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The Interrelation of Blood Urea Nitrogen-to-Albumin Ratio with Three-Month Clinical Outcomes in Acute Ischemic Stroke Cases: A Secondary Analytical Exploration Derived from a Prospective Cohort Study

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Objective: This study targeted elucidating the intricate correlation of the blood urea nitrogen (BUN)-to-albumin (BUN/Alb) ratio with adverse outcomes (AOs) at 3-month in acute ischemic stroke (AIS) cases within a Korean cohort.

Methods: The cohort involved a comprehensive dataset of 1850 AIS cases from a South Korean hospital, spanning from January 2010 to December 2016. To discern the linear relationship of the BUN/Alb ratio with AOs in AIS cases, utilization of a binary logistic regression model (BLRM) was implemented. Additionally, it was attempted to utilize sophisticated statistical techniques, such as generalized additive models (GAMs) and smooth curve fitting methods, to unravel the nonlinear association of the BUN/Alb ratio with AOs in such patients.

Results: The incidence of AOs was determined to be 28.49%, with the median BUN/Alb ratio being 3.85. After adjusting for a number of covariates, the BLRM disclosed that the linear association of BUN/Alb ratio with the risk of AOs particularly in AIS cases did not achieve statistical significance. However, a noticeable nonlinear relationship emerged, with an inflection point identified at 2.86. To the left of this inflection point, the relationship is not statistically significant. On the right side of the inflection point, there was a remarkable 9.47% rise in the risk of AOs (odds ratio (OR) = 1.09, 95% confidence interval (CI): 1.00, 1.19, P = 0.04).

Conclusion: The outcomes illuminate the complex and nonlinear relationship of the BUN/Alb ratio with 3-month AOs in AIS cases. This study established a robust groundwork for the future research, underscoring the potential clinical utility of monitoring the BUN/Alb ratio to enhance the prognostic assessment and management of AIS cases.

Keywords: blood urea nitrogen 1, albumin 2, stroke 3, adverse outcomes 4, cohort study 5

Introduction

Stroke poses a formidable global health concern, occupying the position of the second fundamental etiology of mortality and the third most remarkable contributor to both death and long-term disability on a worldwide scale.[1,2] In particular, ischemic stroke represented a significant majority, comprising 62.4% of all newly diagnosed stroke cases in 2019, highlighting its predominant role in the overall epidemiology of cerebrovascular disorders.[1] Stroke exacts a formidable economic toll on nations and societal frameworks, particularly amplifying its impact in low- and middle-income regions.[2] Planning and providing quality acute stroke care services can reduce the burden of disease following stroke.[2] Therefore, it is vital to identify high-risk patients with poor prognosis in the acute phase of stroke and provide more efficacious treatment and care during hospitalization to improve their prognosis. Previous higher-quality studies have demonstrated that certain clinical biomarkers, such as natriuretic peptides, copeptin, procalcitonin, mannose-binding lectin, adipocyte fatty acid-binding protein, and cortisol are associated with acute ischemic stroke (AIS) prognosis.[3] However, the

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aforementioned parameters are not standard clinical biomarkers and are not readily accessible, highlighting the necessity of obtaining simple and practical indicators. Therefore, we have been looking for simple and easy-to-use indicators that can more accurately predict prognosis at 3 months after stroke.

Our previous study[4] found that the blood urea nitrogen (BUN)-to-creatinine (BUN/Cr) ratio had a non-linear U-shaped relationship with AOs. BUN was negatively correlated with AOs when the BUN/Cr ratio was lower than 21.591. On the contrary, BUN/Cr ratio over 21.591 was positively correlated with AOs. However, BUN/Cr is considered to be a surrogate for plasma osmolality and may primarily reflect the status of renal function. The BUN/Alb ratio has been found to be an effective prognostic biomarker in recent years. It has exhibited remarkable predictive ability in acute kidney injury,[5] sepsis,[6–9] coronary heart disease (CHD),[10] traumatic brain injury,[11] idiopathic pulmonary arterial hypertension,[12] congestive heart failure,[13] aspiration pneumonia,[14] and other diseases. Renal function and nutritional status, as pivotal determinants of systemic health, exert profound and multifaceted influences on recovery trajectories following acute ischemic events.[15] BUN, as a marker reflective of renal function and protein metabolism, assumes escalated clinical significance when elevated, indicating potential renal compromise or augmented protein catabolism. These elevations are typically concomitant with adverse clinical outcomes across a spectrum of acute and chronic conditions, including AIS.[16] Renal impairment exacerbates ischemic and reperfusion injuries via mechanisms, such as fluid overload, electrolyte imbalances, and the accumulation of nephrotoxic uremic solutes.[17] Moreover, renal dysfunction frequently precipitates systemic inflammatory responses, thereby escalating cerebral damage and inhibiting neuroregenerative processes.[18] Conversely, albumin is a canonical plasma protein synthesized by the liver and serves as a barometer of nutritional status and systemic inflammation. Hypoalbuminemia suggests malnutrition and chronic inflammation, which affects immune function and healing, thus further complicating recovery in AIS.[19] consistently correlates with poorer prognostic outcomes across diverse pathologies.[20] The prognostic implications of the BUN/Alb ratio in AIS are underscored by its capacity to encapsulate the dual burdens of renal dysfunction and nutritional inadequacy, both of which significantly hamper recovery post-stroke.[21] Thus, the BUN/Alb ratio, by amalgamating these two critical biomarkers, can be a composite metric that may surpass the prognostic utility of either parameter in isolation.

Despite the extensive body of research, the predictive utility of the BUN/Alb ratio in escalating AIS cases' prognosis following 3-month remains unexplored. Hence, in this investigation, it was attempted to figure out the prognostic potency of the BUN/Alb ratio for adverse outcomes (AOs) in AIS cases following 3-month, assisting clinicians in refining clinical intervention paradigms and elevating patient care standards during the critical phase of stroke, ultimately escalating a superior long-term prognosis.

Materials and Methods

Study Design

Spanning from January 2010 to December 2016, this cohort investigation accurately gathered data from an exclusive prospective registry system established in South Korea.[22] Herein, the principal independent variable under consideration was the BUN/Alb ratio, whereas the dependent variable involved the 3-month clinical outcomes particularly in AIS cases, which were categorized into either AOs or favorable outcomes.

Data Source

Information was derived from the study conducted by Kang et al, titled "Geriatric Nutritional Risk Index Predicts Adverse Outcomes in Acute Ischemic Stroke Cases - Automated Undernutrition Screen Tool". It is noteworthy that this article is open access, governed by the Creative Commons Attribution License. This license permits unrestricted use, distribution, and reproduction in any medium, provided that appropriate credit is given to the original author and source.[22]

Study Population

Drawing on data from a single-center prospective registry in South Korea, initiated in October 2002, an endeavor was undertaken to screen 2084 cases of AIS. These cases were admitted within a 7-day window from the onset of symptoms, spanning the period from January 2010 to December 2016. In accordance with hospital protocol, it was assumed that blood samples for each case were attained from the initial blood draw upon admission. The study adhered to stringent exclusion

criteria, specifically: 1) cases devoid of dysphagia testing or essential laboratory data within the initial 24 hours following admission; 2) cases for which documentation of the modified Rankin Scale (mRS) score at 3 months post-stroke was absent; and 3) known end-stage renal failure. A schematic presentation of patient's selection process is illuminated in Figure 1. The Institutional Review Board of Seoul National University Hospital had previously granted approval for the original study (Approval No. 1009–062-332), thereby waiving the necessity of additional approval for this subsequent secondary analysis.

Variables

The derivation of the BUN/Alb ratio was precisely undertaken through dividing the serum BUN concentration, measured in milligrams per deciliter (mg/dL), by the serum Alb concentration, measured in grams per deciliter (g/dL), thereby yielding a continuous variable. This continuous variable was subsequently stratified into quartiles for analytical purposes, with the quartiles defined as follows: Quartile 1 (Q1): ≤3.04, Quartile 2 (Q2): 3.06–3.83, Quartile 3 (Q3): 3.85–4.87, and Quartile 4 (Q4): ≥4.88.

AIS Cases' Three-Month Outcomes

The assessment of 3-month post-onset outcomes in AIS cases was precisely executed utilizing the mRS score.[23] The exhaustive acquisition of data was executed through detailed outpatient visits or precisely structured telephone interviews.[22] Subsequently, participants were stratified into two distinct cohorts based on their outcomes: those manifesting favorable outcomes, denoted by a mRS score equal to or below 2, and those exhibiting AOs, characterized by an mRS score equal to or above 3.

Missing Data Processing

Among the continuum were a diverse set of variables, including but not limited to white blood cell (WBC), Red blood cell(RBC), the platelet (PLT) count, hemoglobin (HGB) level, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration(MCHC), Red blood cell distribution (RDW), platelet (PLT), total cholesterol (TC), serum triglyceride (TG) levels, low-density lipoproteins cholesterol (LDL-C) levels, high-density lipoproteins cholesterol (HDL-C) levels, alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum

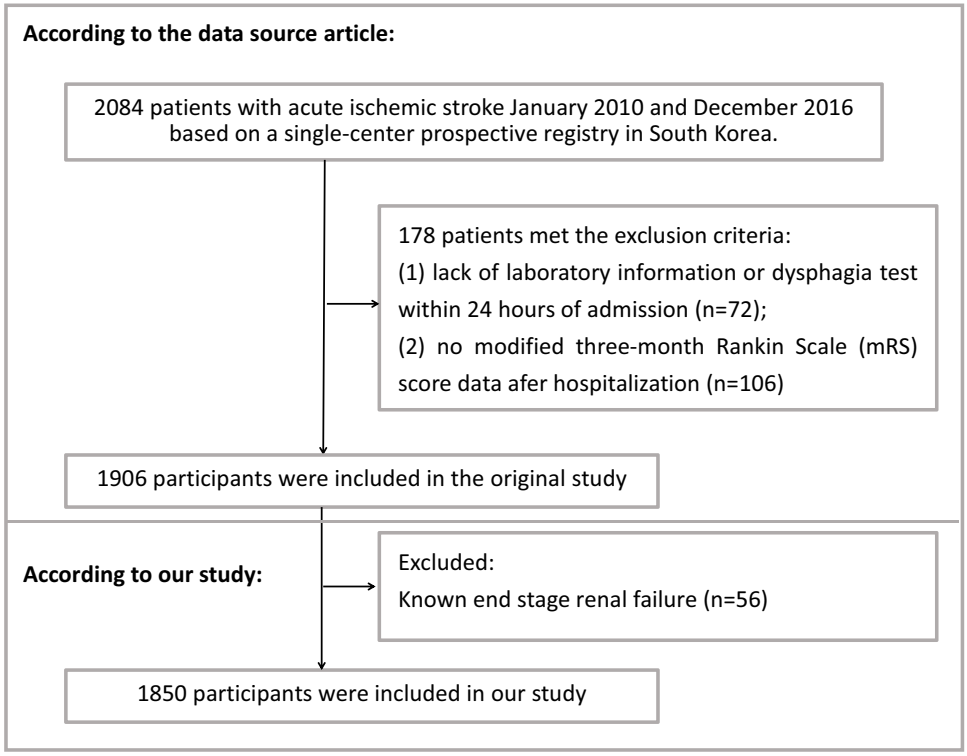

Figure 1 Flowchart of patient selection and exclusion in the original study.

creatinine (Cr), glomerular filtration rate(GFR), serum albumin (ALB), total protein(TP), fasting blood glucose (FBG), activated partial thromboplastin timebody (APTT), fibrinogen (FIB), and mass index (BMI). Within the scope of the present investigation, the occurrences of missing data for pivotal variables, namely TG, HDL-C, LDL-C, FIB, and FBG, amounted to 100 (5.41%), 92 (4.97%), 69 (3.73%), 22 (1.19%), and 130 (7.03%), respectively. To address the potential consequences of these absent covariates on the statistical integrity during the modeling phase, mean imputations were employed as a strategy.

Statistical Analysis

The methodology employed to characterize continuous variables entailed the utilization of descriptive statistics, wherein the expression of variables with a Gaussian distribution was in the format of mean ± standard deviation (SD), while it was attempted to express those displaying a skewed distribution as median (interquartile ranges). Categorical variables underwent thorough delineation using frequencies and percentages. The analytical approach employed a combination of $\chi 2$ tests, one-way analysis of variance (ANOVA), and Kruskal–Wallis *H*-tests to discern variations across distinct BUN/Alb ratio groups. Following a precise assessment for collinearity (Table S1, where variables with VIF values ≥ 5 were systematically excluded), development of three distinct models was undertaken. These encompassed both univariate and multivariate binary logistic regression analyses, aiming to unravel the noticeable relationship of the BUN/Alb ratio with AOs, particularly in AIS cases. The modeling framework featured an unadjusted model, providing an initial insight, followed by a minimally adjusted model that selectively incorporated sociodemographic variables of age and sex. The culmination was a fully adjusted model that comprehensively integrated sociodemographic variables alongside a broad array of clinical features (including WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, history of stroke or TIA, Previous mRS, hypertension, AF, CHD, stroke etiology, smoking status, and NIHSS score). Effect sizes were precisely delineated with 95% confidence intervals (CIs), refined through a synthesis of clinical expertise, insights from the Empower Stats' Covariates module, and outcomes from univariate analysis. Ensuring the robustness of outcomes, sensitivity analysis encompassed categorizing the BUN/Alb ratio into quartiles and scrutinizing trends using P-values. Cases meeting specific criteria—such as DM, abnormal FBG, hypercholesterolemia, elevated BMI, and renal impairment—were rigorously excluded to safeguard data integrity. Potential unmeasured confounding factors were systematically probed using E-values. To unveil potential nonlinearity in the BUN/Alb ratio's association with AOs, sophisticated methodologies were deployed, including generalized additive models (GAMs) and intricately smoothed curve fitting techniques like penalized splines. Detection of nonlinearity prompted the initiation of a recursive algorithm aimed at pinpointing inflection points, thereby catalyzing the development of a two-piece binary logistic regression model (BLRM) operational on either side of these pivotal thresholds. The selection of the most suitable model hinged upon rigorous evaluation via log-likelihood ratio tests and meticulous consideration of categorical implications and diagnostic thresholds.

The outcomes were precisely aligned with the STROBE statement. It was attempted to implement statistical analysis through R and Empower Stats software developed by X&Y Solutions, Inc., which was headquartered in Boston (MA, USA). P-value subordinated 0.05 was regarded to signify statistical significance.[24]

Results

Participants' Characteristics

Following a rigorous screening process on the basis of strict eligibility criteria, this investigation stringently excluded cases that were deficient in either dysphagia testing or requisite laboratory data within the critical initial 24-h window following admission (n = 72), as well as cases for which the mRS scores were not documented at the three-month post-stroke mark (n = 106), and cases with known end-stage renal failure (n = 56). After excluding 234 cases, the final analysis cohort comprised 1850 cases. Table 1 delineates the demographic and clinical features of the study cohort. The cohort involved 60.97% men (1128 individuals). It was attempted to stratify participants into the following age categories: <60 years (425 participants, 22.97%), 60 to <70 years (490 participants, 26.49%), 70 to <80 years (643 participants, 34.76%), and ≥80 years (292 participants, 15.78%). The breakdown of stroke etiology indicated that 588 (31.78%) cases were small-vessel occlusion (SVO), 351 (18.97%) were large-artery atherosclerosis (LAA), 478 (25.84%) were cardiogenic embolism (CE), 168 (9.08%) were other determined etiologies, and 265 (14.32%) were undetermined. The median (interquartile range) of the NIHSS score was 5 (1–11). Participants were further categorized into subgroups

Table 1 Participants' Baseline Characteristics Categorized by the Quartiles of the BUN/Alb Ratio

Characteristics	BUN/Alb Ratio				P
	Q1 (1.14–3.04)	Q2 (3.06–3.83)	Q3 (3.85–4.87)	Q4 (4.88–26.00)	
Number of participants	463	459	458	460	
Demographics					
Age, years					<0.01
<60	184 (39.74%)	110 (23.97%)	75 (16.38%)	56 (11.91%)	
60 to 70	122 (26.35%)	140 (30.50%)	122 (26.64%)	106 (22.55%)	
70 to 80	120 (25.92%)	140 (30.50%)	190 (41.48%)	193 (41.06%)	
≥80	37 (7.99%)	69 (15.03%)	71 (15.50%)	115 (24.47%)	
Gender, n (%)					<0.01
Male	249 (53.78%)	290 (63.18%)	283 (61.79%)	306 (65.11%)	
Female	214 (46.22%)	169 (36.82%)	175 (38.21%)	164 (34.89%)	
Smoking, n (%)	182 (39.31%)	192 (41.83%)	183 (39.96%)	175 (37.23%)	0.55
Hypertension, n (%)	257 (55.51%)	262 (57.08%)	300 (65.50%)	343 (72.98%)	<0.01
DM, n (%)	107 (23.11%)	124 (27.02%)	152 (33.19%)	199 (42.34%)	<0.01
CHD, n (%)	31 (6.70%)	49 (10.68%)	55 (12.01%)	74 (15.74%)	<0.01
AF, n (%)	68 (14.69%)	89 (19.39%)	105 (22.93%)	132 (28.09%)	<0.01
Previous stroke/TIA, n (%)	75 (16.20%)	82 (17.86%)	113 (24.67%)	122 (25.96%)	<0.01
Previous mRS, n (%)					0.093
0	341 (73.65%)	340 (74.07%)	340 (74.24%)	326 (69.36%)	
1	51 (11.02%)	46 (10.02%)	36 (7.86%)	41 (8.72%)	
2	20 (4.32%)	27 (5.88%)	33 (7.21%)	29 (6.17%)	
3	27 (5.83%)	20 (4.36%)	20 (4.37%)	28 (5.96%)	
4	15 (3.24%)	15 (3.27%)	20 (4.37%)	22 (4.68%)	
5	9 (1.94%)	11 (2.40%)	9 (1.97%)	24 (5.11%)	
Clinical features					
BMI (kg/m^2)	23.51 (3.47) 23.40 (21.32–25.69)	23.69 (3.17) 23.53 (21.50–25.63)	23.70 (3.21) 23.61 (21.53–25.62)	23.17 (3.20) 23.27 (20.96–24.91)	0.04
Baseline NIHSS score					<0.01
<6	358 (77.32%)	347 (75.60%)	338 (73.80%)	296 (62.98%)	
6 to 13	65 (14.04%)	68 (14.81%)	70 (15.28%)	95 (20.21%)	
≥14	40 (8.64%)	44 (9.59%)	50 (10.92%)	79 (16.81%)	
WBC ($10^9/L$)	7.46 (6.20–9.15)	7.79 (6.21–9.43)	7.66 (6.25–9.32)	7.85 (6.30–10.10)	0.10
RBC ($10^{12}/L$)	4.52 (4.16–4.87)	4.50 (4.12–4.82)	4.37 (4.03–4.73)	4.12 (3.65–4.53)	<0.01
MCHC (%)	33.90 (33.10–34.50)	33.70 (33.00–34.30)	33.60 (32.80–34.40)	33.50 (32.70–34.20)	<0.01
RDW (%)	12.90 (12.40–13.50)	13.00 (12.50–13.55)	13.20 (12.60–13.60)	13.20 (12.70–14.10)	<0.01
HGB (g/dL)	14.10 (13.00–15.10)	14.10 (12.90–15.10)	13.70 (12.53–14.90)	12.90 (11.40–14.30)	<0.01
HCT (%)	41.60 (38.65–44.70)	41.80 (38.35–44.70)	40.60 (37.50–43.88)	38.40 (34.32–42.20)	<0.01
MCV (fl)	92.40 (89.50–95.20)	92.50 (89.70–95.60)	92.75 (90.12–95.70)	93.55 (90.00–97.00)	<0.01
PLT ($10^9/L$)	230.00 (197.50–271.00)	226.00 (190.00–259.00)	213.00 (176.25–255.50)	199.00 (163.25–248.00)	<0.01
TC (mg/dl)	185.00 (160.50–213.00)	184.00 (155.00–213.50)	179.00 (151.00–204.00)	165.00 (137.00–193.00)	<0.01
TG (mg/dl)	101.00 (77.00–126.00)	103.00 (78.00–138.50)	97.50 (73.00–129.00)	97.00 (74.00–125.50)	0.03
HDL-C (mg/dl)	46.00 (39.00–55.00)	45.00 (38.00–55.00)	44.58 (37.25–53.75)	44.00 (36.00–52.00)	<0.01
LDL-C (mg/dl)	108.00 (90.00–135.00)	110.00 (89.00–136.50)	104.16 (84.00–127.00)	98.50 (74.00–118.00)	<0.01
BUN (mg/dl)	11.00 (9.00–12.00)	14.00 (13.00–15.00)	17.00 (16.00–18.00)	23.00 (21.00–28.00)	<0.01
Cr (mg/dl)	0.78 (0.66–0.90)	0.85 (0.71–0.98)	0.92 (0.76–1.07)	1.09 (0.87–1.39)	<0.01
GFR (%)	90.40 (78.30–103.40)	84.40 (70.65–98.35)	74.70 (63.08–88.60)	63.05 (47.70–77.70)	<0.01
ALT (U/L)	19.00 (14.00–27.00)	18.00 (14.00–26.00)	18.00 (13.00–26.00)	18.00 (12.00–26.00)	0.10
AST (U/L)	23.00 (19.00–29.00)	23.00 (19.00–30.00)	23.00 (19.00–29.75)	23.00 (18.00–30.00)	0.94
ALB (g/dl)	4.20 (4.00–4.40)	4.10 (3.90–4.40)	4.10 (3.80–4.30)	3.90 (3.60–4.10)	<0.01
TP (g/dl)	7.20 (6.90–7.50)	7.10 (6.70–7.40)	7.00 (6.70–7.40)	6.80 (6.40–7.30)	<0.01

(*Continued*)

Table 1 (Continued).

Characteristics	BUN/Alb Ratio				P
	Q1 (1.14–3.04)	Q2 (3.06–3.83)	Q3 (3.85–4.87)	Q4 (4.88–26.00)	
FBG (mg/dl)	99.06 (88.00–112.50)	99.06 (89.00–121.00)	98.00 (84.00–114.00)	97.00 (85.25–112.50)	0.02
FIB (mg/L)	312.00 (274.00–352.00)	321.00 (280.50–362.00)	316.00 (278.00–370.00)	335.00 (292.00–392.00)	
APTT(s)	31.10 (28.80–33.15)	30.60 (28.20–32.80)	30.40 (28.22–32.77)	29.80 (27.60–32.20)	<0.01
Ischemic stroke subtype, n (%)					<0.01
SVO	164 (35.42%)	143 (31.15%)	147 (32.10%)	134 (28.51%)	
LAA	93 (20.09%)	102 (22.22%)	87 (19.00%)	69 (14.68%)	
CE	80 (17.28%)	112 (24.40%)	128 (27.95%)	158 (33.62%)	
Other determined	52 (11.23%)	41 (8.93%)	33 (7.21%)	42 (8.94%)	
Undetermined	74 (15.98%)	61 (13.29%)	63 (13.76%)	67 (14.26%)	
Unfavorable outcome, n (%)	119 (25.70%)	105 (22.88%)	128 (27.95%)	175 (37.23%)	<0.01

Notes: Values are mean ± standard deviation, median (quartile), or number (%).

Abbreviations: BUN/Alb ratio, blood urea nitrogen to albumin ratio; WBC, white blood cell; RBC, Red blood cell; HGB, hemoglobin concentration; HCT, Hematocrit; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, Red blood cell distribution; PLT, platelet; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoproteins cholesterol; BUN, blood urea nitrogen; Cr, serum creatinine; GFR, glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, serum albumin; TP, total protein; FBG, fasting blood glucose; FIB, Fibrinogen; APTT, Activated partial thromboplastin time; BMI, body mass index; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; TIA, transient ischemia attack; mRS, Modified Rankin Scale; LAA, large-artery atherosclerosis; SVO, small-vessel occlusion; CE, cardio embolism; NIHSS, National institute of health stroke scale.

based on BUN/Alb ratio quartiles: Q1: ≤3.04, Q2: 3.06–3.83, Q3: 3.85–4.87, and Q4: ≥4.88. Compared to Q1, Q4 exhibited elevated values of MCV, BUN, and Cr, with reduced levels of RBC, MCHC, GFR, FBG, ALB, TP, HDL-C, TC, PLT, APTT and HGB. Additionally, Q4 featured a higher proportion of those aged ≥ 80 years (24.47%), male (65.11), individuals with hypertension (72.98%), AF (28.09%), previous stroke/TIA (25.96%), CHD (15.74%), DM (42.34%), and cardio embolism cases (33.62%).

Incidence Rate 3-Month AOs in Patients with AIS

A total of 527 participants experienced AOs, translating to an overall incidence rate of 28.49% (26.46–30.58%) (Table 2). Disaggregated by quartiles of the BUN/Alb ratio, the incidence rates were distinctly stratified: in the Q1, the incidence was 25.70% (21.88–29.83%); in the Q2, it was 22.88% (19.21–26.89%); the Q3 exhibited an incidence of 27.95% (23.98–32.19%); and the Q4 demonstrated the highest incidence at 37.23% (32.95–41.68%). These quartile-specific incidence rates unveiled the variable risk associated with differing levels of the BUN/Alb ratio, revealing a remarkable gradient of AO likelihood in the cohort.

Outcomes of the BLRM-Based Univariate Analysis

In the context of univariate analysis focusing on AIS cases, the examination of AOs revealed diverse associations with clinical parameters. Specifically, significantly positive associations were identified between AOs and WBC (OR=1.08,95% CI: 1.04,

Table 2 Incidence Rate of Adverse Outcomes at 3 Months Following the Occurrence of Stroke

BUN/Alb Ratio	Participants (n)	Unfavorable Outcome Events (mRS score ≥3)	Incidence of Unfavorable Outcomes (%) (95% CI)
Total	1850	527	28.49 (26.46–30.58)
Q1 (1.14–3.04)	463	119	25.70 (21.88–29.83)
Q2 (3.06–3.83)	459	105	22.88 (19.21–26.89)
Q3 (3.85–4.87)	458	128	27.95 (23.98–32.19)
Q4 (4.88–26.00)	470	175	37.23 (32.95–41.68)

Abbreviations: BUN/Alb ratio, blood urea nitrogen to albumin ratio; mRS, modified Rankin scale.

1.12), RDW (OR= 1.23,95% CI: 1.15, 1.31), BUN (OR = 1.02, 95% CI: 1.01–1.04), AST (OR = 1.01, 95% CI: 1.00–1.01), FIB (OR = 1.00, 95% CI: 1.00–1.00), and BUN/Alb ratio (OR = 1.15, 95% CI: 1.10–1.21) (all P < 0.05). Furthermore, female participants (OR = 1.66, 95% CI: 1.36–2.04), age group 70–80 years (OR = 1.77, 95% CI: 1.32–2.37), age ≥80 years (OR = 3.90, 95% CI: 2.80–5.44), hypertension (OR = 1.34, 95% CI: 1.08–1.65), DM (OR = 1.45, 95% CI: 1.18–1.80), history of previous stroke/TIA (OR = 1.80, 95% CI: 1.43–2.28), NIHSS score ≥14 (OR = 15.44, 95% CI: 10.99–21.71), AF (OR = 2.09, 95% CI: 1.65–2.63), CE (OR = 1.53, 95% CI: 1.18–1.99), and other determined stroke etiologies (OR = 2.13, 95% CI: 1.49–3.04) exhibited heightened risks of AOs (all P < 0.05). Conversely, RBC (OR=0.56, 95% CI: 0.47, 0.66), MCHC (OR=0.88, 95% CI: 0.81, 0.96), TC (OR = 1.00, 95% CI: 0.99–1.00), TG (OR = 1.00, 95% CI: 0.99–1.00), LDL-C (OR = 1.00, 95% CI: 0.99–1.00), HGB (OR = 0.81, 95% CI: 0.77–0.85), HCT (OR = 0.93, 95% CI: 0.91–0.94), ALT (OR = 0.99, 95% CI: 0.98–1.00), ALB (OR = 0.25, 95% CI: 0.20–0.33), TP (OR =0.67, 95% CI: 0.57, 0.79), FBG (OR = 0.99, 95% CI: 0.99–1.00), and BMI (OR = 0.91, 95% CI: 0.88–0.94) demonstrated inverse relationships with the risk of AOs (Table 3).

Table 3 Determinants of Adverse Outcomes in AIS Assessed Through the Univariate Regression Analysis

Characteristics	OR (95% CI)	P
Demographics		
Age, years		
<60	ref.	
60 to 70	1.18 (0.86, 1.62)	0.31
70 to 80	1.77 (1.32, 2.37)	<0.01
≥80	3.90 (2.80, 5.44)	<0.01
Gender		
Male	ref.	
Female	1.66 (1.36, 2.04)	<0.01
Smoking		
No	ref.	
Yes	0.59 (0.48, 0.74)	<0.01
Hypertension		
No	ref.	
Yes	1.34 (1.08, 1.65)	<0.01
DM		
No,	ref.	
Yes	1.45 (1.18, 1.80)	<0.01
CHD		
No	ref.	
Yes	0.99 (0.72, 1.36)	0.93
AF		
No	ref.	
Yes	2.09 (1.65, 2.63)	<0.01
Previous stroke/TIA		
No	ref.	
Yes	1.80 (1.43, 2.28)	<0.01
Previous mRS		
0	ref.	
1	0.85 (0.58, 1.25)	0.42
2	1.43 (0.94, 2.19)	0.10
3	2.10 (1.37, 3.23)	<0.01
4	8.21 (4.83, 13.96)	<0.01
5	12.06 (6.14, 23.69)	<0.01

(*Continued*)

Table 3 (Continued).

Characteristics	OR (95% CI)	P
Clinical features		
BMI	0.91 (0.88, 0.94)	<0.01
Baseline NIHSS score		
<6	ref.	
6 to 13	6.15 (4.69, 8.06)	<0.01
≥14	15.44 (10.99, 21.71)	<0.01
WBC	1.08 (1.04, 1.12)	<0.01
RBC	0.56 (0.47, 0.66)	<0.01
MCHC	0.88 (0.81, 0.96)	<0.01
RDW	1.23 (1.15, 1.31)	<0.01
HGB	0.81 (0.77, 0.85)	<0.01
HCT	0.93 (0.91, 0.94)	<0.01
MCV	0.99 (0.97, 1.01)	0.24
PLT	1.00 (1.00, 1.00)	0.53
TC	1.00 (0.99, 1.00)	<0.01
TG	1.00 (0.99, 1.00)	<0.01
HDL-C	1.00 (0.99, 1.00)	0.41
LDL-C	1.00 (0.99, 1.00)	0.04
BUN	1.02 (1.01, 1.04)	<0.01
Cr	1.05 (0.80, 1.38)	0.71
GFR	1.00 (1.00, 1.00)	0.68
ALT	0.99 (0.98, 1.00)	0.01
AST	1.01 (1.00, 1.01)	0.02
ALB	0.25 (0.20, 0.33)	<0.01
TP	0.67 (0.57, 0.79)	<0.01
FBG	0.99 (0.99, 1.00)	<0.01
APTT	0.99 (0.97, 1.01)	0.21
FIB	1.00 (1.00, 1.00)	<0.01
BUN/Alb ratio	1.15 (1.10, 1.21)	<0.01
Ischemic stroke subtype		
SVO	ref.	
LAA	0.64 (0.46, 0.89)	<0.01
CE	1.53 (1.18, 1.99)	<0.01
Other determined	2.13 (1.49, 3.04)	<0.01
Undetermined	0.85 (0.60, 1.19)	<0.01

Abbreviations: BUN/Alb ratio, blood urea nitrogen to albumin ratio; WBC, white blood cell; RBC, Red blood cell; HGB, hemoglobin concentration; HCT, Hematocrit; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; RDW, Red blood cell distribution; PLT, platelet; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoproteins cholesterol; BUN, blood urea nitrogen; Cr, serum creatinine; GFR, glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, serum albumin; TP, total protein; FBG, fasting blood glucose; FIB, Fibrinogen; APTT, Activated partial thromboplastin time; BMI, body mass index; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; TIA, transient ischemia attack; mRS, Modified Rankin Scale; LAA, large-artery atherosclerosis; SVO, small-vessel occlusion; CE, cardio embolism; NIHSS, National institute of health stroke scale.

Outcomes of the BLRM-Based Multivariate Logistic Regression Analysis

It was attempted to develop three distinct Bayesian logistic regression models to figure out the intricate relationship of the BUN/Alb ratio with the likelihood of AOs particularly in AIS cases. The unadjusted model unveiled a statistically significant

15% escalation in the risk of AOs with each 1-unit rise in the BUN/Alb ratio (OR = 1.15, 95% CI: 1.10, 1.21, P < 0.01). In the moderately adjusted model, which incorporated a subset of covariates, the risk of AOs increased by 12% per 1-unit increment in the BUN/Alb ratio (OR = 1.12, 95% CI: 1.07, 1.18, P < 0.01), maintaining statistical significance. However, the fully adjusted model, accounting comprehensively for numerous potential confounders in the multivariate logistic regression analysis, did not yield significant outcomes (OR =1.01, 95% CI: 0.89, 1.15, P = 0.86) (Table 4).

Sensitivity Analysis

The sensitivity analysis encompassed an elaborate process that commenced with the transformation of the BUN/Alb ratio from its continuous state into a categorical variable through quartile segmentation. This newly categorized form of the ratio was subsequently reintegrated into the model. The multivariate adjusted model showed that BUN/Alb ratio was not linearly related to AOs at 3 months after stroke.

In a subsequent phase of sensitivity analysis, we undertook a meticulous process of excluding cases that conformed to specific criteria, including TC level ≥200 mg/dL, presence of DM, FBG level ≥6.1 mmol/L, BMI ≥25 kg/m², and serum Cr level ≥1.2 mg/dL. Despite these stringent adjustments aimed at mitigating potential confounders, the previously identified linear association of BUN/Alb ratio with the risk of AOs persisted in its statistical insignificance (all P > 0.05), as evidenced by the data presented in Table 5. This analysis elucidated that the postulated linear relationship of the BUN/Alb ratio with the risk of AOs did not manifest, neither in the overarching study cohort nor in the delineated subgroups.

It is noteworthy that our sensitivity analysis precisely accounted for all covariates, including age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, serum TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, Previous mRS, hypertension, AF, CHD, stroke etiology, smoking, and NIHSS score. It is also noteworthy that Model I for non-DM cases did not include DM as an adjusted covariate. Furthermore, we conducted subgroup analysis based on age, sex, TOAST subtypes, and different HDL-C levels; however, no statistically significant outcomes could be attained (Table S2).

Addressing Nonlinearity via the GAM

The results derived from the multivariate BLRM did not attain statistical significance, revealing the sophisticated nature of nonlinear relationships within the dataset. Furthermore, an in-depth analysis utilizing multivariate-adjusted models, which employed BUN/Alb ratio quartiles as categorical variables, elucidated a noticeable and nonlinear association of BUN/Alb ratio with AOs particularly in AIS cases. This multifaceted relationship highlights the inadequacy of simplistic

Table 4 Examination of the Intricate Relationship Between the BUN/Alb Ratio and Adverse Outcomes 3 Months Post-Stroke Through Diverse Analytical Models

Variable	Crude Model (OR, 95% CI)	P	Model I (OR, 95% CI)	P	Model II (OR, 95% CI)	P
BUN/Alb ratio	1.15 (1.10, 1.21)	<0.01	1.12 (1.07, 1.18)	<0.01	1.01 (0.89, 1.15)	0.86
BUN/Alb ratio (quartiles)						
Q1 (1.14–3.04)	ref.		ref.		ref.	
Q2 (3.06–3.83)	0.86 (0.63, 1.16)	0.32	0.78 (0.57, 1.07)	0.13	0.74 (0.51, 1.08)	0.12
Q3 (3.85–4.87)	1.12 (0.84, 1.50)	0.44	0.99 (0.73, 1.34)	0.92	0.94 (0.65, 1.37)	0.75
Q4 (4.88–26.00)	1.71 (1.30, 2.27)	<0.01	1.40 (1.04, 1.90)	0.03	0.96 (0.63, 1.44)	0.83
P for trend		<0.01		<0.01		0.99

Notes: Crude Model: We did not adjust for any covariates. Model I: We adjusted age and sex. Model II: We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score.

Abbreviations: BUN/Alb ratio, blood urea nitrogen to albumin ratio; WBC, white blood cell; RBC, Red blood cell; MCHC, mean corpuscular hemoglobin concentration; RDW, Red blood cell distribution; TG, triglyceride; LDL-C, low-density lipoproteins cholesterol; Cr, serum creatinine; GFR, glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TP, total protein; FBG, fasting blood glucose; FIB, Fibrinogen; BMI, body mass index; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; TIA, transient ischemia attack; mRS, Modified Rankin Scale; NIHSS, National institute of health stroke scale.

Table 5 Exploration of the Correlation Between the BUN/Alb Ratio and Adverse Outcomes

BUN/Alb Ratio	OR (95% CI)	P
Model I	1.04 (0.88, 1.22)	0.64
Model II	0.97 (0.83, 1.14)	0.72
Model III	1.00 (0.85, 1.16)	0.98
Model IV	1.11 (0.95, 1.29)	0.20
Model V	1.00 (0.87, 1.15)	0.99

Notes: Model I was the sensitivity analysis in participants without DM. We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score. Model II was the sensitivity analysis in participants without BMI ≥25 kg/m2. We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS and NIHSS score. Model III was the sensitivity analysis in participants without TC ≥200 mg/L. We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score. Model IV was the sensitivity analysis in participants without FBG ≥6.1 mmol/L. We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score. Model V was the sensitivity analysis in participants without Cr ≥1.2 mg/dl. We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score.

Abbreviations: OR, odds ratios; CI, confidence; Ref, reference; BUN/Alb ratio, blood urea nitrogen to albumin ratio; WBC, white blood cell; RBC, Red blood cell; MCHC, mean corpuscular hemoglobin concentration; RDW, Red blood cell distribution; TG, triglyceride; LDL-C, low-density lipoproteins cholesterol; Cr, serum creatinine; GFR, glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TP, total protein; FBG, fasting blood glucose; FIB, Fibrinogen; BMI, body mass index; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; TIA, transient ischemia attack; mRS, Modified Rankin Scale; NIHSS, National institute of health stroke scale.

linear models in capturing the complex interactions, thereby necessitating the adoption of more advanced analytical techniques to accurately delineate the underlying mechanisms.

Employing sophisticated statistical methodologies (eg, generalized additive models (GAMs) and smooth curve fitting), while adjusting for an extensive array of covariates encompassing age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, Previous mRS, hypertension, AF, CHD, stroke etiology, smoking, and NIHSS score, revealed a distinctive J-shaped relationship of the BUN/Alb ratio with the likelihood of AOs in AIS cases (Figure 2). To thoroughly capture the intricacies of this relationship, a piecewise BLRM was deployed, accommodating two discernible slopes. The model selection was contingent upon the log-likelihood ratio test during sensitivity analysis, with the P-value for this test being <0.05. Leveraging a recursive algorithm, the inflection point of 2.86 could be achieved. The effect sizes and CIs were precisely computed on both sides of this inflection point through the two-piecewise BLRM. It is noteworthy that on the left side of the inflection point, BUN/Alb ratio is not associated with AOs at 3 months after stroke. On the right side of the inflection point, each unit increase in the BUN/Alb ratio corresponded to a 9.47% reduction in the risk of AOs (OR = 1.09, 95% CI: 1.00, 1.19, P = 0.04) (Table 6).

Discussion

Extracted from an extensive cohort of 2084 AIS cases over a span of 6 years, this investigation ensures a comprehensive representation of diverse cases through a prospective cohort. The primary outcomes can be summarized in the following:

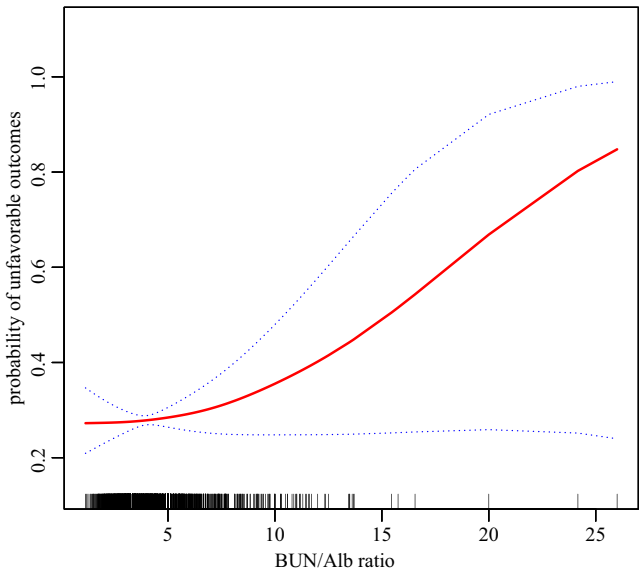

Figure 2 A nonlinear J-shaped relationship was observed between the blood urea nitrogen/albumin ratio (BUN/Alb ratio) and unfavorable outcomes in patients with acute ischemic stroke (AIS).

Firstly, the prevalence of AOs at the 3-month post-AIS was quantified at 28.49%. Secondly, diverging from a linear trajectory, a discernible J-shaped, nonlinear correlation of the BUN/Alb ratio with outcomes at the 3-month post-AIS interval emerged. Thirdly, a consequential threshold effect was attained, delineating a pivotal inflection point at 2.86 for the BUN/Alb ratio. When BUN/Alb ratio is lower than 2.86, the proportion of AOs at 3 months after stroke increases linearly. Fourthly, it was attempted to implement sensitivity analysis, systematically excluding cases with specified conditions, involving TC ≥200 mg/dl, DM, FBG ≥6.1 mmol/L, BMI ≥25 kg/m2, and serum Cr >1.2 mg/dl. Even subsequent to comprehensive adjustment for potential confounders, the linear association of the BUN/Alb ratio with the risk of AOs persisted statistically insignificant. Fifthly, this investigation innovatively stands as the inaugural exploration into the correlation of the BUN/Alb ratio with AOs at the 3-month post-stroke interval. This groundbreaking investigation unveiled a substantial nonlinear J-shaped association of the BUN/Alb ratio with AOs 3-month post-AIS. It was concluded that a BUN/Alb ratio of 2.86 could be associated with a diminished incidence of adverse functional outcomes

Table 6 The Outcomes Derived from the Two-Piecewise Linear Regression Model

Unfavorable Outcome	OR (95% CI)	P
Fitting model by standard linear regression	1.06 (0.98, 1.15)	0.16
Fitting model by two-piecewise linear regression	2.86	
Inflection points of the BUN/Alb ratio		
≤2.86	0.58 (0.34, 1.01)	0.05
>2.86	1.09 (1.00, 1.19)	0.04
P for log-likelihood ratio test	0.03	

Notes: We adjusted age, sex, WBC, RBC, MCHC, RDW, AST, ALT, FBG, FIB, TG, LDL-C, Cr, GFR, TP, FIB, BMI, DM, previous stroke or TIA, hypertension, AF, CHD, stroke etiology, smoking, Previous mRS, and NIHSS score.

Abbreviations: OR, odds ratios; BUN/Alb ratio, blood urea nitrogen to albumin ratio; WBC, white blood cell; RBC, Red blood cell; MCHC, mean corpuscular hemoglobin concentration; RDW, Red blood cell distribution; TG, triglyceride; LDL-C, low-density lipoproteins cholesterol; Cr, serum creatinine; GFR, glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TP, total protein; FBG, fasting blood glucose; FIB, Fibrinogen; BMI, body mass index; DM, diabetes mellitus; CHD, coronary heart disease; AF, atrial fibrillation; TIA, transient ischemia attack; mRS, Modified Rankin Scale; NIHSS, National institute of health stroke scale.

3-month post-AIS. Consequently, the BUN/Alb ratio emerges as a straightforward, innovative, and effective biomarker for prognosticating stroke outcomes. Hence, aligning the BUN/Alb ratio towards 2.86 in the management of AIS cases may result in an enhanced functional prognosis. This discovery serves as a pivotal cornerstone, guiding the trajectory of future research.

BUN and ALB are both low-cost biomarkers that are widely used in clinical practice. BUN is the main end product of human protein metabolism. It is an important index reflecting the status of kidney, protein metabolism and nutritional status and their relationship.[6,25] BUN is filtered through the glomerulus, and is partially reabsorbed in the renal tubule. This process of reabsorption is regulated and controlled by a variety of neurohormonal systems, including the renin-angiotensin-aldosterone system, sympathetic nervous system, and arginine-vasopressin system.[26] BUN an better reflect the severity of renal injury.[5,25] Elevated BUN indicates poor prognosis in multiple disorders, including acute exacerbation of chronic obstructive pulmonary disease, heart failure, aortic dissection, pancreatitis, gastrointestinal bleeding, diabetes mellitus, etc.[27–31] In a study of 3355 Chinese patients, it was found that higher BUN was significantly associated with an increased risk of in-hospital all-cause mortality in AIS patients, and its predictive effect was stronger than that of decreased eGFR and increased Cr or BUN/Cr ratio, suggesting that BUN may be a simple but valuable biomarker for mortality in AIS patients[32]。 However, BUN is affected by multiple factors, such as dietary protein content, dehydration, catabolic status, gastrointestinal bleeding, and age, and has limited prognostic value.

Albumin, which is synthesized in the liver, is a biomarker for hepatocyte function[33], and is a reflection of the body's nutritional status, playing a very notable function not only in molecular and drug transport, but also in the maintenance of effective intravascular colloid osmolality, circulating volume, and Oxidation-reduction status.[34] ALB stands as a pivotal antioxidant within plasma, mitigating apoptosis in renal tubular cells through its scavenging of oxygen free radicals29. Prior research unveiled multifaceted roles of ALB, not only prolonging renal vasodilation to enhance renal perfusion and glomerular filtration, but also exerting a selective inhibitory effect on the expression of vascular cell adhesion molecule 1 induced by tumor necrosis factor-α, alongside thwarting the activation of NF-κB and subsequent monocyte adhesion in human endothelial cells. This selective modulation serves as a protective mechanism against renal injury.[35,36] In addition, ALB promotes DNA synthesis in renal tubular cells through Ca2+-related signaling pathways and is essential for the structural integrity and function of the proximal renal tubules.[37] When the body has liver dysfunction, kidney injury and other conditions, serum ALB levels may also be reduced.[38,39] Hypoproteinemia can worsen pulmonary edema, exacerbate fluid retention, and worsen ischemic heart disease.[40] Hypoalbuminemia is commonly identified in patients with malnutrition or systemic inflammatory response, and hypoalbuminemia is considered to be associated with poor prognosis.[41,42] Meta-analysis unveiled that hypoalbuminemia is an independent predictor of acute kidney injury development and death.[43] In hypoalbuminemia, blood viscosity may be elevated, endothelial function may be impaired, antioxidant capacity decreases, and inhibitory effect on platelet activation or aggregation may be also weakened. These reactions may elevate the possibility of atherothrombosis, which may lead to adverse consequences.[10,44] ALB level may be modulated by a variety of factors, encompassing inflammatory processes, hepatic function, vascular permeability, and catabolic states, thereby constraining its prognostic utility. Consequently, the interaction of BUN with ALB manifests as a multifaceted relationship, potentially indicative of an underlying causal nexus.

Therefore, BAR is a marker that simultaneously reflects nutritional status, protein metabolism, and renal status.[6] Theoretically, it can better predict the prognosis of the disease than BUN or ALB alone, and, as it is easily available. Prior research concluded that a high BUN/Alb ratio could be linked with the adverse prognosis of acute kidney injury,[5] sepsis,[6–9] CHD,[10] traumatic brain injury,[11] idiopathic pulmonary arterial hypertension,[12] congestive heart failure,[13] aspiration pneumonia,[14] and other diseases. It has not been reported that lower BUN/Alb ratio could be linked to poor prognosis. The investigation found that when the BUN/Alb ratio lower than 2.86, the population of the AOs of the stroke at a low level. The rationale for the J-shaped nonlinear relationship between BUN/Alb ratio and AOs at 3-month following AIS remains ambiguous and needs to be explored more comprehensively.

The constraints of this investigation are noteworthy. Firstly, its exclusive concentration on a single center and a predominantly Korean demographic may impede the broader applicability of its conclusions to other ethnic populations, emphasizing the imperative for further research to corroborate and extend the findings across diverse ethnicities. Secondly, the evaluation of the BUN/Alb ratio solely at the point of admission, without subsequent reassessment during

the hospitalization period, emphasizes the necessity for a deeper exploration into potential fluctuations over time to unveil the dynamics of this biomarker more comprehensively. Third, We have not any information on the proportion of subjects who underwent thrombolytic treatment or endovascular treatment, but the proportion of patients receiving these specific treatments was small and had little effect on our findings. Fourth, We have not any information on the proportion of subjects who were regularly being under rehabilitation, and did not assess the use of medications, which could be an important bias of the study. For example, statin use was strongly associated with stroke outcomes.[45,46] This will be the problem that we should pay attention to avoid in the future research.

Conclusions

The present investigation unveiled a notable nonlinear J-shaped correlation of the BUN/Alb ratio with the likelihood of AOs at 3-month among AIS cases. Below the threshold of 2.86, the proportion of the AOs of stroke at a low level, while surpassing this threshold revealed a remarkably significant positive correlation with AOs. The vigilant monitoring of the BUN/Alb ratio may result in valuable insights for identifying cases at the elevated risk of an unfavorable prognosis, assisting clinicians with indispensable guidance in managing such clinical scenarios.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Seoul National University Hospital (protocol code No. 1009–062-332 and date of approval). Ethical exemption was obtained from the ethics committee of the author's institution (Changde Hospital, Xiangya School of Medicine, Central South University).

Informed Consent Statement

The studies involving human participants were reviewed and approved by the Institutional Review Board of Seoul National University Hospital. And the Institutional Review Board waived the need for informed consent (IRB No. 1009–062-332). Ethical exemption was obtained from the ethics committee of the author's institution (Changde Hospital, Xiangya School of Medicine, Central South University).

Data Sharing Statement

All data generated or analysed during this study are included in this published article. Information was derived from the study conducted by Kang et al, titled "Geriatric Nutritional Risk Index Predicts Adverse Outcomes in Acute Ischemic Stroke Cases - Automated Undernutrition Screen Tool".

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As this is a secondary study, the data and explanation of the methodology are mostly drawn from the following studies: Kang et al[22]. We are appreciative of the study's whole authorship team.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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