Clinical application of the HALP score for predicting early neurological deterioration in older patients with acute cerebral infarction

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Abstract. The present study aimed to examine the relationship between the composite biomarker hemoglobin, albumin, lymphocyte and platelet (HALP) score and early neurological deterioration (END) to identify patients predisposed to poor neurological outcomes. A total of 148 older patients with acute ischemic stroke (AIS) who developed END and 283 without END were included. END was defined as an increase of at least two points in the National Institutes of Health Stroke Scale (NIHSS) score within 7 days. Multivariate logistic regression was performed to assess predictors of the HALP score. Receiver Operating Characteristic (ROC) curves and calibration plots were employed to evaluate model performance. The results demonstrated that END occurred in 34.34% of participants. Univariate analysis demonstrated significant differences between the two groups in age, baseline NIHSS score, white blood cell count, lymphocyte count, HALP score, levels of hemoglobin, triglycerides, C-reactive protein, homocysteine, lipoprotein phospholipase A2, and the incidence of infections and mortality (all P<0.05). In multivariate logistic regression, both the HALP score [odds ratio (OR): 0.965; 95% confidence interval (CI): 0.943-0.988; P=0.003) and baseline NIHSS score (OR: 1.169; 95% CI: 1.119-1.220; P<0.001) emerged as independent predictors of END. The areas under the ROC curve for a HALP score <27.69 and NIHSS score >5.5 were 0.727 (95% CI: 0.676-0.778) and 0.868 (95% CI: 0.834-0.903), respectively, with a combined AUC of 0.883 (95% CI: 0.850-0.916). The HALP score demonstrated a significant negative correlation with baseline NIHSS (r=-0.411, P<0.001) and NIHSS at day 7 (r=-0.348, P<0.001). Patients with lower HALP scores exhibited higher rates of END and poorer 90-day functional outcomes. In conclusion, reduced HALP scores were independently associated with END in older patients with AIS, suggesting that HALP may serve as an effective biomarker for the early identification of individuals at elevated risk of unfavorable neurological progression.

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Introduction

Acute ischemic stroke (AIS) remains a leading cause of morbidity, disability and mortality worldwide (1). Despite advances in therapeutic interventions, ~10-40% of patients with AIS experience early neurological deterioration (END) (2). END frequently occurs in older individuals with AIS, resulting in severe neurological impairment and long-term disability, thereby posing a major risk to health and survival. Considering the rapid disease progression observed in elderly patients with AIS (3), the identification of clinically accessible indicators, such as hematological parameters or biomarkers, capable of predicting END is essential to optimize therapeutic strategies and improve prognosis in this population.

Multiple factors, including baseline stroke severity, diabetes, hypertension, atrial fibrillation and stroke subtype, have been recognized as predictors of END (4). Additionally, a meta-analysis has demonstrated that elevated levels of glucose, total cholesterol, triglycerides and white blood cells (WBC) are associated with an increased likelihood of END (5). Nevertheless, the underlying etiology and mechanisms of END in AIS remain insufficiently elucidated. END has been linked to impaired collateral circulation, thrombus extension, cerebral edema and hemorrhagic transformation (6-8). Furthermore, immune-mediated inflammation exerts a key influence across these pathophysiological processes.

Inflammatory activation, coagulation disorders and nutritional deficiency constitute essential pathophysiological mechanisms in AIS and serve as indicators of unfavorable outcomes (9-11). Lymphocytes are integral to post-AIS inflammation and have been identified as predictors of

aggravated ischemic brain injury and neurological deterioration (12). Platelet hyperreactivity heightens the likelihood of thromboembolism and atherosclerotic plaque formation, promoting pathological thrombosis. Once activated, platelets participate in thrombo-inflammatory cascades and tissue injury, enhancing inflammatory responses (13). Anemia and hypoalbuminemia, reflecting malnutrition, have been recognized as risk factors for END (14). Considering the variability in stroke progression, reliance on a single biomarker may be insufficient for accurate END prediction. Hence, integrating multiple biomarkers can enhance predictive precision. The hemoglobin, albumin, lymphocyte and platelet (HALP) score, a composite biomarker that has recently gained attention, provides an integrated measure of systemic inflammatory and nutritional states (15). This index combines indicators of inflammation (lymphocyte and platelet counts) with markers of nutritional status (hemoglobin and albumin) and has demonstrated prognostic significance in several malignancies (16-18). Nonetheless, the association between HALP scores and END in AIS remains uncertain. The present study was designed to determine the predictive significance of the HALP score for END in elderly individuals with AIS.

Materials and methods

Study population. The present retrospective study enrolled elderly patients with AIS admitted to Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School, between January 2018 and December 2021. The inclusion criteria were as follows: (i) age ≥60 years; (ii) diagnosis consistent with the Guidelines for the Diagnosis and Treatment of AIS (19); (iii) availability of complete clinical records, including National Institutes of Health Stroke Scale (NIHSS) scores at admission and discharge as well as modified Rankin Scale (mRS) scores; and (iv) results of routine hematologic and albumin assessments at admission. Patients were excluded if they had: (i) active or chronic inflammatory disorders at admission; (ii) severe hepatic, renal, cardiac, pulmonary, or other vital organ failure; (iii) malignancy or any surgical procedure within the preceding three months; (iv) autoimmune or hematologic neoplastic diseases, or a history of immunosuppressant use; (v) received intravenous thrombolysis or endovascular intervention; or (vi) incomplete clinical information. The study utilized anonymized retrospective data and received approval from the Ethics Committee of Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School (approval 2022-308-01; Nanjing, China). Informed consent was waived by the aforementioned committee.

Data collection. Demographic characteristics (including sex and age), vascular risk factors (hypertension, diabetes, coronary heart disease, prior stroke, atrial fibrillation, smoking and alcohol use), pre-stroke medications (statins, antiplatelet agents and anticoagulants), baseline blood pressure and glucose, as well as baseline laboratory parameters [routine blood counts, albumin, creatinine, lipid profile, homocysteine (Hcy) and lipoprotein phospholipase A2 (Lp-PLA2)] were systematically recorded. Stroke etiology, lesion distribution (anterior or posterior circulation), NIHSS scores at admission and on day 7, and mRS score at 90 days were also documented. All laboratory measurements were performed on fasting venous blood samples obtained on the morning of the second day after admission. Data on lymphocyte count, hemoglobin, platelet count and albumin were used to calculate the HALP score according to the formula: Hemoglobin (g/l) x albumin (g/l) x lymphocyte count (10^9/l)/platelet count (10^9/l). Additional clinical variables, including onset-to-blood collection interval, hospitalization duration, in-hospital infections and fatal outcomes, were also recorded.

Clinical assessment. The etiology of AIS was determined following the Trial of ORG 10172 in Acute Stroke Treatment classification, including large artery atherosclerotic stroke, cardioembolic stroke, small vessel occlusive stroke, ischemic stroke of other determined etiology and ischemic stroke of undetermined etiology. Stroke severity in elderly patients was evaluated using the NIHSS, with scores of ≤8, 9-15, and ≥16 representing mild, moderate and severe stroke, respectively. END was identified as an increase of at least 2 points in the NIHSS score within 7 days after admission. Based on the occurrence of END, participants were categorized into END and non-END groups.

Statistical analysis. Statistical analysis was conducted using SPSS 22.0 (IBM Corp.). Categorical variables were summarized as frequencies and percentages. Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed data were presented as the mean ± standard deviation ($\bar{x} \pm SD$) and analyzed using the independent-samples t-test for two groups, one-way analysis of variance (ANOVA) for multiple groups, and the Student-Newman-Keuls (SNK-q) test for post hoc pairwise comparisons. Data with non-normal distribution were expressed as medians with interquartile ranges and assessed using the Mann-Whitney U test for two groups or the Kruskal-Wallis rank-sum test for multiple groups. Clinical conversion at discharge was designated as the dependent variable, and variables with $P<0.05$ in the univariate analysis were entered into a multivariate logistic regression model. Receiver Operating Characteristic (ROC) analysis was applied to determine the optimal cutoff value, sensitivity and specificity for predicting END. Participants were stratified into tertiles according to HALP scores: Q1 (≤28.11), Q2 (28.11<Q2<44.00) and Q3 (≥44.00). Differences in END incidence among groups were examined using the chi-square test. A heat map illustrated the distribution of cases with varying mRS scores, while Pearson correlation analysis evaluated the relationship between HALP and NIHSS scores. Statistical significance was defined as $P<0.05$.

Results

Baseline characteristics. The flow diagram of patient selection and study cohort formation is presented in Fig. 1. During the study period, 563 elderly patients with AIS were initially included. After further excluding 48 patients who received endovascular therapy, 56 who underwent intravenous thrombolysis, 15 with severe comorbidities and 13 with incomplete clinical data, 431 patients were ultimately included in the analysis. Among them, 254 (58.93%) were men, with a median age of 72 years (62-82 years) and a median baseline NIHSS score of 5 (2-14 points). The non-END group consisted of 283 patients (65.66%),

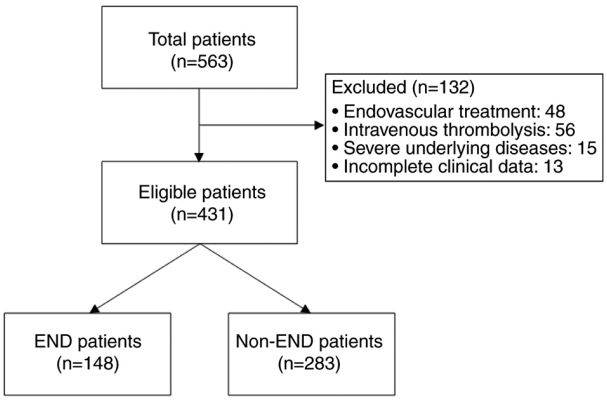

Figure 1. Patient flowchart. END, early neurological deterioration.

and the END group comprised 148 (34.34%). Compared with the non-END group, patients in the END group were older and had higher baseline NIHSS scores. Laboratory analyses indicated significantly elevated leukocyte count, C-reactive protein (CRP), Hcy and Lp-PLA2 levels in the END group. In addition, this group exhibited higher incidences of infectious complications and mortality. In contrast, lymphocyte count, hemoglobin, triglyceride levels and HALP scores were significantly reduced in the END group (P<0.05, Table I).

Risk factors for END. Multivariate logistic regression was performed using END as the dependent variable and factors from Table I with P<0.05 as independent variables. The analysis identified a lower HALP score [odds ratio (OR): 0.965; 95% confidence interval (CI): 0.943-0.988; P=0.003), higher baseline NIHSS score (OR: 1.169; 95% CI: 1.119-1.220; P<0.001) and acute-phase infection (OR: 5.459; 95% CI: 2.096-14.219; P=0.001) as independent predictors of increased END risk (Table II).

Predictive value of HALP score for END. The predictive value of the HALP score, baseline NIHSS score and their combination for END was analyzed through ROC curve evaluation. The area under the curve (AUC) values for predicting END were 0.727 (95% CI: 0.676-0.778), 0.868 (95% CI: 0.834-0.903) and 0.883 (95% CI: 0.850-0.916), respectively. Sensitivity and specificity were 80.62 and 56.08%, 91.20 and 71.29%, and 82.43 and 84.10%, respectively (Table III). The optimal cut-off points were 27.69 for the HALP score and 5.5 for the baseline NIHSS score.

Correlation between HALP scores and NIHSS scores. Pearson correlation analysis determined the association between HALP and NIHSS scores at admission and discharge in older patients with AIS. A significant inverse relationship was observed between HALP and NIHSS scores at admission (r=-0.411; P<0.001) and discharge (r=-0.348; P<0.001), as shown in Fig. 2.

Association between HALP score and clinical status in older patients with AIS. A significant variation in the incidence of END was noted among tertiles of HALP scores (Q1: 59.15%, Q2: 28.47%, Q3: 15.86%; χ^2=158.87; P<0.001) (Fig. 3A). The heat map illustrating patient distribution across HALP tertiles revealed distinct patterns of clinical outcomes. As shown in Fig. 3B, among 431 older patients with AIS, 239 (55.45%) achieved 90-day mRS scores of 0-1. The highest proportion of favorable outcomes (90-day mRS 0-1) occurred in Q3 (104/239, 43.51%), whereas poor outcomes (90-day mRS 5-6) were most frequent in Q1 (39/60, 65.00%). The distribution differences across HALP tertiles were statistically significant (P<0.001).

Discussion

The present study applied the HALP score as an integrated biomarker to evaluate the risk of END in patients with AIS and to determine its association with neurological prognosis. A markedly lower HALP score at admission was linked to an increased likelihood of END among older individuals with AIS. To the best of the authors' knowledge, evidence on the connection between HALP scores and END in this population remains limited. The present results demonstrate the value of the HALP score in predicting post-treatment neurological status and contribute to a more refined understanding of factors influencing END risk factors.

The observed incidence of END (34.34%) exceeded that reported in a recent study (20), possibly due to the advanced age and higher comorbidity burden of the enrolled population. Age-related declines in physical resilience, increased bleeding tendency, and therapeutic challenges such as revascularization delay or thrombolysis failure may contribute to this difference. Furthermore, the adoption of a 7-day observation window for END identification, as opposed to the more conventional 24-72 h intervals (21), may also have influenced the observed incidence. This extended timeframe was selected because pathophysiological processes underlying END, including inflammatory cascades, cerebral edema and infections, often progress beyond 72 h (22), particularly in older patients with more protracted courses. The 7-day window captures these late, clinically relevant deteriorations and aligns with established protocols for vulnerable stroke populations. This longer observation likely contributed to the relatively high-END incidence observed in the cohort of the present study. Consequently, our predictors may encompass both early and subacute deteriorations, underscoring the need for future studies to incorporate time-trend analyses and validate the HALP score across different diagnostic intervals.

Consistent with previous evidence, END was closely related to unfavorable outcomes (23,24). Both univariate and multivariate analyses identified baseline NIHSS scores, infectious events and HALP scores as independent determinants of END in older patients with AIS. The baseline NIHSS score serves as an essential indicator of stroke severity, neurological decline and eventual prognosis. Refining stroke management protocols and shortening the time to reperfusion may protect viable neural tissue and decrease END occurrence (25). Older patients are particularly vulnerable to infections (26), which can trigger severe complications that jeopardize recovery and survival. Hence, prompt detection and prediction of infections, together with timely interventions, may effectively lower the risk of END. Further studies are needed to substantiate and expand upon the current observations.

Accurate prediction of END in clinical settings remains difficult, emphasizing the necessity for simpler and more

Table I. Characteristics of patients with acute ischemic stroke with or without END.

Variables	Total (n=431)	No-END group (n=283)	END group (n=148)	Statistic	P-value
Demographic data					
Age (year, M, IQR)	72.00 (65.00, 82.00)	71.00 (64.00, 81.00)	74.50 (67.50, 84.00)	2.566	0.010[a]
Male (n, %)	254 (58.93)	171 (60.42)	83 (56.08)	0.757	0.384
Onset to blood collection time (h)	40.00 (28.00, 59.00)	39.00 (26.00, 55.00)	45.00 (30.00, 60.50)	1.743	0.081
Stroke risk factors (n, %)					
Hypertension	286 (66.36)	187 (66.08)	99 (66.89)	0.029	0.865
Diabetes	121 (28.07)	77 (27.20)	44 (29.73)	0.306	0.580
CAD	67 (15.55)	47 (16.61)	20 (13.51)	0.709	0.400
Prior stroke	102 (23.67)	62 (21.91)	40 (27.03)	1.410	0.235
Atrial fibrillation	69 (16.01)	44 (15.55)	25 (16.89)	0.131	0.718
Smoking	112 (25.99)	77 (27.21)	35 (23.64)	0.640	0.424
Alcohol	77 (17.86)	50 (17.67)	27 (18.24)	0.022	0.882
Medical history, n (%)					
Antihypertensive	263 (61.02)	167 (59.01)	96 (64.86)	1.400	0.237
Antidiabetic	96 (22.27)	65 (22.97)	31 (20.95)	0.230	0.632
Statin	73 (16.94)	47 (16.61)	26 (17.57)	0.064	0.801
Antiplatelet	83 (19.26)	51 (18.02)	32 (21.62)	0.810	0.368
Anticoagulants	32 (7.42)	19 (6.71)	13 (8.78)	0.606	0.436
Baseline blood pressure (mmHg, $\bar{x}\pm S$)					
SBP	141.31±21.40	142.21±20.81	139.61±22.47	0.054	0.817
DBP	78.58±13.71	79.11±13.30	77.57±14.46	1.033	0.310
Laboratory tests on admission (IQR)					
WBC (10^9/l)	7.10 (5.70, 8.90)	6.70 (5.50, 8.35)	8.20 (6.80, 10.40)	5.901	<0.001[a]
Lymphocyte count (10^9/l)	1.50 (1.10, 2.00)	1.70 (1.30, 2.10)	1.20 (0.85, 1.55)	-7.528	<0.001[a]
Hemoglobin (g/l)	131.50 (118.00, 144.00)	135.00 (122.00, 147.00)	125.00 (114.00, 138.00)	-4.360	<0.001[a]
Platelet count (10^9/l)	196.00 (160.00, 237.00)	194.00 (159.50, 231.50)	200.50 (158.50, 244.50)	0.724	0.469
Albumin (g/l)	36.00 (33.00, 38.40)	36.00 (33.00, 39.00)	35.95 (33.00, 38.30)	-0.192	0.848
HALP score	36.40 (24.36, 49.76)	40.73 (29.83, 56.35)	25.95 (17.99, 39.26)	-7.750	<0.001[a]
CRP (mg/l)	4.30 (2.50, 8.20)	3.60 (2.40, 6.10)	6.80 (3.35, 15.80)	6.313	<0.001[a]
Creatinine (mmol/l)	67.00 (57.00, 79.00)	67.00 (58.00, 79.00)	66.50 (56.00, 80.50)	0.161	0.872
Triglycerides (mmol/l)	1.13 (0.83, 1.67)	1.17 (0.87, 1.76)	0.99 (0.75, 1.36)	-3.659	<0.001[a]
Total cholesterol (mmol/l)	4.04 (3.35, 4.83)	4.05 (3.45, 4.86)	3.91 (3.07, 4.77)	-1.608	0.108
LDL-C (mmol/l)	2.01 (1.31, 2.90)	2.08 (1.40, 2.85)	1.70 (1.17, 3.08)	-1.029	0.303
HDL-C (mmol/l)	1.19 (0.92, 1.66)	1.20 (0.94, 1.52)	1.19 (0.84, 1.93)	-0.043	0.966
Hcy (μmol/l)	5.55 (2.60, 11.10)	5.10 (2.50, 11.10)	7.45 (3.05, 11.00)	1.965	0.049[a]
Lp-PLA2	189.00 (124.00, 324.00)	176.00 (119.00, 322.00)	214.50 (141.50, 360.50)	2.022	0.043[a]
Fasting glucose (mmol/l)	5.11 (4.56, 6.40)	5.04 (4.54, 6.40)	5.27 (4.72, 6.47)	1.886	0.059
Glycohemoglobin (%)	5.90 (5.50, 6.70)	5.90 (5.50, 6.90)	5.80 (5.50, 6.50)	-1.150	0.250
Stroke subtype (n, %)				1.270	0.866
LAA	168 (38.98)	114 (40.28)	54 (36.49)		
SAO	143 (33.18)	91 (32.16)	52 (35.14)		
CE	95 (22.04)	63 (22.26)	32 (21.62)		
Other	25 (5.81)	15 (5.30)	10 (6.76)		
Lesion location (n, %)				0.144	0.704
Anterior cerebral circulation	250 (58.00)	166 (58.66)	84 (56.76)		
Posterior cerebral circulation	181 (42.00)	117 (41.34)	64 (43.24)		
Baseline NIHSS (score, M, IQR)	5.00 (2.00, 14.00)	3.00 (1.00, 6.00)	15.00 (8.00, 21.00)	12.596	<0.001[a]

Table I. Continued.

Variables	Total (n=431)	No-END group (n=283)	END group (n=148)	Statistic	P-value
Baseline NIHSS classification (n, %)				130.052	<0.001[a]
Mild (0, 8)	271 (62.88)	231 (81.63)	40 (27.03)		
Moderate (9, 15)	67 (15.55)	29 (10.25)	38 (25.68)		
Severe (≥16)	93 (21.58)	23 (8.13)	70 (47.30)		
Outcome					
Hospital infection (n, %)	48 (11.14)	10 (3.53)	38 (25.68)	48.142	<0.001[a]
Death (n, %)	7 (1.62)	0 (0.00)	7 (4.73)	13.606	<0.001[a]

Categorical variables were summarized as frequencies and percentages. Normally distributed data were presented as the mean ± standard deviation ($\bar{x} \pm SD$) and analyzed using the independent-samples t-test. Non-normal distribution data were expressed as medians with interquartile ranges and assessed using the Mann-Whitney U test. [a]Significantly different when compared with the no-END group at P<0.05. AIS, Acute ischemic stroke; END, Early neurological deterioration; IQR, interquartile range; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; HALP score, hemoglobin, albumin, lymphocyte and platelet score; CRP, C-reactive protein; Hcy, Homocysteine; Lp-PLA2, lipoprotein phospholipase A2; LAA, large artery atherosclerosis; SAO, small artery occlusion; CE, cardio-embolism; NIHSS, national institute of health stroke scale.

Table II. Logistic regression analysis between the END group (n=148) and non-END group (n=283).

						95% CI	
Variables	B	SE	Wald x^2	P-value	OR	Lower	Upper
Age	0.013	0.014	0.893	0.345	1.013	0.986	1.040
WBC (10^9/l)	0.072	0.053	1.866	0.172	1.075	0.969	1.192
Lymphocyte count (10^9/l)	-0.353	0.309	1.304	0.254	0.703	0.383	1.288
Hemoglobin (g/l)	0.002	0.008	0.071	0.789	1.002	0.987	1.017
HALP score	-0.035	0.012	8.701	0.003[a]	0.965	0.943	0.988
CRP (mg/l)	0.014	0.012	1.287	0.257	1.014	0.990	1.038
Triglycerides	-0.022	0.154	0.020	0.889	0.979	0.723	1.325
Hcy (μmol/l)	-0.015	0.022	0.473	0.491	0.985	0.944	1.028
Lp-PLA2	-0.001	0.001	1.027	0.311	0.999	0.996	1.001
Baseline NIHSS	0.156	0.022	49.512	<0.001[a]	1.169	1.119	1.220
Hospital infection	1.697	0.488	12.075	0.001[a]	5.459	2.096	14.219

Multivariate logistic regression was performed to identify independent predictors of clinical conversion at discharge, incorporating variables significant in univariate analysis (P<0.05). [a]Significantly different when compared with the no-END group at P<0.05. WBC, white blood cell; HALP score, hemoglobin, albumin, lymphocyte and platelet score; Lp-PLA2, lipoprotein phospholipase A2; CI, confidence interval.

effective prognostic systems. Efforts have been directed toward developing refined tools to identify individuals at high risk of END, resulting in the formulation of multiple predictive models. For example, Xie *et al* (27) integrated variables such as NIHSS score, middle cerebral artery stenosis and carotid stenosis into a predictive framework that identified nearly half of patients susceptible to END. This observation is consistent with the present study, which identifies the NIHSS score as a key determinant in evaluating END risk. Nonetheless, the absence of a universally accepted model in clinical practice indicates that a multidimensional assessment including the diverse mechanisms of AIS may yield a more accurate and comprehensive prediction than reliance on a single biomarker.

Infection and malnutrition substantially increase the likelihood of END in patients with stroke (2). The HALP score, a biomarker attracting increasing attention, provides an integrated evaluation of inflammatory and nutritional conditions by combining inflammatory indicators (lymphocyte and platelet counts) with nutritional metrics (hemoglobin and albumin) (15). Within this index, platelets and lymphocytes serve as key parameters reflecting coagulative and inflammatory processes, respectively. A previous study emphasized the regulatory function of platelets in modulating inflammatory activity (28). At thrombotic sites, platelets act as core effector cells in inflammatory cascades, intensifying pathological progression (29). By contrast, lymphocytes participate in modulating inflammation by coordinating tissue repair and

Table III. Clinical value of HALP and NIHSS for predicting END in elderly patients with acute ischemic stroke.

Variables	Threshold	Sensitivity (%)	Specificity (%)	AUC	95% CI
HALP score	27.69	80.62	56.08	0.727	0.676-0.778
Baseline NIHSS	5.5	91.20	71.29	0.868	0.834-0.903
Both	-	82.43	84.10	0.883	0.850-0.916

Receiver operating characteristic curve analysis was performed in the END group (n=148) vs. non-END groups (n=283) to determine the optimal cutoff value, sensitivity and specificity for predicting END. HALP score, hemoglobin, albumin, lymphocyte and platelet score; NIHSS, National Institutes of Health Stroke Scale; END, early neurological deterioration; AUC, area under the curve; CI, confidence interval.

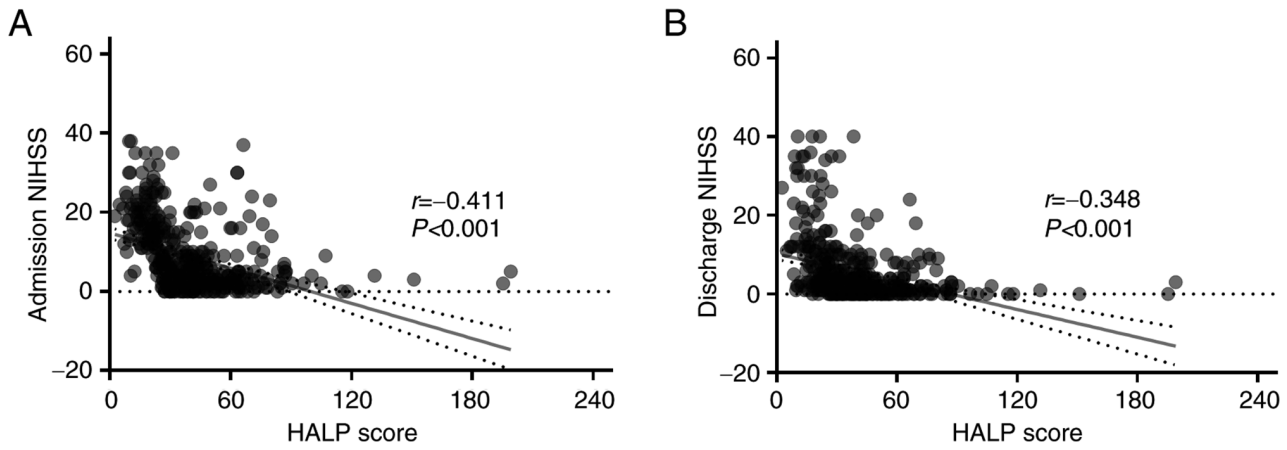

Figure 2. Correlation analysis of HALP score and NIHSS score. Pearson correlation analysis evaluated the relationship between HALP and NIHSS scores in patients with AIS (n=431). (A) HALP scores exhibited a significant negative correlation with NIHSS scores at admission. (B) HALP scores exhibited a significant negative correlation with NIHSS scores at Discharge. HALP score, hemoglobin, albumin, lymphocyte and platelet score; NIHSS, national institute of health stroke scale.

recovery. Some researchers have proposed composite indices, such as the platelet-to-lymphocyte ratio (PLR), to better represent systemic inflammation and thrombosis. Emerging evidence indicates that elevated PLR correlates with reduced overall survival and unfavorable prognosis in stroke populations (30,31). Xu *et al* (32) further demonstrated that increased PLR levels were associated with larger infarct volumes and poorer clinical outcomes in patients with AIS.

The HALP score integrates hematologic and biochemical parameters that reflect interrelated inflammatory and nutritional disturbances inherent to stroke pathophysiology. Hemoglobin and albumin, key constituents of this index, exhibit strong correlations with post-stroke outcomes. Anemia and hypoalbuminemia have been linked to elevated risks of stroke, cardiovascular morbidity and mortality (33,34). Curtelin *et al* (35) demonstrated that reductions in hemoglobin concentration may aggravate neurological deficits in AIS by disrupting cerebral perfusion and intensifying ischemic hypoxia. Albumin serves as an indicator of inflammatory burden and overall disease severity during acute conditions (36). Lymphopenia reflects systemic inflammation and impaired immune homeostasis following stroke, as lymphocytes play a regulatory role in post-ischemic inflammatory cascades, and their depletion is associated with poorer prognosis (12). Platelets contribute to thrombo-inflammatory processes by enhancing thrombosis and releasing proinflammatory mediators (13). Collectively, the HALP score captures the interdependence between inflammatory activity and nutritional status, parameters that together provide an integrated reflection of stroke prognosis.

A prospective cohort study identified a low HALP score as an independent predictor of unfavorable outcomes in patients with AIS (37). Early recognition of END remains essential, as the likelihood of neurological deterioration increases with time. In the present study, HALP scores demonstrated significant negative correlations with NIHSS scores at admission (r=-0.411; P<0.001) and on day 7 (r=-0.348, P<0.001), indicating a moderate association. This relationship suggests that lower HALP scores correspond to more severe neurological impairment reflected by NIHSS values. A marked association was also observed between reduced HALP levels and the development of END within seven days, aligning with prior evidence (37). This association likely reflects the aggravation of ischemic injury induced by systemic inflammatory activation and nutritional deficiency. Moreover, the combined predictive performance of HALP and NIHSS scores for END within 1 week in older patients yielded sensitivities and specificities of 82.43 and 84.10%, respectively. Integration of HALP and NIHSS assessments into clinical evaluation may thus enable earlier identification of high-risk older patients and support more targeted secondary prevention strategies.

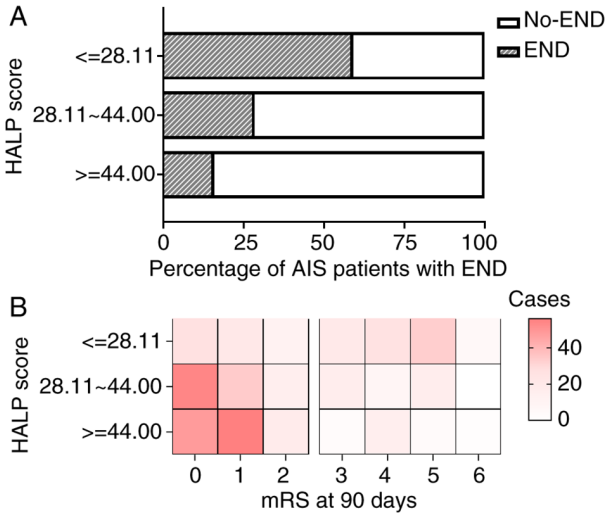

Figure 3. Correlation analysis between HALP score tertiles and outcome of patients with AIS. Patients with AIS (n=431) were categorized into three groups: (Q1, n=142; Q2, n=144; Q3, n=145) based on admission HALP score tertiles. Chi-square test assessed the difference in END incidence, and heat map illustrated the distribution of mRS scores among the tertiles. (A) Incidence of END among groups of patients with AIS stratified by HALP score tertiles. END incidence varied significantly across HALP tertiles (Q1: 59.15%, Q2: 28.47%, Q3: 15.86%; χ^2=158.87; P<0.001); (B) Clinical outcome frequency across HALP score tertiles. The distribution of mRS scores at 90 days differed significantly among the groups (P<0.001), with the highest proportion of favorable outcomes (mRS 0-1) in Q3 and the highest frequency of poor outcomes (mRS 5-6) in Q1. HALP score, hemoglobin, albumin, lymphocyte and platelet score; mRS, modified Rankin scale; AIS, acute ischemic stroke; END, early neurological deterioration.

Other unmeasured variables may also influence the risk of END. Factors such as detailed stroke pathophysiology beyond the TOAST framework (for example, degree of stenosis and plaque morphology), collateral circulation integrity, in-hospital blood pressure control protocols, and specific pharmacologic interventions during the acute phase warrant further investigation. These aspects represent meaningful directions for subsequent studies expanding upon the HALP score framework. In addition, the analysis of 90-day mRS outcomes, an established indicator of long-term post-stroke recovery, demonstrated that a lower admission HALP score correlated with poorer functional outcomes at three months, suggesting its prognostic relevance may extend beyond the acute period. The potential association of the HALP score with long-term recovery, dependency and mortality merits validation through future prospective studies with prolonged follow-up.

In the present study, a lower HALP score at admission exhibited a negative correlation with the NIHSS score and showed a strong association with END occurrence within 7 days, aligning with previous studies. This relationship likely reflects the aggravation of ischemic brain injury induced by systemic inflammatory cascades and malnutrition. The combined predictive performance of HALP and NIHSS scores for END within one week in older patients demonstrated sensitivity and specificity of 82.43 and 84.10%, respectively. Integration of HALP with NIHSS in clinical evaluation enables early recognition of patients at elevated risk of deterioration, allowing for more timely and targeted secondary prevention.

The HALP score, derived from standard admission blood tests, provides a readily obtainable and cost-effective biomarker. Its operational simplicity and bedside practicality confer advantages over more complex indices. Moreover, HALP serves as a valuable parameter for treatment decision-making and triage during the acute phase of stroke, supporting risk stratification that guides individualized management, including intensified therapy and close observation. Nonetheless, large-scale prospective studies with extended follow-up remain essential to verify the prognostic value of HALP in predicting END among older patients with AIS.

The present study has several limitations. First, as a single-center retrospective investigation, potential selection bias cannot be excluded, particularly because patients who received thrombolysis or endovascular therapy were omitted. Although this exclusion enhanced cohort homogeneity and allowed a focused assessment of the HALP score's predictive value, it restricts the applicability of the results to broader stroke populations that include candidates for acute reperfusion therapies. Validation in multicenter, prospective cohorts involving thrombolysis- or thrombectomy-treated patients is required. Second, the observation group included patients whose NIHSS scores increased by ≥2 points within 1 week after stroke onset, without accounting for earlier END events (within 24 or 72 h). Prospective research incorporating temporal trend adjustments is needed to confirm the temporal consistency of the predictive associations. Third, as a retrospective analysis from a single institution, the study lacks external or temporal validation across independent datasets. The predictive model derived in the present study requires replication in larger, multicenter, prospective studies including heterogeneous populations to confirm its reliability and generalizability before clinical implementation. Fourth, several potential confounding variables that might influence END risk were not comprehensively addressed, including detailed imaging parameters of stroke etiology, collateral circulation status, specific blood pressure management strategies during hospitalization and the pharmacologic impact of in-hospital treatments. The absence of these factors constrains the mechanistic interpretation of the findings and should be addressed in future investigations. Finally, the sample size was determined by the number of eligible patients admitted during the defined study period. While the observed associations were statistically significant, this approach remains a methodological limitation. Accordingly, multicenter cohort studies are warranted to further clarify the causal association between HALP scores and END in elderly patients with AIS.

In summary, the analysis indicates that older patients with acute stroke exhibit a higher incidence of END. A reduced HALP score at admission likely represents malnutrition and systemic inflammation, both strongly linked to an elevated risk of END within 1 week. Moreover, integrating HALP with NIHSS scores yields high sensitivity and specificity for END prediction, providing a reliable prognostic indicator that may support clinicians in optimizing therapeutic strategies.

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Availability of data and materials

The data generated in the present study are not publicly available due to ongoing studies using the current data but may be requested from the corresponding author.

Authors' contributions

YJL and LLL designed the experiments, wrote the manuscript and performed statistical analysis. XL performed the experiments. ABG and MMH processed data. YJL and YX contributed to the concept of the present study, design of the experiments, analysis and interpretation of the data, and drafting the manuscript. All authors read and approved the final version of the manuscript. YJL and LLL confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The study protocol was carried out according to the principles of the Helsinki Declaration, approved by the Ethics Committee of Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School (approval no. 2022-308-01; Nanjing, China). Informed consent was waived by the Ethics Committee of Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School. All methods were carried out in accordance with relevant guidelines and regulations.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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