

# Nutritional Status, Dietary Patterns, and Prealbumin as Prognostic Factors in Stroke: An Observational Study

Alparslan Koç<sup>1,\*</sup>, Alevtina Ersoy<sup>2</sup>

<sup>1</sup>Department of Anesthesiology and Reanimation, Erzincan Binali Yıldırım University Menguçek Gazi Training and Research Hospital, Erzincan, Turkey

<sup>2</sup>Department of Neurology, Erzincan Binali Yıldırım University Menguçek Gazi Training and Research Hospital, Erzincan, Turkey

## Correspondence

**Alparslan Koç**, Department of Anesthesiology and Reanimation, Erzincan Binali Yıldırım University Menguçek Gazi Training and Research Hospital, Erzincan, Turkey

Email: dralparslankoc@gmail.com

## History

- Received: May 13, 2024
- Accepted: Jul 24, 2024
- Published Online: Jul 31, 2024

DOI : 10.15419/bmrat.v11i7.904



## Copyright

© Biomedpress. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International license.



## ABSTRACT

**Introduction:** Prealbumin is a protein synthesized by the choroid plexus and liver, playing integral roles in the transport of thyroxine and retinol. Its serum levels are known to decrease in response to conditions such as inflammation, protein deficiency, end-stage liver disease, and malignancy. Notably, decreased serum prealbumin levels have been negatively correlated with the severity of stroke. Given this context, understanding factors that predict functional outcomes and mortality in stroke patients is crucial, particularly the potential role of nutritional status and prealbumin levels. **Methods:** This study targeted a patient population aged 18 to 100 years who were treated for stroke. We systematically recorded levels of prealbumin, albumin, hemoglobin, and the BUN/Cre ratio at three time intervals: on admission, the 5th day, and the 9th day post-admission. In addition, we assessed the severity and functional outcomes using the NIHSS and mRS scores at admission, the 9th day, and upon discharge. Other recorded parameters included Body Mass Index (BMI), daily caloric requirements, NRS-2002 nutritional risk screening scores, chronic disease presence, length of hospital stay, history of infarction, TOAST classification, and dietary patterns. Our study included a total of 57 patients. **Results:** Our findings indicate that there was no significant difference in age between nonsurviving and surviving stroke patients, although deceased patients tended to be older. Notably, prealbumin and albumin levels were significantly higher in surviving patients ( $p < 0.05$ ). The BUN/Cre ratio showed no difference between the groups at the time of admission, but its values on the 5th and 9th days were significantly elevated in nonsurvivors ( $p < 0.01$ ). Furthermore, our analysis revealed that an increase in prealbumin and albumin levels positively influenced patient outcomes. Conversely, higher BUN/Cre ratios and NIHSS scores were associated with poor outcomes, with these differences reaching statistical significance ( $p < 0.01$ ). **Conclusion:** The study established a clear association between prealbumin and albumin levels, the BUN/Cre ratio, NIHSS and mRS scores, and overall nutritional status with the functional outcomes and mortality rates in stroke patients. Our results underscore the importance of closely monitoring nutritional status and these specific biochemical markers as part of the comprehensive management of stroke patients to potentially improve their outcomes.

**Key words:** Malnutrition, stroke, prealbumin, mortality, functional outcome

## INTRODUCTION

In developed countries, stroke mortality ranks after ischemic heart disease and cancer<sup>1</sup>. Malnutrition represents a significant, preventable consequence impacting many stroke victims, typically defined as a protein-energy deficiency. It was reported in 16.3% of patients hospitalized with acute stroke, with this rate increasing to 26.4% by day 7<sup>2</sup>. Malnutrition is associated with fatigue, muscle weakness, and the loss of muscle mass. Additionally, it causes immunosuppression, impaired intestinal function, and hospital infections<sup>3</sup>. After a stroke, levels of plasma cortisol, catecholamines, interleukins, and glucagon, along with acute phase reactants, increase as part of the acute stress response, leading to the rapid loss of muscle mass<sup>4</sup>. It has been demonstrated that just ten days of bed rest can result in a 30% decrease in muscle protein

synthesis and a 6% reduction in leg muscle mass, culminating in a 16% loss of muscle strength in healthy older adults<sup>5</sup>.

Prealbumin is a protein primarily synthesized by the choroid plexus and liver, involved in the transport of thyroxine and retinol. Decreases in serum prealbumin levels, which negatively correlate with stroke severity, can be caused by inflammation, protein deficiency, end-stage liver disease, and malignancy<sup>6,7</sup>. As it is a negative acute-phase reactant, serum concentrations of prealbumin decrease rapidly due to reduced mRNA expression<sup>8</sup>. Malnutrition is expected to occur in the acute phase of a stroke. Initial malnutrition may lead to more complications post-stroke, and it has been reported that malnutrition in the first week predicts poor outcomes for three months<sup>9</sup>. Therefore, nutritional assessment upon hospital admission and

Cite this article : Koç A, Ersoy A. **Nutritional Status, Dietary Patterns, and Prealbumin as Prognostic Factors in Stroke: An Observational Study.** *Biomed. Res. Ther.* 2024; 11(7):6573-6582.

the early identification of patients at risk of malnutrition may be necessary for effective treatment. This study aimed to investigate whether the nutritional status, dietary pattern, and prealbumin levels can predict functional outcomes and mortality in stroke patients.

## METHODS

After obtaining approval, patients aged 18 to 100 years who were treated in the hospital for a stroke were included in the study. Patients were followed and observed for at least 10 days until discharge or death, and laboratory findings and scores were recorded. Informed consent was obtained from all patients or their relatives. In addition, prealbumin, albumin, hemoglobin, and BUN/Cre ratio were recorded on days 0, 5, and 9. The National Institutes of Health Stroke Scale (NIHSS) score and the modified Rankin scale (mRS) score were recorded on admission, on the 9th day, and at discharge. Body mass index (BMI), daily caloric requirements, chronic diseases, length of hospital stay, history of infarction, Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification, dietary pattern, and nutritional risk screening (NRS-2002) scores were also recorded. Oral feeding was preferred when possible, and in patients with poor swallowing function, a nasogastric catheter was placed, and enteral nutrition was started. For patients who could not tolerate enteral nutrition, parenteral nutrition was preferred. Patients who died within ten days after hospitalization, were transferred to the intensive care unit, had liver failure or chronic renal failure, had intracranial hemorrhage, or who experienced further complications were excluded from the study.

### TOAST Classification

According to this classification, patients are divided into five subtypes:

- a. large artery atherosclerosis,
- b. cardioembolism,
- c. small vessel occlusion,
- d. other determined etiologies, and
- e. undetermined etiologies

### NIHSS

The NIHSS, a systematic assessment tool measuring the most common neurological deficits in acute stroke patients, includes assessments of the level of consciousness, gaze, visual field, visual impairment, motor performance of the extremities, sensory deficits,

coordination (ataxia), speech (aphasia), and language (dysarthria), and assesses semiattention (neglect). The scale was created for rapid assessment of neurological function in the early post-stroke period. "A score of 0 is considered normal for all parameters, so the higher the score, the worse the neurological deficit (the highest possible score is 42)."

### mRS

The mRS, used in the follow-up of stroke patients, is a scale that determines the severity of stroke and is used to identify dependency and assess functional improvement (Table 1). According to this scale, those who score 1 or 2 can continue to live independently, and those who score 3 or more can continue to live as dependents.

### NRS-2002

The NRS-2002 scoreboard comprises three parts: disease severity, nutritional status, and age. Scores  $\geq 3$  points indicate the presence of nutritional risk and the need for nutritional therapy.

### Statistical Analyses

The results are expressed as percentages for categorical variables, means for normally distributed variables, and medians (interquartile ranges) for non-normally distributed continuous variables. Continuous variables were compared using t-tests and Mann-Whitney tests, while categorical variables were compared using chi-square tests. Correlations between continuous variables were assessed with Pearson's or Spearman's rank correlation coefficient, depending on distribution status. The severity of the cerebrovascular event was classified as "no or mild (mRS score 0-2: no or only mild neurological symptoms) or severe (mRS score 3-6: moderate or severe disability)" based on the mRS score on day 9. A logistic regression model was used to examine the relationships between the measured parameters, mortality, and high mRS score. Adjusted univariate and multivariate models and reported odds ratios (ORs) and 95% confidence intervals (CIs) were used for all major outcome predictors. A binary logistic regression model that included hypertension, diabetes mellitus, history of stroke, atrial fibrillation, and TOAST subtype was used to examine the ability of these variables to predict the group status. Analyses were performed using the SPSS software package (version 26.0), and  $p < 0.05$  was considered to indicate statistical significance.

**Table 1: The Modified Rankin Scale (mRS)**

Grade	0	1	2	3	4	5	6
Descriptio	No symptoms at all	No significant disability despite symptoms: able to carry out all usual duties and activities	Slight disability: unable to carry out all previous activities but able to look after own affairs without assistance	Moderate disability: requiring some help, but able to walk without assistance	Moderately severe disability: unable to walk without assistance and unable to attend to own bodily needs	Severe disability: bedridden, incontinent, and requiring constant nursing care and attention	Death

### Ethical Principles

The study was carried out in accordance with the Helsinki Declaration of 1975. The ethics committee approval number is Erzurum City Hospital, Erzurum, Turkey (Date: 20.06.2022 No: 2022/08-95).

### RESULTS

Among the 84 patients included in the study, 27 were excluded. Of these, 8 patients died within the first 10 days, 3 had chronic renal failure, 5 experienced intracranial hemorrhage, and 11 were admitted to the intensive care unit due to respiratory distress, sepsis, and the need for anti-edema treatment. The characteristics of the study concerning mortality are shown in **Table 2**.

Of the 57 patients remaining in the study, 20 died after the first 10 days of follow-up. There was no significant difference between the non-surviving and surviving patients, although the deceased patients were older. Prealbumin and albumin levels were significantly higher in surviving patients ( $p < 0.05$ ). When the BUN/Cre ratio was evaluated, there was no difference in admission values. However, the values on the 5<sup>th</sup> and 9<sup>th</sup> days were significantly higher in patients who did not survive ( $p < 0.01$ ). Survival was higher in patients who were enteral-fed ( $p < 0.01$ ). The NIHSS score was significantly higher in patients who did not survive ( $p < 0.01$ ). Compared to baseline and on the 9<sup>th</sup> day, the NIHSS score increased in patients who did not survive and decreased in patients who survived (**Figure 1 a**).

When considering the initial and 9th-day mRS scores, the mRS scores of the nonsurviving patients were significantly higher ( $p < 0.01$ ) (**Figure 1 b**). According to the TOAST classification, the etiologies were cardioembolism in 20 (47.4%) cases, small vessel occlusion in 14 (24.6%), large artery atherosclerosis in 7 (12.3%), and other etiologies in 0 (0%). The size of the

affected vessel was significantly associated with survival ( $p < 0.01$ ). The color Doppler USG findings were as follows: atherosclerotic changes without stenosis in 42 (73.7%), symptomatic internal carotid artery (ICA) stenosis in 5 (8.8%), asymptomatic ICA in 5 (8.8%), bilateral ICA stenosis in 2 (3.5%), and not applicable in 3 patients (5.3%). There was no significant difference in carotid Doppler findings regarding survival. Only the presence of hypertension among chronic diseases was associated with mortality ( $p < 0.01$ ). The results of the logistic regression model for predicting mortality are summarized in **Table 3**.

According to the ROC analysis, prealbumin was a strong predictor of mortality, with an AUC of 0.686 (95% CI 0.523-0.848) on day 5. The optimal cutoff value for predicting mortality was 0.085 g/L, with a sensitivity of 86% and specificity of 50%. The results of the ROC analysis for other independent positive and negative predictors are summarized in **Table 4** and **Figure 2**.

Although there was no correlation between prealbumin levels and initial NIHSS scores, there was a negative, strong correlation with NIHSS scores on the 9<sup>th</sup> day ( $r = -0.716$ ,  $p < 0.01$ ). While there was no correlation between the BUN/Cre ratio and NIHSS score on the 0th day, there was a weak positive correlation on the 9<sup>th</sup> day ( $r = 0.435$ ,  $p < 0.01$ ). There was no correlation between albumin levels and NIHSS scores on the 0<sup>th</sup> day, similar to the findings for the BUN/Cre ratio. However, there was a negative correlation on the 9th day ( $r = -0.480$ ,  $p < 0.01$ ).

Patients were divided into two groups according to their mRS scores and evaluated separately. Those with mRS scores of 0-2 (no neurological deficit or low deficit) had a favorable outcome, whereas those with mRS scores of 3-6 (severe deficit) were classified as having unfavorable outcomes. As shown in **Table 4**, increases in prealbumin and albumin levels positively affected favorable outcomes. In contrast, the

**Table 2: Baseline characteristics of study population**

	N	Survivor	Non-survivor	p-value
Age (Mean ± SD)	75.42 ± 12.75	74.08 ± 10.15	77.9 ± 16.55	0.35
Male/Female	114 (58/56)	74 (34/40)	40 (24/16)	0.31
BMI	26.78 ± 3.78	26.66 ± 4.0	25.87 ± 3.1	0.84
NRS-2002	3.65 ± 1.3	3.73 ± 1.36	3.5 ± 1.23	0.52
Prealbumin 0 <sup>th</sup> day (Mean ± SD)	0.15 ± 0.06	0.16 ± 0.06	0.13 ± 0.07	0.04
Prealbumin 5 <sup>th</sup> day (Mean ± SD)	0.12 ± 0.06	0.13 ± 0.06	0.10 ± 0.07	0.02
Prealbumin 9 <sup>th</sup> day (Mean ± SD)	0.12 ± 0.06	0.13 ± 0.06	0.09 ± 0.07	0.03
Bun/Cre 0 <sup>th</sup> day (Mean ± SD)	21.38 ± 7.88	21.49 ± 9.26	21.17 ± 4.53	0.88
Bun/Cre 5 <sup>th</sup> day (Mean ± SD)	27.26 ± 8.35	25.03 ± 8.31	31.38 ± 6.86	0.00
Bun/Cre 9 <sup>th</sup> day (Mean ± SD)	28.51 ± 9.63	25.05 ± 8.82	34.9 ± 7.73	0.00
Albumin 0 <sup>th</sup> day (Mean ± SD)	36.65 ± 5.79	37.89 ± 4.57	34.36 ± 7.12	0.02
Albumin 5 <sup>th</sup> day (Mean ± SD)	31.23 ± 5.36	33.19 ± 4.13	27.6 ± 5.52	0.00
Albumin 9 <sup>th</sup> day (Mean ± SD)	29.19 ± 5.41	31.66 ± 4.27	24.64 ± 4.24	0.00
Hemoglobin g/dL 0 <sup>th</sup> day (Mean± SD)	13.01 ± 2.26	12.93 ± 2.02	13.18 ± 2.69	0.48
Hemoglobin g/dL 5 <sup>th</sup> day (Mean± SD)	12.33 ± 1.83	12.5 ± 1.62	12.02 ± 2.18	0.34
Hemoglobin g/dL 9 <sup>th</sup> day (Mean± SD)	11.71 ± 2.08	11.96 ± 1.63	11.24 ± 2.7	0.21
Stay of hospital (day)	18.56 ± 12.6	16.65 ± 9.5	22.1 ± 16.64	0.61
Hypertension, n (%)	74 (64.9)	54 (72.9)	14 (35)	0.00
Cardiovascular disease, n (%)	30 (26.3)	20 (27.02)	10 (25)	0.86
Hyperlipidemia, n (%)	8 (7)	6 (8.1)	2 (5)	0.56
Diabetes mellitus, n (%)	34 (29.82)	26 (35.13)	8 (20)	0.23
Atrial fibrillation, n (%)	26 (22.8)	14 (18.91)	12 (30)	0.26
Past cerebral enfarct, n (%)	26 (22.8)	16 (21.62)	10 (25)	0.50
Methallic heart valve, n (%)	8 (7)	4 (5.4)	4 (10)	0.43
tPA therapy n (%)	38 (33.33)	26 (35.139)	12 (30)	0.69
Anticoagulation therapy, n (%)	74 (64.91)	46 (62.16)	28 (70)	0.55
Antiplatelet therapy, n (%)	42 (36.84)	30 (40.5)	12 (30)	0.43
NIHS 0 <sup>th</sup> day (Mean ± SD)	14.18 ± 5.6	11.95 ± 4.87	18.30 ± 4.71	0.00
NIHS 9 <sup>th</sup> day (Mean ± SD)	12.49 ± 7.9	8.51 ± 6	19.85 ± 5.23	0.00
NIHS discharge (Mean ± SD)		7.3 ± 5.3		
MRS 0 <sup>th</sup> day (Mean ± SD)	4.35 ± 0.83	4.14 ± 0.88	4.75 ± 0.55	0.00
MRS 9 <sup>th</sup> day (Mean ± SD)	3.77 ± 1.7	2.95 ± 1.49	5.3 ± 0.73	0.00
MRS discharge (Mean ± SD)		2.61 ± 1.87		
<b>TOAST classification</b>				
a.) Large artery, n (%)	14 (12.3)	10 (71.4)	4 (37.6)	0.00
b.) Small vessels, n (%)	28 (24.6)	26 (92.85)	2 (7.15)	
c.) Cardioembolic, n (%)	32 (28.1)	16 (50)	16 (50)	
d.) Other cause, n (%)	40 (47.4)	28 (70)	12 (30)	

**Abbreviations:** BMI: Body Mass Index, BUN/Cre: Blood Urea Nitrogen/Creatinine, mRS: modified Rankin scale, NIHSS: National Institutes of Health Stroke Scale, SD: Standard deviation, TOAST: Trial of Org 10172 in Acute Stroke Treatment

**Table 3: Independent predictors of mortality**

	OR (95% CI)	Beta	p-value	OR
Prealbumin 0 <sup>th</sup> day	0.00 - 0.00	-	0.00	-
		31.926		31.926
Bun/Cre 9 <sup>th</sup> day	1.007 - 1.222	0.104	0.03	1.110
Albumin 9 <sup>th</sup> day	0.500 - 0.856	-0.424	0.02	-0.654
Hypertension	1.555 - 16.168	1.612	0.00	5.014
Parenteral nutrition	4.71 - 93.944	3.047	0.00	21.048
NIHSS 0 <sup>th</sup> day	1.124 - 1.512	0.265	0.00	1.304
mRS 0 <sup>th</sup> day	1.326 - 11.108	1.345	0.01	3.837

**Abbreviations:** NIHSS: National Institutes of Health Stroke Scale, mRS: Modified Rankin Scale, CI: confidence intervals, OR: Odds ratio, BUN/Cre: Blood nitrogen to creatinin ratio

**Table 4: Best cut-off value, sensitivity and specificity of independent predictors for mortality**

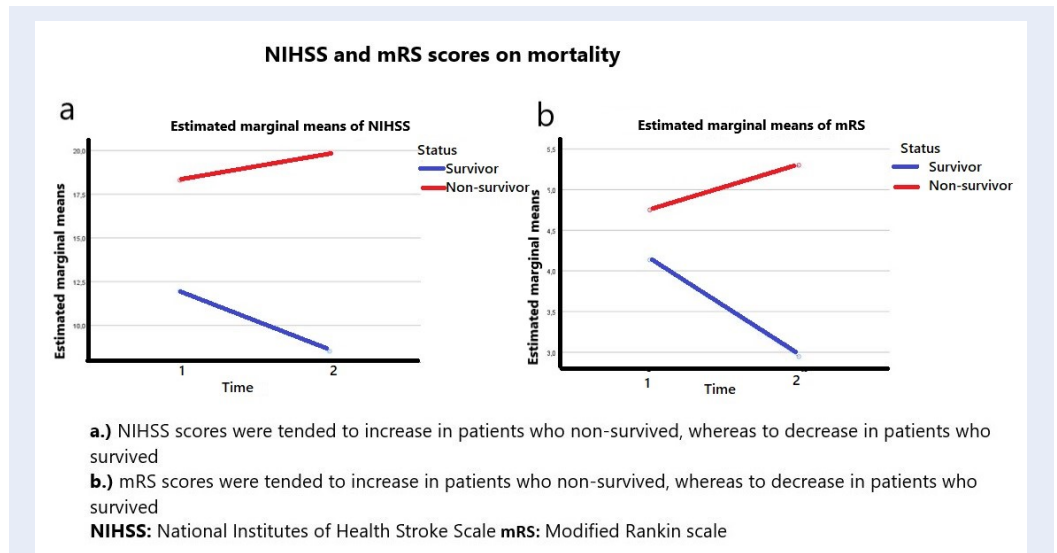
	AUC (95% CI)	Cutt off	p-value	Sensivity (%)	Specificity (%)
<b>Negative predictors</b>					
Prealbümin 0 <sup>th</sup> day	0.662 (0.506 - .0818)	0.10	0.045	86	40
Prealbümin 5 <sup>th</sup> day	0.686 (0.523 - 0.848)	0.085	0.021	89	50
Prealbümin 9 <sup>th</sup> day	0.672 (0.513 - 0.830)	0.075	0.034	91	40
Albümin 0 <sup>th</sup> day	0.657 (0.510 - 0.804)	39.4	0.052	48	85
Albümin 5 <sup>th</sup> day	0.782 (0.657 - 0.906)	32.2	0.000	59	85
Albümin 9 <sup>th</sup> day	0.869 (0.774 - 0.964)	28.5	0.000	75	90
<b>Positive predictors</b>					
BUN/Cre 0 <sup>th</sup> day	0.662 (0.506 - 0.818)	19.85	0.50	70	48
BUN/Cre 5 <sup>th</sup> day	0.686 (0.523 - 0.848)	28.75	0.00	70	75
BUN/Cre 9 <sup>th</sup> day	0.672 (0.513 - 0.830)	28.50	0.00	90	73
mRS 0 <sup>th</sup> day	0.714 (0.575 - 0.852)	4.50	0.00	80	62
NIHSS 0 <sup>th</sup> day	0.822 (0.713 - 0.931)	15.50	0.00	70	79

**Abbreviations:** AUC: Area under curve, BUN/Cre: Blood urea nitrogen to creatinine ratio, NIHSS: National Institutes of Health Stroke Scale, mRS: Modified Rankin scale, CI: Confidence intervals

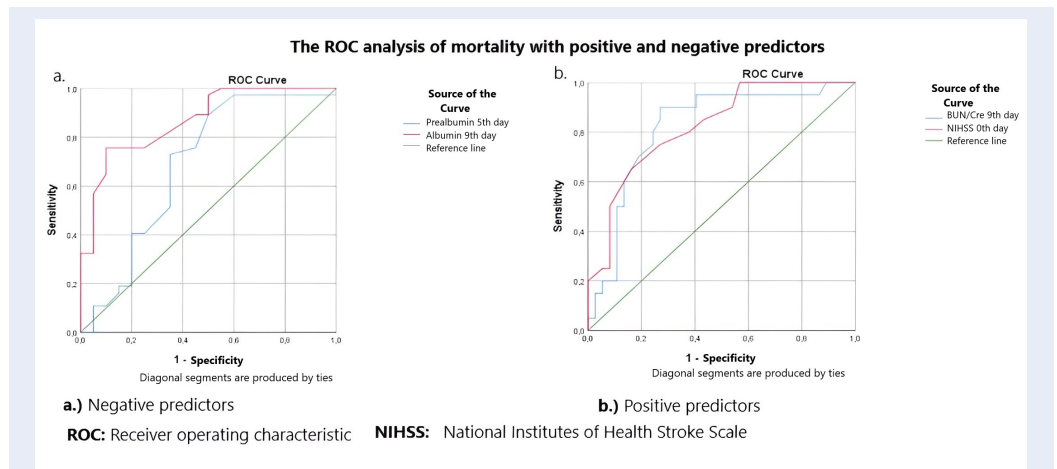
**Table 5: Best cut-off value, sensitivity and specificity of independent predictors for functional outcome**

	AUC (95%)	Cutt-off	p-value	Sensivity (%)	Specificity (%)
<b>Negative predictors</b>					
Prealbumin 0 <sup>th</sup> day	0.656 (0.507 - 0.806)	0.145	0.04	59	74
Albumin 9 <sup>th</sup> day	0.869 (0.774 - 0.964)	28.5	0.00	77	63
<b>Positive predictors</b>					
BUN/Cre 9 <sup>th</sup> day	0.747 (0.615 - 0.878)	28.50	0.00	65	77
NIHSS 0 <sup>th</sup> day	0.844 (0.737 - 0.950)	12.50	0.00	80	77

**Abbreviations:** AUC: Area Under the Curve, BUN/Cre: Blood Urea Nitrogen/Creatinine, NIHSS: National Institutes of Health Stroke Scale



**Figure 1: The NIHSS and mRS scores in patients on the 9th day. (a)** NIHSS scores tended to increase in patients who survived, whereas they tended to decrease in patients who survived. **(b)** mRS scores tended to increase in patients who survived, whereas they tended to decrease in patients who survived.



**Figure 2: ROC analysis of mortality with positive and negative predictors. (a)** Negative predictors, **(b)** Positive predictors.

BUN/Cre ratio and NIHSS score had a negative effect on favorable outcomes, with a significant difference ( $p < 0.01$ ). Upon examining other independent predictors, an unfavorable outcome was observed in patients with diabetes mellitus and those receiving par-enteral nutrition, with the difference being significant ( $p < 0.05$ ). The results of the ROC analysis of other independent positive and negative predictors are summarized in **Table 5** and **Figure 3**.

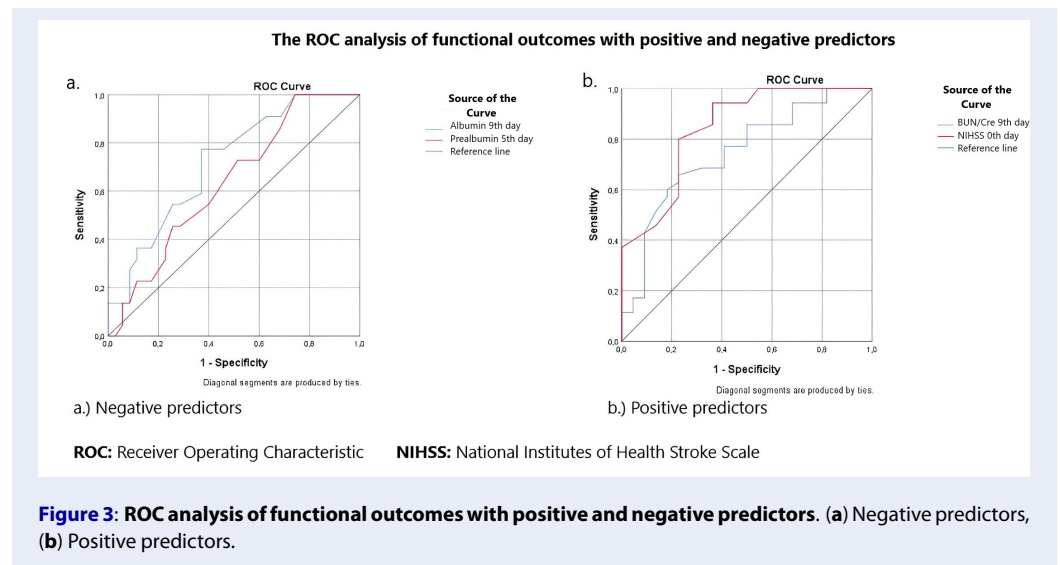
No correlation was found between the NIHSS score or mRS score and age, BMI, NRS-2002 score, pre-

albumin level, BUN/Cre ratio, albumin level, or hemoglobin level when assessing the length of the hospital stay. Additionally, no difference was discovered in the TOAST classification or functional outcome.

## DISCUSSION

The definition of malnutrition, an essential preventable complication, is used to describe several nutritional abnormalities and usually refers to protein-energy inadequacy resulting from a long-term nega-





tive balance of energy and protein<sup>10</sup>. When malnutrition occurs, all fat stores are depleted, and fatty acids are released for energy. However, since fatty acids cannot cross the blood–brain barrier, they cannot be used as an energy source for the brain. Although fatty acids produced in the liver can generate ketone bodies that can cross the blood–brain barrier, they are not an effective energy source for neurons. In stroke patients with reduced oral intake, amino acids become an energy source during the rapid breakdown of muscle protein. This process, along with inflammation, hormonal deficits, and inactivity, leads to a clinical picture with the potential to rapidly develop sarcopenia<sup>11</sup>.

Prealbumin, a plasma protein synthesized by the liver, is an essential predictor of nutritional status. A decrease in prealbumin reflects possible inadequate nutrient intake. Previous studies have shown that low prealbumin levels are associated with poor prognosis in patients with heart failure<sup>12</sup>. Although strong evidence links malnutrition to poor outcomes in ischemic stroke patients<sup>13</sup>, few studies have connected prealbumin levels to mortality in these patients<sup>14</sup>. This article evaluates whether serum prealbumin levels influence functional outcomes and mortality in patients with cerebral infarction.

Several pathophysiological mechanisms can be proposed to explain the link between low prealbumin levels and poor outcomes. Low prealbumin levels likely lead to malnutrition and unfavorable outcomes. The transport of thyroid hormones is the basis for an intriguing hypothesis that may explain the relationship between prealbumin concentration and stroke

severity. Prealbumin transports these hormones from the blood to the cerebrospinal fluid (CSF) through the blood-CSF barrier<sup>15</sup>. Experimental studies have shown that a reduction in prealbumin levels impairs cell survival after ischemic brain injury<sup>16</sup>. Therefore, during cerebral ischemia, damage to the choroid plexus and disrupted blood-CSF barrier may affect the distribution of thyroid hormones in the CSF (and eventually in brain tissue) with decreased prealbumin levels.

Studies have indicated that prealbumin levels may predict mortality in patients with heart failure<sup>17</sup>, renal failure<sup>18</sup>, and coronavirus disease 2019 (COVID-19) pneumonia<sup>19</sup>. A recent study reported an association between prealbumin levels and mortality<sup>14</sup>. In this study, we found that a decrease in prealbumin levels on days 0 and 9 significantly increased mortality. Dehydration is a significant cause of morbidity and mortality in elderly individuals. Many stroke patients become dehydrated, worsening functional outcomes<sup>20</sup>. Dehydration can affect acutely paralyzed patients in several ways, including decreased cerebral blood flow<sup>21</sup>, increased fatigue<sup>22</sup>, and impaired neuroplasticity<sup>23</sup>. Another hypothesis is that dehydration increases blood viscosity and reduces cerebral blood flow due to decreased intravascular volume. Increased hematocrit has been associated with a larger infarct volume in patients with cerebral infarction<sup>24</sup>. A BUN/Cr ratio  $\geq 20$  is a standard laboratory test indicating prerenal azotemia and dehydration. Previous studies have reported an increased BUN/Cr ratio in acute cerebral infarction patients. A BUN/Cr ratio greater than 15 may be a novel predictor of stroke progression<sup>25</sup>. In our study, we evaluated the BUN/Cr

ratios. Although the baseline values were not associated with mortality, the follow-up BUN/Cr ratios were associated with mortality.

Albumin, synthesized by the liver, serves as a transporter of endogenous and exogenous substances in the blood. It has neuroprotective effects in animal models of ischemic stroke<sup>26</sup>. A recent study showed that decreased albumin levels might be associated with mortality in stroke patients<sup>27</sup>. Our study revealed that low albumin levels were associated with mortality, similar to the findings in these studies. The literature has shown that malnutrition in stroke patients can be linked with mortality<sup>28</sup>. Although the association between nutritional status and mortality has not been definitively established in the literature, we found a greater survival rate in patients who received enteral nutrition.

We found that high NIHSS scores increased mortality. Some studies support these findings<sup>29-31</sup>. The strong negative correlation ( $r=-0.716$ ,  $p < 0.01$ ) between prealbumin levels and NIHSS scores in our correlation analysis supports our hypothesis. High mRS scores at admission were associated with mortality. The findings of Deljavan *et al.* support this hypothesis<sup>32</sup>.

We found that high prealbumin and albumin levels positively affected brain functions, which we classified using the mRS score after stroke. In their study, Heifeng *et al.* reported that low prealbumin and albumin levels were associated with unfavorable outcomes<sup>33</sup>. An increase in the BUN/Cr ratio was associated with an unfavorable outcome. Eizenberg *et al.* came to similar conclusions<sup>34</sup>, attributing this result to low intravascular volume. Wu *et al.*, in their study, reported that high NIHSS scores were associated with poor cerebral function<sup>35</sup>. Similarly, high NIHSS scores in this study significantly affected the loss of cerebral function. Although sex and age were not found to be associated with unfavorable outcomes in our study, there are studies on poor cerebral function in older women after stroke<sup>36,37</sup>. Xiaomin *et al.* also concluded that patients who received enteral nutrition had lower unfavorable outcomes than those who received parenteral nutrition, as we found in our study<sup>38</sup>.

Our study has several limitations. It was conducted in a single hospital, and our study cohort was limited to a small group. Only hypotheses were tested, and the sample size was relatively small, which could further limit the generalizability of the results. Future research with larger, diverse cohorts would be beneficial to confirm these observations and further elucidate the mechanisms. Despite these limitations, our study assessed mortality and functional outcomes and drew meaningful conclusions.

## CONCLUSION

In this study, we found that prealbumin, albumin levels, the BUN/Cr ratio, NIHSS, mRS scores, and nutritional status were associated with functional outcomes and mortality, confirming the results of previous studies. We believe these results will be helpful in risk stratification in stroke patients. Although the nutrition team is constantly vigilant, the patient's family's inadequate knowledge of care procedures may have influenced the selection of nutrition forms. Future studies with larger datasets will determine which variables are most important concerning mortality and functional outcomes.

## ABBREVIATIONS

**AUC:** Area Under the Curve, **BMI:** Body Mass Index, **BUN/Cr:** Blood Urea Nitrogen/Creatinine, **CI:** Confidence Interval, **COVID-19:** Coronavirus Disease 19, **CSF:** Cerebrospinal Fluid, **ICA:** Internal Carotid Artery, **mRNA:** Messenger Ribonucleic Acid, **mRS:** modified Rankin scale, **NIHSS:** National Institutes of Health Stroke Scale, **NRS-2002:** Nutritional Risk Screening 2002, **ORs:** Odds Ratios, **ROC:** Receiver Operating Characteristic, **SPSS:** Statistical Package for the Social Sciences, **TOAST:** Trial of Org 10172 in Acute Stroke Treatment, **USG:** Ultrasonography

## ACKNOWLEDGMENTS

None

## AUTHOR'S CONTRIBUTIONS

Koç A.: developed the procedure, analyzed the main data, interpreted the results, wrote the initial draft of the paper, and finalized the manuscript. Ersoy A.: performed the clinical portion of the study and sample collection. All authors have read and approved the final version of the article.

## FUNDING

None

## AVAILABILITY OF DATA AND MATERIALS

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was carried out in accordance with the Helsinki Declaration of 1975. The ethics committee approval number is Erzurum City Hospital, Erzurum,



Turkey (Date: 20.06.2022 No: 2022/08-95. Before initiating any procedures, all patients provided informed consent by signing the appropriate documentation.

## CONSENT FOR PUBLICATION

Not applicable.

## COMPETING INTERESTS

The authors declare that they have no competing interests.

## REFERENCES

- Scherbakov N, Doehner W. Sarcopenia in stroke-facts and numbers on muscle loss accounting for disability after stroke. *Journal of Cachexia, Sarcopenia and Muscle*. 2011;2(1):5–8. PMID: 21475676. Available from: <https://doi.org/10.1007/s13539-011-0024-8>.
- Kim S, Byeon Y. Comparison of nutritional status indicators according to feeding methods in patients with acute stroke. *Nutritional Neuroscience*. 2014;17(3):138–44. PMID: 23863463. Available from: <https://doi.org/10.1179/1476830513Y.0000000078>.
- Klempir J, Sarbochova I, Ruzickova L, Bezuchova E, Gal O, Srp M. Guidelines for nutritional support in stroke. *Czech and Slovak Neurology and Neurosurgery*. 2020;83(6):667–73.
- Arsava EM, Aydoğdu İ, Güngör L, İşçT, Yaka E. Nutritional Approach and Treatment in Patients with Stroke, An Expert Opinion for Turkey. *Türk Noroloji Dergisi*. 2018;24(3):226–42. Available from: <https://doi.org/10.4274/tnd.92603>.
- Kortebein P, Ferrando A, Lombeida J, Wolfe R, Evans WJ. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. *Journal of the American Medical Association*. 2007;297(16):1772–4. PMID: 17456818. Available from: <https://doi.org/10.1001/jama.297.16.1772-b>.
- a Yi, Young V. Transthyretin (prealbumin) in health and disease: nutritional implications. *Annual review of nutrition*. 1994;14(1):495–533. PMID: 7946531. Available from: <https://doi.org/10.1146/annurev.nu.14.070194.002431>.
- Chang KC, Lee HC, Huang YC, Hung JW, Chiu HE, Chen JJ. Cost-effectiveness analysis of stroke management under a universal health insurance system. *Journal of the Neurological Sciences*. 2012;323(1-2):205–15. PMID: 23046751. Available from: <https://doi.org/10.1016/j.jns.2012.09.018>.
- Johnson AM, Merlini G, Sheldon J, Ichihara K, of Clinical Chemistry Scientific Division Committee on Plasma Proteins (C-PP) IF, (IFCC) LM. Clinical indications for plasma protein assays: transthyretin (prealbumin) in inflammation and malnutrition. *Clinical Chemistry and Laboratory Medicine*. 2007;45(3):419–26. PMID: 17378745. Available from: <https://doi.org/10.1515/CCLM.2007.051>.
- Yoo SH, Kim JS, Kwon SU, Yun SC, Koh JY, Kang DW. Undernutrition as a predictor of poor clinical outcomes in acute ischemic stroke patients. *Archives of Neurology*. 2008;65(1):39–43. PMID: 18195138. Available from: <https://doi.org/10.1001/archneurol.2007.12>.
- Corrigan ML, Escuro AA, Celestin J, Kirby DF. Nutrition in the stroke patient. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition*. 2011;26(3):242–52. Available from: <https://doi.org/10.1177/0884533611405795>.
- Hasselbalch SG, Knudsen GM, Jakobsen J, Hageman LP, Holm S, Paulson OB. Brain metabolism during short-term starvation in humans. *Journal of Cerebral Blood Flow and Metabolism*. 1994;14(1):125–31. PMID: 8263048. Available from: <https://doi.org/10.1038/jcbfm.1994.17>.
- Wang W, Ren D, Wang CS, Li T, Yao HC. High sensitivity C-reactive protein to prealbumin ratio measurement as a marker of the prognosis in acute coronary syndrome. *Scientific Reports*. 2019;9(1):11583. PMID: 31399624. Available from: <https://doi.org/10.1038/s41598-019-48189-y>.
- Shen HC, Chen HF, Peng LN, Lin MH, Chen LK, Liang CK. Impact of nutritional status on long-term functional outcomes of post-acute stroke patients in Taiwan. *Archives of Gerontology and Geriatrics*. 2011;53(2):e149–52. PMID: 20801531. Available from: <https://doi.org/10.1016/j.archger.2010.08.001>.
- Ambrosius W, Michalak S, Kazmierski R, Andrzejewska N, Kozubski W. Predictive value of serum transthyretin for outcome in acute ischemic stroke. *PLoS One*. 2017;12(6):e0179806. PMID: 28636639. Available from: <https://doi.org/10.1371/journal.pone.0179806>.
- Richardson SJ, Wijayagunaratne RC, D'Souza DG, Darras VM, Herck SLV. Transport of thyroid hormones via the choroid plexus into the brain: the roles of transthyretin and thyroid hormone transmembrane transporters. *Frontiers in Neuroscience*. 2015;9:66. PMID: 25784853. Available from: <https://doi.org/10.3389/fnins.2015.00066>.
- Santos SD, Lambertsen KL, Clausen BH, Akinc A, Alvarez R, Finsen B. CSF transthyretin neuroprotection in a mouse model of brain ischemia. *Journal of Neurochemistry*. 2010;115(6):1434–44. PMID: 21044072. Available from: <https://doi.org/10.1111/j.1471-4159.2010.07047.x>.
- Han S, Wang C, Tong F, Li Y, Li Z, Sun Z. Value of the Neutrophils/Prealbumin Ratio and Its Combination With the GWTG-HF Score in Predicting In-Hospital Mortality in Patients With Heart Failure. *The American Journal of Cardiology*. 2022;172:62–7. PMID: 35341578. Available from: <https://doi.org/10.1016/j.amjcard.2022.02.027>.
- Huu DN, Quy QDB, Minh TN, Duc LN, Dinh CT, Trung KN. Low serum prealbumin concentration predicts long-term mortality in maintenance hemodialysis patients with hepatitis B and/or C virus infections. *JGH Open: An Open Access Journal of Gastroenterology and Hepatology*. 2021;5(12):1344–50. PMID: 34950777. Available from: <https://doi.org/10.1002/jgh3.12677>.
- Zuo P, Tong S, Yan Q, Cheng L, Li Y, Song K, et al. Decreased prealbumin level is associated with increased risk for mortality in elderly hospitalized patients with COVID-19. *Nutrition (Burbank, Los Angeles County, Calif)*. 2020;78:110930. PMID: 32854020. Available from: <https://doi.org/10.1016/j.nut.2020.110930>.
- Rodriguez GJ, Cordina SM, Vazquez G, Suri MF, Kirmani JF, Ezzeddine MA. The hydration influence on the risk of stroke (THIRST) study. *Neurocritical Care*. 2009;10(2):187–94. PMID: 19051062. Available from: <https://doi.org/10.1007/s12028-008-9169-5>.
- Hillis AE, Ulatowski JA, Barker PB, Torbey M, Ziai W, Beauchamp NJ. A pilot randomized trial of induced blood pressure elevation: effects on function and focal perfusion in acute and subacute stroke. *Cerebrovascular Diseases (Basel, Switzerland)*. 2003;16(3):236–46. PMID: 12865611. Available from: <https://doi.org/10.1159/000071122>.
- Acciarresi M, Bogousslavsky J, Paciaroni M. Post-stroke fatigue: epidemiology, clinical characteristics and treatment. *European Neurology*. 2014;72(5-6):255–61. PMID: 25277765. Available from: <https://doi.org/10.1159/000363763>.
- Ogren SO. Central serotonin neurones in avoidance learning: interactions with noradrenaline and dopamine neurones. *Pharmacology, Biochemistry, and Behavior*. 1985;23(1):107–23. PMID: 2994116. Available from: [https://doi.org/10.1016/0091-3057\(85\)90138-8](https://doi.org/10.1016/0091-3057(85)90138-8).
- Harrison MJ, Pollock S, Kendall BE, Marshall J. Effect of haematocrit on carotid stenosis and cerebral infarction. *Lancet*. 1981;2(8238):114–5. PMID: 6113481. Available from: [https://doi.org/10.1016/S0140-6736\(81\)90298-1](https://doi.org/10.1016/S0140-6736(81)90298-1).
- Schrock JW, Glasenapp M, Drogell K. Elevated blood urea nitrogen/creatinine ratio is associated with poor outcome in patients with ischemic stroke. *Clinical Neurology and Neurosurgery*. 2012;114(7):881–4. PMID: 22333035. Available from: <https://doi.org/10.1016/j.clineuro.2012.01.031>.

26. Idicula TT, Waje-Andreassen U, Brogger J, Naess H, Thomassen L. Serum albumin in ischemic stroke patients: the higher the better. The Bergen Stroke Study. *Cerebrovascular Diseases (Basel, Switzerland)*. 2009;28(1):13–7. PMID: 19420917. Available from: <https://doi.org/10.1159/000215938>.
27. Kocatürk M, Kocatürk Ö. Assessment of relationship between C-reactive protein to albumin ratio and 90-day mortality in patients with acute ischaemic stroke. *Neurologia i Neurochirurgia Polska*. 2019;53(3):205–11. PMID: 31145464.
28. Hao R, Qi X, Xia X, Wang L, Li X. Malnutrition on admission increases the in-hospital mortality and length of stay in elder adults with acute ischemic stroke. *Journal of Clinical Laboratory Analysis*. 2022;36(1):e24132. PMID: 34877710. Available from: <https://doi.org/10.1002/jcla.24132>.
29. Magdon-Ismail Z, Ledneva T, Sun M, Schwamm LH, Sherman B, Qian F. Factors associated with 1-year mortality after discharge for acute stroke: what matters? *Topics in Stroke Rehabilitation*. 2018;25(8):576–83. PMID: 30281414. Available from: <https://doi.org/10.1080/10749357.2018.1499303>.
30. Algin A, Inan I. The role of radiologic, clinical and biochemical parameters in prediction of stroke mortality. *Neurosciences (Riyadh)*. 2019;24(2):110–4. PMID: 31056542. Available from: <https://doi.org/10.17712/nsj.2019.2.20180021>.
31. Olum S, Muyingo A, Wilson TL, Demaerschalk BM, Hoxworth JM, Zhang N, et al. Stroke Mortality Outcomes in Uganda. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2021;30(5):105661. Available from: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105661>.
32. Deljavan R, Farhoudi M, Sadeghi-Bazargani H. Stroke in-hospital survival and its predictors: the first results from Tabriz Stroke Registry of Iran. *International Journal of General Medicine*. 2018;11:233–40. PMID: 29950884. Available from: <https://doi.org/10.2147/IJGM.S158296>.
33. Mao H, Wu Q, Lin P, Mo J, Jiang H, Lin S. Derivation of a Prediction Rule for Unfavorable Outcome after Ischemic Stroke in the Chinese Population. *Journal of Stroke and Cerebrovascular Diseases*. 2019;28(1):133–41. PMID: 30337207. Available from: <https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.09.025>.
34. Eizenberg Y, Grossman E, Tanne D, Koton S. Admission Hydration Status and Ischemic Stroke Outcome-Experience from a National Registry of Hospitalized Stroke Patients. *Journal of Clinical Medicine*. 2021;10(15):3292. PMID: 34362078. Available from: <https://doi.org/10.3390/jcm10153292>.
35. Wu Z, Zeng M, Li C, Qiu H, Feng H, Xu X. Time-dependence of NIHSS in predicting functional outcome of patients with acute ischemic stroke treated with intravenous thrombolysis. *Postgraduate Medical Journal*. 2019;95(1122):181–6. PMID: 30975729. Available from: <https://doi.org/10.1136/postgradmedj-2019-136398>.
36. Phan HT, Blizzard CL, Reeves MJ, Thrift AG, Cadilhac DA, Sturm J. Factors contributing to sex differences in functional outcomes and participation after stroke. *Neurology*. 2018;90(22):e1945–53. PMID: 29703773. Available from: <https://doi.org/10.1212/WNL.0000000000005602>.
37. Roy-O'Reilly M, McCullough LD. Age and Sex Are Critical Factors in Ischemic Stroke Pathology. *Endocrinology*. 2018;159(8):3120–31. PMID: 30010821. Available from: <https://doi.org/10.1210/en.2018-00465>.
38. Li X, Yang Y, Ma ZF, Gao S, Ning Y, Zhao L. Enteral combined with parenteral nutrition improves clinical outcomes in patients with traumatic brain injury. *Nutritional Neuroscience*. 2022;25(3):530–6. PMID: 32431234. Available from: <https://doi.org/10.1080/1028415X.2020.1765114>.