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Association between blood–urea–nitrogen-to-albumin ratio and in-hospital mortality in patients diagnosed with coronavirus disease 2019: a retrospective cohort study

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Abstract

Background The blood–urea–nitrogen-to-albumin ratio (BAR) is recognized as a novel prognostic indicator; however, there is a limited number of studies investigating the relationship between BAR and in-hospital mortality associated with coronavirus disease 2019 (COVID-19). Therefore, the present investigation aims to explore the correlation between BAR and in-hospital mortality in patients with COVID-19 in China.

Methods This retrospective observational study enrolled a cohort of 1027 patients diagnosed with COVID-19 between December 2022 and March 2023. Multivariate Cox regression analyses were used to ascertain the independent association between BAR and in-hospital mortality among patients with COVID-19. Furthermore, stratified analyses were used to investigate potential interaction effects with variables, such as age, sex, COVID-19 Severity, hypertension, coronary artery disease, and diabetes mellitus.

Results A total of 117 patients (11.4%) died from various causes during hospitalization. Subsequent to adjustment for confounding variables, patients in the highest BAR tertile exhibited an elevated risk for in-hospital mortality relative to those in the lowest tertile (hazard ratio [HR] 2.44 [95% confidence interval CI 1.24–4.79]) when BAR was treated as a categorical variable. When considering BAR as a continuous variable, a 6% increase in the prevalence of in-hospital mortality was observed for each 1-unit increase in BAR (adjusted HR 1.06 [95% CI 1.03–1.08]; $P < 0.001$). Stratified analyses revealed a consistent association between BAR and in-hospital mortality due to COVID-19.

Conclusions BAR exhibited a significant relationship with in-hospital mortality in patients with COVID-19, suggesting that a higher BAR is associated with a poorer prognosis. However, further research is required to confirm these findings.

Keywords Blood–urea–nitrogen-to-serum albumin ratio (BAR), COVID-19, In-Hospital mortality

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Background

The novel coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1], results in multiorgan dysfunction impacting the lungs, heart, gastrointestinal tract, nervous system, and renal system [2]. This global

pandemic has significantly endangered human lives, health, and wealth. The cumulative crude mortality rate has been reported to be 2.3%, escalating to 49% among patients with severe disease [3]. This has imposed a substantial strain on global medical health services. Laboratory biomarkers, including procalcitonin (PCT), D-dimer, lactate dehydrogenase (LDH), ferritin, interleukin (IL)−6, C-reactive protein (CRP), and cytokine assays have been scrutinized for their potential contribution toward diagnostic confirmation and therapeutic guidance in patients with COVID-19 [4].

Blood–urea–nitrogen (BUN), a derivative of protein metabolism, is a significant marker of renal function, volume depletion, nutritional status, and is linked with mortality across various diseases [5]. Albumin (ALB) is the most prevalent plasma protein in the human body [6] and has numerous physiological functions, including preservation of osmotic pressure, binding and transportation of drugs, neutralization of free radicals, and regulation of fluid equilibrium [7, 8]. Furthermore, it serves as an indicator of malnutrition [9]. In relation to COVID-19, Huang et al. [10] analyzed 299 patients and recorded hypoalbuminemia in 106, concluding that hypoalbuminemia served as an independent prognosticator of mortality.

The BUN-to-ALB ratio (BAR) has been recognized as a novel short-term prognostic index [11]. A meta-analysis further implied that an elevated BAR led to a threefold increment in the risk for an unfavorable prognosis among patients hospitalized for COVID-19[12]. However, it is crucial to acknowledge that the severity of COVID-19 and mortality rates can fluctuate based on racial and epidemiological factors across different countries and phases of the pandemic [13, 14].

Nevertheless, during the pandemic phase in China, an insufficient number of studies examined the relationship between BAR and in-hospital mortality attributable to COVID-19. As such, the objective of the present investigation was to explore the connection between BAR values and in-hospital mortality among Chinese patients with COVID-19, aiming to provide reference material for clinical management.

Materials and methods

Study design and participants

This retrospective study encompassed 1134 patients, aged over 18 years, who were hospitalized with a diagnosis of COVID-19 in the Department of Internal Medicine at Jinzhou Medical University First Affiliated Hospital from December 2022 to March 2023. Diagnosis of COVID-19 was confirmed through nasopharyngeal swabs and polymerase chain reaction assays positive for SARS-CoV-2.

Data regarding patient demographic features, medical history, treatment(s) administered, and laboratory investigations were sourced from primary patient medical records. Variables collected included demographic details, such as age, sex, alcohol consumption, and smoking status. Vital signs, including body temperature (T), respiratory rate (RR), heart rate, systolic blood pressure, diastolic blood pressure, and Body Mass Index (BMI) were documented. Hospital-related features, including length of hospital stay and application of mechanical ventilation (MV), noninvasive ventilation (NIV), and high-flow oxygen were also noted. The presence or absence of symptoms, such as cough, fever, and comorbidities including hypertension (HTN), diabetes mellitus (DM), coronary heart disease (CHD), cardiovascular disease, cancer, and chronic obstructive pulmonary disease (COPD), were recorded. Biochemical markers including aspartate aminotransferase (AST), alanine aminotransferase (ALT), glutamine aminotransferase, ALB, BUN, creatinine, C-reactive protein (CRP), potassium, sodium, and chloride levels were measured. Hematology tests comprised white blood cell count (WBC), neutrophilic granulocyte percentage, lymphocyte percentage, platelet count, and hemoglobin (HB). In addition, in-hospital mortality rates and the incidence of acute kidney injury (AKI) were documented. All data were gathered within the initial 24 h of patient admission to the hospital. Standard laboratory tests were used to evaluate all parameters.

Inclusion and exclusion criteria

The inclusion criteria were patients aged over 18 years who were hospitalized in the Department of Internal Medicine at Jinzhou Medical University First Affiliated Hospital due to a confirmed diagnosis of COVID-19 between December 2022 and March 2023. Exclusion criteria included the presence of chronic kidney disease, chronic liver disease, incomplete covariate data, missing data for BUN and ALB, as well as pregnant individuals. Initially, 1134 patients were deemed potentially eligible for this study, as illustrated in Fig. 1. However, after applying the inclusion and exclusion criteria, data from 1027 patients were ultimately included in the analysis.

The outcome of interest for this study was in-hospital mortality, which was characterized as any death occurring during patient hospitalization or within 24 h of discharge from hospital. BAR (mg/g) was calculated using the initial serum BUN (mg/dL) divided by serum ALB (g/dL). Severe COVID-19 was defined by the presence of any of the following conditions: dyspnea with a RR $\geq$ 30/min; SaO2 $\leq$ 93% on room air; arterial PaO2/fraction of inspired oxygen (FiO2) $\leq$ 300 mmHg; or lung lesion progression > 50% on computed tomography within 24–48 h

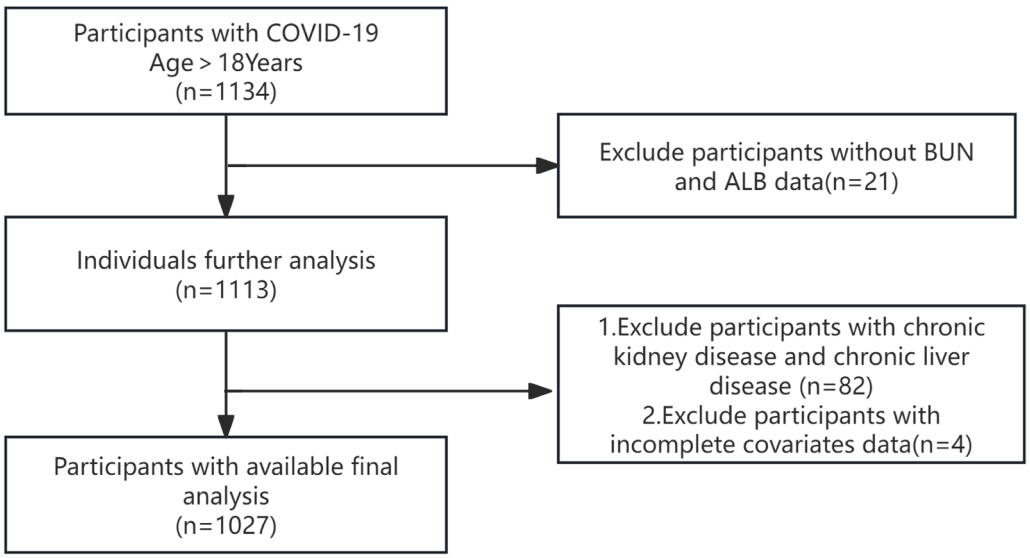

Fig. 1 Flow chart of the study

[15].This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received approval from the Ethics Review Board of the First Affiliated Hospital of Jinzhou Medical University (No.KYLL2024143). Given the retrospective nature of the study and the use of anonymized patient data, requirements for informed consent were waived.

Sample size

To determine the required sample size for this study, we reviewed existing literature reporting a hospitalization mortality rate of 15.9% among COVID-19 patients [16]. Based on this figure, we calculated that a minimum of 883 participants would be needed to achieve 90% statistical power with a significance level set at 0.01 [17].Furthermore, accounting for a potential dropout rate of 20%, we have adjusted our target recruitment number to 1,104 participants. This adjustment ensures that we can ultimately secure 883 evaluable subjects, thereby preserving the statistical integrity and accuracy of our findings.

Statistical analysis

Descriptive statistics were used to delineate basic patient characteristics. The Kolmogorov–Smirnov test was used to ascertain whether the variables adhered to a normal distribution. Continuous variables are expressed as either mean ± standard deviation (SD) or median (interquartile range [IQR]). Categorical variables are expressed as absolute value and percentage. The chi-squared test was used to analyze categorical variables. Comparisons between groups for normally distributed continuous variables were performed using one-way analysis of variance, while non-normally distributed continuous variables were subjected to the Kruskal–Wallis test.

The study cohort was segmented into tertiles based on continuous BAR values with the following distribution: tertile I (BAR, 1.134–3.932 [$n=341$]); tertile II (BAR, 3.944–5.793 [$n=343$]); and tertile III (BAR, 5.811–48.3 [$n=343$]). To determine the relationship between BAR and in-hospital mortality, both univariate and multivariate analyses were performed via Cox proportional hazards regression. The regression analysis incorporated adjustments for various factors using 3 models: model 1, adjusted for sex, age, COVID-19 Severity; model 2, adjusted for model 1 plus CHD, HTN, DM, cancer, CVD and COPD; model 3, adjusted for model 2 plus platelet count and HB levels. Cox regression models were used to determine interaction and subgroup analyses were predicated on age, sex, COVID-19 severity, HTN, DM, and CHD.

The study examined and compared the Kaplan–Meier survival probabilities among patients with COVID-19 during hospitalization, applying the log-rank test among the various BAR tertiles. All statistical tests were two-tailed and differences with $P<0.05$ were considered to be significant. Statistical software used for the analyses included R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) and Free Statistics Software version 1.8 [18].

Results

The present investigation initially included 1134 patients diagnosed with COVID-19; however, 25 were excluded from the analysis due to inadequate data

regarding BUN, ALB, and other covariates. In addition, 82 patients with a confirmed history of chronic kidney disease or chronic liver disease were excluded. Consequently, the final sample size comprised 1,027 eligible participants. A flow-diagram illustrating the participant selection process is presented in Fig. 1.

The demographic attributes, vital signs, symptoms, co-existing conditions, therapeutic measures, laboratory results, and patient outcomes of the 1027 study participants are summarized in Table 1. Among the study participants, there were 569 males (55.4%), and the mean age of the population was 72.1 ± 13 years. The in-hospital mortality rate was 11.4%, with HFNC use, invasive ventilation, and MV rates of 9.5%, 3.3%, and 2.9%, respectively. The most prevalent co-existing conditions included HTN (46.4%), CHD (30.2%), DM (27.0%), cerebrovascular disease (21.1%), oncological conditions (12.2%), and COPD (6.4%). The median length of hospital stay was 11.0 days. Fever symptoms were reported in 70.3% of patients, whereas 73.2% experienced cough symptoms.

As shown in Supplementary Table 1, univariate analyses revealed significant associations between various factors and in-hospital mortality in patients with COVID-19 (all $p < 0.05$). These variables included age, T, RR, history of HTN, use of HFNC, NIV, MV, COVID-19 Severity, AKI, and WBC, neutrophilic granulocyte percentage, lymphocyte percentage, HB, AST, ALB, BUN, BAR, and creatinine levels. Nevertheless, after adjusting for potential confounding factors based on the results of the univariate analysis, the multivariate analysis revealed a significant association between BAR and in-hospital mortality. Hazard ratios (HRs) and 95% confidence intervals (CIs) are summarized in Table 2. The HRs remained robust between the unadjusted and adjusted models in all 3 models ($P < 0.05$). In the unadjusted model, a difference of 1 unit of BAR was associated with a 9% difference in in-hospital mortality (HR 1.09 [95% CI 1.07–1.11]). In the fully adjusted model (i.e., model 3), for each additional 1 unit of BAR, the effect size increased by 6% (HR 1.06 [95% CI 1.03–1.08]).

For further sensitivity analysis, the continuous variable BAR was classified into tertiles, with the initial category serving as the baseline reference. Participants within the highest BAR tertile exhibited an elevated risk for in-hospital mortality compared with those in the lowest BAR tertile (HR 2.44 [95% CI 1.24–4.79]). Kaplan–Meier survival curves, depicted in Fig. 2, were used to evaluate in-hospital mortality among patients with COVID-19 with various BAR levels. In addition, stratified and interaction analyses were used to examine whether the association between BAR and in-hospital mortality remained consistent across various subgroups, including age, sex, COVID-19 severity, HTN, CHD, and DM. The findings from these analyses were consistent (Fig. 3).

Discussion

Results of the current study provide evidence supporting an independent association between BAR and adverse outcomes in individuals diagnosed with COVID-19. Increased BAR was found to be significantly associated with decreased survival rates among patients with COVID-19.

Studies have substantiated that the BAR prognosticates long-term mortality in patients with acute myocardial infarction within the intensive care setting, in addition to forecasting mortality in hospitalized geriatric cohorts [19] and patients experiencing acute pulmonary thromboembolism [20, 21].One investigation identified a substantial link between augmented BAR and diminished survival in septic individuals admitted to intensive care units in the United States [22]. In addition, BAR was found to independently prognosticate 30-day mortality and disease severity in patients with *Escherichia coli* bacteremia [23]. Zeng et al. [24] reported that elevated BAR robustly and independently predicated all-cause mortality during hospitalization and at a 90-day interval in individuals experiencing acute exacerbation of COPD. A meta-analytical review confirmed the association of BAR with adverse prognoses in patients with community-acquired pneumonia [25]. It has also been demonstrated that BAR, along with BUN and ALB levels, can reliably predict emergency and in-hospital mortality in patients with COVID-19, with BAR being more reliable than BUN and ALB alone [16, 26].Ata et al. [27] reported that BAR was an even better independent predictor of in-hospital mortality than BUN or ALB in patients with severe SARS-CoV-2 infection. The BAR has emerged as a significant prognostic marker for evaluating patient outcomes and mortality rates in various medical conditions, including pneumonia and its severity grading, cardiovascular diseases, and gastrointestinal diseases [25, 28–31].The precise pathophysiological mechanisms linking the blood–urea–nitrogen-to-albumin ratio (BAR) with increased mortality risk in hospitalized COVID-19 patients remain unclear; however, several potential mechanisms may be involved. Oxidative stress and inflammation: In patients with COVID-19, the aberrant activation of immune cells, such as macrophages and neutrophils, leads to elevated levels of reactive oxygen species (ROS). This state of oxidative stress exacerbates cellular damage, resulting in the release of intracellular genetic material and subsequently triggering toxic stress responses in epithelial cells, which may cause pulmonary edema and

Table 1 Demographic characteristics, symptoms treatment, laboratory findings and outcome of the patients with COVID-19 stratified by tertiles of BAR

Variables	Total ($n=1027$)	T1 ($n=341$) (1.134–3.932)	T2 ($n=343$) (3.944–5.793)	T3 ($n=343$) (5.811–48.3)	p
Sex, *n* (%)					
Male	569 (55.4)	146 (42.8)	199 (58)	224 (65.3)	< 0.001
Age, (y)	72.1 ± 13.0	65.8 ± 14.5	73.3 ± 11.2	77.1 ± 10.2	< 0.001
LOS, (day)	11.0 (7.0, 15.0)	10.0 (7.0, 13.0)	11.0 (8.0, 15.0)	12.0 (7.0, 17.0)	0.002
Drinking status, *n* (%)					
Never	891 (86.8)	297 (87.1)	298 (86.9)	296 (86.3)	0.301
Ever	52 (5.1)	11 (3.2)	20 (5.8)	21 (6.1)	
Current	84 (8.2)	33 (9.7)	25 (7.3)	26 (7.6)	
Smoking status, *n* (%)					
Never	850 (82.8)	289 (84.8)	290 (84.5)	271 (79)	0.005
Ever	113 (11.0)	24 (7)	37 (10.8)	52 (15.2)	
Current	64 (6.2)	28 (8.2)	16 (4.7)	20 (5.8)	
T(℃)	36.8 ± 0.6	36.7 ± 0.5	36.8 ± 0.6	36.8 ± 0.6	0.243
COVID-19 Severity, n (%)	356 (34.7)	68 (19.9)	112 (32.7)	176 (51.3)	< 0.001
P(bpm)	85.4 ± 16.8	85.0 ± 15.6	84.0 ± 17.0	87.3 ± 17.6	0.034
RR(bpm)	20.7 ± 3.9	20.0 ± 2.5	20.8 ± 4.0	21.2 ± 4.7	< 0.001
SBP(mmHg)	135.5 ± 21.5	136.1 ± 20.1	135.2 ± 21.6	135.1 ± 22.9	0.796
DBP(mmHg)	78.5 ± 13.3	80.0 ± 12.9	77.8 ± 13.1	77.9 ± 13.9	0.058
BMI(kg/m^2)	24.2 ± 4.1	24.7 ± 4.0	24.3 ± 4.1	23.6 ± 4.2	0.008
Fever, *n* (%)	722 (70.3)	228 (66.9)	249 (72.6)	245 (71.4)	0.223
Cough, *n* (%)	752 (73.2)	256 (75.1)	255 (74.3)	241 (70.3)	0.309
CHD, *n* (%)	310 (30.2)	99 (29)	99 (28.9)	112 (32.7)	0.475
DM, *n* (%)	277 (27.0)	71 (20.8)	95 (27.7)	111 (32.4)	0.003
HTN, *n* (%)	477 (46.4)	141 (41.3)	160 (46.6)	176 (51.3)	0.033
COPD, *n* (%)	66 (6.4)	18 (5.3)	23 (6.7)	25 (7.3)	0.545
Cancer, *n* (%)	125 (12.2)	38 (11.1)	47 (13.7)	40 (11.7)	0.556
CVD, *n* (%)	217 (21.1)	55 (16.1)	73 (21.3)	89 (25.9)	0.007
HFNC, *n* (%)	98 (9.5)	15 (4.4)	29 (8.5)	54 (15.7)	< 0.001
NIV, *n* (%)	34 (3.3)	7 (2.1)	7 (2)	20 (5.8)	0.006
MV, *n* (%)	30 (2.9)	0 (0)	13 (3.8)	17 (5)	< 0.001
AKI, *n* (%)	202 (19.7)	72 (21.1)	64 (18.7)	66 (19.2)	0.7
Non-survivor, *n* (%)	117 (11.4)	11 (3.2)	35 (10.2)	71 (20.7)	< 0.001
WBC(10^9/L)	6.4 (4.7, 8.8)	6.0 (4.5, 7.8)	6.4 (4.6, 8.4)	7.0 (5.2, 10.5)	< 0.001
Lymphocyte, (%)	14.3 (8.4, 22.4)	18.1 (12.5, 26.7)	15.5 (8.9, 23.8)	9.6 (5.6, 16.0)	< 0.001
NEU(%)	74.1 ± 13.6	70.1 ± 12.4	72.7 ± 13.5	79.6 ± 13.1	< 0.001
Hb(g/L)	126.4 ± 25.3	130.0 ± 33.1	127.0 ± 18.3	122.2 ± 21.6	< 0.001
Platelet (10^9/L)	210.2 ± 94.7	221.6 ± 89.6	212.4 ± 90.1	196.6 ± 102.4	0.002
ALT(U/L)	23.0 (15.0, 35.0)	22.0 (15.0, 33.0)	21.0 (14.0, 34.0)	25.0 (17.0, 40.0)	0.009
AST(U/L)	24.0 (18.0, 36.0)	22.0 (17.0, 29.0)	24.0 (17.0, 36.0)	29.0 (19.0, 44.0)	< 0.001
BUN(mmol/L)	5.7 (4.5, 7.7)	4.0 (3.5, 4.7)	5.8 (5.2, 6.4)	8.9 (7.6, 11.6)	< 0.001
ALB(g/L)	34.3 ± 5.0	37.2 ± 4.4	34.4 ± 4.2	31.3 ± 4.7	< 0.001
CREA (umol/L)	69.0 (56.8, 89.0)	60.1 (51.3, 71.7)	68.6 (58.0, 81.8)	87.2 (68.3, 121.2)	< 0.001
CRP(mg/L)	46.5 (14.7, 97.2)	24.5 (6.5, 61.7)	49.0 (16.0, 93.7)	72.2 (28.6, 133.0)	< 0.001
Potassium (mmol/L)	3.8 ± 0.6	3.7 ± 0.5	3.8 ± 0.5	3.9 ± 0.6	< 0.001
Sodium (mmol/L)	137.3 ± 6.0	137.7 ± 4.1	136.8 ± 7.6	137.4 ± 5.8	0.143
Chlorine (mmol/L)	103.5 ± 7.1	103.5 ± 4.2	103.1 ± 8.2	103.8 ± 8.0	0.48

CHD Coronary heart disease, *DM* Diabetes mellitus, *HTN* Hypertention, *COPD* Chronic obstructive pulmonary disease, *CVD* Cerebrovascular disease, *RR* Respiratory rate, *T* Body temperature, *HFNC* High flow nasal cannula, *MV* Mechanical ventilation, *NIV* Noninvasive ventilation, *AKI* Acute kidney injury, *LOS* Length of stay, *BMI* Body mass index, *CRP* C-reactive protein, *bpm* Breaths per minute, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *WBC* White blood count, *NEU%* Neutrophilic granulocyte percentage, *HB* Hemoglobin, *ALB* Albumin, *BUN* Blood–urea–nitrogen, *BAR* Blood–urea–nitrogen-to-serum albumin ratio, *AST* Aspartate transaminase, *ALT*

Table 1 (continued)

Alanine transaminase, *SD* Standard deviation, *IQR* Interquartile range, *CI* Confidence interval, *HR* Hazard ratio

Table 2 Multivariable cox regression analysis to assess the association between BAR and in-hospital mortality

Variable	*n*. event(%)	Unadjusted		Model1		Model2		Model3	
		HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*
BAR(mg/g)	117 (11.4)	1.09 (1.07 ~ 1.11)	< 0.001	1.06 (1.04 ~ 1.08)	< 0.001	1.06 (1.03 ~ 1.08)	< 0.001	1.06 (1.03 ~ 1.08)	< 0.001
Tertiles									
T1	11 (3.2)	1(Ref)		1(Ref)		1(Ref)		1(Ref)	
T2	35 (10.2)	2.74 (1.39 ~ 5.42)	0.004	1.91 (0.96 ~ 3.79)	0.066	1.88 (0.94 ~ 3.75)	0.074	1.9 (0.95 ~ 3.8)	0.069
T3	71 (20.7)	4.95 (2.61 ~ 9.39)	< 0.001	2.62 (1.35 ~ 5.09)	0.005	2.54 (1.3 ~ 4.97)	0.006	2.44 (1.24 ~ 4.79)	0.009
P for Trend	117 (11.4)		< 0.001		0.003		0.005		0.009

Model 1 Adjusted for sex + age + COVID-19 Severity

Model 2 Adjusted for model1 + Coronary heart disease + Hypertention + Diabetes mellitus + Cancer + chronic obstructive pulmonary disease + Cerebrovascular Disease

Model 3 Adjusted for model2 + Hemoglobin + Platelet

BAR Blood–urea–nitrogen-to-serum albumin ratio, *CI* confidence interval, *HR* Hazard ratio, *Ref* reference

uncontrolled inflammatory responses. These factors collectively contribute to severe clinical outcomes, including multiple organ dysfunction and death [32, 33]. Albumin oxidation and cytokine storm: Due to SARS-CoV-2 infection, serum albumin may undergo oxidation, becoming part of a positive feedback loop in the inflammatory response. Activated leukocytes synthesize cytokines, enhancing the release of pro-inflammatory cytokines, which may trigger a cytokine storm. This cytokine storm further intensifies inflammation and tissue damage, potentially leading to critical clinical conditions or mortality [34]. In addition, low serum albumin levels may significantly impact endothelial dysfunction. The reduction in albumin synthesis, coupled with an increase in inflammatory catalysts, contributes to a heightened systemic inflammatory state [35]. Renal injury and vascular damage: COVID-19 and associated inflammatory mediators directly induce widespread endothelial injury, resulting in decreased levels of vasodilators, such as nitric oxide. This vasoconstrictive response diminishes renal perfusion, leading to prerenal azotemia. Furthermore, endothelial injury activates the coagulation cascade, resulting in microvascular damage and disseminated intravascular coagulation (DIC), which are closely associated with COVID-19-related renal impairment. In addition, SARS-CoV-2 may exert direct effects on the kidneys through viral tropism, leading to cellular damage within the renal tissue and complement activation, thereby further increasing the risk of renal injury [36, 37]. Further well-designed clinical studies with large sample sizes are necessary to investigate and elucidate the mechanisms underlying the relationship between BAR and COVID-19-related hospital mortality.

This study had several notable strengths. First, the BAR indicator was determined through a straightforward and cost-effective approach. Second, to mitigate potential confounding factors, we incorporated both continuous and categorical independent variables, thereby reducing the likelihood of errors in data analysis and bolstering the reliability of the conclusions. Finally, subgroup analyses were performed, yielding no significant interactions, thus fortifying the robustness of this investigation.

Nevertheless, several limitations should be acknowledged. First, this retrospective study was conducted at a single medical center, possibly introducing confounding and bias. Second, the serum levels of BUN and albumin may be influenced by factors, such as dietary composition, nutritional status, and muscle loss. Due to the limitations of our data, we were unable to obtain information regarding these factors, which may introduce selection bias into our study. Third, we undertook multiple statistical analyses on a non-randomized cohort. Although these analyses provide important insights into the interrelationships of variables, the involvement of multiple comparisons increases the likelihood of Type I errors. Thus, it is essential to approach the interpretation of results with caution. Future investigations should consider implementing more rigorous randomized design methodologies to substantiate our findings. Fourth, this study exclusively utilized the initial BAR measured at admission for analysis. Given that BAR may vary with treatment and disease progression, this single-point

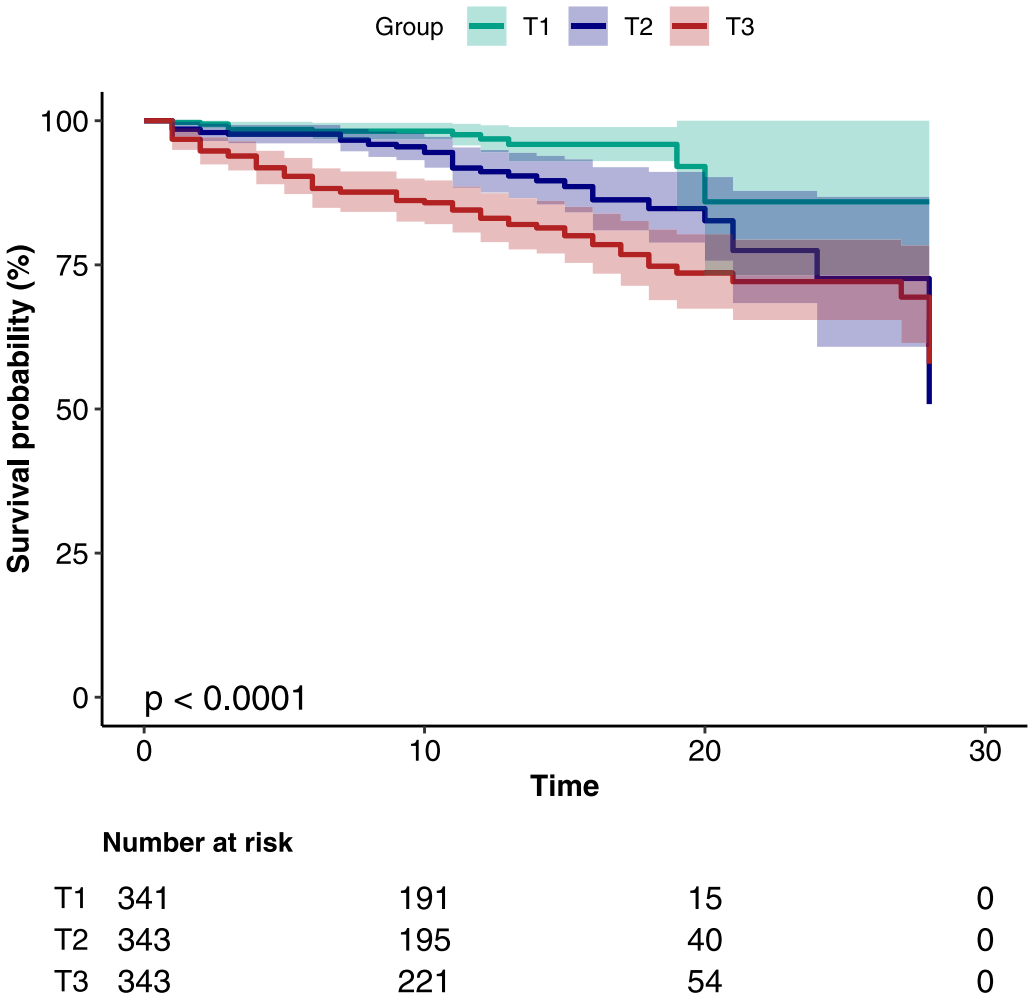

Fig. 2 Kaplan–Meier curves indicates the association between the BAR and in-hospital mortality of patients with COVID-19. Only patients with a hospital length of stay ≤ 28 days are displayed

measurement approach may introduce bias. Therefore, we recommend that future research incorporate repeated measurements to better observe the dynamic characteristics of BAR over time, allowing for a more comprehensive analysis. Fifth, considering the missing data rates of 23.6% for BMI and 15.3% for CRP in this study, we chose to present these variables only in the data description. However, after excluding the missing values, the results of the multivariate analysis remained stable. Finally, this study predominantly focused on a population infected with the Omicron variant of SARS-CoV-2 during the COVID-19 pandemic in China, restricting its generalizability to other populations. Therefore, additional research is warranted to address these limitations, validate the findings, and further explore the results obtained.

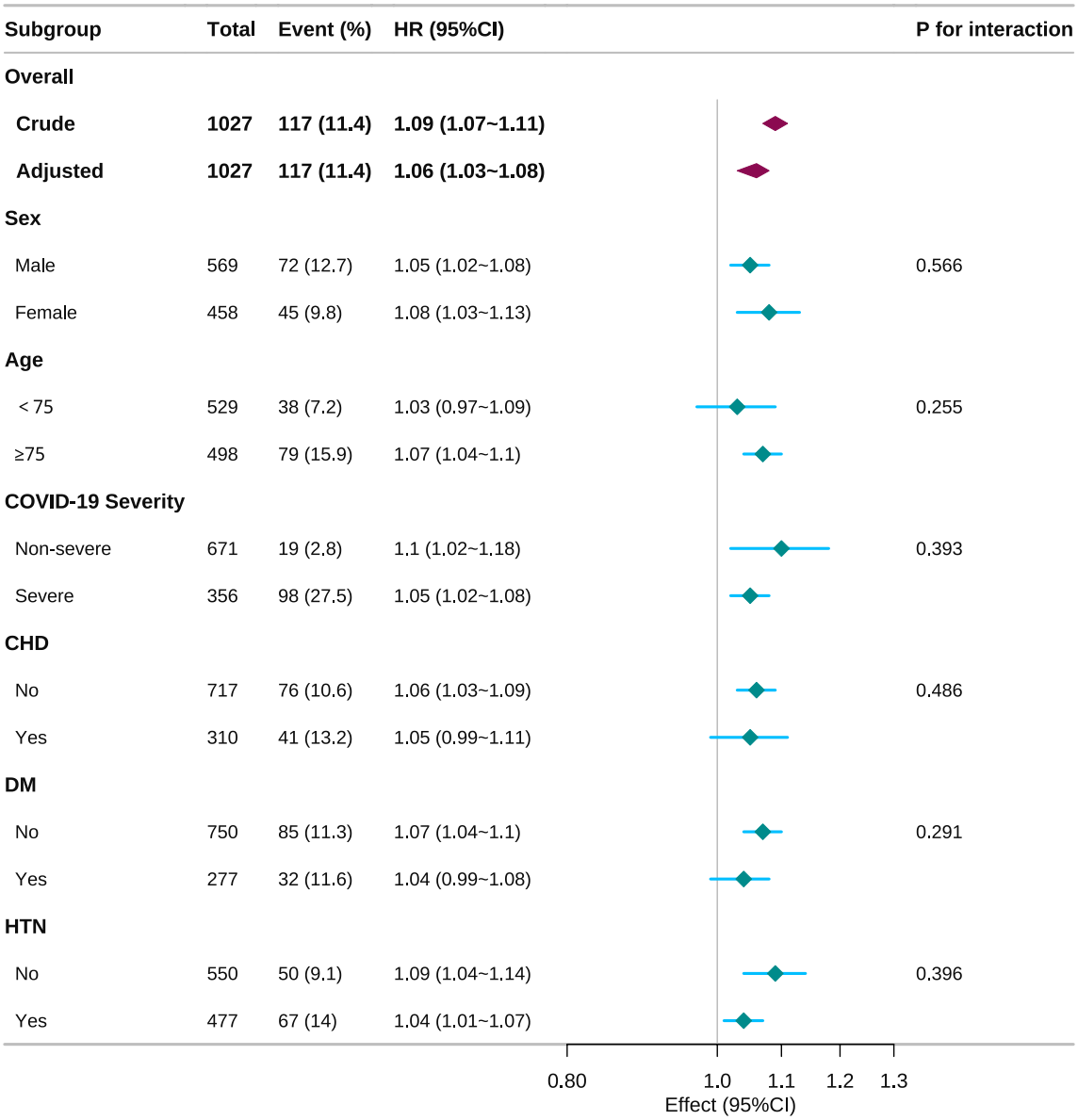

Fig. 3 Association between BAR and in-hospital mortality according to baseline characteristics. Each stratification was adjusted for age, sex, COVID-19 Severity, coronary heart disease, hypertention, diabetes mellitus, cancer, chronic obstructive pulmonary disease, cerebrovascular disease, platelet, and hemoglobin, except the stratification factor itself

Conclusion

In this study, we identified a correlation between initial BAR and in-hospital mortality among patients with COVID-19. Our findings indicate a significant association between elevated BAR levels and decreased survival rates in individuals affected by COVID-19.

Abbreviations

ALB	Albumin
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BAR	Blood–urea–nitrogen-to-albumin ratio
BUN	Blood–urea–nitrogen
T	Body temperature
WBC	White blood cell
CHD	Coronary heart disease
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
DM	Diabetes mellitus
HFNC	High-flow nasal cannula
HB	Hemoglobin
HTN	Hypertension
MV	Mechanical ventilation
NIV	Non-invasive ventilation

BMI	Body mass index
AKI	Acute kidney injury
RR	Respiratory rate
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

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Author contributions
D P designed the study, collected data, and performed statistical analyses. R Z drafted the manuscript, and all the authors have read and approved the final manuscript.

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Availability of data and materials
The datasets are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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