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ORIGINAL RESEARCH

Relationship Between Lymphocyte-Associated Inflammatory Markers and Post-Stroke Cognitive Impairment

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Objective: To determine whether differences in lymphocyte-related inflammatory markers in the ultra-early phase of stroke (within 24 hours of onset) are associated with post-stroke cognitive impairment in the early recovery phase (within 30 days of stroke onset), and to further assess the predictive value of these markers.

Methods: The study population consisted of patients who underwent rehabilitation treatment at the Rehabilitation Department of Hebei University Affiliated Hospital between December 2024 and June 2025, within 30 days of stroke onset, ie, during the early recovery phase of stroke. Patients were grouped based on whether they developed cognitive impairment. A retrospective analysis was conducted of patients' blood markers and neurological deficit scores within 24 hours of stroke onset to examine the relationship between ultra-early blood markers and neurological deficits and post-stroke cognitive impairment.

Results: There were no significant differences in baseline data between the two groups. However, the proportion of hemorrhagic stroke patients was significantly higher in the PSCI group than in the non-PSCI group (39.7% vs 18.8%, P=0.026<0.05). NLR and NIHSS scores showed significant differences between the two groups. Multivariate analysis indicated that NIHSS (OR=1.297, 95% CI: 1.167–1.442, p<0.001) was independently associated with PSCI, while NLR (OR=1.107, 95% CI: 0.995–1.231, p=0.063) showed a borderline association with PSCI. MLR showed differences between the two groups in univariate analysis (P=0.018) but was excluded in multivariate analysis. ULR did not show significant differences.

Conclusion: NIHSS is a strong predictive factor (P < 0.05), with a cut of value of 12 calculated by the ROC curve. NLR is at the threshold for an independent risk factor. Subsequent ROC curves indicate that NLR has low diagnostic sensitivity but high specificity, making it more suitable for screening rather than diagnostic use. MLR and ULR did not demonstrate high predictive value; further studies should be conducted to expand the sample size, perform subgroup analyses, and increase follow-up.

Keywords: post-stroke cognitive impairment, NIHSS, NLR, MLR, ULR

Background

The 2020 China Stroke Report shows that the prevalence of stroke in China is 1,114.8 per 100,000 people, the annual incidence rate is 246.8 per 100,000 people, and the mortality rate is 149.49 per 100,000 people. China has become the country with the highest lifetime risk of stroke and the heaviest disease burden globally.[1] Post-stroke cognitive impairment (PSCI) refers to a clinical syndrome characterized by cognitive impairment that occurs after a stroke event and persists for up to six months. According to literature reports, approximately one-third of stroke patients experience.[2] The diagnosis of PSCI is typically based on clinical assessment, neuropsychological assessment, and neuroimaging. The Montreal Cognitive

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Assessment (MoCA) and the Mini-Mental State Examination (MMSE) are the most widely used cognitive tests in PSCI research.[3] However, both are subject to copyright restrictions, which pose challenges for research. Meanwhile, the new cognitive test Mini-Cog, which is simple to administer and time-efficient, can aid in detecting the early stages of cognitive impairment. In a post-hoc analysis of a population-based study of older adults in the United States, the Mini-Cog scores classified as "possibly impaired" or "possibly normal" using the algorithm were comparable to those of the MMSE with a cutoff point of 25 in terms of sensitivity (76% vs 79%) and specificity (89% vs 88%) for dementia.-Cog, which was scored as "possibly impaired" or "possibly normal" by the algorithm, showed similar sensitivity (76% vs 79%) and specificity (89% vs 88%) for dementia compared to the MMSE with a cutoff point of 25. These results were comparable to those obtained using traditional neuropsychological assessments (sensitivity 75%, specificity 90%).[4] A meta-analysis indicated that for cognitive impairment (including dementia and mild cognitive impairment) in primary care settings, Mini-Cog showed 73% sensitivity and 84% specificity. In secondary care settings, Mini-Cog showed 73% sensitivity and 76% specificity[5] All performed well.

In addition to clinical examinations, neuropsychological assessments, and imaging studies, various blood biomarkers have become a focal point of research. By measuring indicators associated with brain injury in the early stages of stroke, it is possible to predict the occurrence of PSCI, which aids in the early identification of PSCI and facilitates further rehabilitation interventions. Inflammatory factors are closely associated with cognitive impairment. Clinically, lymphocyte-related inflammatory markers, such as the neutrophil-lymphocyte ratio (NLR), have been shown to have predictive value in a prospective cohort study of cognitive impairment following ischemic stroke. Peripheral NLR levels are significantly elevated in PSCI patients.[3]

Another inflammatory marker closely related to lymphocytes—the monocyte-to-lymphocyte ratio (MLR)—is more commonly used in the prediction of cardiovascular disease.[6] The serum uric acid to lymphocyte ratio (ULR) has been validated as a new lymphocyte-related inflammatory marker with superior predictive value for hemorrhagic stroke compared to uric acid or lymphocyte levels alone in a large prospective cohort study conducted in China.[7] This study was conducted to further clarify whether differences in inflammatory markers, especially lymphocyte-related inflammatory markers, in the ultra-early stage of stroke (within 24 hours of onset), including hemorrhagic stroke, are associated with post-stroke cognitive impairment in the early recovery stage (within 30 days of stroke onset).[8]

Research Methods

This study is a retrospective study targeting patients who underwent rehabilitation therapy at the Rehabilitation Department of Hebei University Affiliated Hospital between December 2024 and June 2025, specifically those within 30 days post-stroke, ie, in the early recovery phase of stroke. The study population was divided into an observation group (PSCI group) and a control group (non-PSCI group) based on the occurrence of cognitive impairment. A retrospective analysis was conducted of blood markers and neurological deficit scores within 24 hours of stroke onset, to investigate the relationship between ultra-early blood markers and neurological deficits and the occurrence of cognitive impairment after stroke.

Refer to previous literature,[3] the inclusion criteria are as follows: (1) age ≥ 18 years; (2) confirmed by cranial computed tomography (CT) or magnetic resonance imaging (MRI);[2] (3) Patients who have experienced a stroke within the past 30 days, are in the early stages of recovery, have stable conditions, are conscious, can speak fluently, and are able to cooperate with rehabilitation assessments and treatments; (4) Patients who visited the Department of Neurology, Department of Neurosurgery, Department of Critical Care Medicine, or other relevant departments at Hebei University Affiliated Hospital within 24 hours of experiencing a stroke, with complete clinical data and traceable medical records from within 24 hours of the onset of symptoms.

Refer to previous literature,[3] the exclusion criteria are as follows: (1) Patients who had been diagnosed with cognitive impairment disorders prior to the stroke, including Alzheimer's disease, frontotemporal dementia, Parkinson's disease dementia, Lewy body dementia, mixed dementia, and other types of cognitive impairment or dementia caused by various reasons; (2) Patients unable to cooperate with cognitive function assessments, including those with severe aphasia, hearing impairments, dysarthria, impaired consciousness, visual impairments, or those unable to write normally due to limb dysfunction caused by stroke; (3) Patients with unstable conditions who are unable to cooperate with assessments and rehabilitation therapy, including but not limited to those with severe illnesses such as cardiovascular diseases (eg, severe heart failure, severe arrhythmias), renal diseases (eg, renal failure), pulmonary diseases (eg, severe pneumonia,

respiratory failure), etc.; (4) Patients who had conditions prior to the stroke that could trigger inflammatory and immune responses (eg, acute infections, tumors, blood disorders, autoimmune diseases, recent major surgeries, or trauma); (5) Patients who had been taking medications that could interfere with the inflammatory and immune systems prior to the stroke (eg, antibiotics, corticosteroids, immunosuppressants, targeted therapies, etc).; (6) Patients with a history of recurrent strokes.

Based on the Mini-Cog score, patients were divided into a post-stroke cognitive impairment (PSCI) group and a group without post-stroke cognitive impairment. This study complies with the World Medical Association's Declaration of Helsinki and has been approved by the Ethics Committee of Hebei University Affiliated Hospital (the Ethics Committee of Affiliated Hospital of Hebei University:HDFYLL - KY - 2024 - 120).

Data Collection

Baseline Characteristics

Age, sex, body mass index (BMI), educational attainment (elementary, middle school, university),smoking and alcohol use,were collected.

Clinical Variables

This included past medical history (including coronary heart disease, diabetes, and hypertension, the definition criteria are a previous clear diagnosis of a related disease and/or long-term use of therapeutic drugs prior to onset, stroke type (hemorrhagic or ischemic).

Observation Indicators

Extract and analyze medical records from the acute phase within 24 hours of onset, extracting data on neutrophils, lymphocytes, monocytes, and uric acid, and calculate NLR, MLR, and ULR. Uric acid levels were analyzed using the Fusion biochemical analyzer from Johnson & Johnson, and blood cell counts were measured using the XN-L™ Series blood analyzer from Sysmex Corporation. Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS) to evaluate neurological deficit scores.[9]

Cognitive Function Assessment and Grouping

The official Chinese version of the Mini-Cog official website was used to assess the cognitive function of the patients, which was truncated into a control group (no cognitive impairment group) and an observation group (cognitive impairment group) with 4 points.

The sample size calculation formula is: $n = \frac{Z^2 \times p \times (1-p)}{d^2}$ where the expected prevalence rate (P) is 1/3 (33%) as described in the background section above, the confidence interval is 95%, and the allowable error is 0.1. The minimum sample size calculated is 85 cases, which will be assessed by therapists who are trained and proficient in using the Mini-Cog. A total of 127 cases were ultimately included in this study, 69 in the control group and 58 in the observation group.

Statistical Analysis

Descriptive statistical analysis was conducted. Data were categorized as either count data or measurement data. Measurement variables included age, BMI, NIHSS score, MLR, NLR, and ULR. Count variables included sex, education level, smoking status, alcohol use, history of chronic conditions (coronary heart disease, diabetes, hypertension), stroke type.(The normality test for the measurement data revealed a skewed distribution except for age and BMI, where the mean ± standard deviation was used to describe the centralized and discrete trends, and the *t*-test was used to compare the differences between the groups, while the rest were statistically described using quartiles, and the Mann–Whitney test in non-parametric tests was used to compare the differences between the groups. Measurements were described using percentages and the chi-square test was used to compare differences between groups. Box scatter plots of data distribution for MLR, NLR, ULR, and NIHSS scores were also plotted for the two groups of data. Statistical analyses were performed using SPSS software, version 25.0. Graphs were created using GraphPad Prism, version 10.0.

All variables were included in univariate logistic regression analysis to investigate their association with PSCI. All variables with P values < 0.1 were included in the subsequent multivariate logistic regression model. Based on the logistic regression results, the receiver operating characteristic (ROC) curve was used to assess the potential predictive performance for PSCI. All statistical analyses were defined as statistically significant with a two-sided P value < 0.05. Regression analysis was performed using SPSS 25.0, and ROC curves were plotted using MedCalc 23.0.9, which automatically calculated the cutoff value, sensitivity, and specificity.

Results

Demographic Data

A total of 127 post-stroke patients were included in this study, including 69 in the group with normal cognitive function (control group) and 58 in the group with post-stroke cognitive impairment (observation group). In terms of age (control group: 60.64 ± 11.26 years, observation group: 57.03 ± 13.61 years; p = 0.100), body mass index (BMI, control group: 25.99 ± 3.77, observation group: 27.14 ± 3.58; p = 0.845), gender distribution (percentage of males: 63.8% in the control group, 69.0% in the observation group; p = 0.538), education level (p = 0.538), and the number of post-stroke cognitively impaired patients in the observation group. 0.538), educational level (p = 0.551), smoking history (p = 0.229), and alcohol consumption history (p = 0.553) did not show statistical differences, and the baseline demographic characteristics of the two groups were balanced. The details are shown in Table 1.

Clinical Data

In this study, the clinical data of the two groups were compared and analyzed. The results showed no significant differences in the prevalence of a history of coronary heart disease (21.7% in the control group versus 12.1% in the observation group; p = 0.151), diabetes mellitus (33.3% versus 29.3%, respectively; p = 0.627), and hypertension (78.3% versus 72.4%, respectively; p = 0.445), and there was a significant difference in the distribution of the nature of the strokes (p = 0.026). p = 0.026). The proportion of hemorrhagic strokes was significantly higher in the observation group than in the control group (39.7% versus 18.8%, respectively), whereas infarctive strokes predominated in the control group (81.2% versus 60.3%, respectively). The details are shown in Table 2.

Table 1 Demographic Data of Patients with Stroke

Data	Control Group (N=69)	Observation Group (N=58)	*p*-value
Age (mean ± standard deviation)	60.64±11.255	57.03±13.606	0.100
BMI (mean ± standard deviation)	25.99±3.773	27.14±3.575	0.845
Sex (%)			0.538
Male	44(63.8)	40(69.0)	
Female	25(36.2)	18(31.0)	
Education level(%)			0.551
Elementary school	14(20.3)	15(25.9)	
Middle school	48(69.6)	35(60.3)	
University	7(10.1)	8(13.8)	
Smoking (%)			0.229
No	43(62.3)	30(51.7)	
Yes	26(37.7)	28(48.3)	
Drinking (%)			0.553
No	44(63.8)	34(58.6)	
Yes	25(36.2)	24(41.4)	

Notes: Observation group: cognitive impairment group, Control group: normal cognitive function group, $p < 0.05$ indicates significant difference.

Table 2 Clinical Data of Patients with Stroke

Data	Control Group (N=69)	Observation Group (N=58)	*p*-value
History of coronary heart disease (%)			0.151
No	54(78.3)	51(87.9)	
Yes	15(21.7)	7(12.1)	
History of diabetes (%)			0.627
No	46(66.7)	41(70.7)	
Yes	23(33.3)	17(29.3)	
History of hypertension (%)			0.445
No	15(21.7)	16(27.6)	
Yes	54(78.3)	40(72.4)	
Nature of stroke (%)			0.026
Infarction	56(81.2)	35(60.3)	
Bleeding	13(18.8)	23(39.7)	

Notes: Observation group: cognitive impairment group, Control group: normal cognitive function group, $p < 0.05$ indicates significant difference.

Observations

Degree of neurological damage: the National Institutes of Health Stroke Scale (NIHSS) scores were significantly higher in the observation group than in the control group (11.95 ± 5.56 vs 6.41 ± 3.72; p<0.001), and the median comparison [11.50 (interquartile range 8.00–16.00) vs 6.00 (interquartile range 3.00–10.00)] Inflammatory markers: The NLR values in the PSCI patient group (6.019 ± 5.040; median 3.939, IQR 2.352–8.295) were significantly higher than those in the non-PSCI patient group (3.896 ± 3.111; median 3.016, IQR 2.194–4.492), with a statistically significant difference (P = 0.012). Monocyte-lymphocyte ratio (MLR): The MLR value in the observation group (0.439 ± 0.312; median 0.348, IQR 0.234–0.500) was higher than that in the control group (0.326 ± 0.144; median 0.277, IQR 0.225–0.399), with the difference being at the threshold and not reaching statistical significance (P = 0.066). Uric acid-lymphocyte ratio (ULR): There was no significant statistical difference in ULR values between the two groups (P = 0.97). The ULR in the observation group was 218.59 ± 156.25 (median 165.78, IQR 120.54–301.65), and the control group had a ULR of 202.31 ± 105.68 (median 191.06, IQR 118.75–253.54). Detailed data are shown in Table 3, and data distribution is illustrated in Figures 1–4.

Logistic Regression Analysis of the Relationship Between Various Variables and PSCI

Univariate logistic regression analysis showed that lesion location, NLR, MLR, NIHSS, and PSCI were significantly associated (all p < 0.05). After adjusting for variables with p < 0.1 in univariate logistic regression analysis, multivariate logistic regression analysis revealed that NIHSS (OR = 1.297, 95% CI: 1.167–1.442, p < 0.001) was independently associated with PSCI, and NLR (OR = 1.107, 95% CI: 0.995–1.231, p = 0.063) was marginally associated with PSCI. Detailed data are presented in Table 4.

Table 3 Observation Index Data

Data	Control Group (N=69)					Observation Group (N=58)					*p*-value
	(mean±SD)	Q1	Mdn	Q3	IQR	(mean±SD)	Q1	Mdn	Q3	IQR	
NHISS	6.41±3.723	3.00	6.00	10.00	7.00	11.95±5.564	8.00	11.50	16.00	8.00	0.000
NLR	3.896±3.111	2.194	3.016	4.492	2.298	6.019±5.040	2.352	3.939	8.295	5.943	0.012
ULR	202.30±95.68	118.75	191.06	253.54	124.340	218.59±156.25	120.54	165.78	301.65	182.792	0.971
MLR	0.326±0.144	0.225	0.277	0.399	0.174	0.439±0.312	0.234	0.348	0.5	0.266	0.066

Notes: Observation group: cognitive impairment group, Control group: normal cognitive function group, IQR = Q3 - Q1,$p < 0.05$ indicates significant difference.

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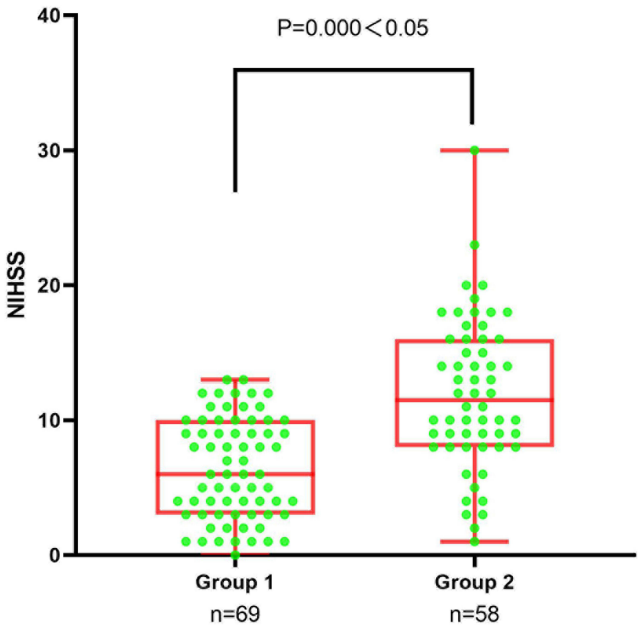

Figure 1 NIHSS score data distribution map. (Group 1 Control group: Normal cognitive function group, Group 2 Observation Group: Cognitive impairment group, $p < 0.05$ indicates significant differences).

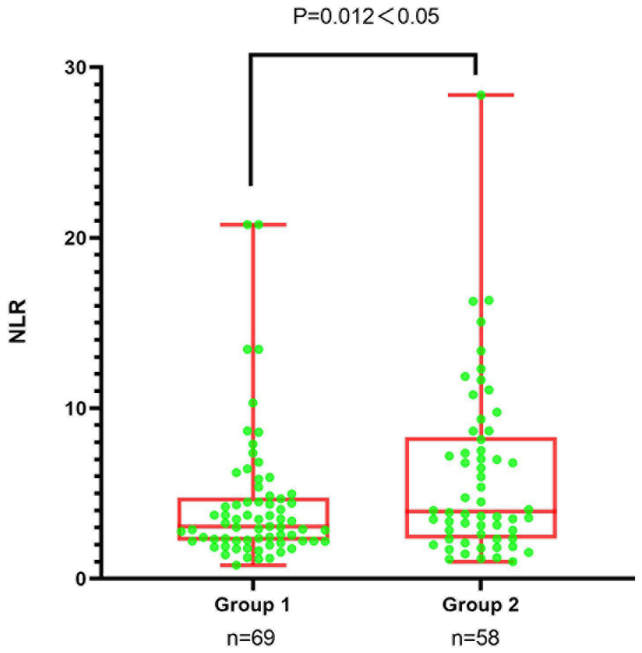

Figure 2 NLR data distribution map. (Group 1 Control group: Normal cognitive function group, Group 2 Observation Group: Cognitive impairment group, $p < 0.05$ indicates significant differences).

ROC Analysis of NIHSS and NLR for Predicting PSCI

ROC analysis was used to assess the diagnostic value of NHISS and NLR for PSCI. The area under the ROC curve (AUC) was 0.787 (95% CI: 0.706–0.855), significantly higher than the random prediction level (P < 0.0001). The optimal diagnostic cutoff point, determined based on the Youden index, was >12 points, with a sensitivity of 44.83% and

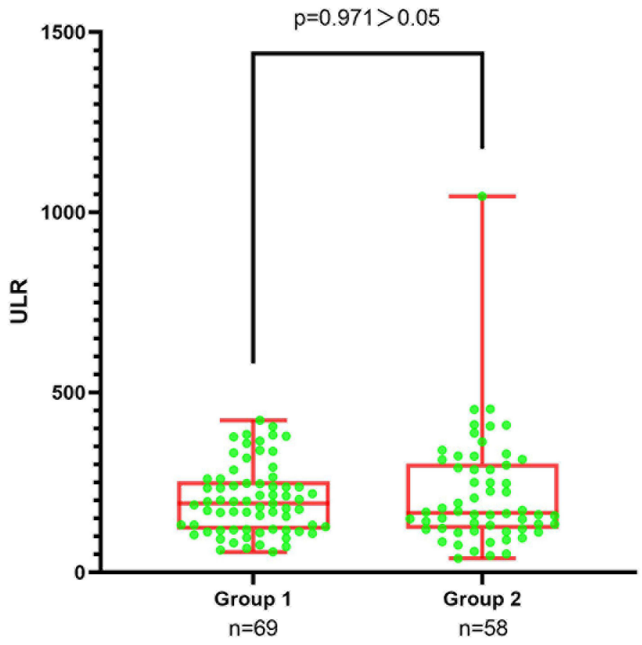

Figure 3 ULR data distribution map. (Group 1 Control group: Normal cognitive function group, Group 2 Observation Group: Cognitive impairment group, $p < 0.05$ indicates significant differences).

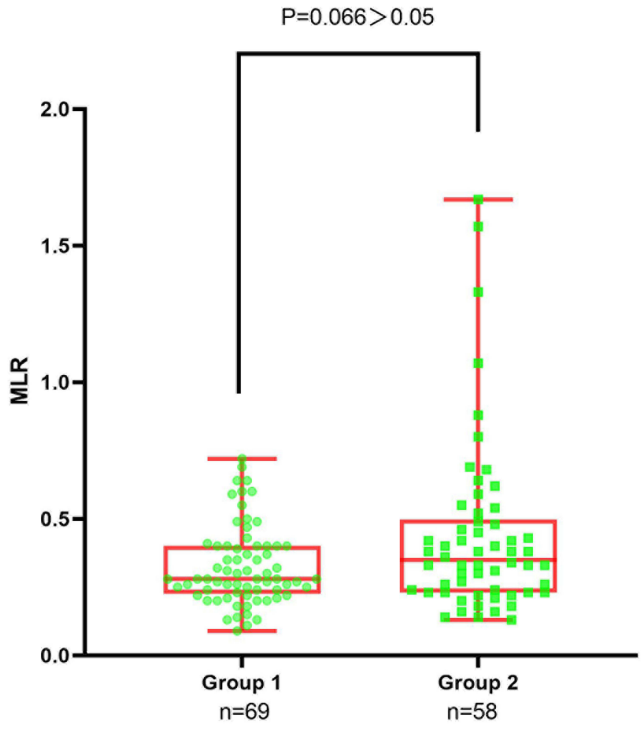

Figure 4 MLR data distribution map. (Group 1 Control group: Normal cognitive function group, Group 2 Observation Group: Cognitive impairment group, $p < 0.05$ indicates significant differences).

specificity of 97.10%. The area under the curve (AUC) for NLR was 0.630 (95% CI: 0.540–0.714), significantly higher than the random level (P = 0.0107). The optimal diagnostic cutoff value was >6.44, with a sensitivity of 39.66% and specificity of 88.41%. See Figures 5 and 6.

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Table 4 Univariate and Multivariate Logistic Regression Analysis

Data	Single Factor Analysis		Multiple-Factor Analysis	
	OR(95%CI)	p	OR(95% CI)	p
Baseline Data				
Age	1.004(0.976,1.033)	0.782		
BMI	1.035(0.942,1.137)	0.4788		
Sex	0.792(0.377,1.663)	0.538		
Education level				
Elementary school		0.505		
Middle school	0.750(0.209,2.691)	0.659		
University	0.547(0.174,1.718)	0.301		
Smoking	1.171(0.576,2.380)	0.663		
Drinking	0.805(0.393,1.649)	0.553		
Clinical Data				
Coronary heart disease	1.386(0.551,3.483)	0.488		
Diabetes	1.206(0.567,2.566)	0.627		
Hypertension	1.256(0.553,2.852)	0.586		
Nature of disease	0.353(0.159,0.787)	0.011**	0.796(0.305,2.076)	0.641
Observational Index				
NIHSS	1.304(1.177,1.445)	0.000**	1.297(1.167,1.442)	0.000
NLR	1.153(1.037,1.283)	0.009**	1.107(0.995,1.231)	0.063
ULR	1.001(0.998,1.004)	0.473		
MLR	9.832(1.470,65.750)	0.018**	1.353(0.071,25.875)	0.841

Note: **denotes $p < 0.05$.
Abbreviations: NIHSS, National Institutes of Health Stroke Scale; NLR, neutrophil-to-lymphocyte ratio; ULR, uric acid to lymphocyte ratio; MLR, mononuclear-to-lymphocyte ratio.

Discussion

In this study, through detailed baseline data collection and statistical analysis, it was found that there were no statistically significant differences between the experimental group and the control group in terms of key demographic characteristics

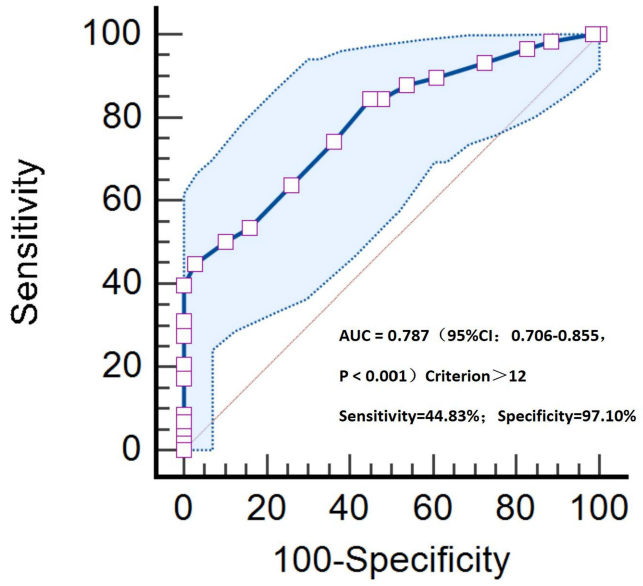

Figure 5 NHISS receiver operating characteristic curve graph.

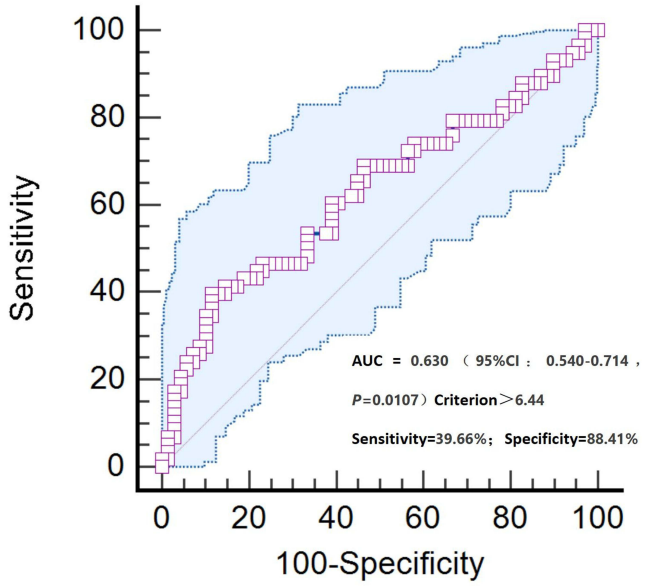

Figure 6 NLR receiver operating characteristic curve graph.

and social behavioral factors, including age distribution (mean age and age range), gender ratio (proportion of males and females), years of education and educational attainment, smoking history, and drinking history (all p-values were >0.05). This excellent baseline comparability provides a critical foundation for the reliability of the study conclusions.

In previous studies, most research has focused on ischemic stroke. However, this study included both ischemic and hemorrhagic stroke. Statistical results showed significant differences in stroke type between the two groups. Compared with the control group, the proportion of intracerebral hemorrhage was significantly higher in the observation group (39.7% in the observation group, control group 18.8%). Single-factor analysis also showed significant differences, but this factor was gradually eliminated in subsequent multi-factor regression analysis, indicating that stroke type is not an independent risk factor for PSCI. In China, 69.9–79.8% of new strokes are ischemic strokes.[8] Due to differences in etiology, research on complications associated with hemorrhagic stroke is less extensive than that on ischemic stroke. In a prospective cohort study examining the progression of cognitive dysfunction following intracerebral hemorrhage, which included imaging characteristics such as hematoma morphology and volume, white matter hyperintensities, and large artery stenosis, an independent negative correlation was found between cognitive recovery and hemorrhage in the dominant hemisphere. Compared to hemorrhage in the non-dominant hemisphere, hemorrhage in the dominant hemisphere was more likely to severely impair the strategic domain, thereby affecting cognitive function.[10] This study did not include imaging data. Future studies could incorporate patients' imaging data for subgroup analysis to more clearly elucidate the relationship between injury location, extent, and patients' cognitive decline and long-term recovery.

In this study, there was a significant difference between the two NLR groups (P=0.012<0.05), which is consistent with previous studies.[3] A prospective cohort study on peripheral immunity and cognitive impairment after acute mild ischemic stroke found that elevated NLR levels increase the risk of PSCI, with the most significant effect observed in individuals aged 50 to 65 years, and significantly improve the predictive efficacy of PSCI.[11] This study also confirmed this finding after including patients with hemorrhagic stroke. The NLR has emerged as a new indicator of inflammatory status, reflecting an imbalance between neutrophil-mediated systemic pro-inflammatory activity and impaired lymphocyte immune regulatory function. This dysregulation of the immune response may be associated with the pathological process of PSCI. Neutrophils can release peroxidase and form extracellular traps, thereby causing oxidative damage to brain tissue; while stress-induced reduction in lymphocyte numbers may weaken immune surveillance and neural repair functions.[12,13] Subsequent multivariate analysis revealed that NLR was at the threshold for an independent risk factor.

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The subsequent ROC curve indicated that NLR had low diagnostic sensitivity but high specificity, making it more suitable for screening applications than diagnostic use.

In addition to NLR, this study also included MLR as an observational indicator. MLR has previously been used in cardiovascular research and studies on post-stroke depression. A large cross-sectional study using the NHANES database to investigate the relationship between MLR and cardiovascular disease found that MLR was positively correlated with cardiovascular events. High MLR serves as a marker for increased risk of cardiovascular diseases, including congestive heart failure, coronary heart disease, and stroke, reflecting the body's state in chronic inflammation and immune responses.[6] A meta-analysis on the role of NLR, and MLR in depression in post-stroke depression research also suggested that MLR was significantly higher in patients with post-stroke depression than in non-depressed patients, which may be related to neuroinflammation.[14] Post-stroke inflammatory damage may affect the hippocampus and parahippocampal gyrus.[15] This further affects cognition. Therefore, this study included MLR for the first time. In the univariate analysis, the odds ratio was very high, and the confidence interval (1.47–65.75) was very wide, indicating that the estimate was not accurate enough and may have been limited by the sample size. In the future, the sample size can be further expanded, or subgroup analysis can be performed to further clarify the predictive value of MLR for PSCI.

ULR is a novel serum biomarker that combines uric acid levels and lymphocyte counts. Previous studies have reported that individuals with higher serum uric acid concentrations exhibit milder cognitive decline, and that uric acid levels are negatively correlated with the severity of dementia.[16] Lymphocytes play a regulatory or protective role in adaptive immunity, and lymphocytopenia indicates impaired immune function. Both are related to the body's inflammatory state and immune response. Therefore, ULR can theoretically provide valuable insights into patients' inflammatory states and related health risks.[17] A prospective cohort study conducted in China showed that ULR, as a novel inflammatory biomarker, is significantly associated with the risk of hemorrhagic stroke in Chinese adults.[7] This study is the first to use ULR in a predictive study of PSCI. The results showed no statistical difference between the two groups, but Figure 3 shows that ULR is more dispersed in the PSCI group. Further research is needed to determine clinically significant thresholds and to assess changes in ULR levels over time through multicenter, longitudinal studies.

In this study, the NIHSS demonstrated strong predictive value. The NIHSS is a 15-item functional disability scale used to assess stroke severity. It was originally developed in 1989 and is a reliable, valid, and sensitive tool for measuring stroke severity, suitable for use in both clinical practice and research. It can be applied to patients with language and cognitive impairments and has been widely adopted worldwide.[18] NIHSS can predict ischemic volume after ischemic stroke.[19] It is also linked to cognitive decline.[20] In a retrospective study of patients with ischemic stroke, a NIHSS score ≥5 was found to be an independent risk factor for cognitive impairment.[21] This study included both ischemic and hemorrhagic strokes. The NIHSS was a strong predictor ($P < 0.05$), with a cutoff value of 12 calculated using the ROC curve. This may be related to the inclusion of patients with hemorrhagic strokes, who tend to have more severe acute-phase conditions and higher NIHSS scores. Future studies may further analyze the cutoff values for different patient subgroups.

Conclusion

Unlike most previous studies, this study included stroke patients with ischemic stroke and hemorrhagic stroke. In addition to NLR, MLR and ULR were also introduced for the first time to evaluate PSCI. Patients were divided into PSCI and non-PSCI groups based on mini-cog scores. A comparison of baseline data and clinical data between the two groups revealed no significant differences in baseline data. In clinical data, the proportion of hemorrhagic patients in the PSCI group was significantly higher than that in the non-PSCI group (39.7% vs 18.8%, $P=0.026<0.05$), indicating significant differences between the two groups. However, this difference was excluded in subsequent multivariate analysis, suggesting that stroke type is an independent risk factor for non-PSCI. In the observational indicators section, the NIHSS score showed significant differences between the two groups, serving as an independent risk factor for PSCI ($P = 0.000 < 0.05$), with a ROC curve cutoff value of 12 points, demonstrating extremely high specificity (97.1%). However, the NLR had limited predictive efficacy for post-stroke cognitive impairment. MLR showed differences between the two groups in univariate analysis ($P=0.018$) but was excluded in multivariate analysis. Combined with the wide confidence interval, further research is needed. ULR did not show obvious differences, but the data distribution plot showed high

variability and the presence of extreme data. Future studies could expand the sample size and conduct subgroup analyses to determine its predictive value.

This study has certain limitations: it is a retrospective study with a limited sample size, some variables have high data variability, and no subgroup analysis was conducted. Future studies could expand the sample size, conduct prospective clinical trials, extend the follow-up period, incorporate imaging results to analyze the impact of different lesion locations on PSCI, and perform subgroup analyses. Additionally, incorporating the platelet-to-lymphocyte ratio (PLR) and the Systemic Immune-Inflammation Index (SII) could further clarify the association between inflammatory markers and PSCI, providing guidance for the early identification and treatment of PSCI in clinical practice.

Abbreviations

PSCI, post-stroke cognitive impairment; MMSE, mini-mental state examination; MoCA, Montreal cognitive assessment; NLR, Neutrophil-lymphocyte Ratio; MLR, Monocyteto-lymphocyte Ratio; ULR, Uric acid to Lymphocyte Ratio; NIHSS, National Institute of Health stroke scale.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author (Cai-Hong Cui) on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Affiliated Hospital of Hebei University (HDFYLL-KY-2024-120). A written informed consent was obtained from legal guardian of all participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors have contributed significantly to the manuscript and declare that the work is original and has not been submitted or published elsewhere. None of the authors have any conflict of interest to declare for this work.

References

1. Wang Y-J, Li Z-X, Gu H-Q, et al. China stroke statistics 2019: a 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 prevention and institute for global neuroscience and stroke collaborations. *Stroke Vasc Neurol*. 2020;5(3):211–239. doi:10.1136/svn-2020-000457
2. Wang K, Dong Q, Yu J, et al. Expert consensus on the management of post-stroke cognitive impairment 2021. *Chin J Stroke*. 2021;16(4):376–389. doi:10.3969/j.issn.1673-5765.2021.04.011
3. Huang W, Liao L, Liu Q, et al. Predictive value of circulating inflammatory biomarkers for early-onset post-stroke cognitive impairment: a prospective cohort study. *Front Neurol*. 2025;16. doi:10.3389/fneur.2025.1565613
4. Borson S, Scanlan JM, Chen P, et al. The Mini-Cog as a screen for dementia: validation in a population-based sample. *J Am Geriatrics Soc*. 2003; 10:1451–1454.
5. Abayomi SN, Sritharan P, Yan E, Saripella A, Alhamdah Y, Englesakis M. Maria Carmela Tartaglia,et al.2024."The diagnostic accuracy of the Mini-Cog screening tool for the detection of cognitive impairment—A systematic review and meta-analysis". *PLoS One*. 2024;19(3):e0298686. doi:10.1371/journal.pone.0298686

6. Li X, Zhang L, Du Y, et al. Association between monocyte-to-lymphocyte ratio and cardiovascular diseases: insights from NHANES data. *Diabetol Metab Syndr*. 2025;17(1). doi:10.1186/s13098-025-01640-9
7. Tian X, Wang P, Chen S, Zhang Y, Zhang X, Xu Q. Yanxia L, et al. Association of serum uric acid to lymphocyte ratio, a novel inflammatory biomarker, with risk of stroke: a prospective cohort study. *CNS Neurosci Ther*. 2023;29(4):1168–1177. doi:10.1111/cns.14094
8. Chinese Society of Neurology,Neurorehabilitation Society. Chinese society of neurology,cerebrovascular disease society, chinese society of neurology. Guidelines for early rehabilitation of stroke in China [J]. *Chin J Neurol*. 2017;50(6):405–412. doi:10.3760/cma.j.issn.1006-7876.2017.06.002
9. Baik M, Lee H, Hyung lee IH, et al.Early depression screening and short-term functional outcome in hospitalized patients for acute ischemic stroke. *Front Neurol*. 2022;13. doi:10.3389/fneur.2022.950045
10. Gong L, Gu Y, Qiuyue Q, et al. Prognostic factors for cognitive recovery beyond early poststroke cognitive impairment (PSCI): a prospective cohort study of spontaneous intracerebral hemorrhage. *Front Neurol*. 2020;11. doi:10.3389/fneur.2020.00278
11. Zhao P, Zhang G, Wang Y, et al. Peripheral immunity is associated with cognitive impairment after acute minor ischemic stroke and transient ischemic attack. *Sci Rep*. 2024;14(1). doi:10.1038/s41598-024-67172-w
12. Chen Q, Wu M, Tang Q, Yan P, Zhu L. Age-related alterations in immune function and inflammation: focus on ischemic stroke. *Aging Dis*. 2024;15(3):1046–1074. PMID: 37728582; PMCID: PMC11081165. doi:10.14336/AD.2023.0721-1
13. Halazun HJ, Mergeche JL, Mallon KA, Connolly ES, Heyer EJ. Neutrophil-lymphocyte ratio as a predictor of cognitive dysfunction in carotid endarterectomy patients. *J Vasc Surg*. 2014;59(3):768–773. PMID: 24571940; PMCID: PMC3959110. doi:10.1016/j.jvs.2013.08.095
14. Cheng Y, Wang Y, Wang X, Jiang Z, Zhu L, Fang S. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio in depression: an updated systematic review and meta-analysis. *Front Psychiatry*. 2022;13. doi:10.3389/fpsyt.2022.893097
15. Monje ML, Toda H, Palmer TD. Inflammatory blockade restores adult hippocampal neurogenesis. *Science*. 2003;302(5651):1760–1765. PMID: 14615545. doi:10.1126/science.1088417
16. Pu Z. Associations of serum oxidative stress markers with cognitive impairment and behavioral and psychological symptoms in Alzheimer's disease. *Wenzhou Med Univer*. 2017.
17. Zhao J, Liu K, Dai Q, et al.Association of serum uric acid to lymphocyte ratio with clinical outcomes in cerebral venous sinus thrombosis. *J Inflamm Res*. 2024;17:9379–9389. doi:10.2147/JIR.S490407
18. Kwah LK, Diong J. National institutes of health stroke scale (NIHSS). *J Physiother*. 2014;1:61.
19. Gottesman RF, Kleinman JT, Davis C, et al. The NIHSS-Plus: improving cognitive assessment with the NIHSS. *Behav Neurol*. 2010;22(1–2):11–-15. doi:10.1155/2010/123903
20. Ishiwata A, Nogami A, Nishimura T, Kanamaru T, Suzuki K, Suda S. Cognitive assessment in patients with acute stroke: exploring early intervention for dementia. *Clinl Neurol Neurosurg*. 2025;249:108748. doi:10.1016/j.clineuro.2025.108748
21. Li Y, Geng W, Zhang X, Mi B. Risk factors and characteristics analysis of cognitive impairment in patients with cerebral infarction during recovery period. International. *Int J Neurosci*. 2025;135(8):863–868. doi:10.1080/00207454.2024.2336189