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Nutrition-associated markers and outcomes among patients receiving enteral nutrition after ischemic stroke: a retrospective cohort study

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Abstract

Background Early nutrition after acute ischemic stroke is crucial. We explored early enteral nutrition for stroke patients and evaluated changes in blood indicators as a predictor of stroke prognosis.

Methods All hospitalized stroke patients receiving enteral nutrition were included in the study. We retrospectively collected the protein, energy, fat, and carbohydrate values for 7 days after admission. Serum albumin, total protein, and hemoglobin values were reviewed at admission and at one week. The main outcome indicators were the Modified Rankin Score, Barthel Index, and Quality of Life at 3 months.

Results A total of 354 patients (mean age, 70.7 years; 59.0% male) were included. The change in serum albumin at day 7 relative to at admission was positively correlated with the Quality of Life score ($p=0.001$), the Barthel Index ($p=0.004$), and the modified Rankin Score ($p=0.029$). The change in total protein at day 7 relative to at admission was positively correlated with the Quality of Life score ($p=0.002$), the Barthel Index ($p=0.001$), and the modified Rankin score ($p=0.011$). The change in hemoglobin values at day 7 relative to at admission was positively correlated with the Barthel Index ($p=0.037$ but not with the Quality of Life score ($p=0.237$) or the modified Rankin score ($p=0.730$).

Conclusions Improved nutrition-related blood indicators one week after admission were independently associated with good stroke outcomes. Nutritional support for acute ischemic stroke patients during the early hospitalization stage appears to be advisable.

Trial registration This review was a retrospective cohort study. The study was retrospectively registered in the Chinese Clinical Trial Registry (No: ChiCTR2300077228). Registration date: 1/11/2023.

Highlights

- we explored the possible value of early enteral nutrition for stroke patients and evaluated changes in blood indicators as a predictor of stroke prognosis.
- we found that improved nutrition-related blood indicators at one week after admission were independently associated with good stroke outcomes.

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Keywords Stroke, Ischemic stroke, Enteral nutrition, Modified rankin score, European quality of life scale, Barthel index

Introduction

Critically ill patients with stroke frequently present with a decreased level of consciousness, severe dysphagia, and impaired gastrointestinal function, which are major risk factors for malnutrition [1]. Malnutrition one week after admission has been associated with increased mortality and complications and with poor functional prognosis [2]. Thus, current guidelines recommend that critically ill stroke patients with a decreased level of consciousness or prolonged severe dysphagia receive early (starting within the first 72 h) enteral tube feeding [3]. However the optimal caloric goal in early enteral nutrition for critically ill stroke patients remains unclear [4–6]. Malnutrition is one of the most common complications of stroke patients, accumulating evidence suggests that patients' nutritional status at admission is a determinant of stroke outcome: higher nutritional risk scores were associated with poor outcomes at three months after stroke [7 –8]. Many malnutrition risk screening tools are commonly used, including Nutrition Risk Screening 2002 and Malnutrition General Screening Tool [9], but these tools are more suitable for patients with clear awareness and good communication than for ischemic stroke patients, for whom data collection is complicated, and body weight changes, diet changes, and laboratory measurements are easily affected by subjective factors. Few reports have evaluated nutrition-associated markers during hospitalization and stroke outcome. Total protein and serum albumin values at the time of presentation of ischemic stroke were found to be a significant predictor of outcomes [10], and early correction of hypoalbuminemia has been suggested to reduce the risk of poor outcomes [11]. Some researchers [12] have expressed concern that high concentrations of hemoglobin increase blood viscosity, thereby increasing blood pressure and worsening the cardiovascular function in stroke patients. Overall, changes in nutrition-associated markers has not been clarified. These results prompt questions over which nutrition-related blood indicators can help clinical nutrition strategies? In this study, we evaluated nutritional intake for patients with ischemic stroke during the acute stroke period (one week after admission) and the association of nutritional intake with markers of patients' outcomes. We also examined the relationship between changes in nutrition-associated markers at day 7 relative to at admission and outcomes three months after the onset of ischemic stroke.

Materials and methods

Study design and participants

This is a single-center, investigator initiated, retrospective, cohort study of nutritional strategies and outcomes in patients receiving enteral nutrition after ischemic stroke. This review was reported in line with The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)Statement, completed checklist was upload as an additional file (supplementary file 1) [13]. The study was approved by the ethics committee of the West China Hospital, Sichuan University (Approval number: 2023(1845)). The patients were treated between January 2020 and September 2022, with final follow-up in November 2022.

Inclusion criteria were the following: (1) first onset of stroke confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) examination; (2) aged 18 years or older; (3)with a water-swallow test score of 3 or more; (4) enteral nutrition through a nasogastric tube within 48 h after stroke; (5) need enteral nutrition at least 7 days after stroke.

Exclusion criteria were the following: (1)unstable vital signs; (2)receiving total parenteral nutrition; (3)pre-stroke dementia or disability, or had a history of gastrectomy or enterectomy.

Withdrawal criteria were the following: (1) refusing to continue to participate in the study; (2) development of an acute disease or decompensation of chronic disease with the risk of a potential impact on the study results (repeated stroke, acute myocardial infarction, non-compensated diabetes, etc.); (3) patients with 20% absence of data.

Clinical data collection

The following clinical variables were collected from the hospital information system (HIS): age; gender; and comorbid disease, such as hypertension, diabetes mellitus, chronic coronary artery disease, hyperlipidemia, and atherosclerosis. Stroke severity was assessed at admission according to the National Institutes of Health Stroke Scale (NIHSS) [14] and the Modified Barthel Index (MBI).

Modified Barthel Index (MBI): is a measure of activities of daily living (ADL), which shows the degree of independence of a patient from any assistance. It is an important method used to evaluate the capacity of participants to conduct 10 different ADLs, considered basic ADLs, thus providing a quantitative estimation of their independence level [15].

Assessment of nutritional status on admission

Nutritional status was evaluated with the Nutrition Risk Screening 2002. Serum albumin, total protein, and hemoglobin values were determined on each patient at least twice: once at admission and once at 7–10 days. Changes (Δ) in these indexes were defined as the values measured at 7–10 days minus the values measured at admission.

Assessment of nutrition intake

We collected patients' daily nutritional intake during the week of admission (caloric intake; protein intake; fat intake; and carbohydrate intake from all sources, including enteral nutrition, parenteral nutrition, protein supplements, and energy-containing medications).

Outcomes

The prespecified primary outcome was the modified Rankin score (mRS) at day 90. The mRS is an ordinal scale that ranges from 0 (no symptoms) to 6 (death) [16]. The prespecified secondary outcomes were the score of NIHSS, MBI, swallowing function, and quality of life at day 90.

The quality of life (QoL) was assessed with the Chinese version of the European Quality of Life Measurement Scale (EQ-5D) [17], which consisted of the EQ-5D descriptive system, the European Five Dimensions Questionnaire Visual Analogue Scale (EQ-VAS), and the utility index. The EQ-5D descriptive system measured participants' health status in three levels of severity (no problems, moderate problems, and extreme problems) with five dimensions: mobility (MO), self-care (SC), usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD) [18]. The EQ-VAS score was recorded on a scale with anchor points 0 (worst health state) and 100 (best health state), which reflected patients' knowledge of health (40). A higher EQ-5D utility index indicated higher levels of QoL [19]. Previous studies have confirmed EQ-5D's reliability and validity in China [18].

Swallowing function was assessed with the Functional Oral Intake Scale (FOIS) of Crary et al. [20]. documented to have good reliability, validity, and sensitivity for objectively determining and monitoring the oral intake of patients with neurogenic dysphagia. It is an ordinal scale with 7 tiers that assesses the oral intake of food and liquids. Levels 1 to 3 indicate tube dependency, and levels 4 to 7 indicate total oral intake. Level 1 indicates complete impairment of oral intake; level 7 indicates that the patient has complete oral intake regardless of food consistency or type.

In addition, the occurrence of the following adverse events within 3 months after discharge were recorded: recurrence of stroke, cardiovascular events, vascular-related surgeries, systemic embolism, and epileptic seizures.

Sample size calculation

Data collected from a pilot study was used to calculate the sample size. According to pilot study, based on the correlation between nutritional status indicators (serum albumin) and MBI, $\beta=1.605$, covariate variance accounted for 0.0009, and main variable variance accounted for 0.024. If $\alpha=0.05$, $1-\beta=0.8$, multiple linear regression analysis was used, and the theoretical sample size in PASS2021 was calculated to be 312 people. Considering the 5% loss rate in pilot study, the sample size was expanded by 5%, the actual sample size required was about 329 people. 408 patients receiving post-stroke enteral nutrition initially entered the study.

Statistical analysis

The latent class growth model (LCGM) was used to classify energy intake curves of the patients. The number of latent classes was set to 3 to minimize Bayesian information criterion (BIC), and quadratic function was used for the growth curve. The likelihood ratio test (LRT) bootstrap method was used for model estimation, and the number of bootstraps was 200. The patients were divided into class 1, class 2, class 3 based on the energy intake curve.

For descriptive analysis, categorical variables were reported as counts (%), and continuous variables were reported as mean ± standard deviation (min–max), except that the length of stay variable was reported as median. Baseline characteristics were compared between the 3 classes using analysis of variance (ANOVA) for continuous variables and the Chi-Squared test for categorical variables. Multivariable linear regression was used to investigate the relationship between mean energy intake and blood indexes or outcomes (except occurrence of adverse events), and covariates were known confounders (age, gender, and NHISS score). Multivariable linear regression was also used to explore correlations between Δ blood indexes and outcomes. When the relationship between energy intake curve classes and outcomes was presented, multivariable linear regression was performed with class 1 as the reference group. Multivariable logistic regression was conducted to show the relationship between mean energy intake or energy intake curve class and occurrence of adverse events. LCGM was performed in M plus 8.3; other analysis and plotting was performed in R 4.2.3.

Results

Clinical characteristics and outcome

Between January 2020 and September 2022, 408 patients receiving post-stroke enteral nutrition initially entered the study. After strict inclusion and exclusion criteria were applied (detailed exclusion reasons in Figs. 1), 354 patients were included.

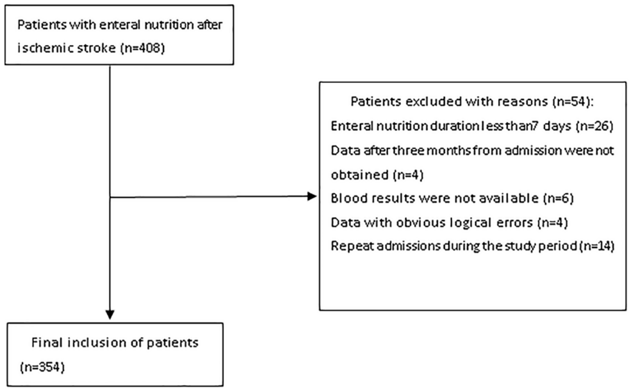

Fig. 1 Flowchart of study selection and screening

Baseline clinical characteristics of the 354 patients are listed in Table 1. The mean age ± standard deviation of the 354 patients with stroke was 70.68 ± 14.13 years. There were 209 participants (59.04%) were male. According to their energy intake curves, the patients were divided into three classes (Fig. 2). No significant differences were found in age, gender, NIHSS score, Body Mass Index (BMI), or comorbid disease (except diabetes) among the classes (all $p > 0.05$). Significant differences (all $p < 0.05$) among the classes were found in Bartel Index, diabetes, and length of stay.

The impact of energy intake on blood indexes and outcomes

No significant relationship was found between the mean of energy intake during the first 7 days following admission and Δ serum albumin, Δ total protein, or Δ hemoglobin (all $p > 0.05$; Table 2). Similarly, the mean of energy intake within 7 days had no significant relationship with occurrence of adverse events, mRS at 3 month, Barthel Index changes, and EQ at 3 months (all $p > 0.05$, Table 2).

Variations in outcomes among the three energy intake curve classes

Outcomes (occurrence of adverse events, mRS at 3 month, Δ Barthel Index, and EQ at 3 months) showed no significant difference among the three classes, as shown in Table 3.

The relationship of changes of blood indexes and outcome

Figure 3 shows the relationship between Δ albumin, total protein, and hemoglobin values and outcomes (mRS at 3 months, Δ Barthel Index, and EQ at 3 months). Higher Δ albumin and Δ total protein values were significantly associated with better outcomes (all $p < 0.05$). Δ hemoglobin was significantly correlated with Δ Barthel Index ($p = 0.037$), but had no significant correlation with mRS at 3 months or EQ at 3 months (both $p > 0.05$). Additionally, Δ blood indexes had no significant relationship

Table 1 Baseline characteristics of the enteral nutrition population

	Total (*n*=354)	Class 1 (*n*=138)	Class 2 (*n*=36)	Class 3 (*n*=180)	*P*-value
Age (years)	70.68±14.13	71.13±13.38	70.47±13.60	70.37±14.84	0.890
Gender (%)					
Male	209 (59.04)	79 (57.25)	24 (66.67)	106 (58.89)	0.591
Female	145 (40.96)	59 (42.75)	12 (33.33)	74 (41.11)	
Severity					
National Institutes of Health Stroke Scale (NIHSS)	14.15±7.35	14.31±7.39	14.51±7.69	13.96±7.28	0.874
Nutrition Risk Screening 2002 (NRS2002)	2.76±0.97	2.75±0.77	3.08±1.34	2.70±1.02	0.097
Barthel index (BI)	13.93±19.49	10.58±15.40	15.97±18.32	16.08±22.09	0.035
Comorbid disease					
Hypertension	245 (69.21)	99 (71.74)	27 (75.00)	119 (66.11)	0.408
Diabetes	119 (33.62)	50 (36.23)	18 (50.00)	51 (28.33)	0.030
Hyperlipidemia	43 (12.15)	16 (11.59)	4 (11.11)	23 (12.78)	0.931
Coronary artery disease	175 (49.44)	64 (46.38)	15 (41.67)	96 (53.33)	0.289
Atherosclerosis	121 (34.18)	52 (37.68)	8 (22.22)	61 (33.89)	0.218
Blood index (admission)					
Albumin (Alb)	38.89±4.57	38.68±4.79	38.89±4.95	39.05±4.34	0.773
Total protein (TP)	66.38±6.92	66.47±6.30	67.55±8.61	66.07±7.01	0.494
Hemoglobin (Hb)	128.59±23.13	129.46±22.61	133.06±34.15	127.02±20.71	0.307
Length of stay (days)	15.58±8.45	13.88±6.65	18.49±12.86	16.32±8.41	0.004
Provided nutrition (average of 7 days)					
Energy intake (kcal/day)	795.81±287.48	868.91±232.87	1029.51±326.53	693.04±273.69	<0.001
Protein intake (g/day)	30.31±18.88	35.18±11.26	40.73±15.35	27.10±11.39	<0.001
Fat intake (g/day)	31.64±12.74	30.52±10.65	40.10±20.46	28.24±22.62	0.003
Carbohydrate intake (g/day)	100.30±43.29	114.02±35.23	121.99±39.64	85.51±44.45	<0.001

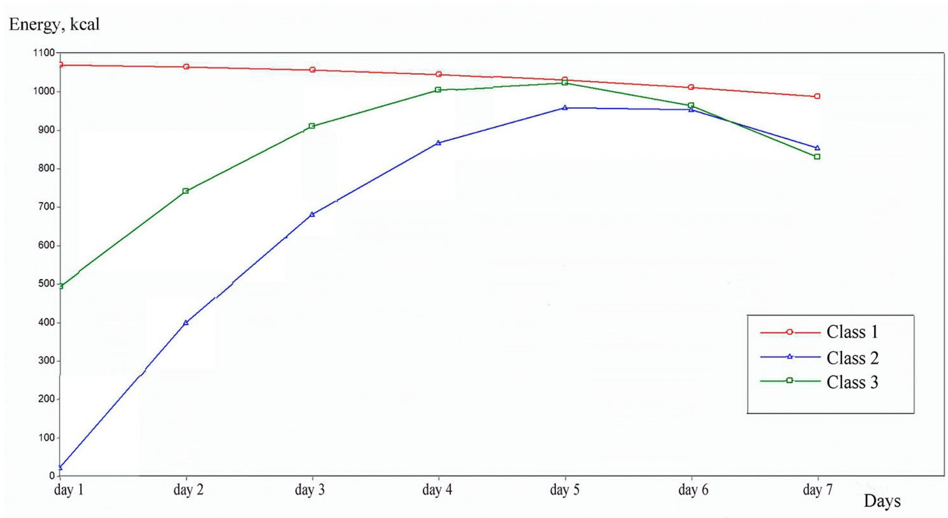

Fig. 2 Three different energy intake curve classes

Table 2 Relationship between energy intake and blood indexes or outcomes

	beta	p
ΔAlb	−0.00044	0.648
ΔTP	−0.00201	0.125
ΔHb	−0.00137	0.669
Occurrence of adverse events	0.000354	0.558
mRS at 3 months	6.76E-07	0.998
ΔBarthel	0.000205	0.974
EQ at 3 months	−0.00060	0.914

ΔAlb, change in albumin at day 7 relative to at admission; ΔTP, change in total protein at day 7 relative to at admission; ΔHb, change in hemoglobin at day 7 relative to at admission; ΔBarthel, change in Barthel Index at 3 months relative to at admission; mRS, modified Rankin score; EQ, the European Quality of Life Measurement Scale

Table 3 The relationship between energy intake curve classes and outcomes

	beta	*p*
Class1	Reference	
Occurrence of adverse events		
Class 2	−0.435	0.507
Class3	−0.364	0.322
mRS at 3 months		
Class 2	0.0712	0.822
Class 3	−0.0509	0.79
ΔBarthel		
Class 2	−5.495	0.405
Class 3	−2.440	0.541
EQ at 3 months		
Class 2	1.494	0.792
Class 3	1.850	0.59

with occurrence of adverse events (all $p>0.05$, data not shown).

Discussion

The main finding of this study on patients receiving enteral nutrition after ischemic stroke was that serum albumin and total protein values during the first week were positively correlated with three outcome markers: modified Rankin scale; Barthel Index; and European Quality of Life Measurement Scale. The timing of placement of enteral feeding tubes after the occurrence of stroke has received attention as a potentially important determinant in outcomes [21–23]. In this study, all patients were given enteral nutrition within 48 h, which accords with current guidelines and expert consensus recommendations, so the timing of gastric tube insertion was not addressed [1, 24]. We registered the daily intake of energy, protein, carbohydrates, and fats in stroke patients admitted for enteral nutrition for more than 7 days. LCGM was used to classify energy curves, but, unfortunately, none fit the three modes well, our cohort of patients was unable to provide this evidence. However, when we used LRT bootstrap to analyze the relationship between the values of nutrition-related blood indicators and outcomes, changes in the indicators one week after admission were independently associated with good stroke outcomes. These findings suggest that parenteral nutrition support for acute ischemic stroke patients during their early hospitalization (within one week after admission) improves their outcomes.

Previous literature suggested that Serum biomarkers was associated with the prognosis of ischemic stroke [25], may help predict the prognosis of critically ill patients and make early decisions for their treatment [26]. Among the numerous biomarkers, serum albumin,

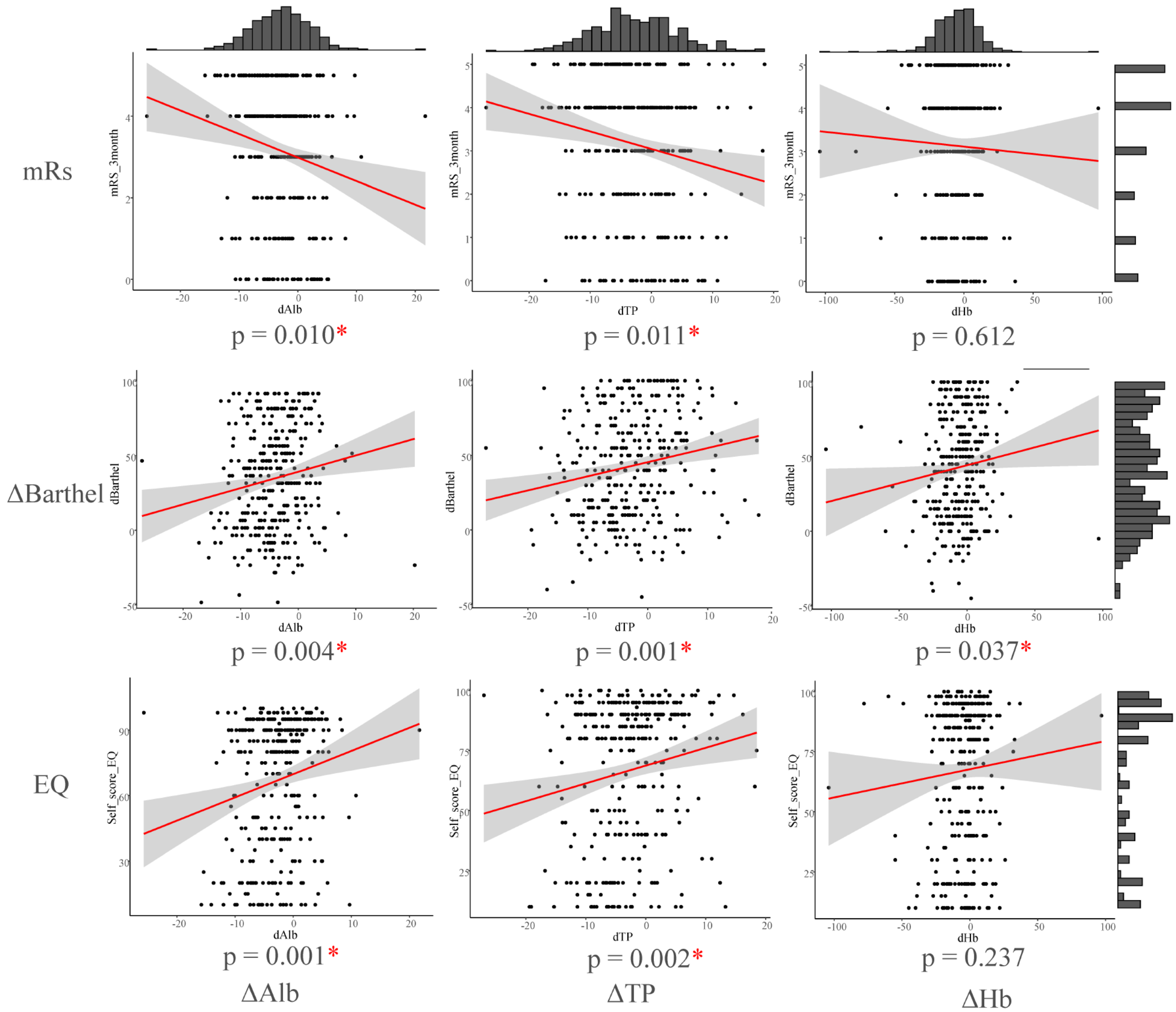

Fig. 3 Changes in nutrition-related blood indicators and patients' clinical outcomes. mRs, Modified Rankin Scale; ΔBarthel, change in Barthel Index at 3 months relative to at admission; EQ, European Quality of Life Measurement Scale; ΔAlb, change in albumin at day 7 relative to at admission; ΔTP, change in total protein at day 7 relative to at admission; ΔHb, change in hemoglobin at day 7 relative to at admission. * $P<0.05$

total protein and hemoglobin are commonly used predictors of morbidity and mortality in critically ill patients [27–28]. A relatively high level decreases the risk of poor outcomes in patients with acute ischemic stroke [29–30]. Meanwhile, we need to note that the nutritional status of patients at admission would help decrease the risk of poor outcomes, but cannot be intervened easy, especially the impact of changes in nutritional blood indicators on patient outcomes after nutrition management.

An inverse relationship between the concentration of serum albumin, stroke risk, and functional outcome has been described [31], and the prognostic capability of the serum albumin value in acute ischemic stroke has been demonstrated by the effect of serum albumin at admission on patients' functional outcome [32–33]. Investigators of these studies concluded that trials should be conducted to determine if correction of hypoalbuminemia in acute ischemic stroke patients would decrease the risk of poor outcomes. Patients with low serum total protein levels are prone to malnutrition, which may be related to their low protein reserves, reduced intake, and high disease-related consumption of nutrients. Our findings on serum albumin and total serum protein values in relation to outcomes in acute ischemic stroke patients are in agreement with the published results. Hemoglobin also is an indicator that may reflect the risk of malnutrition in older adults; [34] it can reflect iron metabolism and the body's protein status. However, in the present study, changes in hemoglobin were only weakly correlated with the outcome indicators: hemoglobin concentrations were positively correlated with Barthel Index score but not with the EQ score or mRS score. Our study has limitations. First, it is a retrospective cohort study conducted at a single site, so the findings have limited generalizability. Second, the amount of nutritional intake was evaluated at only one week, so our findings do not reflect patients' nutritional intake during the overall hospitalization. Finally, our study is a retrospective study, with unpredictable consequences due to uncertain data collection. Hence, prospective studies with a larger number and diverse population of patients carried out for a longer duration are required to determine whether early nutritional intervention improves stroke-patient outcomes.

Conclusion

Improved nutrition-related blood indicators one week after admission were independently associated with good stroke outcomes in ischemic stroke patients. Enteral nutritional support for these patients during early hospitalization appears to be important for their care.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03812-y.

Supplementary Material 1

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Author contributions

R.W. and L.C. wrote the main manuscript text and prepared the figures and tables. R.W., YY.H., and P.Z. performed the data collection. R.W., L.C. and L. F. performed the study design and data interpretation. All authors contributed to the design of the research, to the analysis and interpretation of the data, and to writing, reviewing and editing. All authors approved the final version of the manuscript submitted for publication. All authors reviewed and approved the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The research data in the study was retrieved from the Research Database. The datasets were fully de-identified and there were no patient identifiers, therefore, informed consent was not required from all participants. The study was approved by the ethics committee of the West China Hospital, Sichuan University (Approval number: 2023(1845)). All methods were carried out in accordance with the principles expressed in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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