

RESEARCH ARTICLE

Malnutrition on admission increases the in-hospital mortality and length of stay in elder adults with acute ischemic stroke

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Abstract

Purpose: Malnutrition, as determined by the Controlling Nutritional Status (CONUT), has an effect on the 3-month and long-term prognosis of stroke patients. The association between malnutrition and in-hospital mortality has not been well established. We aimed to investigate the relationship between the CONUT score on admission and in-hospital mortality and length of stay (LOS) in elderly patients with acute ischemic stroke (AIS).

Methods: This study analyzed controls and patients with AIS. Malnutrition was determined using the CONUT score. A CONUT score of 5–12 was defined as undernutrition status. Based on the CONUT scores, the patients were divided into the low CONUT (0–4) and high CONUT (5–12) groups.

Results: In total, 1079 participants were recruited, comprising 288 controls and 791 AIS patients. Among the 791 patients, 64 (8.1%) had malnutrition and 63 (7.9%) had an in-hospital death. Compared to the controls, the AIS patients presented higher CONUT scores, higher proportion of in-hospital mortality (8.0%), and longer length of stay. Malnutrition was independently associated with in-hospital mortality in the AIS patients (adjusted odds ratio: 3.77, 95% confidence interval [CI]: 1.55–9.15; $p = 0.003$). The general linear models showed an association between the CONUT score and LOS ($\beta = 0.574$, 95% CI: 0.208–0.934; $p = 0.002$). Furthermore, the effect of the interaction between infection and nutrition status on in-hospital mortality showed borderline statistical significance ($p = 0.06$).

Conclusions: Malnutrition estimated by the CONUT score on admission can be a predictor of in-hospital mortality and increased LOS in elderly AIS patients.

KEYWORDS

controlling nutritional status score, lymphocyte, malnutrition, mortality, nutrition, serum albumin, stroke, total cholesterol

1 | INTRODUCTION

Stroke is one of the leading causes of increased disability-adjusted life-years¹ and the years of life lost.² Moreover, it is the

second-leading cause of mortality worldwide,³ with majority of these deaths occurring in low-income and middle-income countries.⁴ China had a higher estimated global lifetime risk of stroke than that of the global average level (39.3% vs. 24.9%).⁵ Although

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recent data have highlighted the marked increase in stroke prevalence and incidence but an overall stable mortality rate, the absolute number of stroke patients increases steadily as the Chinese population continues to grow and age.⁶ Moreover, stroke incidence and associated mortality also increase with age,⁷ especially in those aged ≥ 75 years.⁶ Considering the steady increase in life expectancy, the incidence of stroke is also expected to be more than double over the next 30 years, mainly among the elderly patients aged ≥ 75 years.⁸

Malnutrition in hospitalized patients is a common unrecognized problem, especially in the elderly,⁹ and it appears to exacerbate brain damage and contribute to adverse outcomes.¹⁰ Stroke patients are prone to malnutrition mainly due to dysphagia, impaired consciousness, perception deficits, and cognitive dysfunction.¹¹ Additionally, those presenting an undernourished status on admission tend to have more complications during hospitalization (eg, pneumonia, other infections, bedsores, and gastrointestinal bleeding), longer length of stay (LOS), and higher hospitalization costs as compared to those presenting a nourished status.¹² Therefore, an early assessment of the nutritional status on admission is strongly recommended by the clinical nutrition guidelines in neurology.¹¹

Several assessment tools reflecting the nutrition status have been used, one of which is the Controlling Nutritional Status (CONUT) score system. This system was initially proposed as a convenient and effective assessment tool for screening the comprehensive nutritional status in cases of hospital undernutrition.¹³ Subsequently, it was established as a prognostic predictor of various cancers,¹⁴ coronary artery disease (CAD),¹⁵ heart failure,¹⁶ and atrial fibrillation.¹⁷ Few studies have identified that a malnourished status determined by the CONUT score on admission is associated with an increased risk of short-term and long-term mortality in patients with ischemic stroke.^{18,19} However, whether the CONUT score is an effective indicator of in-hospital mortality in the elderly (age ≥ 75 years) with acute ischemic stroke (AIS) remains unclear. Hence, the primary aim of this study was to demonstrate the association between malnutrition on admission and in-hospital mortality as well as LOS in elderly AIS patients aged ≥ 75 years.

2 | MATERIALS AND METHODS

2.1 | Study population

We conducted a study at the Department of Neurology of the Second Hospital of Tianjin Medical University in Tianjin, China. Patients who were diagnosed with AIS and admitted to the hospital between January 1, 2014, and July 31, 2020, were enrolled. The inclusion criteria were ischemic stroke diagnosis, age ≥ 75 years, and complete blood and biochemical indexes. The exclusion criteria were missing laboratory data of serum albumin, total lymphocyte count (TLC), and total cholesterol (TC); patients with hematological diseases or history of cirrhosis and malignancy; and previous/ongoing intravenous thrombolysis treatment. After applying the aforementioned exclusion criteria to the 2706 AIS patients, 791 AIS patients

were included in the final analysis. The CONUT scores were calculated for these patients to determine the association with in-hospital mortality and LOS (Figure 1). Meanwhile, the age-matched control group ($n = 288$) included contemporaneously hospitalized patients admitted to hospital for disorders not related to acute stroke.

2.2 | Ethics

The study was approved by the Ethics Committee of the Second Hospital of Tianjin Medical University, and informed consent was provided by all participants.

2.3 | Data collection and risk factor definitions

AIS was defined as a cerebral, spinal, or retinal infarction caused by vascular factors resulting in acute focal or global neurological dysfunction lasting >24 hours, with or without ischemic evidence on computerized tomography or magnetic resonance imaging. According to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification,²⁰ the types of stroke can be classified into the following five clinical subtypes: large artery atherosclerosis (LAA), cardioembolism (CE), small artery occlusion (SAO), stroke of other determined cause (SOD), and stroke of undetermined cause (SUD). The National Institutes of Health Stroke Scale (NIHSS) score was used to estimate the stroke severity. The baseline clinical characteristics on admission were obtained from our electronic medical record system. This included age, sex, personal history (drinking and smoking), medical history (hypertension, diabetes mellitus, CAD, heart failure, atrial fibrillation, hyperlipidemia, stroke or transient ischemic attack, and leucocytopenia), systolic blood pressure (SBP) and diastolic blood pressure (DBP) data, laboratory findings, clinical manifestations affecting the nutrition status (consciousness disorder and dysphagia), infection during hospitalization, LOS, and

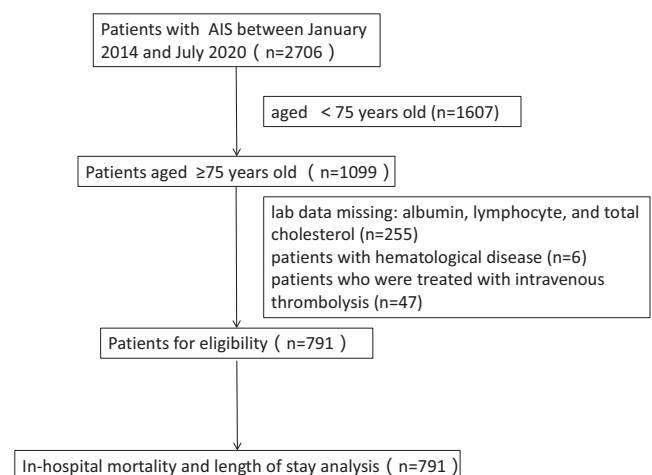


FIGURE 1 Flow chart of screening patients with acute ischemic stroke

hospitalization expenses. Venous blood was collected in the morning of the second day of admission with an 8-hour fasting condition for blood examination.

Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or ongoing treatment with antihypertensive medications. Diabetes mellitus was defined as fasting blood glucose level ≥ 7.0 mmol/L or random glucose level ≥ 11.1 mmol/L on two measurements, or if there was a previous diagnosis of diabetes and/or use of hypoglycemic agents. Hyperlipidemia was defined as ongoing treatment with cholesterol-reducing agents, triglyceride level > 200 mg/dl, or TC level > 240 mg/dl. Based on the smoking status, patients were classified as never, former, or current smokers.²¹ Individuals who had smoked almost every day for > 1 year were defined as current smokers. Alcohol drinkers were defined as those who consumed alcohol at least once per week for > 1 year. We calculated the eGFR by using the following Modification of Diet in Renal Disease Study equation²²:

$$\text{eGFR} = 186 \times \text{standardized serum creatinine}^{-1.154} \\ \times \text{age}^{-0.203} \times 0.742 \text{ (if female).}$$

Reduced renal function was defined as eGFR < 60 ml/min/1.73 m².²³ Due to the lack of height and weight records, the body mass index could not be calculated. Infection during hospitalization was defined by the presence of pneumonia or urinary tract infection, as diagnosed by the clinicians.

2.4 | Nutritional evaluation

Patients were diagnosed with anemia according to the World Health Organization criteria, that is, hemoglobin concentration < 13 g/dl in men and < 12 g/dl in women.²⁴ The details of CONUT score are listed in Table S1. The CONUT score range is 0–12. Based on the score, the nutrition status can be classified into four levels: normal (0–1), light (2–4), moderate (5–8), and severe (9–12).¹³ In this study, 0–4 was considered as low CONUT score and 5–12 as high CONUT score; the higher the score, the poorer the nutrition. High CONUT score was defined as malnutrition (moderate and severe malnutrition).

2.5 | Outcomes

The primary outcome of this analysis was all-cause death during hospitalization, and the secondary outcome was LOS. The LOS was measured from the day of admission to the day of death or discharge.

2.6 | Statistical analysis

Continuous variables are presented as means \pm standard deviations or medians (interquartile ranges). According to the normality of the data distribution, the student's *t* test or Mann–Whitney *U* test was

performed to compare the low CONUT and high CONUT groups. Categorical variables are expressed as counts and proportions. The significance of the intergroup differences was evaluated using Pearson's chi-square test or Fisher's exact test. Multiple linear regression analysis was conducted for LOS.²⁵ We performed univariate logistic regression analysis to calculate the *p*-value and analyzed the association between the dependent variables and covariates. We further analyzed the covariates with a univariable *p*-value < 0.05 using the multivariable logistic model to analyze the association between the nutrition status and in-hospital mortality or LOS. Statistical analysis was performed using the Statistical Product and Service Solutions, version 25.0.

3 | RESULTS

3.1 | Baseline demographics and clinical characteristics on admission

Table 1 shows the baseline demographics and clinical characteristics at admission of all participants. This study enrolled 1079 participants, comprising 288 controls and 791 AIS patients, who were hospitalized between January 1, 2014, and July 31, 2020. In this sample of both cases and controls, the median age was 82 years, 532 (49.3%) participants were female, 214 (19.8%) were current smokers, and 232 (21.5%) had infection. There were several differences between the controls and cases. The AIS patients presented a higher proportion of atherogenic diseases (diabetes, 42.0% and hyperlipidemia, 67.1%), more cardiac complications (heart failure, 17.8% and atrial fibrillation, 30.8%), higher CONUT scores, and poorer outcomes (higher in-hospital mortality [8.0%] and longer LOS) as compared to the controls.

Of the 791 AIS patients, 373 (47.2%) were female and the median NIHSS score was 4, and patients with consciousness disorder accounted for 8.1% ($n = 64$) and those with dysphagia for 7.6% ($n = 60$). Of these AIS patients, 64 (8.1%) belonged to the high CONUT group and the remaining 727 (91.9%) to the low CONUT group. As compared to the low CONUT group, the high CONUT group had higher NIHSS score and higher proportion of patients with consciousness disorder on admission ($p < 0.05$). The complications of heart failure, atrial fibrillation, and anemia were more prevalent in those with malnutrition than in those without ($p < 0.05$). Patients with malnutrition were more likely to have poorer hospital outcomes and a higher mortality rate than those without (23.4% vs. 6.6%). With respect to laboratory investigations, the white blood cell (WBC) count and high-sensitivity C-reactive protein (hs-CRP) level tended to be higher in patients with malnutrition than in those without, reflecting a stronger inflammatory response in the former. There were no significant differences between the high and low CONUT groups with respect to age, sex, SBP, stroke types, infection during hospitalization, dysphagia, and medical history (hypertension, diabetes mellitus, CAD, history of stroke, or transient ischemic attack) ($p > 0.05$ for all).

TABLE 1 Baseline demographics and clinical characteristics at admission of all participants

Variables	Control (n = 288)	Ischemic stroke Total (n = 791)	p value	Ischemic stroke		p value
				Low CONUT (n = 727)	High CONUT (n = 64)	
Age, years	81 (78–85)	82 (78–85)	0.147	82 (78–85)	82 (78–88)	0.407
Female, n (%)	159 (55.2)	373 (47.2)	0.019	342 (47.0)	31 (48.4)	0.830
SBP, mmHg	145 (131–160)	153 (138–169)	<0.001	154 (139–170)	148 (130–169)	0.089
DBP, mmHg	80 (70–87)	81 (79–90)	0.001	82 (74–91)	78 (69–88)	0.006
Current smoking, n (%)	42 (14.6)	172 (21.7)	0.009	164 (22.6)	8 (12.5)	0.061
Current drinking, n (%)	25 (8.7)	98 (12.4)	0.090	93 (12.8)	5 (7.8)	0.246
NIHSS score	1 (0–4)	4 (1–8)	<0.001	4 (1–8)	9 (3–14)	<0.001
TOAST Classification, n (%)						0.035
LAA	–	245 (31.0)		223 (30.7)	22 (34.4)	
CE	–	156 (19.7)		135 (18.6)	21 (32.8)	
SAO	–	324 (41.0)		307 (42.2)	17 (26.6)	
SOD	–	3 (0.4)		3 (0.4)	0	
SUD	–	63 (8.0)		59 (8.1)	4 (6.3)	
Infection, n (%)	36 (12.5)	196 (24.8)	<0.001	174 (23.9)	22 (34.4)	0.064
Clinical manifestations						
Consciousness disorder, n (%)	12 (4.2)	64 (8.1)	0.026	53 (7.3)	11 (17.2)	0.005
Dysphagia, n (%)	18 (6.3)	60 (7.6)	0.454	54 (7.4)	6 (9.4)	0.573
Medical history						
Hypertension, n (%)	222 (77.1)	569 (71.9)	0.091	525 (72.2)	44 (68.8)	0.554
Diabetes mellitus, n (%)	92 (31.9)	332 (42.0)	0.003	308 (42.4)	24 (37.5)	0.450
Coronary artery disease, n (%)	197 (68.4)	395 (49.9)	<0.001	358 (49.2)	37 (57.8)	0.189
Heart failure, n (%)	20 (6.9)	141 (17.8)	<0.001	119 (16.4)	22 (34.4)	<0.001
Atrial fibrillation, n (%)	50 (17.4)	244 (30.8)	<0.001	216 (29.7)	28 (43.8)	0.020
Hyperlipidemia, n (%)	127 (44.1)	531 (67.1)	<0.001	500 (68.8)	31 (48.4)	0.001
Stroke or TIA, n (%)	92 (31.9)	278 (35.1)	0.327	253 (34.8)	25 (39.1)	0.494
Anemia, n (%)	95 (33.0)	300 (38.0)	0.133	255 (35.1)	45 (70.3)	<0.001
CONUT score	1 (0–2)	1 (0–3)	<0.001	1 (0–2)	5 (5–7)	<0.001
Laboratory data						
White blood cells, count/mL	6500 (5300–7980)	6960 (5750–8990)	<0.001	6900 (5740–8900)	8095 (5800–11650)	0.013
Lymphocyte count, count/mL	1520 (1117–1970)	1330 (960–1720)	<0.001	1370 (1010–1760)	705 (560–1185)	<0.001
Hemoglobin, g/dL	12.9 (12.0–14.2)	13.0 (11.7–14.2)	0.872	13.13 ± 2.50	11.10 ± 2.63	<0.001
Total cholesterol, mg/dL	416.16 (351.08–485.23)	413.51 (349.97–479.91)	0.920	417.05 (356.84–481.68)	374.55 (303.91–475.93)	0.012
Serum albumin, g/dL	3.93 (3.72–4.16)	3.86 (3.59–4.18)	0.005	3.91 (3.67–4.20)	2.98 (2.68–3.29)	<0.001
Hs-CRP, mg/L	2.86 (1.08–7.21)	4.82 (1.99–22.89)	<0.001	4.81 (1.91–22.74)	33.76 (6.29–183.09)	<0.001
eGFR, ml/min/1.73 m ²	79.19 (64.25–95.61)	80.93 (61.32–98.60)	0.962	81.05 (63.26–98.98)	62.69 (40.43–90.53)	<0.001

(Continues)

TABLE 1 (Continued)

Variables	Control (n = 288)	Ischemic stroke Total (n = 791)	p value	Ischemic stroke		p value
				Low CONUT (n = 727)	High CONUT (n = 64)	
In-hospital mortality, n (%)	0 (0)	63 (8.0)	<0.001	48 (6.6)	15 (23.4)	<0.001
LOS (median and IQ)	13 (9–14)	13 (10–17)	<0.001	13 (10–17)	14.50 (11.25–22.00)	0.010

Abbreviations: CE, cardioembolism; CONUT, Controlling Nutritional Status; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; Hs-CRP, high-sensitivity c-reactive protein; LAA, large artery atherosclerosis; LOS, length of stay; NIHSS, National Institutes of Health Stroke Scale; SAO, small artery occlusion; SBP, systolic blood pressure; SOD, stroke of other determined cause; SUD, stroke of undetermined cause; TIA, transient ischemic attack; TOAST, Trial of Org 10172 in Acute Stroke Treatment.

TABLE 2 Comparison of in-hospital death and length of stay between participants with stroke or not

Dependent variable	In-hospital mortality		Length of stay	
	OR (95% CI)	p value	β coefficient (95% CI)	p value
NIHSS score	1.12 (1.06–1.18)	<0.001	0.16 (0.07–0.26)	0.001
Infection	0.57 (0.27–1.21)	0.145	3.47 (2.31–4.64)	<0.001
CONUT score	1.35 (1.12–1.62)	0.002	0.50 (0.20–0.80)	0.001

Note: Both in-hospital mortality and length of stay were adjusted for age, sex, NIHSS, SBP, DBP, current smoking, infection, consciousness disorder, diabetes mellitus, coronary artery disease, heart failure, atrial fibrillation, hyperlipidemia, CONUT, white blood cells, and hs-CRP.

Abbreviations: CONUT, Controlling Nutritional Status; DBP, diastolic blood pressure; hs-CRP, high-sensitivity c-reactive protein; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

3.2 | In-hospital outcomes of all participants (controls and cases)

The risk factors for in-hospital mortality and LOS are reported in Table 2. The multivariate logistic regression analysis was performed for in-hospital mortality, which showed that NIHSS score was associated with in-hospital mortality (odds ratio [OR]: 1.12, 95% confidence interval [CI]: 1.06–1.18). A similar association was observed between CONUT score and in-hospital mortality (OR: 1.35, 95% CI: 1.12–1.62). General linear regression analysis conducted for LOS showed that the NIHSS score was associated with an increase in the LOS ($\beta = 0.16$, 95% CI: 0.07–0.26). Additionally, there was an association between the CONUT score and LOS ($\beta = 0.50$, 95% CI: 0.20–0.80; $p = 0.001$). Moreover, infection and CAD were both associated with an increase in LOS ($\beta = 3.47$, 95% CI: 2.31–4.64 and $\beta = 1.28$, 95% CI: 0.28–2.28, respectively) (Table S2). However, the association between infection and in-hospital mortality was not statistically significant after adjustment for all confounders.

3.3 | In-hospital outcomes between the high and low CONUT groups

We first performed univariate logistic regression analysis of the risk factors associated with in-hospital mortality (Model 1; Table S3). We found that age, sex, NIHSS, stroke types, infection during

hospitalization, heart failure, atrial fibrillation, hyperlipidemia, WBC count, hs-CRP level, and CONUT score were associated with in-hospital mortality. However, the effect of anemia on in-hospital mortality was not statistically significant. After adjusting for age and sex in Model 1, the risk of in-hospital mortality in patients with high CONUT score was significant as compared to those with low CONUT score (adjusted OR: 4.38, 95% CI: 2.27–8.44; $p < 0.001$) (Model 1; Table S3). We further performed another multivariate logistic regression analysis in Model 2 by adjusting for covariates with p -values < 0.05 in the univariate analysis and anemia, which has been shown to influence stroke outcomes. The adjusted risk for some factors (age, sex, stroke types, etc.) did not differ significantly between the two CONUT groups (Table S3). However, the adjusted risk of in-hospital mortality in the high CONUT group showed a significant increase as compared to the low CONUT group (adjusted OR: 3.77, 95% CI: 1.55–9.15; $p = 0.003$) (Figure 2).

The factors influencing LOS were estimated by conducting general linear regression analysis in patients with AIS (Table S4). The univariate analysis revealed that the CONUT score, infection, CAD, and NIHSS score were positively associated with LOS ($p < 0.01$) (Table 3). After adjustment for age, sex, NIHSS score, stroke types, CAD, atrial fibrillation, history of stroke, WBC count, hs-CRP level, CONUT score, and infection, the general linear models showed an association between CONUT score and LOS ($\beta = 0.574$, 95% CI: 0.208–0.934; $p = 0.002$). Moreover, infection showed a stronger association with LOS than did NIHSS score ($\beta = 4.335$, 95%

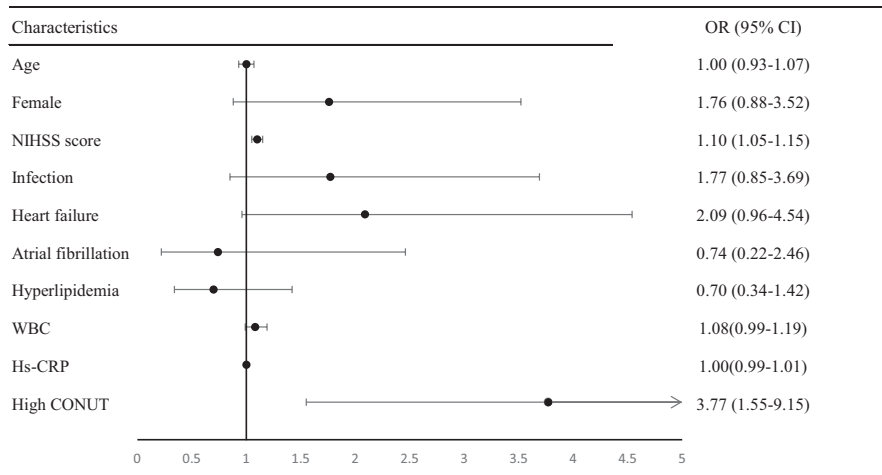


FIGURE 2 In-hospital mortality of AIS patients: univariate and multivariable analyses

TABLE 3 Length of stay of ischemic stroke patients: univariate and multivariable analyses

Variables	Univariate analysis		Multivariate analysis	
	β coefficient (95% CI)	<i>p</i> value	β coefficient (95% CI)	<i>p</i> value
Infection	5.367 (4.025–6.708)	<0.001	4.335 (2.932–5.777)	<0.001
CAD	2.065 (0.852–3.278)	0.001	2.042 (0.830–3.254)	0.001
NIHSS score	0.304 (0.206–0.403)	<0.001	0.169 (0.062–0.276)	0.002
CONUT score	0.952 (0.598–1.306)	<0.001	0.574 (0.208–0.934)	0.002

Abbreviations: CAD, Coronary artery disease; CONUT, Controlling Nutritional Status; NIHSS, National Institutes of Health Stroke Scale.

CI: 2.932–5.777; $p < 0.001$ and $\beta = 0.169$, 95% CI: 0.062–0.276; $p = 0.002$, respectively); CAD was associated with an increase in LOS ($\beta = 2.042$, 95% CI: 0.830–3.254; $p = 0.001$) (Table 3).

3.4 | Subgroup analysis on the effect of the high and low CONUT scores on the in-hospital mortality

We conducted subgroup analyses after stratification according to age, sex, anemia, renal dysfunction, heart failure, atrial fibrillation, infection during hospitalization, and hyperlipidemia (Figure 3). A significantly higher risk of in-hospital mortality was found in the high CONUT group as compared to the low CONUT group for the following factors: age ≥ 80 years, female sex, presence of anemia, no dyslipidemia, no reduced renal function, history of heart failure, no atrial fibrillation, and no infection ($p < 0.05$ for all). There were no interactions between the nutrition status and any of the subgroup factors, except for infection. However, the effect of the interaction between infection and nutrition status on the in-hospital mortality showed a borderline statistical significance ($p = 0.06$).

4 | DISCUSSION

Our findings indicate that the CONUT score is a predictor of in-hospital mortality in AIS patients aged ≥ 75 years and that high

CONUT scores are associated with increased in-hospital mortality and LOS.

A previous study demonstrated that malnutrition on admission increased the risk of poor prognosis in stroke patients based on the Malnutrition Universal Screening Tool (MUST).²⁶ The MUST was used to estimate the risk of malnutrition in stroke patients within 48 hours of admission, thus identifying patients who would benefit the most from medical nutrition therapy.¹¹ The MUST assesses weight loss in the past 3–6 months and no nutritional intake for >5 days, thus reflecting the relative long-term nutrition status. However, it is difficult to obtain accurate data for MUST when patients have decreased levels of consciousness and cognitive impairment. The nutrition score is needed to reflect the comprehensive state at the onset of acute stroke. This study is the first to compare the CONUT scores between the control and AIS groups. The results revealed that patients with AIS had higher CONUT scores and increased in-hospital mortality rate and LOS as compared to the controls, which reflected the acute changes in the comprehensive nutrition status. The CONUT score, comprising the serum albumin level, TLC, and TC level, is a comprehensive index that reflects the protein storage and lipid metabolism, as well as the immunity and inflammatory status. Furthermore, it assesses malnutrition conveniently and objectively using the conventional blood biochemical tests. Thus, the CONUT score is a preferred choice to evaluate the nutrition status.²⁷

Association between each component of the CONUT and AIS has been demonstrated. As a predictor, low serum albumin levels are

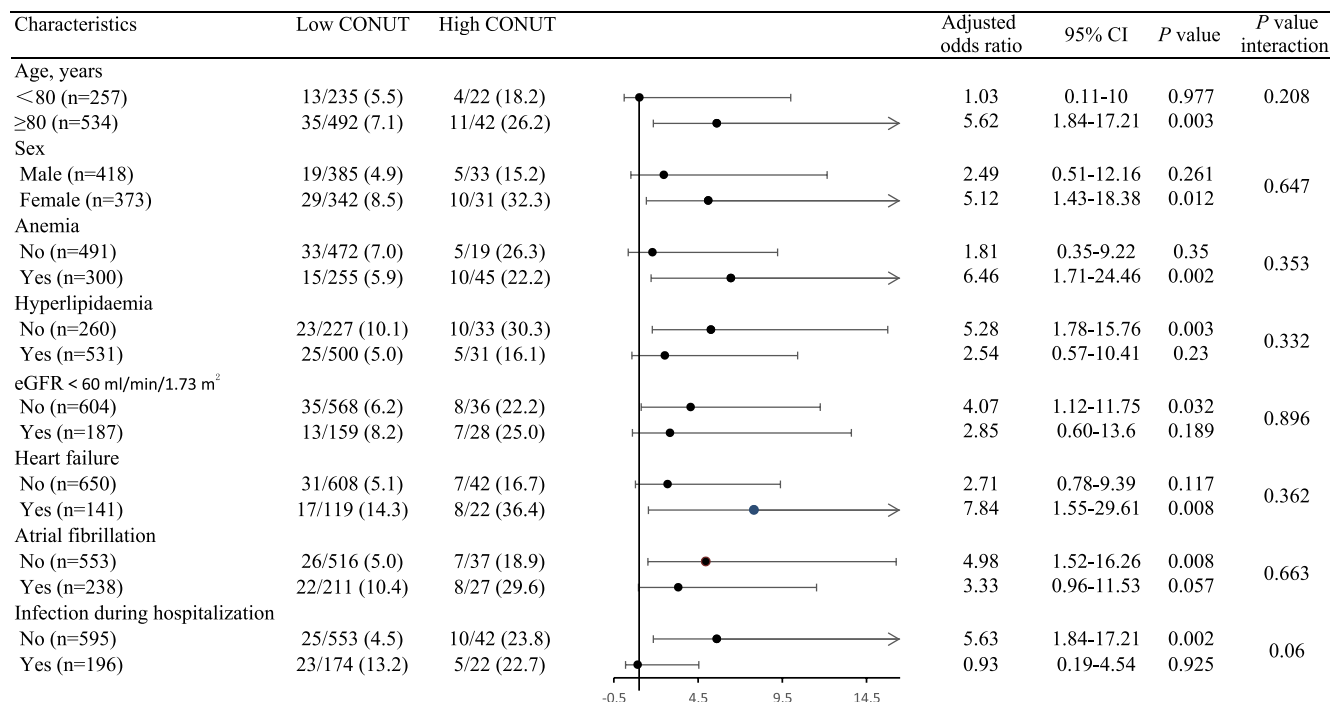


FIGURE 3 Subgroup analysis for the effect of the high versus low CONUT score on in-hospital mortality

associated with short-term and long-term mortality in hospitalized patients^{28,29} and poor outcomes in AIS patients.^{30,31} The main mechanisms could be attributed to the neuroprotective role played by albumin in ischemic stroke, such as antioxidant defense, antagonism of leukocyte adhesion, anti-thrombotic effects, decreasing cellular immunity, and sustained neuronal metabolism.^{30,31} TC is a good indicator of dietary intake.³² Previous studies have shown that low TC levels represent poor nutritional status, increased inflammation, and increased risk of death in aged non-stroke patients.^{33,34} For patients with AIS, an association between low TC levels and short-term and long-term mortality has been reported.^{35,36} TLC is one of systemic inflammation markers, and its reduced level represents a decrease in the immunity and inflammatory status,³⁷ which play a key role in the pathogenesis of stroke.³⁸ Low TLC levels are associated with an increased risk of in-hospital death and longer LOS in hospitalized patients.³⁹

In this study, we found that there was no difference in the association between the CONUT score and in-hospital mortality of the AIS patients in the different stroke subgroups. However, a previous study explored the association between malnutrition at admission, as determined by the CONUT score, and poor 3-month prognosis in different stroke subgroups.⁴⁰ Their study clarified that malnutrition was independently associated with adverse outcomes in the patients classified as cardioembolic stroke, and stroke of other etiologies (determined and undetermined etiologies).⁴⁰ This could be because low baseline serum albumin levels increased the risk of cardioembolic and cryptogenic stroke.⁴¹ However, the phenomenon was not found in our study. This difference may be due to the higher age composition and the higher proportion of LAA and SAO in the present study.

The high risk of malnutrition in patients with stroke is associated with reduced level of consciousness, dysphagia, infection, etc.⁴² Normal dietary and fluid intake are affected by dysphagia, leading to malnutrition and aspiration pneumonia.⁴³ However, there was no significant difference in dysphagia between the two CONUT groups in our study. This could be attributed to the age of the enrolled patients, which was different from that in other studies. Our study recruited elderly patients aged ≥ 75 years with similar history of stroke, which can lead to dysphagia due to pseudobulbar paralysis. Besides, decrease in physical function in the elderly participants, including poor dentition and gastrointestinal changes, can cause swallowing problems.

Our findings also showed that the effect of the interaction between infection and CONUT score on the in-hospital mortality showed borderline statistical significance. Further studies with a larger sample size might elicit results that are more relevant. The association between infection and nutrition status has been demonstrated that malnutrition is associated with the development of pneumonia and urinary tract infection,^{44,45} which increases the risk of in-hospital mortality.⁴⁶ Nutrition therapy has a possible effect on decreasing the incidence of infections according to some prior studies with limited sample size that were conducted on older stroke patients.^{47,48} Whether the tailored nutritional intervention can improve the in-hospital mortality in stroke patients remains to be explored.

There are several limitations in this study. First, this was a single-center study with a small sample size. There might have been some selection bias. Second, it has been reported that preexisting malnutrition before the stroke onset and poor nursing care were the risk factors for undernutrition in stroke patients.⁴⁹ Excluding patients

with a pre-morbid modified Rankin scale score of 3–5 could eliminate this effect to some extent. However, we were not able to obtain the history of nursing care and preexisting malnutrition. Third, we evaluated the stroke-associated mortality based on the CONUT score on admission. It is unknown whether dysphagia, inadequate care, depression, or other unmeasured confounders exacerbated malnutrition and whether post-stroke enteral nutrition effectively improved the nutrition status. Without considering these factors, the change in the CONUT score might lead to a bias. Although this study is based on a small sample, the findings suggest that the CONUT score is an independent predictor of in-hospital mortality and LOS in AIS patients aged ≥ 75 years. Further prospective studies should be conducted to identify that whether nutritional intervention, early screening for dysphagia, and enhanced hospital care can improve the prognosis in elderly patients with AIS.

5 | CONCLUSION

Malnutrition on admission, as determined by the CONUT score, was associated with an increased the risk of in-hospital mortality and LOS in AIS patients aged ≥ 75 years.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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