 (14.0)	6 (12.5)	.79
Dyslipidemia	142 (86.6)	45 (93.8)	.18

Continued

TABLE I. Patients' Clinical Characteristics, Through 90-Day Prognosis (N = 212)^a (Continued)

Variable	Good prognosis group (n = 164)	Poor prognosis group (n = 48)	P value
Cerebral hemorrhage	10 (6.1)	1 (2.1)	.46
Smoking	77 (47.0)	17 (35.4)	.16
Alcohol use	74 (45.1)	16 (33.3)	.15
CHA ₂ DS ₂ -VASc score, mean (SD)	4 (3-6)	4 (3-5)	.56
HAS-BLED score, mean (SD)	2 (2-4)	2 (2-3)	.87
CHADS2 score, mean (SD)	1 (0-3)	1 (0-2)	.44
OCSP classifications, No. (%)			<.001
Partial anterior circulation infarction	91 (55.5)	18 (37.5)	
Total anterior circulation infarcts	0 (0.0)	6 (12.5)	
Posterior circulation infarction	63 (38.4)	24 (50.0)	
Lacunar infarction	10 (6.1)	0 (0.0)	
Lesion characteristics, No. (%)			<.001
Single large lesion	31 (18.9)	19 (39.6)	
Single small-area lesion	93 (56.7)	2 (4.2)	
Multiple and fused lesions	40 (24.4)	27 (56.3)	
Antiplatelet regimen, No. (%)	144 (87.8)	45 (93.8)	.24
Anticoagulation regimen, No. (%)			.26
None	151 (92.1)	46 (95.8)	
Warfarin	8 (4.9)	0 (0.0)	
Direct oral anticoagulants	5 (3.0)	2 (4.2)	
Therapeutic strategy, No. (%)			.17
None	152 (92.7)	46 (95.8)	
Intravenous thrombolysis	9 (5.5)	0 (0.0)	
Thrombectomy	2 (1.2)	2 (4.2)	
Combined strategy	1 (0.6)	0 (0.0)	
Length of stay, median (IQR), d	15 (13-20)	14 (12-18)	.19
NIHSS score at admission, median (IQR)	5 (4-7)	12 (8-18)	<.001
NIHSS score at discharge, median (IQR)	3 (1-4)	10 (7-22)	<.001
mRS score at admission, median (IQR)	2 (2-3)	5 (4-5)	<.001
mRS score at discharge, median (IQR)	2 (1-3)	4 (4-5)	<.001
mRS score at 90 d, median (IQR)	1 (0-2)	4 (3-6)	<.001
Death, No. (%)	0 (0.0)	15 (31.3)	<.001

 CHA_2DS_2 -VASc, congestive heart failure, hypertension, age \geq 75 y (doubled), diabetes, stroke (doubled), vascular disease, age 65 y to 74 y ,and sex category (female); HAS-BLED, hypertension, abnormal kidney and liver function, stroke, bleeding; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OCSP, Oxfordshire Community Stroke Project.

SI conversion factor: To convert from mm Hg to kPa, multiply by 0.133.

P < .05 was considered statistically significant.

^a Some percentages in this table may not add up to 100 as a result of rounding.

scores at admission (median [IQR], 12 [8-18] vs 5 [4-7]), higher NIHSS scores at discharge (median [IQR], 10 [7-22] vs 3 [1-4]), higher mRS scores at admission (median [IQR], 5 [4-5] vs 2 [2-3]), higher mRS scores at discharge (median [IQR], 4 [4-5] vs 2 [1-3]), higher

90-day mRS scores (median [IQR], 4 [3-6] vs 1 [0-2]), and a higher mortality rate (31.3% vs 0%) (all *P* < .001).

The comparison of laboratory examination results between the good prognosis group and the poor prognosis group is presented in Table II. There was a significant

TABLE II. Patients' Laboratory Values at 90-Day Follow-Up

Variable	Good prognosis group (n = 164)	Poor prognosis group (n = 48)	P value ^a
White blood cell count, median (IQR), ×10 ⁹ /L	6.8 (5.8-8.3)	6.8 (5.3-7.9)	.17
Red blood cell count, mean (SD), ×10 ¹² /L	4.5 (0.5)	4.5 (0.5)	.76
Platelet count, median (IQR), ×10 ⁹ /L	204 (176-259)	207 (172-243)	.64
Hemoglobin, median (IQR), g/L	140 (130-149)	137 (123-151)	.59
Lymphocytes, median (IQR), ×10 ⁹ /L	1.8 (1.4-2.1)	1.6 (1.3-1.8)	.03
Neutrophils, median (IQR), ×10 ⁹ /L	4.2 (3.4-5.7)	4.1 (3.2-5.4)	.55
Red blood cell distribution width-SD, median (IQR), fL	42.6 (40.9-44.6)	42.3 (40.4-45.0)	.59
High-sensitivity C-reactive protein, median (IQR), mg/L	3.2 (0.9-9.8)	3.7 (1.3-12.4)	.22
Alanine aminotransferase, median (IQR), U/L	17 (12-26)	17 (12-23)	.42
Aspartate aminotransferase, median (IQR), U/L	20 (17-25)	19 (16-25)	.58
Triglycerides, median (IQR), mmol/L	1.2 (0.9-1.6)	1.2 (1.0-1.8)	.76
Total cholesterol, median (IQR), mmol/L	4.1 (3.4-4.8)	3.9 (3.4-4.8)	.82
High-density lipoprotein cholesterol, median (IQR), mmol/L	1.0 (0.9-1.1)	1.0 (0.9-1.2)	.88
Low-density lipoprotein cholesterol, median (IQR), mmol/L	2.5 (1.9-3.1)	2.4 (2.0-3.1)	.91
Urea nitrogen, median (IQR), mmol/L	4.8 (3.8-6.1)	4.9 (4.1-6.0)	.61
Creatinine, median (IQR), µmol/L	67.5 (54.4-79.0)	67.8 (57.4-84.8)	.31
Uric acid, median (IQR), µmol/L	290 (236-359)	315 (224-360)	.82
Fasting glucose, median (IQR), mmol/L	5.8 (5.1-7.4)	5.4 (5.1-6.8)	.32
Glycated hemoglobin, median (IQR), %	6.1 (5.6-7.2)	6.2 (5.7-7.7)	.31
Direct bilirubin, median (IQR), µmol/L	2.9 (2.3-3.8)	2.9 (1.8-4.1)	.57
B-type natriuretic peptide, median (IQR), pg/mL	209.7 (69.0-434.5)	207.7 (37.0-433.7)	.32
International normalized ratio, median (IQR)	1.00 (0.95-1.10)	1.00 (0.94-1.10)	.69
Dimerized plasmin fragment D, median (IQR), µg/L	151.0 (93.0-370.3)	164.5 (114.0-388.0)	.17

SI conversion factor: To convert U/L to μ kat/L, multiply by 0.0167. To convert a percentage of total hemoglobin to a proportion of total hemoglobin, multiply by 0.01. To convert pg/mL to ng/L, multiply by 1. To convert μ g/mL to nmol/L, multiply by 5.476.

^a P < .05 was considered statistically significant.

difference in lymphocyte count between the 2 groups (1.8 [1.4-2.1] vs 1.6 [1.3-1.8] \times 10°/L; P = .03). There were no significant differences in complete blood cell count, lipid profiles, liver function, kidney function, fasting blood glucose, B-type natriuretic peptide levels, or coagulation function between the 2 groups (all P > .05).

A multivariate analysis was conducted to determine the factors associated with poor prognosis in patients with cardiogenic stroke. Based on the results of the univariate analysis presented in Table I and Table II, several variables with significant differences were selected as covariates for inclusion in the multivariate analysis. These variables included white blood cell count (P = .17), dimerized plasmin fragment D values (P = .17), dyslipidemia (P = .18), smoking use (P = .16), alcohol use (P = .15), length of stay (P = .19), peripheral artery disease (P = .20), OCSP classification (P < .001), lesion characteristics (P < .001), NIHSS score at admission (P < .001), stroke or transient ischemic attack (P = .10), coronary heart disease (P = .14) and lymphocyte count (P = .03). The results of the multivariate analysis are presented in Table III and show that in both forward and backward stepwise models, NIHSS score at admission was closely associated with poor prognosis in patients with cardiogenic stroke, thereby identifying this score as a statistically significant factor. A higher NIHSS score at admission was associated with a worse prognosis.

To further evaluate the predictive performance of NIHSS score at admission for patient prognosis, receiver operating characteristic curve analysis was performed as shown in Figure 2. The analysis demonstrated that NIHSS score at admission had a good predictive ability for the 90-day prognosis when the threshold was set at 7 (area under the curve, 0.937 [95% CI, 0.895-0.965]; P < .001), with a sensitivity of 85.42% and specificity of 85.37%.

Discussion

The main findings of this study support the important clinical significance of and innovation in the prognostic assessment and treatment of cardioembolic stroke. Accurate assessment of the prognosis of cardioembolic stroke is crucial for formulating appropriate treatment strategies in clinical practice. The findings of this study

TABLE III. Multivariable Analysis for Independent Factors of Poor Prognosis in Patients With Cardiogenic Stroke

	Forward stepwise		Backward stepwise	
Variable	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value ^a
White blood cell count	NA	NA	NA	NA
Dimerized plasmin fragment D	NA	NA	NA	NA
Lymphocytes	NA	NA	NA	NA
OCSP classifications	NA	NA	NA	NA
Lesion characteristics	NA	NA	NA	NA
NIHSS at admission	2.7 (1.9-3.8)	<.001	2.6 (1.9-3.6)	<.001
Stroke or transient ischemic attack	NA	NA	0.08 (0.02-0.41)	.079
Coronary artery disease	NA	NA	NA	NA
Peripheral artery disease	NA	NA	NA	NA
Dyslipidemia	NA	NA	NA	NA
Alcohol use	0.08 (0.02-0.41)	.002	NA	NA
Smoking	NA	NA	NA	NA
Length of stay	NA	NA	NA	NA

SI conversion factor: To convert U/L to µkat/L, multiply by 0.0167. To convert a percentage of total hemoglobin to a proportion of total hemoglobin, multiply by 0.01. To convert pg/mL to ng/L, multiply by 1. To convert µg/mL to nmol/L, multiply by 5.476.

 $^{^{\}rm a}$ P < .05 was considered statistically significant.

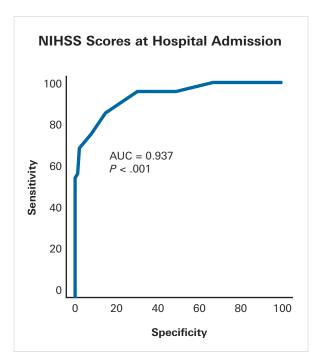


Fig. 2 Receiver operating characteristic curve of NIHSS scores at admission for predicting poor 90-day prognosis in patients with cardioembolic stroke.

AUC, area under the curve; NIHSS, National Institutes of Health Stroke Scale.

P < .05 was considered statistically significant.

emphasize the importance of NIHSS score at admission, lesion characteristics, and lymphocyte count in the prognostic assessment of cardioembolic stroke. These indicators can help physicians better evaluate the prognostic risk of patients and provide a basis for individualized treatment and rehabilitation plans. Early intervention and active rehabilitation measures are furthermore crucial for improving the prognosis and quality of life of patients with cardioembolic stroke. Further research is needed, however, to deepen a clinical understanding of the pathogenesis and prognostic impact of cardioembolic stroke to facilitate more effective clinical decision-making and intervention measures.

Cardioembolic stroke is a common and serious disease with multiple underlying mechanisms, including vascular changes, hemodynamic alterations, and thrombus formation.¹⁵ Recent studies have shown that the pathogenesis of cardioembolic stroke is a complex process involving multiple interacting factors. Vascular changes are one of the important factors in the occurrence of cardioembolic stroke, and atherosclerosis is the most common cause of cardioembolic stroke. Atherosclerot-

ic lesions narrow the arterial vessel wall, form plaques, and increase the risk of thrombus formation. Studies have shown a higher incidence of hypertension, diabetes, and hyperlipidemia in patients with cardioembolic stroke, which are closely related to atherosclerosis. Cardioembolic stroke presents with a variety of symptoms, including sudden facial paralysis, limb weakness, language disorders, and sensory loss. The appearance of these symptoms is related to cerebral blood supply interruption or localized cerebral infarction. Recent studies have also found a high prevalence of carotid artery plaques in patients with cardioembolic stroke, which may be related to the progression of atherosclerosis and thrombus formation.

In addition to vascular changes, hemodynamic alterations are important factors in cardioembolic stroke. Cardiac conditions, such as myocardial infarction and arrhythmias, can lead to reduced cardiac function, resulting in a decreased pumping capacity of the heart and affecting the blood supply to the brain. 19 Conditions such as valvular heart disease and heart failure may also increase the risk of cardioembolic stroke.²⁰ The present study reached a similar conclusion and found that atrial arrhythmias and left atrial thrombosis were the leading causes of cardiogenic stroke, though there was no significant difference in these causes between the good prognosis and poor prognosis groups. The study found that men accounted for the majority of patients with cardioembolic stroke and that there were age differences between the prognosis groups. Common risk factors included a history of hypertension, smoking, diabetes, and hyperlipidemia. These risk factors are closely related to the formation of atherosclerosis and the occurrence of cardiovascular diseases. According to the results of multivariate analysis, NIHSS score at admission was an important indicator for predicting poor prognosis in patients with cardioembolic stroke. A higher NIHSS score was associated with a poorer prognosis, which may reflect the severity of brain damage and the severity of functional impairment. This finding is consistent with the latest research results, which highlight the importance of the NIHSS score at admission in the prognostic assessment of patients with cardioembolic stroke.²¹ In addition, it was found that lesion characteristics and lymphocyte count were closely related to the prognosis of cardioembolic stroke, though these were not directly independent factors in the subsequent multivariate analysis. In the poor prognosis group, patients were more likely to have total anterior circulation infarcts, posterior

circulation infarcts, and larger lesion areas, which may reflect the association between the extent and severity of brain damage and prognosis. ²² There was also a significant difference in the lymphocyte count between the good prognosis group and the poor prognosis group, which may be related to the patient's immune status and inflammatory response. ²³ These findings provide new clues for the prognostic assessment and individualized treatment of cardioembolic stroke.

The current study has yielded findings regarding prognostic factors in cardioembolic stroke that further validate the viewpoints in existing literature. The NIHSS score at admission has been widely studied for its ability to predict the prognosis of, and is considered an important indicator for, cardioembolic stroke. The current study also confirmed the close correlation between NIHSS score at admission and prognosis. A high NIHSS score at admission was significantly associated with poor outcomes, such as a higher NIHSS score at discharge, a higher 90-day mRS score, and a higher mortality rate. This result is consistent with the findings of other studies, which emphasize the importance of the NIHSS score in assessing stroke severity and prognostic risk.^{24,25} In addition, the current study observed the impact of lesion characteristics on the prognosis of cardioembolic stroke. Patients in the poor prognosis group were more likely to have single large-area lesions and multiple confluent lesions while patients in the good prognosis group was dominated by single small-area lesions. This finding is consistent with the results of other studies, which supports the importance of lesion characteristics in the prognosis of cardioembolic stroke. Large-area lesions and confluent lesions may indicate more severe brain tissue damage and functional deficits, resulting in poorer prognosis.26 The current study, however, also differed in some ways from related studies. For example, in the current study, the correlation between OCSP classification and prognosis was more evident. Patients in the poor prognosis group were more likely to have total anterior circulation infarcts and posterior circulation infarcts while patients in the good prognosis group were more likely to have partial anterior circulation infarcts. This result may be related to differences between regions or sample populations and requires further research for confirmation.

The observed association between specific lesion characteristics and poor prognosis can be attributed to the impact of lesion location and size on brain function. Total anterior circulation infarcts and posterior circulation infarctions are often associated with extensive brain

damage and affect critical areas responsible for motor, sensory, and cognitive functions. Total anterior circulation infarcts typically involve larger infarcts that can lead to severe disability while posterior circulation infarction can affect vital structures such as the brainstem and cerebellum, resulting in significant neurological deficits.²⁷ Multiple confluent lesions may indicate widespread embolic events or secondary thrombotic processes, both of which can exacerbate brain injury and complicate recovery. These factors collectively contribute to the observed poor prognosis in patients with these lesion characteristics. The association between lymphocyte count and prognosis in cardioembolic stroke may be linked to lymphocytes' role in inflammation and immune response following stroke. Lymphopenia, or a lower lymphocyte count, is often associated with a heightened inflammatory response and increased susceptibility to infections, both of which can negatively impact recovery and prognosis.²⁸ In addition, lymphocytes play a crucial role in modulating the immune response and promoting neuroprotection. Reduced lymphocyte levels could impair these protective mechanisms, leading to worse outcomes.29

This study offers several innovative outlooks on the prognostic assessment of cardioembolic stroke. First, although NIHSS score and lesion characteristics are established prognostic factors, the current study is innovative in its comprehensive approach and its specific focus on a Chinese population. Multiple factors, including NIHSS score at admission, detailed lesion characteristics, and extensive laboratory examinations were integrated into a multivariate analysis, conducted to identify a combination of factors associated with poor prognosis in cardioembolic stroke. This holistic approach provided a more nuanced and comprehensive understanding of patients' disease status and prognostic risk than those of previous studies, especially within the context of the Chinese health care system and treatment protocols. Second, the study's use of receiver operating characteristic curve analysis to evaluate the predictive ability of NIHSS score at admission is not just a replication of existing methods but includes a novel application and validation within a specific cohort of Chinese patients with cardioembolic stroke. The high predictive performance observed underscores the utility of the NIHSS score as a simple and effective tool for early identification of and intervention for prognostic risks in this particular patient group, considering the unique characteristics and treatment processes of the Chinese population.

Study Limitations

Despite the innovations of this study, several limitations need to be noted. First, this study adopted a single-center design with a relatively small sample size. This limitation may affect the reliability and generalizability of its findings. The patient population from a single center may not fully represent the diversity seen in broader clinical settings, which can introduce potential selection bias. The study's results should therefore be interpreted with caution when applied to other populations. To validate and generalize the study's findings, further large-scale, multicenter studies will be necessary.

Second, this study focused on only a few factors related to the prognosis of cardioembolic stroke, and other potential influencing factors were not considered. Future research can further expand the range of factors to comprehensively evaluate the prognostic risk of patients with cardioembolic stroke. Another limitation of the current study was the absence of routine transesophageal echocardiography for all patients. This technique is recognized as the most accurate method for identifying cardiac sources of emboli, but because of practical constraints, not all patients in the cohort received transesophageal echocardiography. Instead, the study relied on the TOAST classification system and comprehensive clinical evaluations performed by experienced clinicians to diagnose cardiogenic stroke. In addition, the study primarily relied on the collection and analysis of clinical data, which makes it difficult to explore in-depth mechanisms and changes in biological markers. Combining clinical data with laboratory research could provide a more comprehensive understanding and interpretation of future study results.

Conclusion

The current study comprehensively evaluated the clinical characteristics, prognostic factors, and laboratory examinations of patients with cardioembolic stroke. Close associations between NIHSS score at admission, lesion characteristics, and lymphocyte count with prognosis were identified. These findings provide new perspectives and strategies for individualized treatment and prognostic prediction as well as scientific evidence for improving the prognosis and quality of life of patients with cardioembolic stroke. Further research is needed to deepen clinical understanding of the pathogenesis and prognostic impact of cardioembolic stroke to facilitate more effective clinical decision-making and intervention measures.

Article Information

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References

- Shirokov EA. Cardiogenic ischemic stroke. Article in Russian. Klin Med (Mosk). 2014;92(11):5-9. https://pubmed.ncbi.nlm.nih.gov/25796939/
- Davis WD, Hart RG. Cardiogenic stroke in the elderly. Clin Geriatr Med. 1991;7(3):429-442.
- Strandberg M, Mustonen P, Taina M, Korpela J, Vanninen S, Hedman M. Etiology, diagnostics and treatment of cardiogenic stroke. *Duodecim*. 2016;132(18):1625-1633.
- Kamel H, Healey JS. Cardioembolic stroke. *Circ Res.* 2017;120(3):514-526. doi:10.1161/ CIRCRESAHA.116.308407
- Kapil N, Datta YH, Alakbarova N, et al. Antiplatelet and anticoagulant therapies for prevention of ischemic stroke. Clin Appl Thromb Hemost. 2017;23(4):301-318. doi:10.1177/1076029616660762
- Wang L, Chen Y, Shen W, et al. A bibliometric analysis of cardioembolic stroke from 2012 to 2022. *Curr Probl Cardiol*. 2023;48(3):101537. doi:10.1016/j.cpcardiol.2022.101537
- Maida CD, Norrito RL, Daidone M, Tuttolomondo A, Pinto A. Neuroinflammatory mechanisms in ischemic stroke: focus on cardioembolic stroke, background, and therapeutic approaches. *Int J Mol Sci.* 2020;21(18):6454. doi:10.3390/ ijms21186454
- Piccardi B, Giralt D, Bustamante A, et al. Blood markers of inflammation and endothelial dysfunction in cardioembolic stroke: systematic review and meta-analysis. *Biomarkers*. 2017;22(3-4):200-209. doi:10.1080/1354750X.2017.1286689
- Bahit MC, Sacco RL, Easton JD, et al; RE-SPECT ESUS Steering Committee and Investigators. Predictors of atrial fibrillation development in patients with embolic stroke of undetermined source: an analysis of the RE-SPECT ESUS trial. Circulation. 2021;144(22):1738-1746. doi:10.1161/ CIRCULATIONAHA.121.055176
- Sarfo FS, Ovbiagele B, Akpa O, et al; SIREN. Risk factor characterization of ischemic stroke subtypes among West Africans. *Stroke*. 2022;53(1):134-144. doi:10.1161/ STROKEAHA.120.032072

- Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1):35-41. doi:10.1161/01.STR.24.1.35
- Kwah LK, Diong J. National Institutes of Health Stroke Scale (NIHSS). J Physiother. 2014;60(1):61. doi:10.1016/j. jphys.2013.12.012
- Zhang J, Chen S, Shi S, et al. Direct endovascular treatment versus bridging therapy in patients with acute ischemic stroke eligible for intravenous thrombolysis: systematic review and meta-analysis. *J Neurointerv Surg.* 2022;14(4):321-325. doi:10.1136/neurintsurg-2021-017928
- Asdaghi N, Jeerakathil T, Hameed B, et al. Oxfordshire Community Stroke Project classification poorly differentiates small cortical and subcortical infarcts. Stroke. 2011;42(8):2143-2148. doi:10.1161/ STROKEAHA.111.613752
- Mac Grory B, Emmer BJ, Roosendaal SD, Zagzag D, Yaghi S, Nossek E. Carotid web: an occult mechanism of embolic stroke. *J Neurol Neurosurg Psychiatry*. 2020;91(12):1283-1289. doi:10.1136/jnnp-2020-323938
- O'Carroll CB, Barrett KM. Cardioembolic stroke. Continuum (Minneap Minn). 2017;23(1, Cerebrovascular Disease):111-132. doi:10.1212/CON.00000000000000419
- Diener HC, Easton JD, Hart RG, Kasner S, Kamel H, Ntaios G. Review and update of the concept of embolic stroke of undetermined source. *Nat Rev Neurol*. 2022;18(8):455-465. doi:10.1038/s41582-022-00663-4
- Deniz C, Altunan B, Aykaç Ö, Özdemir AÖ.
 Coexistence of external carotid artery embolus and internal carotid artery occlusion in acute ischemic stroke: an indicator of cardioembolic etiology? J Stroke Cerebrovasc Dis. 2022;31(9):106630. doi:10.1016/j. jstrokecerebrovasdis.2022.106630
- van Diepen S, Katz JN, Albert NM, et al; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. Circulation. 2017;136(16):e232-e268. doi:10.1161/ CIR.000000000000000525

- Kelley RE, Kelley BP. Heart-brain relationship in stroke. *Biomedicines*. 2021;9(12):1835. doi:10.3390/ biomedicines9121835
- Zhao Y, Han Y, Sun W, Zhang Y. Clinical symptoms, etiology and prognosis of acute bilateral posterior circulation cerebral infarction. *Int J Gen Med.* 2022;15:2787-2793. doi:10.2147/IJGM.S351560
- Mead GE, Lewis SC, Wardlaw JM, Dennis MS, Warlow CP. How well does the Oxfordshire Community Stroke Project classification predict the site and size of the infarct on brain imaging? *J Neurol Neurosurg Psychiatry*. 2000;68(5):558-562. doi:10.1136/jnnp.68.5.558
- Faura J, Bustamante A, Miró-Mur F, Montaner J. Stroke-induced immunosuppression: implications for the prevention and prediction of post-stroke infections. *J Neuroinflammation*. 2021;18(1):127. doi:10.1186/s12974-021-02177-0
- Kazi SA, Siddiqui M, Majid S. Stroke outcome prediction using admission NIHSS in anterior and posterior circulation stroke. J Ayub Med Coll Abbottabad. 2021;33(2):274-278.
- Zeng YY, Zhang WB, Cheng L, et al. Cardiac parameters affect prognosis in patients with non-large atherosclerotic infarction. *Mol Med.* 2021;27(1):2. doi:10.1186/s10020-020-00260-5
- Lv YK, Huang LP, Fang ZW, et al. Relationship between size and location of infarction beside lateral ventricle and motor recovery following rehabilitation. *NeuroRehabilitation*. 2022;51(3):527-532. doi:10.3233/NRE-220132
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*. 1991;337(8756):1521-1526. doi:10.1016/0140-6736(91)93206-o
- Ren H, Liu X, Wang L, Gao Y. Lymphocyte-to-monocyte ratio: a novel predictor of the prognosis of acute ischemic stroke. *J Stroke Cerebrovasc Dis.* 2017;26(11):2595-2602. doi:10.1016/j.jstrokecerebrovasdis.2017.06.019
- Yang YL, Wu CH, Hsu PF, et al. Systemic immuneinflammation index (SII) predicted clinical outcome in patients with coronary artery disease. *Eur J Clin Invest*. 2020;50(5):e13230. doi:10.1111/eci.13230