

# Hemoglobin, Albumin, Lymphocyte, and Platelet Score is Associated With Adverse Clinical Outcomes of Acute Ischemic Stroke: A Prospective Cohort Study

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## Research article

**Keywords:** acute ischemic stroke, cohort study, HALP score, death

**Posted Date:** July 29th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-38304/v1>

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# Abstract

## Background

The combined index of hemoglobin, albumin, lymphocyte and platelet (HALP) is considered as a novel score to reflect systemic inflammation and nutritional status. This study aimed to investigate the association between HALP score and adverse clinical events in patients with acute ischemic stroke (AIS).

## Methods

This study prospectively included patients with AIS within 24 hours of admission to the First Affiliated Hospital of Zhengzhou University. The primary outcomes were all-cause death within 90 days and 1 year. The secondary outcomes included stroke recurrence and combined vascular events. The association between HALP score and adverse clinical outcomes was analyzed using Cox proportional hazards.

## Results

A total of 1337 patients were included. Patients in the highest tertile of HALP score had a lower risk of death within 90 days and 1 year (Hazard ratio: 0.20 and 0.30; 95% confidence intervals: 0.06–0.66 and 0.13–0.69,  $P$  for trend  $< 0.01$  for all) compared with the lowest tertile after adjusting relevant confounding factors. Similar results were found for secondary outcomes. Subgroup analyses further confirmed these association. Adding HALP score to the conventional risk factors improved prediction of death in patients with AIS within 90 days and 1 year (net reclassification index, 38.63% and 38.68%; integrated discrimination improvement, 2.43% and 2.57%;  $P < 0.02$  for all).

## Conclusions

High HALP score levels were associated with decreased risk of adverse clinical outcomes within 90 days and 1 year after stroke onset, suggesting that HALP score may serve as a powerful indicator for AIS.

## Background

Stroke is the leading cause of death and long-term disability worldwide; recurrent stroke worsens the outcome and even increases mortality[1, 2]. Exploring new predictors of stroke prognosis can help improve patients' clinical outcomes and contribute to more effective secondary prevention. Inflammation, abnormal blood coagulation, and poor nutritional status are associated with poor prognosis of acute ischemic stroke (AIS)[3–5]. Lymphocytes have key regulatory functions in post-stroke inflammation; lower lymphocyte counts were associated with increased infarct volume, neurological deterioration, and poor prognosis after ischemic stroke[6, 7]. Platelet hyperactivity increases the risk of thromboembolism and atherosclerotic lesions and may lead to abnormal thrombosis which exacerbates inflammation

response[8]. Anemia and hypoalbuminemia are manifestations of poor nutritional status and have been identified as risk factors for cerebrovascular events that may lead to poor prognosis in patients with AIS[9, 10]. Anemia and lower albumin levels at admission may adversely affect the prognosis of stroke and can be used as indicators for stroke recurrence[11, 12].

The hemoglobin, albumin, lymphocyte and platelet (HALP) score is considered to be an easily calculated marker of systemic inflammation and nutritional status[13, 14] and has been confirmed as a significant prognostic factor in patients with pancreatic cancer, esophageal squamous cell carcinoma, and bladder cancer[15, 16]. However, it is unknown whether HALP score is associated with the adverse clinical events of AIS. Therefore, our study aimed to investigate the predictive value of HALP score in a large cohort of patients with AIS.

## Methods

### Study Design and Population

The study was a prospective consecutive hospital-based cohort study. We enrolled patients with AIS within 24 hours of onset from the Ischemic Cerebrovascular Disease Database of the First Affiliated Hospital of Zhengzhou University from January 2015 to June 2018, which has been published previously[17, 18]. The diagnosis of AIS was based on the criteria of the World Health Organization (WHO)[19]. The database was approved by the Ethics Committee and informed consent forms were obtained from all patients or their relatives.

The exclusion criteria were as follows: (✗) patients with active or chronic inflammatory disease; (✗) autoimmune diseases or using immunosuppressant drugs; (✗) patients with neoplastic hematologic disorder; (✗) patients without blood cell count data; and (✗) severe liver and kidney dysfunction.

### Clinical Assessment

Baseline clinical information was obtained from case report forms at admission, including demographic characteristics, medical histories, imaging features, and medication use. The severity of AIS was assessed blindly according to the National Institutes of Health Stroke Scale (NIHSS) at admission[20].

### Laboratory Assay

Laboratory tests were obtained within 24 hours of admission, including the serum albumin, hemoglobin, lymphocyte, and platelet levels. The blood counts were analyzed using an autoanalyzer (Beckman Coulter Hematology Analyzer LH750, USA). All the serum biochemical parameters were assayed using an automatic biochemical analyzer (Roche COBAS 8000 automatic biochemical analyzer). The HALP score

was calculated according to the following formula: hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L) / platelets (/L).

## Outcome Assessments

The primary outcomes were all-cause death within 90 days and 1 year. The secondary outcomes included stroke recurrence and combined vascular events (stroke recurrence and all-cause death) within 90 days and 1 year. Patients enrolled were followed up by face-to-face or telephone interviews at 90 days and 1 year after stroke onset.

## Statistical Analyses

Continuous variables with normal distribution were expressed as mean ± standard deviation (SD) and skewed distribution were expressed as medians with interquartile ranges (median, IQR). Categorical variables were expressed as frequencies and percentages (n, %). Patients were classified into three groups based on the HALP score tertiles. The nonparametric Wilcoxon test or Kruskal-Wallis test was used to compare group differences for continuous variables, and the  $\chi^2$  test was used for categorical variables. The cumulative incidence risks of adverse clinical events across baseline HALP score were calculated with Kaplan-Meier curves and compared by log-rank test. Multivariate Cox proportional hazards models were used to assess the risk of adverse clinical outcomes with HALP score tertiles. C statistics, net reclassification index (NRI), and integrated discrimination improvement (IDI) were used to evaluate the incremental predictive ability of HALP score beyond the conventional model. Optimal HALP score cut-off points were obtained using receiver operating characteristic curve (ROC) analysis. Finally, subgroup analyses were conducted to assess the robustness of association between HALP score and adverse clinical outcomes of AIS. Interactions between HALP score and subgroup variables on the adverse clinical outcomes were tested in the models with interaction terms by the likelihood ratio test, adjusting for the aforementioned covariates unless the variable was used as a subgroup variable. Statistical analysis was performed using IBM SPSS software version 24.0 (SPSS, Inc, Chicago, IL, USA) and R (version 3.5.0). A two-tailed value of  $P < 0.05$  was considered statistically significant.

## Results

### Baseline Characteristics

A total of 1337 patients were included in our analysis (see Additional file 1). The baseline characteristics were balanced between the patients included and excluded (see Additional file 2). The mean age of the patients was 61 years and 30.5% of them were female. Compared with the higher HALP score patients, those with a lower HALP score were more likely to be older, had lower lymphocyte, hemoglobin and albumin levels, and had higher platelet counts and baseline NIHSS scores (Table 1).

Table 1  
Baseline Characteristics of Patients According to the HALP score tertiles

Variable	Overall	HALP score tertiles			P value
		Tertile 1 < 36.65	Tertile 2 36.65–54.42	Tertile 3 > 54.42	
Patients, n	1337	445	446	446	–
Age, years, mean ± SD	60.55 ± 12.45	63.20 ± 12.45	60.24 ± 11.92	58.20 ± 12.48	< 0.001
Female, n (%)	408 (30.5)	179 (40.2)	123 (27.6)	106 (23.8)	< 0.001
Smoking, n (%)	564 (42.2)	146 (32.8)	188 (42.2)	230 (51.6)	< 0.001
Alcohol consumption, n (%)	419 (31.3)	120 (27.0)	133 (29.8)	166 (37.2)	0.003
Hypertension, n (%)	809 (60.5)	274 (61.6)	268 (60.1)	267 (59.9)	0.852
Diabetes, n (%)	311 (23.3)	97 (21.8)	97 (21.7)	117 (26.2)	0.191
Stroke history, n (%)	322 (24.1)	114 (25.6)	99 (22.2)	109 (24.4)	0.479
Coronary heart disease, n (%)	159 (11.9)	61 (13.7)	48 (10.8)	50 (11.2)	0.343
Atrial fibrillation, n (%)	88 (6.6)	42 (9.4)	26 (5.8)	20 (4.5)	0.009
Hemoglobin, g/l, median (IQR)	138 (20)	132 (23)	138 (17)	144 (19)	< 0.001
Albumin, g/l, median (IQR)	40.9 (4.7)	39.6 (4.8)	40.9 (4.2)	41.8 (4.5)	< 0.001
Lymphocyte, 10 <sup>9</sup> /l, median (IQR)	1.7 (0.9)	1.2 (0.6)	1.7 (0.6)	2.2 (0.7)	< 0.001
Platelet, 10 <sup>9</sup> /l, median (IQR)	207 (77)	234 (87)	209 (72)	186 (59)	< 0.001
NIHSS, median (IQR)	3 (4)	4 (6)	3 (4)	3 (4)	< 0.001
HALP = hemoglobin, albumin, lymphocyte, and platelet; NIHSS = National Institute of Health Stroke Scale					

## Association Between Halp Score And Adverse Clinical Outcomes

The cumulative incidence of death, stroke recurrence, and combined vascular events within 90 days of follow-up were 2.8%, 1.8%, and 4.5%, respectively, while the cumulative incidence within 1 year were 4.6%, 4.7%, and 8.8%. All Kaplan-Meier curves showed that patients in the lowest tertile of HALP score had the highest incidence of death, stroke recurrence and combined vascular events within 90 days and at 1 year (log-rank  $P < 0.05$  for all, Fig. 1 and see Additional file 3).

After adjustment for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease, atrial fibrillation, and baseline NIHSS score, higher levels of HALP score were associated with a decreased risk of death within 90 days and 1 year (Table 2). The adjusted Hazard ratios (95% confidence intervals) for the highest vs lowest tertile of HALP score were 0.20 (0.06–0.66) for death at 90 days and 0.30 (0.13–0.69) at 1 year. Similar results were observed for stroke recurrence and combined vascular events within 90 days and 1 year (Table 2).

Table 2  
HRs (95% CIs) for adverse clinical outcomes according to HALP score tertiles

Outcomes	Outcomes within 90 days				Outcomes within 1 year		
	HALP score tertiles	Events, n (%)	Unadjusted Model	Adjusted Model*	Events, n (%)	Unadjusted Model	Adjusted Model*
<b>Death</b>							
	Tertile 1	24 (5.4)	Reference	Reference	38 (8.5)	Reference	Reference
	Tertile 2	10 (2.2)	0.41 (0.20–0.86)	0.57 (0.27–1.20)	16 (3.6)	0.41 (0.23–0.74)	0.58 (0.32–1.04)
	Tertile 3	3 (0.7)	0.12 (0.04–0.41)	0.20 (0.06–0.66)	7 (1.6)	0.18 (0.08–0.40)	0.30 (0.13–0.69)
	<i>p</i> for trend	< 0.001	< 0.001	0.004	< 0.001	< 0.001	0.002
<b>Stroke</b>							
	Tertile 1	14 (3.1)	Reference	Reference	31 (7.0)	Reference	Reference
	Tertile 2	6 (1.3)	0.42 (0.16–1.08)	0.43 (0.16–1.11)	17 (21.0)	0.52 (0.29–0.94)	0.48 (0.27–0.88)
	Tertile 3	4 (0.9)	0.27 (0.09–0.83)	0.28 (0.09–0.84)	15 (21.0)	0.45 (0.24–0.84)	0.41 (0.22–0.77)
	<i>p</i> for trend	0.028	0.013	0.014	0.022	0.008	0.003
<b>Combined vascular events</b>							
	Tertile 1	35 (7.9)	Reference	Reference	63 (14.2)	Reference	Reference
	Tertile 2	18 (4.0)	0.50 (0.29–0.89)	0.62 (0.35–1.10)	33 (7.4)	0.51 (0.33–0.77)	0.60 (0.39–0.92)
	Tertile 3	7 (1.6)	0.19 (0.09–0.44)	0.27 (0.12–0.61)	22 (4.9)	0.33 (0.20–0.54)	0.42 (0.25–0.69)

HR, Hazard Ratio; CI, Confidence Interval; HALP = hemoglobin, albumin, lymphocyte, and platelet.  
\*Adjusted for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease and atrial fibrillation and baseline NIHSS scores

	Outcomes within 90 days			Outcomes within 1 year		
<i>p</i> for trend	< 0.001	< 0.001	0.001	< 0.001	< 0.001	< 0.001
HR, Hazard Ratio; CI, Confidence Interval; HALP = hemoglobin, albumin, lymphocyte, and platelet. *Adjusted for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease and atrial fibrillation and baseline NIHSS scores						

Based on the ROC analysis, the area under the curve of HALP score for predicting death were 0.730 (95% CI: 0.705–0.754) at 90 days and 0.714 (95% CI: 0.689–0.738) at 1 year (see Additional file 4).

## Incremental Predictive Ability Of Halp Score

The incremental predictive ability of HALP score to predict adverse clinical outcomes after AIS is presented in Table 3. Adding HALP score to the conventional model, which included age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease, atrial fibrillation, and baseline NIHSS scores, significantly improved the predictive ability for death within 90 days and 1 year (NRI: 38.63% and 38.68%; IDI: 2.43% and 2.57%,  $P < 0.02$  for all). Similar results were found in combined vascular events but not for stroke recurrence within 90 days and 1 year after AIS onset.

Table 3  
Reclassification and discrimination statistics for adverse clinical outcomes by HALP score

	C statistic		NRI (Continuous), %		IDI, %	
	Estimate (95% CI)	P Value	Estimate (95% CI)	P Value	Estimate (95% CI)	P Value
Outcomes within 90 days						
Death						
Conventional Model	0.801 (0.778–0.822)		Reference		Reference	
Conventional Model + HALP score	0.823 (0.801–0.843)	0.325	38.63 (6.92–70.35)	0.017	2.43 (0.50–4.37)	0.014
Stroke						
Conventional Model	0.722 (0.698–0.746)		Reference		Reference	
Conventional Model + HALP score	0.730 (0.705–0.753)	0.840	28.43 (10.69–67.54)	0.154	0.89 (0.13–1.64)	0.021
Combined vascular events						
Conventional Model	0.753 (0.729–0.776)		Reference		Reference	
Conventional Model + HALP score	0.777 (0.754–0.799)	0.231	33.17 (8.17–58.16)	0.009	1.65 (0.29–3.02)	0.018
Outcomes within 1 year						
Death						
Conventional Model	0.804 (0.782–0.825)		Reference		Reference	

Conventional Model adjusted for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease and atrial fibrillation and baseline NIHSS scores. HALP = hemoglobin, albumin, lymphocyte, and platelet; CI, Confidence Interval; IDI, Integrated Discrimination Improvement; NRI, Net Reclassification Index

	C statistic		NRI (Continuous), %		IDI, %	
Conventional Model + HALP score	0.826 (0.804–0.846)	0.192	38.68 (13.97–63.39)	0.002	2.57 (0.98–4.16)	0.002
Stroke						
Conventional Model	0.604 (0.577–0.630)		Reference		Reference	
Conventional Model + HALP score	0.622 (0.595–0.648)	0.429	22.59 (1.81–46.99)	0.070	0.52 (0.15–0.90)	0.006
Combined vascular events						
Conventional Model	0.652 (0.626–0.678)		Reference		Reference	
Conventional Model + HALP score	0.686 (0.661–0.711)	0.035	26.65 (8.32–44.99)	0.004	1.47 (0.71–2.23)	< 0.001
Conventional Model adjusted for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease and atrial fibrillation and baseline NIHSS scores. HALP = hemoglobin, albumin, lymphocyte, and platelet; CI, Confidence Interval; IDI, Integrated Discrimination Improvement; NRI, Net Reclassification Index						

## Subgroup Analyses

An optimal HALP score cut-off point level was obtained from the ROC analysis and low HALP score levels were associated with the death after adjustment for age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease, atrial fibrillation, and baseline NIHSS score (Fig. 2). The adjusted Hazards ratio were 0.30 (95% CI: 0.15–0.59) within 90 days and 0.35 (95% CI: 0.21–0.60) at 1 year. In the subgroup analyses, negative associations between HALP score and death were observed in most subgroups. No statistical significance between HALP score and these factors on primary outcome was observed (all *P* for interaction > 0.05). Similar results were observed for stroke recurrence and combined vascular events within 90 days and 1 year (see Additional file 5).

## Discussion

We explored the prognostic value of the novel index HALP score in patients with AIS in this prospective cohort study and found that higher levels of HALP score at admission were highly associated with a decreased risk of death, stroke recurrence and combined vascular events within 90 days and 1 year.

Ischemic stroke initiates with gradual or sudden cerebral hypoperfusion, including oxidative stress, hemostatic activation, inflammation, and eventually leads to a corresponding loss of neurological function[21]. Ischemic brain tissue activates leukocytes and promotes their migration to the ischemic site by releasing pro-inflammatory chemokines[22]. The inflammation triggers the process of thrombosis, in which platelets participate in adhesion, release reaction, and aggregation[8]. Lymphocytes play an important role in the elimination and repair of inflammation[23]. Albumin has a neuroprotective effect because of its antagonism of oxidation, stagnant, thrombosis, and leukocyte adhesion[24, 25]. Hemoglobin has oxygen-carrying capacity and can affect the energy balance in the penumbra[26]. Studies have shown that each of these indicators is a predictor of stroke prognosis[7, 9, 27, 28]. Further, serum albumin and hemoglobin concentration have predictive value for stroke recurrence and combined events[11, 12]. The new indicator HALP score is based on the combination of the four hematological parameters mentioned above. Our study showed that HALP score was associated with the risk of death, stroke recurrence and combined vascular events within 90 days and 1 year after AIS. These results suggested that decreased HALP score could be an independent risk factor of adverse clinical outcomes.

So far, no study has investigated the association between HALP score and AIS. Recent studies have shown that the HALP score can reflect the inflammation-nutritional status of patients[14, 29], and has been proved to be an important prognostic indicator for patients with pancreatic cancer[13], esophageal squamous cell carcinoma[15], and bladder cancer[16]. Anemia and thrombosis could exacerbate inflammation while lymphocytes reduce inflammation[30]. Since Seltzer[31] proposed that admission serum albumin levels and total lymphocyte counts evaluate immediate nutritional status of patients, serum albumin has been considered as an indicator of nutritional status. Some studies also suggest that albumin reflects the severity of inflammation and illness in acute diseases[32]. It is widely accepted that the inflammatory response and nutritional status are correlated with the prognosis of patients with stroke[5, 33, 34]. HALP score is obtained by hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L) / platelets (/L), which makes it a cost effective, simple parameter to easily assess the inflammation-nutritional status. This finding may be significant because instant inflammation-nutritional status assessment can help clinicians assess prognosis and formulate appropriate treatment plans.

There were some limitations to this study. First, this was a single-center study; therefore, there may be a selection bias. Second, the potential influence of previously received treatments, such as thrombolytic therapy, oral anti-platelet, and statins were not considered. Third, we only obtained the hemoglobin, albumin levels, lymphocyte, and platelet count at admission but did not present the dynamic change of HALP score at different stages. Therefore, multicenter cohort studies are still needed to validate the findings.

## Conclusion

Our study indicated association between HALP score and risk of death, stroke recurrence and combined vascular events within 90 days and 1 year, suggesting that HALP score at admission may act as a powerful indicator of adverse clinical events in patients with AIS.

# Abbreviations

AIS

acute ischemic stroke; HALP:the hemoglobin, albumin, lymphocyte and platelet; mRS:modified Rankin Scale; NIHSS:National Institutes of Health Stroke Scale; NRI:net reclassification index; IDI:integrated discrimination improvement.

# Declarations

## Ethics approval and consent to participate

The study was approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University. Informed consent forms were obtained from all patients or their relatives.All informed consent obtained from study participants is written.

## Consent for publication

Not applicable

## Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request, subject to permission from the relevant ethics committees at the hospital and university.

## Competing interests

The authors declare that they have no competing interests.

## Funding

This study was supported by the National Natural Science Foundation of China (81571158) and the Education Department of Henan Province (16A320054, 172102310086).No funding body had any role in the design, data collection, analysis, interpretation of data or writing the manuscript.

## Authors' contributions

BS, YMXu designed the overall study with contributions fromMMN, FB, JW and SLS. MKT designedand carried out experiments and collected and analyzeddata with YFL, XW, XT, LLP, XW, LYZ and WXS.MKT wrote the manuscript. BS supervised this study, designed experiments and edited thepaper. All authors critically reviewed the manuscript and approvedthe submitted version.

## Acknowledgments

We thank the study participants and the clinical staff for their support and contribution to this study.

## References

1. Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet Glob Health*. 2013;1(5):e259-81. doi:10.1016/s2214-109x(13)70089-5.
2. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project Stroke. 1994;25 2:333–7. doi:10.1161/01.str.25.2.333.
3. Esenwa CC, Elkind MS. Inflammatory risk factors, biomarkers and associated therapy in ischaemic stroke. *Nat Rev Neurol*. 2016;12 10:594–604. doi:10.1038/nrneurol.2016.125.
4. de Lau LM, Leebeek FW, de Maat MP, Koudstaal PJ, Dippel DW. A review of hereditary and acquired coagulation disorders in the aetiology of ischaemic stroke. *Int J Stroke*. 2010;5 5:385–94. doi:10.1111/j.1747-4949.2010.00468.x.
5. Collaboration FT. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. *Stroke*. 2003;34 6:1450–6. doi:10.1161/01.str.0000074037.49197.8c.
6. Baird AE. The forgotten lymphocyte: immunity and stroke. *Circulation*. 2006;113 17:2035–6. doi:10.1161/circulationaha.105.620732.
7. Kim J, Song TJ, Park JH, Lee HS, Nam CM, Nam HS, et al. Different prognostic value of white blood cell subtypes in patients with acute cerebral infarction. *Atherosclerosis*. 2012;222 2:464–7. doi:10.1016/j.atherosclerosis.2012.02.042.
8. del Zoppo GJ. The role of platelets in ischemic stroke. *Neurology*. 1998;51(3 Suppl 3):9–14. doi:10.1212/wnl.51.3\_suppl\_3.s9.
9. Milionis H, Papavasileiou V, Eskandari A, D'Ambrogio-Remillard S, Ntaios G, Michel P. Anemia on admission predicts short- and long-term outcomes in patients with acute ischemic stroke. *Int J Stroke*. 2015;10(2):224–30. doi:10.1111/ijvs.12397.
10. Tanne D, Molshatzki N, Merzeliak O, Tsabari R, Toashi M, Schwammenthal Y. Anemia status, hemoglobin concentration and outcome after acute stroke: a cohort study. *BMC Neurol*. 2010;10:22. doi:10.1186/1471-2377-10-22.
11. Chang JY, Lee JS, Kim BJ, Kim JT, Lee J, Cha JK, et al. Influence of Hemoglobin Concentration on Stroke Recurrence and Composite Vascular Events. *Stroke*. 2020;51 4:1309–12. doi:10.1161/strokeaha.119.028058.
12. Zhang Q, Lei YX, Wang Q, Jin YP, Fu RL, Geng HH, et al. Serum albumin level is associated with the recurrence of acute ischemic stroke. *Am J Emerg Med*. 2016;34 9:1812–6. doi:10.1016/j.ajem.2016.06.049.

13. Xu SS, Li S, Xu HX, Li H, Wu CT, Wang WQ, et al. Haemoglobin, albumin, lymphocyte and platelet predicts postoperative survival in pancreatic cancer. *World J Gastroenterol.* 2020;26 8:828–38. doi:10.3748/wjg.v26.i8.828.
14. Shen XB, Zhang YX, Wang W, Pan YY. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score in Patients with Small Cell Lung Cancer Before First-Line Treatment with Etoposide and Progression-Free Survival. *Med Sci Monit.* 2019;25:5630–9. doi:10.12659/msm.917968.
15. Cong L, Hu L. The value of the combination of hemoglobin, albumin, lymphocyte and platelet in predicting platinum-based chemoradiotherapy response in male patients with esophageal squamous cell carcinoma. *Int Immunopharmacol.* 2017;46:75–9. doi:10.1016/j.intimp.2017.02.027.
16. Peng D, Zhang CJ, Gong YQ, Hao H, Guan B, Li XS, et al. Prognostic significance of HALP (hemoglobin, albumin, lymphocyte and platelet) in patients with bladder cancer after radical cystectomy. *Sci Rep.* 2018;8 1:794; doi:10.1038/s41598-018-19146-y.
17. Song B, Hu R, Pei L, Cao Y, Chen P, Sun S, et al. Dual antiplatelet therapy reduced stroke risk in high-risk patients with transient ischaemic attack assessed by ABCD3-I score. *Eur J Neurol.* 2019;26 4:610–6. doi:10.1111/ene.13864.
18. Zhao L, Wang R, Song B, Tan S, Gao Y, Fang H, et al. Association between atherogenic dyslipidemia and recurrent stroke risk in patients with different subtypes of ischemic stroke. *Int J Stroke.* 2015;10 5:752–8. doi:10.1111/ijs.12471.
19. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ.* 1980;58(1):113–30.
20. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, et al. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke.* 1989;20 7:864–70. doi:10.1161/01.str.20.7.864.
21. Brouns R, De Deyn PP. The complexity of neurobiological processes in acute ischemic stroke. *Clin Neurol Neurosurg.* 2009;111 6:483–95. doi:10.1016/j.clineuro.2009.04.001.
22. Kim JY, Park J, Chang JY, Kim SH, Lee JE. Inflammation after Ischemic Stroke: The Role of Leukocytes and Glial Cells. *Exp Neurobiol.* 2016;25 5:241–51. doi:10.5607/en.2016.25.5.241.
23. Ren X, Akiyoshi K, Dziennis S, Vandenbark AA, Herson PS, Hurn PD, et al. Regulatory B cells limit CNS inflammation and neurologic deficits in murine experimental stroke. *J Neurosci.* 2011;31 23:8556–63. doi:10.1523/jneurosci.1623-11.2011.
24. Taverna M, Marie AL, Mira JP, Guidet B. Specific antioxidant properties of human serum albumin. *Ann Intensive Care.* 2013;3 1:4. doi:10.1186/2110-5820-3-4.
25. Lam FW, Cruz MA, Leung HC, Parikh KS, Smith CW, Rumbaut RE. Histone induced platelet aggregation is inhibited by normal albumin. *Thromb Res.* 2013;132 1:69–76. doi:10.1016/j.thromres.2013.04.018.
26. Kimberly WT, Lima FO, O'Connor S, Furie KL. Sex differences and hemoglobin levels in relation to stroke outcomes. *Neurology.* 2013;80 8:719–24. doi:10.1212/WNL.0b013e31828250ff.

27. Dzedzic T, Slowik A, Szczudlik A. Serum albumin level as a predictor of ischemic stroke outcome. *Stroke*. 2004;35 6:e156-8. doi:10.1161/01.STR.0000126609.18735.be.
28. Du J, Wang Q, He B, Liu P, Chen JY, Quan H, et al. Association of mean platelet volume and platelet count with the development and prognosis of ischemic and hemorrhagic stroke. *Int J Lab Hematol*. 2016;38 3:233–9. doi:10.1111/ijlh.12474.
29. Peng D, Zhang CJ, Tang Q, Zhang L, Yang KW, Yu XT, et al. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy. *BMC Urol*. 2018;18 1:20; doi:10.1186/s12894-018-0333-8.
30. Barlas RS, Honney K, Loke YK, McCall SJ, Bettencourt-Silva JH, Clark AB, et al. Impact of Hemoglobin Levels and Anemia on Mortality in Acute Stroke: Analysis of UK Regional Registry Data, Systematic Review, and Meta-Analysis. *J Am Heart Assoc*. 2016;5:8. doi:10.1161/jaha.115.003019.
31. Seltzer MH, Bastidas JA, Cooper DM, Engler P, Slocum B, Fletcher HS. Instant nutritional assessment. *JPEN J Parenter Enteral Nutr*. 1979;3 3:157–9. doi:10.1177/014860717900300309.
32. Eckart A, Struja T, Kutz A, Baumgartner A, Baumgartner T, Zurfluh S, et al. Relationship of Nutritional Status, Inflammation, and Serum Albumin Levels During Acute Illness: A Prospective Study. *Am J Med*. 2019. doi:10.1016/j.amjmed.2019.10.031.
33. Fu Y, Liu Q, Anrather J, Shi FD. Immune interventions in stroke. *Nat Rev Neurol*. 2015;11 9:524–35. doi:10.1038/nrneurol.2015.144.
34. Martineau J, Bauer JD, Isenring E, Cohen S. Malnutrition determined by the patient-generated subjective global assessment is associated with poor outcomes in acute stroke patients. *Clin Nutr*. 2005;24 6:1073–7. doi:10.1016/j.clnu.2005.08.010.

## Figures

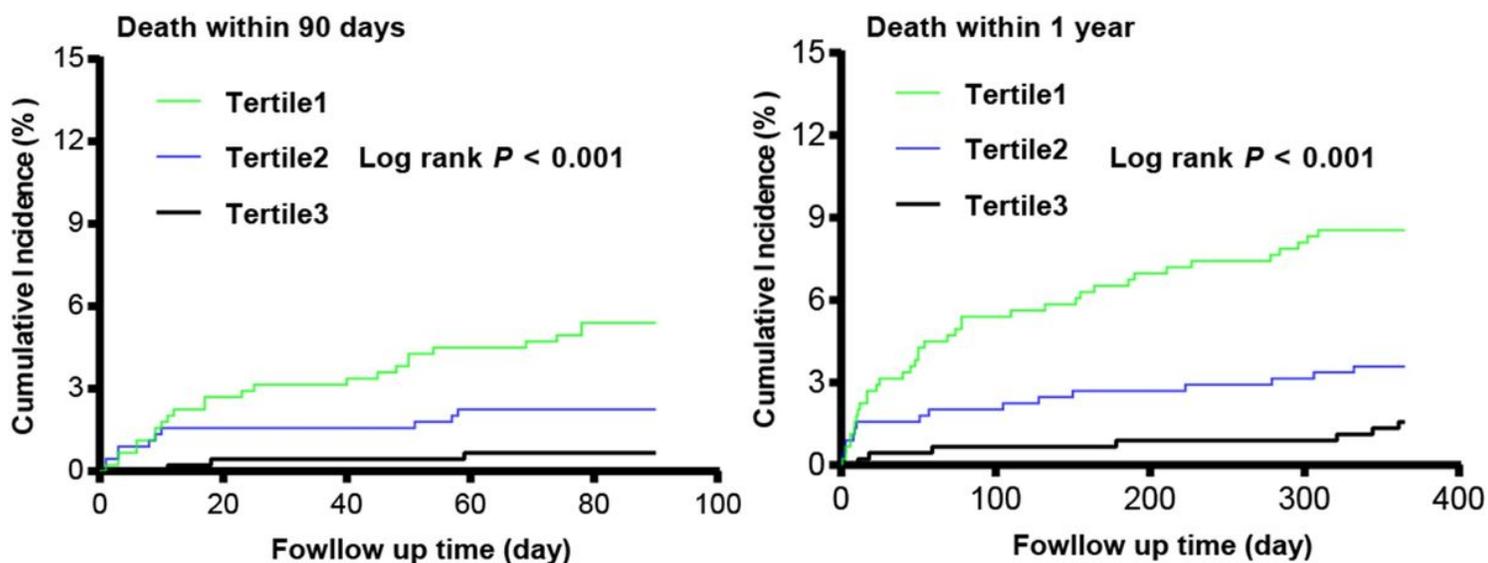
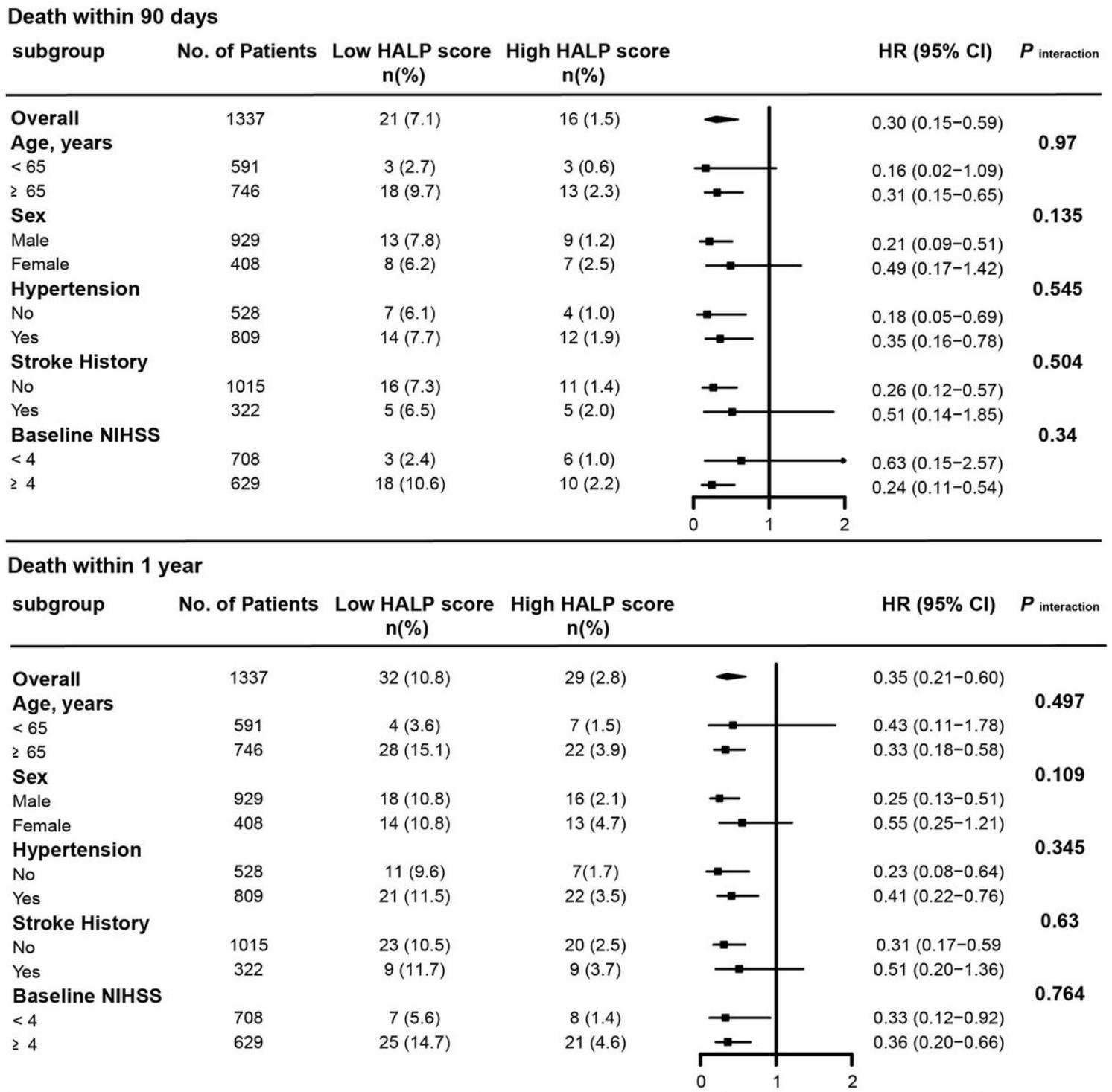


Figure 1

Kaplan-Meier curves of cumulative incidence (%) of death by tertiles of HALP score at 90-days and 1-year follow-up.



**Figure 2**

Subgroup analyses of the association between HALP score and death within 90 days and 1 year. In the multivariate models, confounding factors, such as age, sex, smoking, alcohol consumption, history of hypertension, diabetes, ischemic stroke, coronary heart disease and atrial fibrillation and baseline NIHSS

scores were included unless the variable was used as a subgroup variable. HR, Hazard Ratio; CI, Confidence Interval; HALP = hemoglobin, albumin, lymphocyte, and platelet

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