Liu *et al. BMC Neurology* (2024) 24:351
https://doi.org/10.1186/s12883-024-03763-4

BMC Neurology

RESEARCH Open Access

Association between base excess and mortality in critically ill patients with ischemic stroke: a retrospective cohort study

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Abstract

Background Base excess (BE) is associated with mortality from many diseases. However, the relationship between BE and mortality in patients with ischemic stroke remains uncertain. Our aim is to investigate the relationship between BE values upon admission to the ICU and mortality rates in critically ill stroke patients.

Methods The current study enrolled 1,572 patients with ischemic stroke (863 males and 709 females). The associations of BE with intensive care unit (ICU), hospital, 28-day, and 1-year mortalities were assessed using multivariable logistic regression or Cox proportional hazards model. The potential impact of the Sequential Organ Failure Assessment (SOFA) score (< 5 or ≥ 5) on the prognostic value of BE was further evaluated with interaction and subgroup analyses.

Results BE values less than − 3 mmol/L, greater than 3 mmol/L, and within − 3 to 3 mmol/L (normal BE) were observed in 316 (20.1%), 175 (11.1%), and 1,081 (68.8%) patients, respectively. The restricted cubic splines analyses revealed that a U-shaped curve between BE and the mortality risk. Multivariable analysis indicated that patients with low BE (<-3 mmol/L) had higher rates of ICU mortality (odds ratio [OR], 1.829; 95% confidence interval [CI], 1.281–2.612; $P = 0.001$), hospital mortality (OR, 1.484; 95% CI, 1.077–2.045; $P = 0.016$), 28-day mortality (hazard ratio [HR], 1.522; 95% CI, 1.200–1.929; $P = 0.001$), and 1-year mortality (HR, 1.399; 95% CI, 1.148–1.705; $P = 0.001$) than patients with normal BE. Subgroup analyses showed consistent results pertaining to SOFA scores ≥ 5.

Conclusions In critically ill patients with ischemic stroke, an initial BE of <-3 mmol/L at ICU admission may indicate an increased risk of ICU, hospital, 28-day, and 1-year mortalities.

Keywords Ischemic stroke, Base excess, Mortality, Intensive care units, Cohort study

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Introduction

Stroke is the most common severe manifestation of cerebrovascular disease and the leading cause of disability [1]. In 2019, there were 7.63 million cases of incident ischemic stroke, and 3.29 million deaths from ischemic stroke [2]. Stroke keeps the second material reason of death and disability worldwide [3, 4]. Studies suggest that acute stroke needing ICU admission is associated with a poor prognosis [5].

Previous studies have shown that acid-base imbalance is associated with poor prognosis in stroke patients [6]. Base excess (BE) refers to the acid consumption when titrating 1 L whole blood to neutral pH (pH=7.4) at 37 ℃, under PCO_2=40mmHg and complete oxygenation of hemoglobin [7]. The calculation formula for BE in clinical practice is as follows: BE = (HCO_3^- - 24.8) + β (pH-7.40), where 24.8 and 7.40 are the reference, ideal HCO_3^- (mmol/L) and pH values, and β is the buffer power (mmol/L) of non-carbonic weak acids [8]. Compared with the normal range of BE (−3 mmol/L≤BE≤3 mmol/L), low BE values represent metabolic acidosis, while high BE values represent metabolic alkalosis [9]. Previous studies have demonstrated that BE is related to mortality in patients with congestive heart failure (CHF) [10], acute kidney injury (AKI) [11], multiple trauma [12], and sepsis [13]. Among them, a U-shaped relationship between BE and mortality risk has been reported in patients with CHF or AKI [10, 11]. However, the relationship between BE and mortality in critically ill patients with ischemic stroke remains unclear. Being a crucial instrument for evaluating the acid-base equilibrium of patients within the intensive care unit, BE potentially correlates with unfavorable prognoses among stroke patients [14]. Delving into the correlation between BE levels upon ICU admission and the prognostic outcomes in stroke patients may contribute to refining patient care practices in clinical settings. Consequently, we performed a retrospective observational cohort study of data in the Multiparameter Intelligent Monitoring in Intensive Care IV (MIMIC-IV) database to evaluate the correlation between BE and mortality in patients with ischemic stroke in the ICU.

Methods

Study design

This was an observational, retrospective cohort study based on the data from the MIMIC-IV database (version 2.2), authorized by the Institutional Review Boards (IRB) of Beth Israel Deaconess Medical Centre (Boston, MA) and Massachusetts Institute of Technology (MIT; Cambridge, MA). As there is pre-existing institutional review board approval in the MIMIC-IV database, we were exempt from IRB approval from our institution. This database is a broad, freely available database containing health-related data of over 380,000 patients admitted to the Beth Israel Deaconess Medical Centre from 2008 to 2019 [15]. To protect patient privacy, patients in the database are anonymous [15]. All the authors completed the essential online training and gained permission to access the MIMIC database.

Study population

Patient information was gained from the MIMIC-IV database. The inclusion criteria were (1) first hospital admission, (2) age≥18 years old. The exclusion criteria were (1) patients without a diagnosis of ischemic stroke, as defined by the International Classification of Diseases (ICD)-9 or ICD-10 codes, (2) patients without an initial BE at ICU admission, and (3) patients with ICU length of stay≤24 h.

BE and outcomes

According to the first record of BE from arterial blood at ICU admission, the patients were divided into three groups: low BE group (BE < -3 mmol/L), normal BE group (-3 mmol/L≤BE≤3 mmol/L), and high BE group (BE>3 mmol/L). The central outcome indicators in our study were ICU and hospital mortalities. The secondary outcome indicator was 28-day mortality and 1-year mortality. ICU mortality referred to death before the first ICU discharge for all causes. Meanwhile, ICU, hospital, and 28-day mortalities were considered short-term mortality, and 1-year mortality was considered long-term mortality.

Data extraction

All patient data were extracted from the MIMIC-IV database: age, sex, ethnicity, length of ICU stay, Sequential Organ Failure Assessment (SOFA) score at admission, use of mechanical ventilation (invasive, and non-invasive), medication from one day before admission to the time before the first measurement of BE (including vasopressors, vasodepressor, sedatives, anticoagulant, and mannitol), comorbidities (diabetes, hypertension, malignant neoplasm, heart failure, hyperlipemia, chronic hepatic failure, chronic respiratory failure, chronic kidney disease, sepsis, disseminated intravascular coagulation [DIC], pneumonia and diarrhea), first measurement of BE at ICU admission, and study outcomes (including ICU death, hospital death, 28-day death and 1-year death). All the diseases were classified using the ICD-9 or ICD-10 codes. Data were obtained using SAS version 9.4 (SAS Institute, Cary, NC).

Statistical analysis

Continuous variables were presented as medians and inter-quartile ranges (IQRs) and compared using the Kruskal–Wallis test. Categorical variables were presented

as frequencies with percentages and compared using the Chi-squared test. To assess the impact of BE on the outcomes, this study used univariable and multivariable logistic regression models for ICU mortality and hospital mortality and Cox proportional hazards models for 28-day mortality and 1-year mortality. In multivariable regression analyses, four models were established to show the modeling process, which could support the stability of the association between the BE and mortality. Model 1 was adjusted for the SOFA score. Model 2 was adjusted for the covariates included in model 1 plus age, sex, and ethnicity. Model 3 was adjusted for the covariates included in model 2 and the admission diagnoses. Model 4 was adjusted for the covariates included in model 3 and the treatment measures. The R squares of each model is provided in supplementary table. The SOFA score is an indicator of organ dysfunction related to the prognosis of patients [16]. Interaction and subgroup analyses were proceeded to confirm whether the impact of BE on mortality invariable in each subgroup (SOFA score [<5 vs. ≥5]). In subgroup analysis, covariates include demographic characteristics and treatment measures. A two-sided *P*-value<0.05 was considered statistically significant. All data analyses were accomplished using SPSS version 18.0 (IBM Corp, Armonk, NY).

Result

Individual selection and baseline characteristics

From the 50,920 adult patients extracted from the MIMIC-IV database, exclude the following patients: 47,664 without a diagnosis of ischemic stroke, 1,618 without an initial BE at ICU admission, and 66 with ICU stays≤24 h. Eventually, 1,572 patients were included (Fig. 1). A total of 570 patients (36.3%) experienced cerebral infarction as a result of precerebral artery occlusion, 912 patients (58.0%) due to cerebral artery occlusion, and 185 patients (11.8%) due to various other factors, including cerebral venous thrombosis. The 1179 (75.0%) patients were aged≥60 years, 863 (54.9%) were male, and 979 (62.3%) were White. The median (IQR) of SOFA score was 5 (3–7). The median (IQR) of BE at ICU admission was 0 (-3–2) mmol/L. The patients were divided

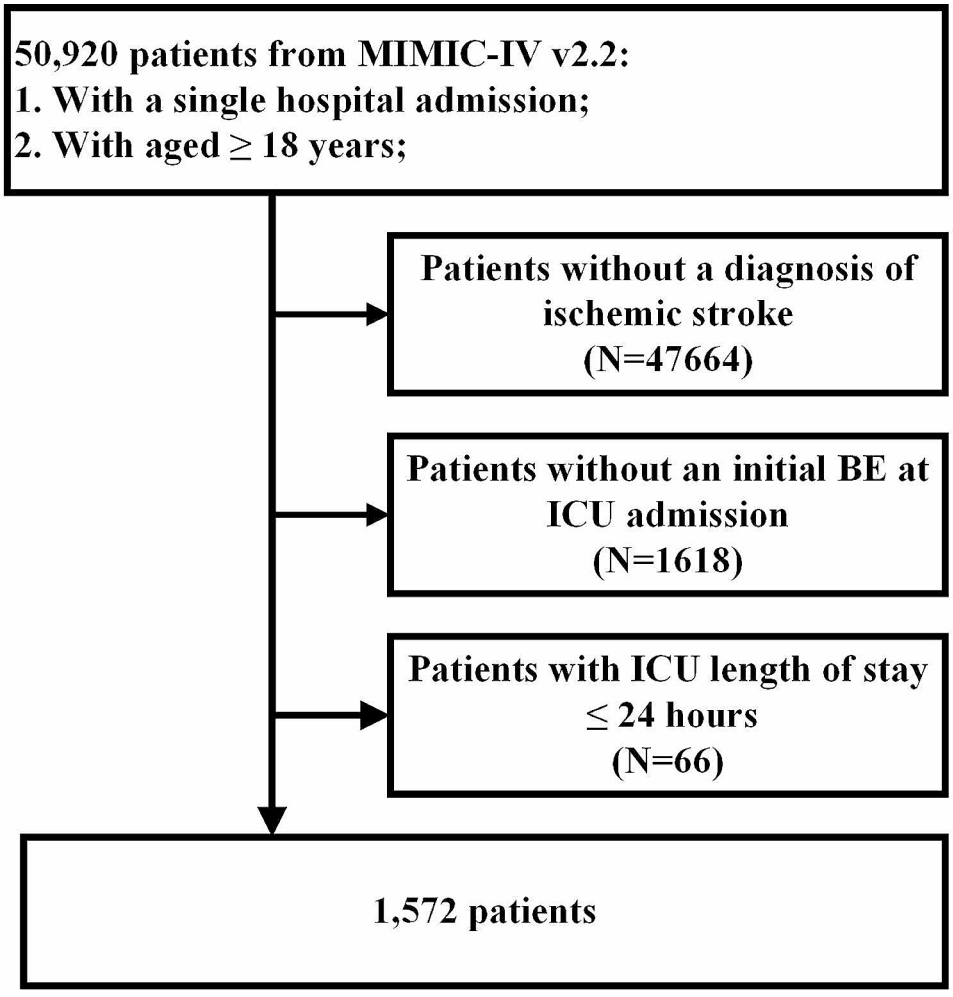

Fig. 1 Participant selection. MIMIC-IV, Multiparameter Intelligent Monitoring in Intensive Care IV; BE, Base Excess; ICU, Intensive Care Unit

into three groups according to the BE: <-3 mmol/L (316, 20.1%), -3 to 3 mmol/L (1081, 68.8%), and >3 mmol/L (175, 11.1%). The age ($P=0.029$), SOFA score ($P<0.001$), treatment measures (vasoactive drugs [$P<0.001$], mannitol [$P=0.012$], and mechanical ventilation [$P=0.017$]), and diagnoses (hyperlipemia [$P=0.007$], heart failure [$P<0.001$], chronic kidney disease [$P=0.007$], and sepsis [$P<0.001$]) were significant different among the three groups (Table 1).

Association of BE with mortality

The low BE group showed higher ICU mortality and hospital mortality than the normal (24.4% versus 12.9%, $P<0.001$, respectively; 30.7% versus 20.7%, $P<0.001$, respectively) and high BE groups (24.4% versus 14.9%, $P=0.015$, respectively; 30.7% versus 19.4%, $P=0.008$, respectively) (Fig. 2-a, b). Kaplan–Meier survival curves showed that the survival probability of 28-day and 1-year were lower in the low BE group than in the normal BE group ($P<0.001$; $P<0.001$) (Fig. 2-c, d). To visualize the

Table 1 Demographic characteristics of normal, low, and high BE groups

Characteristics	Total ($n=1572$)	Base excess (mmol/L)			*P*-value
		-3–3 ($n=1081$)	< -3 ($n=316$)	> 3 ($n=175$)	
Base excess (mmol/L), median (IQR)	0 (-3–2)	0 (-1–1)*	-6 (-9 – -5)	5 (4–7)*	< 0.001
Stroke, n (%)					
Due to occlusion of precerebral arteries	570 (36.30)	424 (39.20)	71 (22.50)	75 (42.90)	< 0.001
Due to occlusion of cerebral arteries	912 (58.00)	610 (56.40)	205 (64.90)	97 (55.4)	0.021
Other cerebral infarction	185 (11.80)	121 (11.20)	53 (16.80)	11 (6.30)	0.001
Age, n (%)					0.029
Age ≥ 60 years	1179 (75.00)	812 (75.10)	224 (70.90)	143 (81.70)*	
Age < 60 years	393 (25.00)	269 (24.90)	92 (29.10)	32 (18.30)*	
Sex, n (%)					0.705
Male	863 (54.90)	598 (55.30)	167 (52.80)	98 (56.00)	
Female	709 (45.10)	483 (44.70)	149 (47.20)	77 (44.00)	
Ethnicity, n (%)					0.175
White	979 (62.30)	672 (62.20)	188 (59.50)	119 (68.00)	
Other	593 (37.70)	409 (37.80)	128 (40.50)	56 (32.00)	
SOFA score, median (IQR)	5 (3–7)	4 (3–6)*	8 (5–10)	4 (2–7)	< 0.001
Treatment measures, n (%)					
Vasoactive drugs	246 (15.60)	135 (12.50)*	96 (30.40)	15 (8.60)	< 0.001
Sedative	594 (37.80)	400 (37.00)	134 (42.40)	60 (34.30)	0.131
Anticoagulant	94 (6.00)	65 (6.00)	14 (4.40)	15 (8.60)	0.179
Mannitol	29 (1.80)	23 (2.10)*	0 (0.00)	6 (3.40)	0.012
Mechanical ventilation	647 (41.20)	423 (39.10)*	152 (48.10)	72 (41.10)	0.017
Admission diagnosis, n (%)					
Diabetes	554 (35.20)	376 (34.80)	108 (34.20)	70 (40.00)	0.369
Hyperlipemia	835 (53.10)	586 (54.20)*	145 (45.90)	104 (59.40)	0.007
Hypertension	1214 (77.20)	844 (78.10)	232 (73.40)	138 (78.90)	0.191
Malignant neoplasm	150 (9.50)	97 (9.00)	33 (10.40)	20 (11.40)	0.491
Heart failure	449 (28.60)	267 (24.70)*	113 (35.80)	69 (39.40)*	< 0.001
Chronic hepatic failure	5 (0.30)	4 (0.40)	1 (0.30)	0 (0.00)	0.722
Chronic respiratory failure	3 (0.20)	2 (0.20)	1 (0.30)	0 (0.00)	0.741
Chronic kidney disease	322 (20.50)	199 (18.40)*	83 (26.30)	40 (22.90)	0.007
Sepsis	1134 (72.10)	748 (69.20)*	316 (83.50)	122 (69.70)	< 0.001
DIC	21 (1.30)	12 (1.10)	7 (2.20)	2 (1.10)	0.313
Pneumonia	299 (19.00)	197 (18.20)	72 (22.80)	30 (17.10)	0.153
Diarrhea	65 (4.10)	42 (3.90)	16 (5.10)	7 (4.00)	0.649
Outcome, n (%)					
ICU mortality	242 (15.40)	139 (12.90)*	77 (24.40)	26 (14.90)*	< 0.001
Hospital mortality	355 (22.60)	224 (20.70)*	97 (30.70)	34 (19.40)*	0.001
28-day mortality	420 (26.70)	264 (24.40)*	117 (37.00)	39 (22.30)	< 0.001
1-year mortality	624 (39.70)	389 (36.00)*	165 (52.20)	70 (40.00)	< 0.001

SOFA: Sequential Organ Failure Asses; IQR, inter-quartile range; DIC, disseminated intravascular coagulation; ICU, intensive care unit

*Significantly different versus the low base excess group (*P* values < 0.05 are statistically significant)

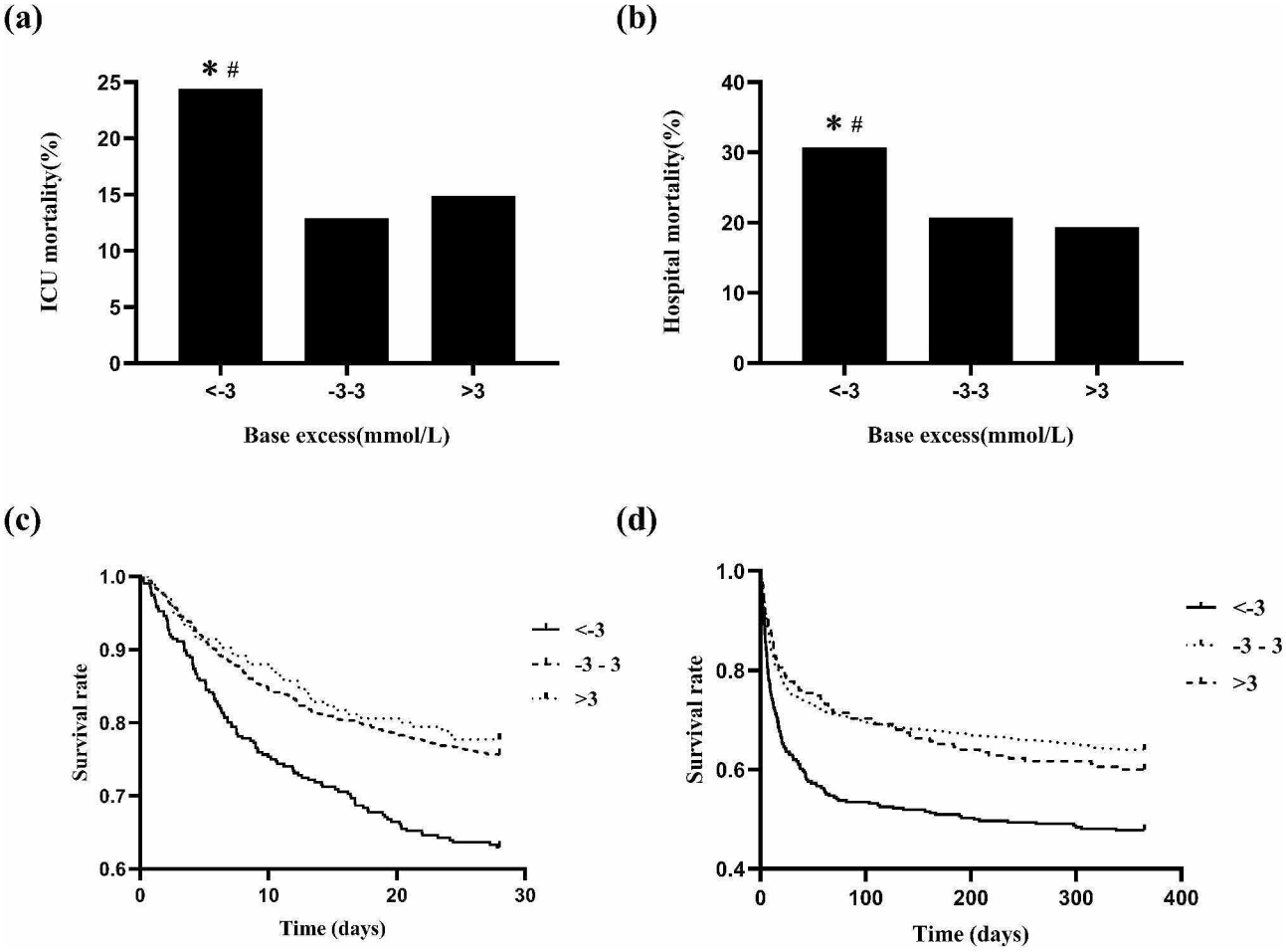

Fig. 2 Comparison of ICU, hospital, 28-days and 1-year mortalities among different BE groups. ICU, Intensive Care Unit; BE, Base Excess

relationship between BE and mortalities, we use the restricted cubic splines (RCS) analyses. The RCS analyses revealed that a U-shaped curve between BE and the mortality risk (Fig. 3). Further, the low BE group showed higher rates of ICU (odds ratio [OR], 2.183, 95% confidence interval [CI], 1.597–2.984), hospital (OR, 1.695, 95% CI, 1.280–2.244), 28-day (hazard ratio [HR], 1.664, 95% CI, 1.339–2.069), and 1-year (HR, 1.678, 95% CI, 1.399–2.014) mortality than the normal BE group in the univariable regression analyses. After multivariable adjustment, the outcomes were consistent with those gained in the univariable regression analyses (ICU mortality: OR, 1.829 [95% CI, 1.281–2.612]; hospital mortality: OR, 1.484 [95% CI, 1.077–2.045]; 28-day mortality: HR, 1.522 [95% CI, 1.200–1.929]; 1-year mortality: HR, 1.399 [95% CI, 1.148–1.705]) (Table 2). There is no significant difference in the mortality rates between the normal BE group and the high BE group.

Sensitivity analyses for association of BE with ICU/hospital/28-day/1-year mortality

The probable interaction effects of BE and diverse variables (SOFA score≥5 [n=861] and SOFA score<5 [n=711], lactate level≥2 mmol/L [n=570], lactate level<2 mmol/L [n=807]) on mortality were appraised. The interaction effect between BE and SOFA score was only observed with the outcome of 28-day mortality (ICU mortality, $P_{interaction}$ = 0.269; hospital mortality, $P_{interaction}$ = 0.307; 28-day mortality, $P_{interaction}$ < 0.001; 1-year mortality, $P_{interaction}$ = 0.223). No interaction effect between BE and lactate was observed (ICU mortality, $P_{interaction}$ = 0.542; hospital mortality, $P_{interaction}$ = 0.158; 28-day mortality, $P_{interaction}$ = 0.087; 1-year mortality, $P_{interaction}$ = 0.096).

To validate our findings, we analyzed the association between BE and mortality in subgroup of SOFA score. In the subgroup analyses, the low BE group had a higher risk of ICU mortality (OR, 2.494, 95% CI, 1.653–3.762), hospital mortality (OR, 1.840, 95% CI, 1.276–2.652), 28-day mortality (HR, 1.765, 95% CI, 1.332–2.338), and 1-year mortality (HR, 1.717, 95% CI, 1.363–2.163)

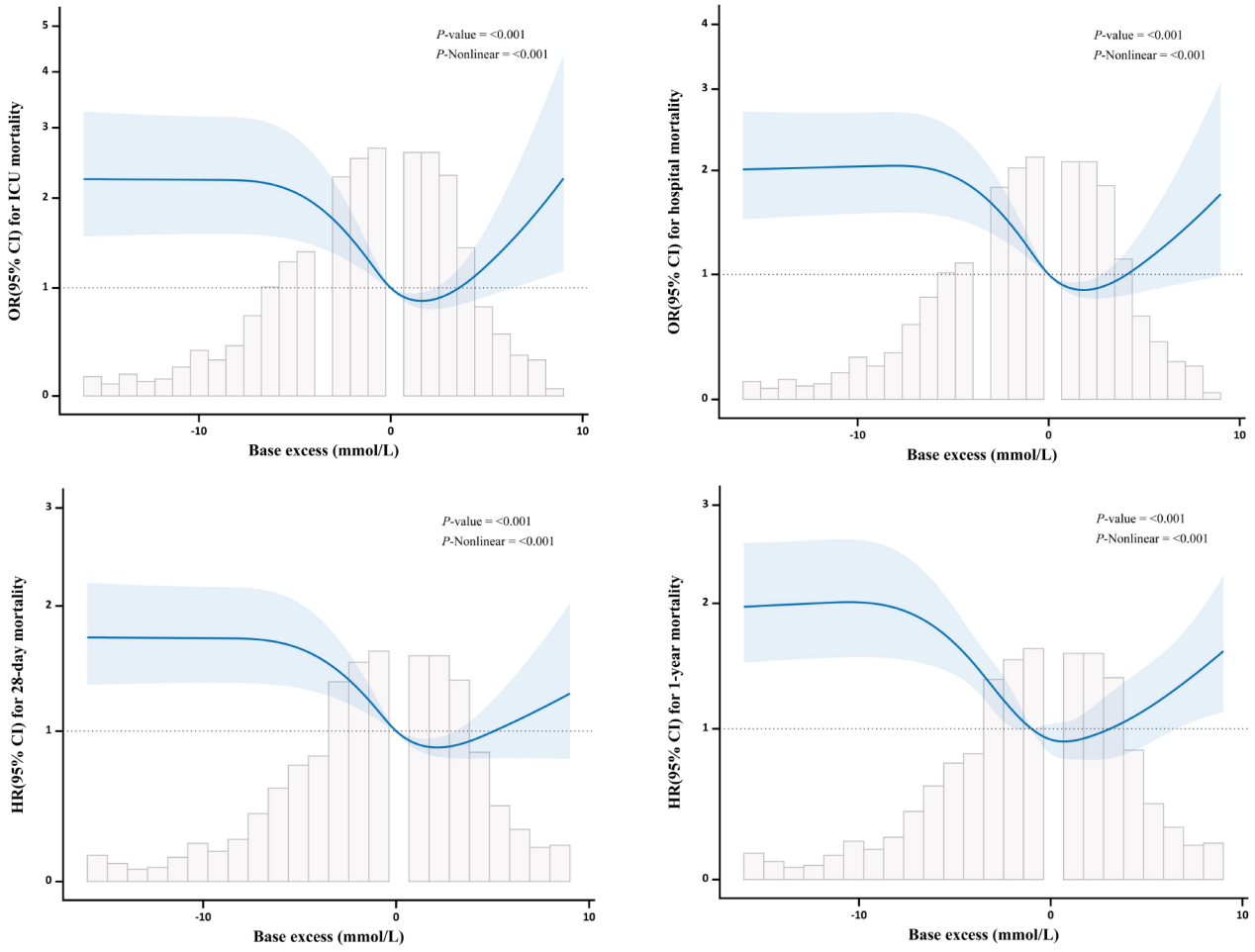

Fig. 3 The restricted spline curves for the association between BE change level and the incidence of outcomes in the whole population. OR, Odds Ratio; CI, Confidence Interval; ICU, Intensive Care Unit; HR, Hazard Ratio

than the normal BE group in the subgroup of SOFA score≥5(Fig. 4). In the subgroup of SOFA score<5, no significant difference in the mortality rates between the normal BE group and the low BE group (Fig. 4).

Discussion

We performed a retrospective cohort study to explore the association between BE and mortality in critically ill patients with ischemic stroke. Our study showed that patients with low BE values (<-3 mmol/L) had higher risks of ICU, hospital, 28-day, and 1-year mortalities than those with normal BE values (-3 mmol/L≤BE≤3 mmol/L). No significant difference in the mortality rates between the normal group and the high group.

The severity of the metabolic acid-base disorder can affect the regulation of cerebral blood flow, thereby affecting the prognosis of stroke patients [17]. Effective predictors are vital for managing stroke patients in the critical care unit [18]. BE is one of the common markers of acid–base balance disorders [7], serving as a useful biochemical marker of shock, which is an indicator for immediate physiological assessment and resuscitation initiation as well as a predictor of prognosis in many diseases [12, 19]. A retrospective study of 2441 patients with multiple traumas in the ICU indicated that BE was an independent predictor of 72-h mortality [20]. Another study also showed that BE was a suitable predictor of mortality in patients in the ICU for medical causes [21]. Previous studies have shown a U-shaped relationship between BE value and all-cause mortality in patients with congestive heart failure or acute kidney injury [10, 11]. Cheng et al. divided 14,238 ICU patients with AKI into five groups according to BE and found that compared with normal BE (−3 to 3 mEq/L), both low BE (BE≤−3 mEq/L) and high BE (BE≥9 mEq/L) increased the risk of 30-day ICU mortality [11]. Another study used the group with 3<BE≤2 mEq/L as the reference population found that both low and high BE increased the risk of all-cause mortality in patients with CHF in the ICU [10]. However, the ability of BE value to predict outcomes in critically

Table 2 ORs and HRs with 95% CIs for the association between base excess and ICU/hospital/28-day/1-year mortality

Regression models	Base excess (mmol/L)				
	-3–3	< -3		> 3	
ICU mortality		**OR (95%CI)**	***P*-value**	**OR (95%CI)**	***P*-value**
Event, n (%)	139 (12.90)	77 (24.40)		26 (14.90)	
Univariable model	1 (ref)	2.183 (1.597–2.984)	< 0.001	1.183 (0.752–1.860)	0.468
Multivariable Model 1	1 (ref)	1.768 (1.263–2.475)	0.001	1.193 (0.757–1.880)	0.447
Multivariable Model 2	1 (ref)	1.780 (1.264–2.507)	0.001	1.229 (0.775–1.949)	0.381
Multivariable Model 3	1 (ref)	1.795 (1.266–2.546)	0.001	1.293 (0.809–2.066)	0.283
Multivariable Model 4	1 (ref)	1.829 (1.281–2.612)	0.001	1.190 (0.737–1.921)	0.477
Hospital mortality		**OR (95%CI)**	***P*-value**	**OR (95%CI)**	***P*-value**
Event, n (%)	124 (20.70)	97 (30.70)		34 (19.40)	
Univariable model	1 (ref)	1.695 (1.280–2.244)	< 0.001	0.923 (0.617–1.379)	0.695
Multivariable Model 1	1 (ref)	1.448 (1.072–1.957)	0.016	0.928 (0.620–1.388)	0.715
Multivariable Model 2	1 (ref)	1.454 (1.069–1.978)	0.017	0.938 (0.622–1.415)	0.760
Multivariable Model 3	1 (ref)	1.460 (1.066–2.001)	0.019	0.955 (0.628–1.452)	0.829
Multivariable Model 4	1 (ref)	1.484 (1.077–2.045)	0.016	0.877 (0.572–1.344)	0.547
28-day mortality		**HR (95%CI)**	***P*-value**	**HR (95%CI)**	***P*-value**
Event, n (%)	264 (24.40)	117 (37.00)		39 (22.30)	
Univariable model	1 (ref)	1.664 (1.339–2.069)	< 0.001	0.901 (0.644–1.261)	0.543
Multivariable Model 1	1 (ref)	1.499 (1.187–1.893)	0.001	0.908 (0.649–1.271)	0.573
Multivariable Model 2	1 (ref)	1.489 (1.180–1.879)	0.001	0.895 (0.639–1.253)	0.517
Multivariable Model 3	1 (ref)	1.482 (1.173–1.873)	0.001	0.928 (0.660–1.304)	0.668
Multivariable Model 4	1 (ref)	1.522 (1.200-1.929)	0.001	0.884 (0.628–1.244)	0.480
1-year mortality		**HR (95%CI)**	***P*-value**	**HR (95%CI)**	***P*-value**
Event, n (%)	389 (36.00)	165 (52.20)		70 (40.00)	
Univariable model	1 (ref)	1.678 (1.399–2.014)	< 0.001	1.104 (0.856–1.424)	0.446
Multivariable Model 1	1 (ref)	1.468 (1.207–1.785)	< 0.001	1.119 (0.867–1.443)	0.387
Multivariable Model 2	1 (ref)	1.483 (1.221–1.802)	< 0.001	1.079 (0.836–1.392)	0.559
Multivariable Model 3	1 (ref)	1.405 (1.153–1.711)	0.001	1.052 (0.812–1.363)	0.701
Multivariable Model 4	1 (ref)	1.399 (1.148–1.705)	0.001	1.051 (0.811–1.361)	0.707

Multivariable Model 1 was adjusted for the SOFA score

Multivariable Model 2 was adjusted for model 1 plus age, sex, and ethnicity

Multivariable Model 3 was adjusted for model 2 plus admission diagnoses including diabetes, hypertension, hyperlipemia, malignant neoplasm, chronic kidney disease, heart failure, chronic hepatic failure, chronic respiratory failure, sepsis, disseminated intravascular coagulation, pneumonia and diarrhea

Multivariable Model 4 was adjusted for model 3 plus treatment measures, including vasoactive drugs, sedatives, anticoagulants, mannitol, mechanical ventilation

ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; OR, odds ratio; HR, hazard ratio; CI, confidence interval

ill patients with ischemic stroke remains blurred. Owing to the intricate nature of severe patients' conditions and the prevalence of various complications, multiple factors, including conditions like diabetes, can influence patients' BE levels. To mitigate the influence of complications on research outcomes, we incorporate a comprehensive range of complications that may impact the research findings into the covariates. After adjusting for confounding factors, our results showed that low BE was associated with higher rates of ICU, hospital, 28-day, and 1-year mortalities than normal BE.

The mechanism underlying the relationship between BE and ischemic stroke remains unclear. Previous studies have shown that when an ischemic stroke occurs, the presence of the thrombus decreases cerebral blood flow, resulting in acidosis due to a lack of glucose, production of lactate, and an increase in the level of carbon dioxide (CO_2). The accumulation of acidic substances in the brain can promote edema and necrosis of nerve cells, resulting in the generation of proinflammatory cytokines that cause inflammation and oxidative stress [22, 23]. Brain acidosis also can also cause neuronal injury via glutamate-induced neuronal apoptosis, wherein alterations in the functions of intracellular proteins eventually induce the death of neurons and glial cells [24–26]. Furthermore, acidosis induces the activation of neuronal acid-sensing ion channel 1, which can cause neuronal death [27–29]. Pericytes, contractile cells that form an integral part of the blood–brain barrier, are destroyed by ischemia, potentially causing irreversible capillary constriction and breakdown of the blood–brain barrier [30]. The exact biological mechanism underlying the association between metabolic acidosis and outcomes of patients with ischemic stroke remains to be elucidated.

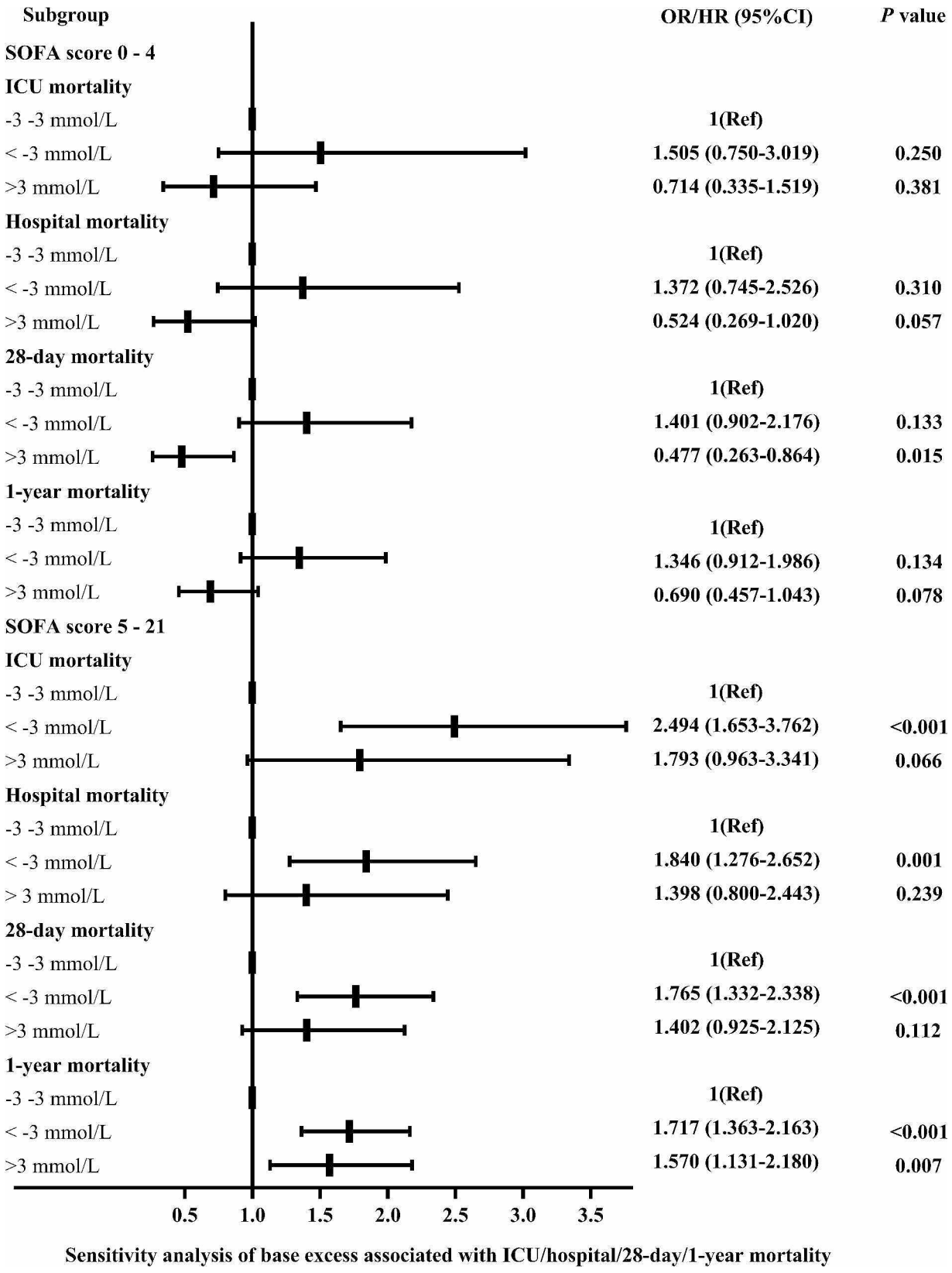

Fig. 4 Multivariate logistic regression analysis for BE change associated with mortality stratified by different subgroup. BE, Base Excess; SOFA, Sequential Organ Failure Assessment; ICU, Intensive Care Unit; OR, Odds Ratio; HR, Hazard Ratio; CI, Confidence Interval

The SOFA score is used to assess the acute morbidity of critical illness at a population level and is considered a potent indicator of the risk of ICU mortality [31, 32]. Lactate level is perceived as a predictor of mortality in ICU patients [21, 33, 34]. To explore whether the results persisted when the clinical status severity changed, we conducted interaction by dividing the subjects into two groups according to their SOFA score on the first day of ICU admission (<5 or ≥5) as well as into two groups according to their lactate levels (<2 or ≥2 mmol/L). The blood lactate level serves as an indicator of tissue anaerobic metabolism. Prior research has demonstrated a correlation between elevated blood lactate levels and a reduction in BE [35]. But no interaction between lactate and BE was observed in the mortality of stroke patients, which may suggest that BE may be independent of lactate in predicting the prognosis of stroke patients. We analyzed the association between BE and mortality in the subgroup of SOFA score. Our findings showed that in the presence of a high SOFA score, low BE (<-3 mmol/L) was strongly associated with high rates of ICU, hospital, 28-day and, 1-year mortalities. Therefore, the BE of patients with high SOFA scores should be closely monitored in clinical practice.

This study has some limitations. First, the MIMIC-IV is a single-center database, hence, selection bias (i.e., Berkson's bias) was inevitable. The recruited patients were from various ICUs, including coronary, medical, and surgical care ICUs. Various healthcare professionals may opt for distinct timings when conducting BE testing on patients, potentially resulting in notable selection bias. Nevertheless, their data may mirror real situations of ICU patients. Furthermore, the MIMIC-IV database is deficient in imaging data for confirming the diagnosis of cerebral infarction in patients and records of commonly used treatment measures for cerebral infarction patients in clinical practice (such as interventional surgery). Subsequent studies should focus on evaluating the influence of surgical and alternative treatment interventions on patient prognostication. Secondly, we only extracted records of the first measurement of BE at ICU admission without considering the first hospitalization record and changes afterward in BE. However, the first record of BE at ICU admission can allow prompt and convenient prediction of the prognoses of patients. Thirdly, although we adjusted our models for as many covariates as possible and processed a sequence of sensitivity analyses, given the retrospective design, some cofactors, such as the administration of bicarbonate, were not included. At last, in the regression analysis, the U-shaped relationship between BE and mortalities exhibited by the RCS curve did not appear, possibly due to the number of patients with BE>3mmol/L being insufficient. In the future, multicenter prospective studies can demonstrate the association between BE and outcomes in critically ill patients with ischemic stroke.

Conclusion

BE of <-3 mmol/L at ICU admission may be correlated with high ICU, hospital, 28-day, and 1-year mortalities in patients with ischemic stroke. Patients with ischemic stroke who have high SOFA scores may need careful supervision when their initial BE value <-3 mmol/L.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03763-4.

Supplementary Material 1

Acknowledgements

We appreciate the researchers at the MIT Laboratory for Computational Physiology and collaborating research groups to keep MIMIC-IV databases available.

Author contributions

Jueheng Liu wrote the main manuscript; Jueheng Liu, Jiamei Li and Xuting Jin conducted the data curation and analysis; Jueheng Liu and Jiamei Li prepared figures and tables; Jiajia Ren, Ruohan Li, Jingjing Zhang, Ya Gao, Xiaochuang Wang and Gang Wang revised the draft. All authors reviewed the manuscript.

Funding

This study was supported by the National Natural Science Foundation of China (81770057), the Top Young Talents Project of the "Special Support Program for High-Level Talents" in Shaanxi, China, and the Xi'an Jiaotong University Medical "Basic-Clinical" Integration Innovation Project (YXJLRH2022060).

Data availability

The data supporting the results of this study are from the MIMIC-IV database. https://doi.org/10.13026/6mm1-ek67.

Declarations

Ethics approval and consent to participate

As there is pre-existing institutional review board approval in the MIMIC-IV database, we were exempt from IRB approval from our institution.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 21 November 2023 / Accepted: 15 July 2024
Published online: 18 September 2024

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