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Association between albumin-corrected anion gap level and all-cause mortality in patients with gastrointestinal bleeding

A retrospective cohort study of the MIMIC-IV database

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Abstract

This study explores the association of albumin-corrected anion gap (ACAG) level and all-cause mortality in patients with gastrointestinal bleeding (GIB). Data in this retrospective cohort study were extracted from the medical information mart for intensive care IV database. Univariate and multivariate Cox proportional hazards models were utilized for evaluation of hazard ratio (HR) of 30- and 90-day all-cause mortality in different ACAG levels. Subgroup analysis of age, gender, complications and mechanical ventilation was conducted to investigate this relationship in patients with different characteristics. Among 1933 eligible participants, 390 died in 30 days and 540 died in 90 days. After adjusting for covariates, the concentration of ACAG elevated 1 mmol/L, the risk of 30-day all-cause mortality and 90-day all-cause mortality increased 0.064 (95% confidence interval [CI]: 1.046–1.084) and 0.061 (95% CI: 1.044–1.078), respectively. Compared to a normal ACAG level, a high ACAG level was associated with increased risk of both 30-day (HR = 1.620, 95% CI: 1.281–2.049) and 90-day (HR = 1.572, 95% CI: 1.287–1.921) all-cause mortality. The restricted cubic spline curves indicated a linear correlation between ACAG and all-cause mortality in GIB patients. Additionally, this positive association between ACAG and increased mortality risk was significant in age, gender, non-hypertension, non-diabetes mellitus, sepsis, atrial fibrillation, non-heart failure, nonmechanical ventilation, and mechanical ventilation subgroups (all $P < .05$). An elevated ACAG level was associated with increased risk of mortality in GIB patients, with a linear correlation. However, the specific mechanism that ACAG level linked to mortality risk in GIB patients still needs clarification.

Abbreviations: ACAG = albumin-corrected anion gap, AF = atrial fibrillation, AG = anion gap, ALT = alanine aminotransferase, BUN = blood urea nitrogen, Cr = creatinine, CI = confidence interval, DM = diabetes mellitus, GIB = gastrointestinal bleeding, HF = heart failure, HR = hazard ratio, ICU = intensive care unit, INR = international normalized ratio, M = median, MBP = mean blood pressure, MIMIC-IV = medical information mart for intensive care IV, PTT = partial thromboplastin time, Q_1 = 1st quartiles, Q_3 = 3rd quartiles, RBC = red blood cell, RR = respiration rate.

Keywords: albumin, all, cause mortality, corrected anion gap, gastrointestinal bleeding, IV database, MIMIC

1. Introduction

Gastrointestinal bleeding (GIB) is a common cause for presentation in the emergency room and hospitalization, and usually categorized to upper or lower GIB. In the United States, >3,00,000 hospital admissions annually are due to patients with upper gastrointestinal bleeding, and similarly, acute lower gastrointestinal bleeding is a common reason for hospitalization.[1,2] They are both associated with significant utilization of hospital resources, as well as considerable morbidity and mortality. Therefore, identifying risk factors of GIB is significant for prevention of patients' mortality risks and formulation of clinical management strategies.

Anion gap (AG) represents the differences between unmeasured anions and cations and is determined by subtracting the sum of serum chloride and bicarbonate concentrations from the sum of sodium concentrations.[3] AG can reflect acid–base balance and is associated with the prognosis of various diseases, such as cerebral infarction, sepsis, coronary artery disease, cardiogenic shock, and acute myocardial infarction.[4–8]

The author has no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

This study does not include research on identifiable human material and data, and all the study methods were performed in compliance with the Helsinki Declaration. Since the study data were extracted from the MIMIC-IV databases that were publicly available, according to national regulations, ethical approval has been waived from the IRB of Langfang Health Vocational College. Also, the need for consent to participate was waived by the IRB of Langfang Health Vocational College.

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A recent study showed there is a potential linear relationship between AG and 90-day all-cause mortality in critically ill GIB patients.[9] Nevertheless, AG levels can be significantly affected by serum albumin concentrations, especially in critically ill patients with reduced albumin levels.[10] Albumin as the main negatively charged protein in plasma, normally contributes to the AG, and when albumin levels decrease, the reduction in negative charges lowers the AG, which can obscure the detection of metabolic disruptions.[11] Hence, the albumin-corrected anion gap (ACAG) was introduced to address this limitation.[12] The ACAG is calculated by adding a correction factor based on albumin concentrations to the traditional AG, accounting for hypoalbuminemia, and can provide a more accurate representation of metabolic disturbances.[13] Studies have revealed the associations of ACAG with mortality risk of multiple diseases, including acute myocardial infarction, acute ischemic stroke and acute pancreatitis.[11,14,15] However, the relationship between ACAG and prognosis in GIB patients is still unclear.

Herein, this study aims to explore the association of ACAG levels with all-cause mortality in patients with GIB and hope to provide some information for investigation for indexes related to GIB prevention and mortality risk management.

2. Materials and methods

2.1. Study design and participants

Data in this retrospective cohort study were extracted from the medical information mart for intensive care IV (MIMIC-IV) database. The MIMIC-IV survey encompasses clinical information from over 1,90,000 real patients and 4,50,000 hospitalizations recorded at the Beth Israel Deaconess Medical Center in Boston, MA, USA in 2008 to 2019. It provides detailed information on patients' demographics, laboratory tests, medications, vital signs, surgical procedures, disease diagnoses, medication management, and follow-up survival status.

In this study, 6210 patients diagnosed with GIB in the MIMIC-IV database were initially included. In the MIMIC-IV, diagnosis of GIB was defined as a clinically significant bleeding event diagnosed by a physician (manifesting as coffee-ground emesis, hematemesis, melena, or hematochezia) or the presence of blood in the upper or lower gastrointestinal tract identified during endoscopic evaluation.[16] The exclusion criteria were stayed in the intensive care unit (ICU) for <24 hours, missing information on AG or ACAG, and without survival data. The final sample size for analysis was 1933. The MIMIC-IV database has obtained informed consent from participants and has been approved by the institutional review boards of related organizations. Since it is publicly available, according to relevant law and regulations, ethical approval informed consent has been waived by the institutional review board of Langfang Health Vocational College.

2.2. Calculation of ACAG

The formula used for ACAG calculation was as follows: ACAG (mmol/L) = AG + [4.4 – Albumin (g/dL)] × 2.5.[17] In this study, GIB patients were divided into normal ACAG group and high ACAG group based on their serum ACAG levels, with cutoff value of 20 mmol/L.[18]

2.3. Covariable selection

Variables as potential covariates associated with all-cause mortality were selected from the database, including age, gender, race, heart rate (HR), mean blood pressure (MBP), respiration rate (RR), SpO_2, atrial fibrillation (AF), diabetes mellitus (DM), heart failure (HF), hypertension, liver cirrhosis, malignancy, renal dysfunction, sepsis, the glasgow coma scale score, vancomycin, mechanical ventilation, alanine aminotransferase (ALT), blood urea nitrogen (BUN), chloride, creatinine (Cr), fasting blood glucose, hemoglobin, international normalized ratio (INR), platelet, partial thromboplastin time (PTT), and red blood cell (RBC) distribution width. All laboratory indicators were the first detected and recorded data within 24 hours of admission to the ICU.

2.4. Outcomes

The study outcome was 30- and 90-day all-cause mortality. Death information was obtained from hospitalization record, and that on discharged patients' death was accessed from the United States Social Security Death Index.

2.5. Statistical analysis

The Kolmogorov–Smirnov test was used to identify the distribution of continuous data, and the study data were all non-normal distribution parameters. Continuous variables were presented by median values with quartiles [M (Q_1, Q_3)], and the Kruskal–Wallis test was used for comparation between normal ACAG group and high ACAG group. Categorical variables were described by frequency with percentiles [N (%)], and chi-square test (χ^2) was utilized for comparation between 2 groups.

Kaplan–Meier survival analysis was utilized to assess the incidence rate of all-cause mortality between normal ACAG group and high ACAG group, and their differences were assessed through log-rank tests. Cox proportional hazards models were used to calculate the hazard ratio (HR) and 95% confidence interval between the ACAG level and all-cause mortality in GIB patients. Model 1 was an unadjusted model. Model 2 was adjusted for gender, race, age, HR, MBP, RR, SpO_2, ALT, BUN, chloride, Cr, fasting blood glucose, hemoglobin, INR, platelet, PTT, and RBC distribution width. Model 3 adjusted for AF, DM, HF, hypertension, liver cirrhosis, malignancy, renal dysfunction, sepsis, stroke, vancomycin, mechanical ventilation, and glasgow coma scale in addition to the model 2.

Moreover, we analyzed the nonlinear association between ACAG levels with all-cause mortality using a restricted cubic spline regression model. Subgroup analysis of age, gender, hypertension, DM, sepsis, AF, HF, and mechanical ventilation was also conducted to investigate the association of ACAG levels with 30- and 90-day all-cause mortality in GIB patients with different characteristics. Two-side $P < .05$ represented statistically significant. All statistics analyses were completed by SAS 9.4 (SAS Institute, Cary) and R version 4.2.3 (2024-01-24 ucrt).

3. Results

3.1. Characteristics of participants

Initially, 6210 patients diagnosed with GIB were included. After excluding those who stayed in the ICU for <24 hours (n = 1326), missing information on AG or ALB (n = 21) or without survival data (n = 2930), a total of 1933 participants were eligible for further analysis (Fig. 1). Among the total population, the number of patients died in 30 days and in 90 days was 390 (20%) and 540 (28%), respectively. Comparation of characteristics of participants in normal ACAG level group (n = 1305) and high ACAG level group (n = 628) was shown in Table 1. The median age of GIB patients in normal ACAG level group was significantly higher than that in high ACAG level group (66 years old vs 64 years old). Patients in high ACAG level group had higher levels of HR (97 bpm vs 89 bpm), RR (20 insp/min vs 19 insp/min), ALT (36 IU/L vs 26 IU/L), BUN (42 mg/dL vs 25 mg/dL), Cr (2.15 mg/dL vs 1.00 mg/dL), INR (1.60 vs 1.40), PTT (66 years old vs 64 years old) and AG (66 years old vs 64 years old), comparing to those in normal ACAG

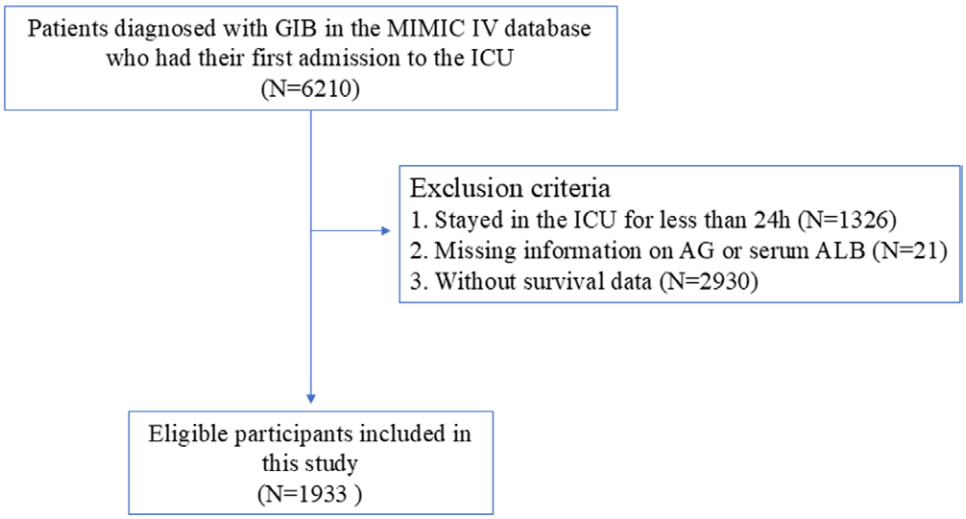

Figure 1. Flowchart of participants screening.

Table 1

Characteristics of GIB patients with different ACAG levels.

Variables	Total (n = 1933)	Normal ACAG (n = 1305)	High ACAG (n = 628)	*P*
Male, n (%)	1205 (62)	813 (62)	392 (62)	.959
Age, yr, *M* (Q_1, Q_3)	65 (55, 76)	66 (55, 77)	64 (54, 75)	.028
Race, n (%)				.017
Black	231 (12)	137 (10)	94 (15)	
White	498 (26)	344 (26)	154 (25)	
Others	1204 (62)	824 (63)	380 (61)	
HR, bpm, *M* (Q_1, Q_3)	91 (78, 106)	89 (76, 104)	97 (82, 112)	<.001
MBP, mm Hg, *M* (Q_1, Q_3)	80 (69, 93)	81 (71, 93)	78 (67, 90)	.002
RR, insp/min, *M* (Q_1, Q_3)	19 (16, 23)	19 (16, 22)	20 (17, 25)	<.001
SpO_2, %, *M* (Q_1, Q_3)	98 (95, 100)	98 (96, 100)	98 (95, 100)	.381
AF, n (%)	661 (34)	436 (33)	225 (36)	.294
DM, n (%)	751 (39)	483 (37)	268 (43)	.017
HF, n (%)	734 (38)	486 (37)	248 (39)	.34
Hypertension, n (%)	1007 (52)	714 (55)	293 (47)	<.001
Liver cirrhosis, n (%)	763 (39)	489 (37)	274 (44)	.009
Malignancy, n (%)	483 (25)	330 (25)	153 (24)	.66
Renal dysfunction, n (%)	193 (10)	79 (6.1)	114 (18)	<.001
Sepsis, n (%)	1477 (76)	938 (72)	539 (86)	<.001
GCS, n (%)	15 (15, 15)	15 (15, 15)	15 (15, 15)	<.001
Vancomycin, n (%)	1457 (75)	913 (70)	544 (87)	<.001
Mechanical ventilation, n (%)	444 (23)	287 (22)	157 (25)	.141
ALT, IU/L, *M* (Q_1, Q_3)	29 (17, 61)	26 (16, 51)	36 (19, 99)	<.001
BUN, mg/dL, *M* (Q_1, Q_3)	28 (17, 49)	25 (16, 39)	42 (23, 69)	<.001
Chloride, mmol/L, *M* (Q_1, Q_3)	104 (99, 109)	105 (101, 109)	101 (96, 107)	<.001
Cr, mg/dL, *M* (Q_1, Q_3)	1.20 (0.80, 2.10)	1.00 (0.70, 1.50)	2.15 (1.25, 4.00)	<.001
FBG, mg/dL, *M* (Q_1, Q_3)	117 (96, 160)	117 (97, 156)	117 (94, 170)	.498
HB, g/dL, *M* (Q_1, Q_3)	9.40 (8.10, 11.00)	9.40 (8.20, 11.00)	9.40 (7.80, 10.90)	.225
INR, *M* (Q_1, Q_3)	1.40 (1.20, 1.80)	1.40 (1.20, 1.70)	1.60 (1.30, 2.10)	<.001
Platelet, K/μL, *M* (Q_1, Q_3)	149 (90, 226)	149 (94, 218)	149 (83, 239)	.818
PTT, s, *M* (Q_1, Q_3)	33 (28, 41)	32 (28, 39)	36 (29, 46)	<.001
RBC distribution width, m/μL, *M* (Q_1, Q_3)	3.11 (2.65, 3.64)	3.13 (2.69, 3.64)	3.07 (2.59, 3.64)	.079
AG, mmol/L, *M* (Q_1, Q_3)	15 (12, 18)	13 (11, 15)	20 (18, 23)	<.001
ALB, mmol/L, *M* (Q_1, Q_3)	3.00 (2.50, 3.40)	3.00 (2.60, 3.40)	2.90 (2.40, 3.30)	<.001
ACAG, mmol/L, *M* (Q_1, Q_3)	18.0 (15.3, 21.3)	16.5 (14.5, 18.3)	23.3 (21.3, 26.1)	<.001
30-d mortality, n (%)	390 (20)	202 (15)	188 (30)	<.001
90-d mortality, n (%)	540 (28)	297 (23)	243 (39)	<.001

Statistics analyses included the Kruskal–Wallis test and chi-square test.

ACAG = albumin-corrected anion gap, AF = atrial fibrillation, AG = anion gap, ALB = albumin, ALT = alanine aminotransferase, BUN = blood urea nitrogen, Cr = creatinine, DM = diabetes mellitus, FBG = fasting blood glucose, GCS = glasgow coma scale, GIB = gastrointestinal bleeding, HB = hemoglobin, HF = heart failure, HR = heart rate, INR = international normalized ratio, M = median, MBP = mean blood pressure, PTT = partial thromboplastin time, Q_1 = 1st quartile, Q_3 = 3rd quartile, RBC = red blood cell, RR = respiration rate.

level group. Oppositely, the median levels of MBP (81 mm Hg vs 78 mm Hg), chloride (105 mmol/L vs 101 mmol/L) and ALB (3.00 mmol/L vs 2.90 mmol/L) were significantly higher in normal ACAG level group than those in high ACAG level group. Besides, the proportions of patients with AF, liver cirrhosis, renal dysfunction, sepsis and vancomycin were

significantly higher in high ACAG level group than those in normal ACAG level group (all $P < .05$).

3.2. Association of ACAG levels with all-cause mortality in GIB patients

Figure 2 was the Kaplan–Meier curves of participants in different ACAG level groups. It could be clearly seen that the survival probability was significantly lower in GIB patients with high ACAG levels than those with normal ACAG levels. Then, Cox proportional hazards analysis results suggested that after adjusting for all covariates (Table 2), the concentration of ACAG elevated 1 mmol/L, the risk of 30-day all-cause mortality and 90-day all-cause mortality increased 0.064 (95% confidence interval[CI]: 1.046–1.084) and 0.061 (95% CI: 1.044–1.078), respectively (all $P < .01$). Compared to a normal ACAG level, a high ACAG level was associated with increased risk of both 30-day (HR = 1.620, 95% CI: 1.281–2.049) and 90-day (HR = 1.572, 95% CI: 1.287–1.921) all-cause mortality. The restricted cubic spline curves indicated a linear correlation between ACAG and all-cause mortality in GIB patients (Fig. 3).

Furthermore, the relationship between ACAG and 30-day (Fig. 4) and 90-day (Fig. 5) all-cause mortality was investigated in different subgroups. The positive association between ACAG level and increased 30-day mortality risk was significant in age <65 years (HR = 1.50, 95% CI: 1.06–2.13), age ≥ 65 years (HR = 1.89, 95% CI: 1.36–2.62), male (HR = 1.789=, 95% CI: 1.32–2.40), female (HR = 1.53, 95% CI: 1.03–2.27), non-hypertension (HR = 1.89, 95% CI: 1.37–2.59), non-DM (HR = 1.77, 95% CI: 1.32–2.36), sepsis (HR = 1.66, 95% CI: 1.29–2.14), non-AF (HR = 1.54, 95% CI: 1.16–2.06), AF (HR = 1.86, 95% CI: 1.20–2.88), non-HF (HR = 1.87, 95% CI: 1.41–2.48), nonmechanical ventilation (HR = 1.40, 95% CI: 1.06–1.83), and mechanical ventilation (HR = 2.98, 95% CI: 1.82–4.89) subgroups. Regarding to high ACAG level and 90-day mortality, in subgroups of age < 65 years, age ≥ 65 years,

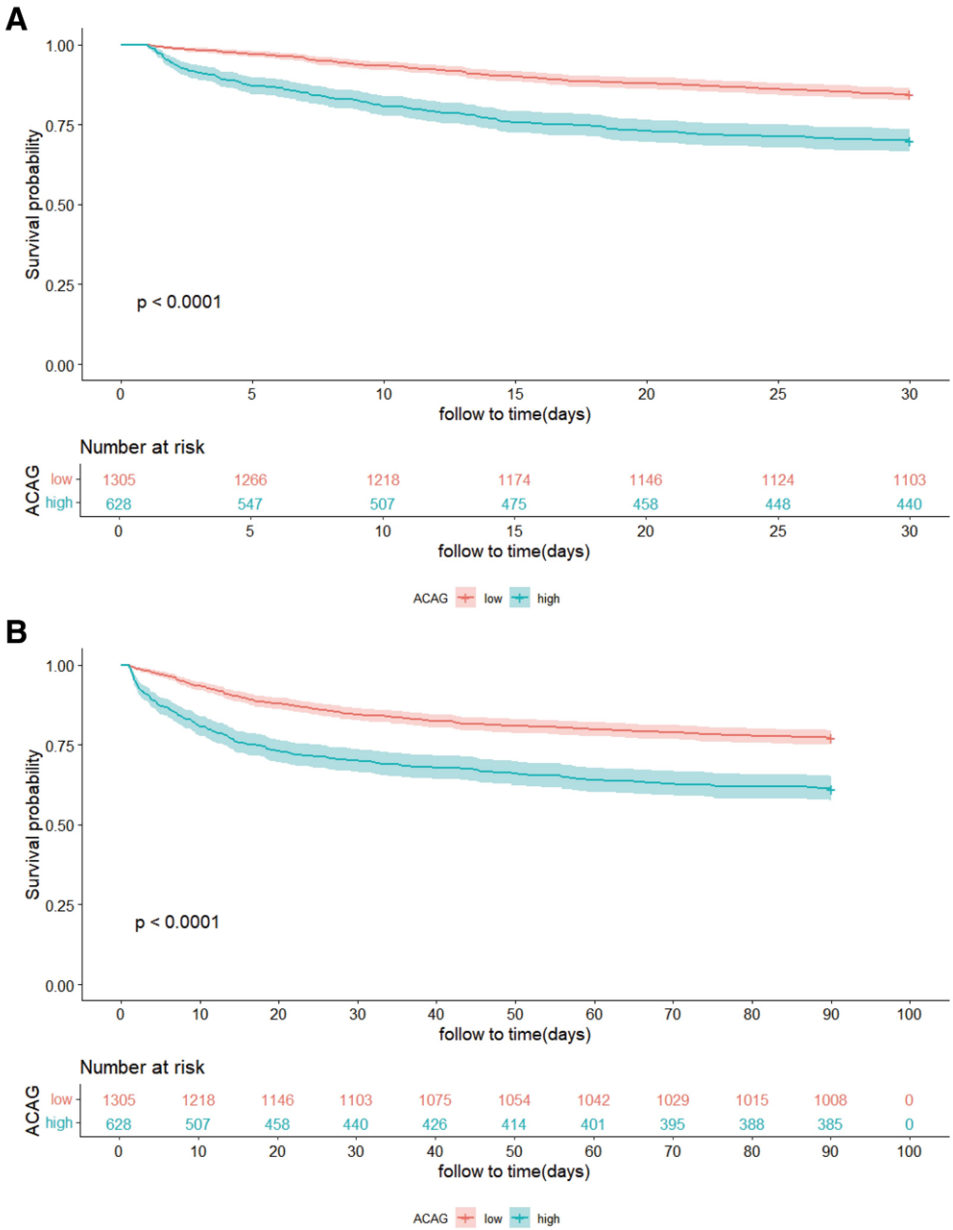

Figure 2. KM curves of survival probability of GIB patients with normal and high ACAG levels. ACAG = albumin-corrected anion gap, GIB = gastrointestinal bleeding, KM = Kaplan–Meier.

Table 2

Associations of ACAG levels with all-cause mortality in patients with GIB.

	Model 1		Model 2		Model 3	
Variables	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
30-d mortality						
ACAG, mmol/L	1.085 (1.070–1.100)	<.001	1.088 (1.073–1.104)	<.001	1.064 (1.046–1.084)	<.001
Normal ACAG level	Ref		Ref		Ref	
High ACAG level	2.190 (1.796–2.672)	<.001	2.214 (1.815–2.701)	<.001	1.620 (1.281–2.049)	<.001
90-d mortality						
ACAG, mmol/L	1.075 (1.062–1.089)	<.001	1.079 (1.065–1.093)	<.001	1.061 (1.044–1.078)	<.001
Normal ACAG level	Ref		Ref		Ref	
High ACAG level	1.971 (1.663–2.335)	<.001	2.003 (1.691–2.374)	<.001	1.572 (1.287–1.921)	<.001

Model 1: Unadjusted model.

Model 2: Adjusted for gender, race, age, HR, MBP, RR, SpO_2, ALT, BUN, chloride, Cr, FBG, HB, INR, platelet, PTT, and RBC distribution width.

Model 3: Adjusted for gender, race, age, HR, MBP, RR, SpO_2, ALT, BUN, chloride, Cr, FBG, HB, INR, platelet, PTT, RBC distribution width, AF, DM, HF, hypertension, liver cirrhosis, malignancy, renal dysfunction, sepsis, stroke, vancomycin, mechanical ventilation, and GCS.

ACAG = albumin-corrected anion gap, CI = confidence interval, GIB = gastrointestinal bleeding, HR = hazard ratio, Ref = reference.

male, non-hypertension, non-DM, sepsis, non-AF, AF, non-HF, nonmechanical ventilation and mechanical ventilation, this association was significant (all $P < .05$).

4. Discussion

In this retrospective cohort study, we explored the association between ACAG and all-cause mortality in patients with GIB. The results suggested a linear correlation between ACAG and 30- and 90-day all-cause mortality, respectively. An elevated ACAG concentration was significantly associated with increased risk of all-cause mortality. Compared to patients with normal ACAG levels, those who with high ACAG levels had increased all-cause mortality risk. Additionally, this positive relationship between ACAG and increased mortality risk was significant in patients with different characteristics.

Previous studies have reported the potential prediction value of ACAG in prognosis of multiple diseases. Pan et al[19] suggested higher 28-day mortality in high ACAG group among septic patients with cirrhosis. Another study identified that the elevated ACAG is an independent risk factor for both short-term and long-term mortality in AIS patients.[11] Studies based on the MIMIC-IV database have also provided evidence linking ACAG to the risk of mortality in ICU patients.[18,20,21] For example, Chen et al[22] reported that the incidence of severe disorder of consciousness, in-hospital mortality, and long-term mortality were gradually increased as ACAG levels. A latest study based on the MIMIC-IV database showed that AG has a positive association with increased ICU mortality and 90-day all-cause mortality risk in GIB patients, after adjusting for confounders, which was a linear correlation.[9] Similarly, in the present study, we extracted GIB patients' data from the MIMIC-IV database, which includes large sample of real ICU patients and their clinical information, and investigate the relationship between ACAG and 30- and 90-day all-cause mortality.[9] The results showed that an elevated level of ACAG was linked to increased risk of all-cause mortality, with a linear correlation. Compared to Liu et al's study, we utilized ACAG instead of AG, because it can avoid effect from reduced serum albumin concentrations in critically ill patients. Since no research has explored the role of ACAG in GIB mortality risk, our findings may fill the gap in literature, provide evidence for further investigation of markers for poor prognosis in this population, and further contribute to risk stratification and management strategy in clinical practice.

Specific biological mechanism that links ACAG with mortality in GIB is still unclarified. Existence evidence may provide support for speculation of the potential mechanism. In the ICU, GIB is a common complication for various diseases, such as kidney failure,[23] liver cirrhosis,[24] and acute respiratory failure.[25] Kidney diseases may cause inadequate erythropoietin production, and consequential anemia and GIB may be catastrophic in patients who are already anemic.[26] At the same time, in kidney diseases, when acid excretion falls below acid production, acid accumulation occurs.[27] This state of acid–base imbalance can be sensitively detected by ACAG. In addition to the kidneys and lungs, the liver also plays an important role in the regulation of the acid–base equilibrium. The liver is involved in the regulation of acid–base equilibrium via 4 pathophysiological mechanisms, including ALB homeostasis, lactic acid metabolism, urea production and ketogenesis.[28] A previous study showed that due to the high prevalence of hypoalbuminemia in liver cirrhosis patients with sepsis, utilizing the ACAG could offer a more precise evaluation of acid load.[19] Besides, ICU patients are frail and often have other comorbidities such as DM and CVDs. Particularly, patients with ischemic heart disease, peripheral artery disease, and stroke may be on antithrombotic medications, and those who have bleeding when they have risk factors, or a history of ischemic events are difficult to manage. Therefore, timely monitoring serum ACAG may be beneficial to identify potential mortality risk in the ICU patients with GIB.

Moreover, the relationship between ACAG and 30- and 90-day all-cause mortality was significant in GIB patients with different age, gender, with/without complications, with/without mechanical ventilation. GIB, especially upper gastrointestinal bleeding, is a common reason for hospital admission in older adult patients and carries a high morbidity and mortality if not properly managed.[29] In fact, it can be seen in all age group patients. According to our findings, a high level of ACAG in GIB patients with any age was associated with increased mortality risk. We observed a significant gender difference in association between ACAG and increased 90-day mortality risk, but the specific mechanism is unclear. A study has suggested that female patients treated with direct oral anticoagulants have a higher risk of GIB versus male patients, but this difference is not observed in vitamin K antagonist patients.[30] In GIB patients with non-hypertension, non-DM or non-HF, positive relationship between ACAG and all-cause mortality risk was significant. One possible reason to explain this difference may be that medication treatment regimens commonly used by patients with these comorbidities often have the potential to disrupt metabolic balance and thus have been particularly noted by clinicians and have received certain preventive measures. Also, as mentioned before, patients with sepsis or AF, results on ACAG and mortality risk in the present study were in accordance with previous conclusions. Additionally, it has been reported that in ICU patients who used mechanical ventilation, a higher ACAG level was associated with a higher risk of acute kidney injury.[31] Our findings

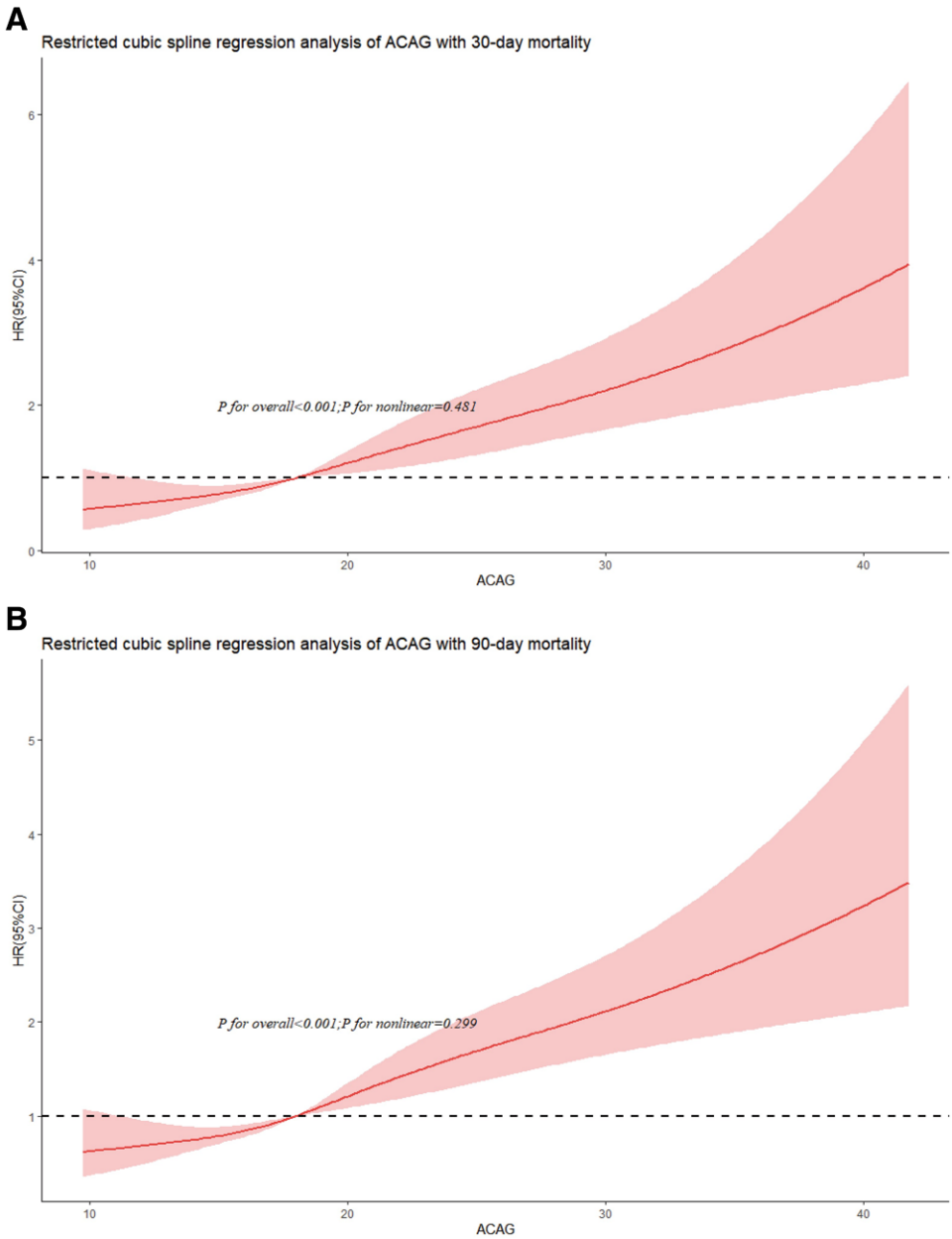

Figure 3. RCS curves of association between ACAG and 30- and 90-d all-cause mortality in GIB patients. ACAG = albumin-corrected anion gap, GIB = gastrointestinal bleeding, RCS = restricted cubic spline.

supplemented that in GIB patients, an elevated ACAG level was associated with higher risk of mortality no matter whether they received mechanical ventilation or not.

This study first investigated the association between ACAG level and all-cause mortality in ICU patients with GIB, which provided some information for identifying index of potential mortality risk, and new insights for clinical management of these patients. However, limitations could not be ignored for results explanation. Firstly, because of the retrospective study design, recall bias and selection bias are unavoidable, and the causal association between ACAG and mortality risk has not been concluded. Secondly, in addition to ALB, serum level of ACAG may be influenced by various confounding, although we have included multiple covariates such as BUN, RBC distribution, liver cirrhosis, renal dysfunction, sepsis, stroke, and mechanical ventilation in adjustment of multivariate models, other factors that the MIMIC database not recorded are not considered. Furthermore, participants in this study were from a single medical center that limited the extrapolation of the results. Multicenter prospective cohort study is expected to verify the association between ACAG and all-cause mortality risk in GIB patients as well as clarify the underlying mechanisms.

5. Conclusion

This study based on data from the MIMIC-IV database observed a linear correlation between ACAG and 30- and 90-day all-cause mortality in GIB patients, indicating that patients with a high level of ACAG may have increased mortality risk. However, the specific mechanism that serum ACAG level may help identify the potential risk of all-cause mortality in ICU patients with GIB still needs to be clarified.

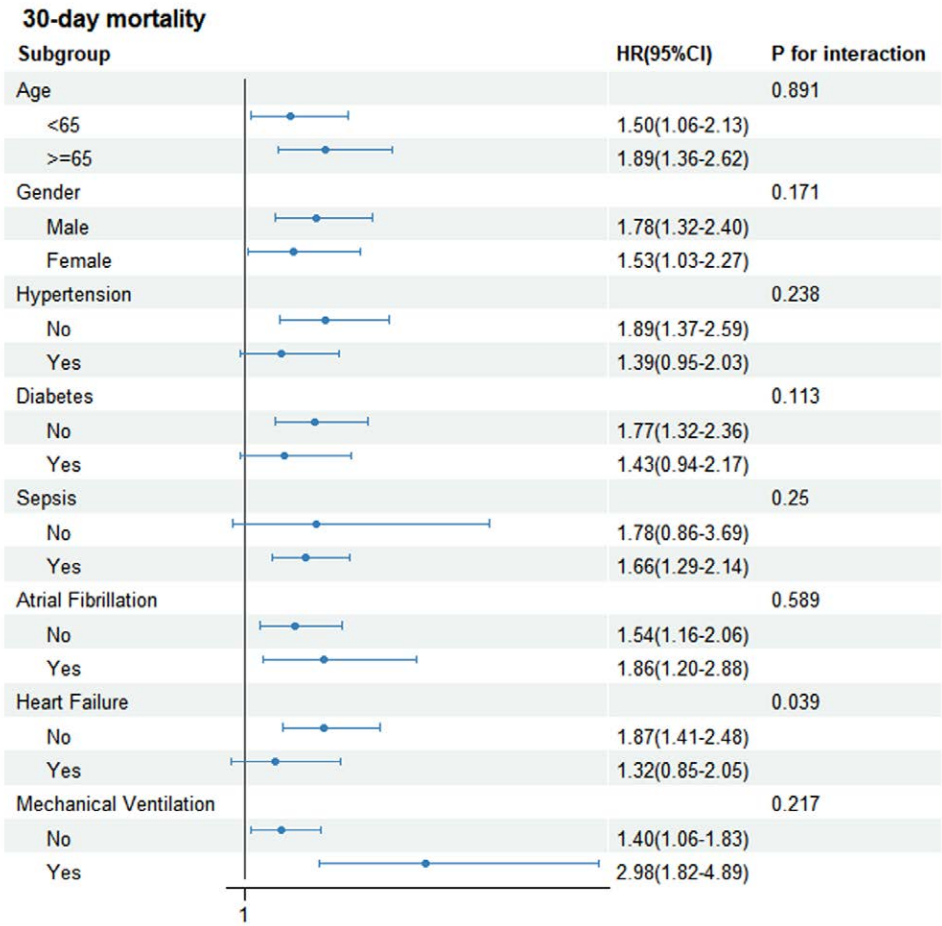

Figure 4. Subgroup analysis on association of ACAG with 30-d all-cause mortality in GIB patients. ACAG = albumin-corrected anion gap, GIB = gastrointestinal bleeding.

Author contributions

Conceptualization: Qian Wang.
Data curation: Qian Wang.
Formal analysis: Qian Wang.
Investigation: Qian Wang.
Methodology: Qian Wang.
Project administration: Qian Wang.
Resources: Qian Wang.
Software: Qian Wang.
Supervision: Qian Wang.
Validation: Qian Wang.
Visualization: Qian Wang.
Writing – original draft: Qian Wang.
Writing – review & editing: Qian Wang.

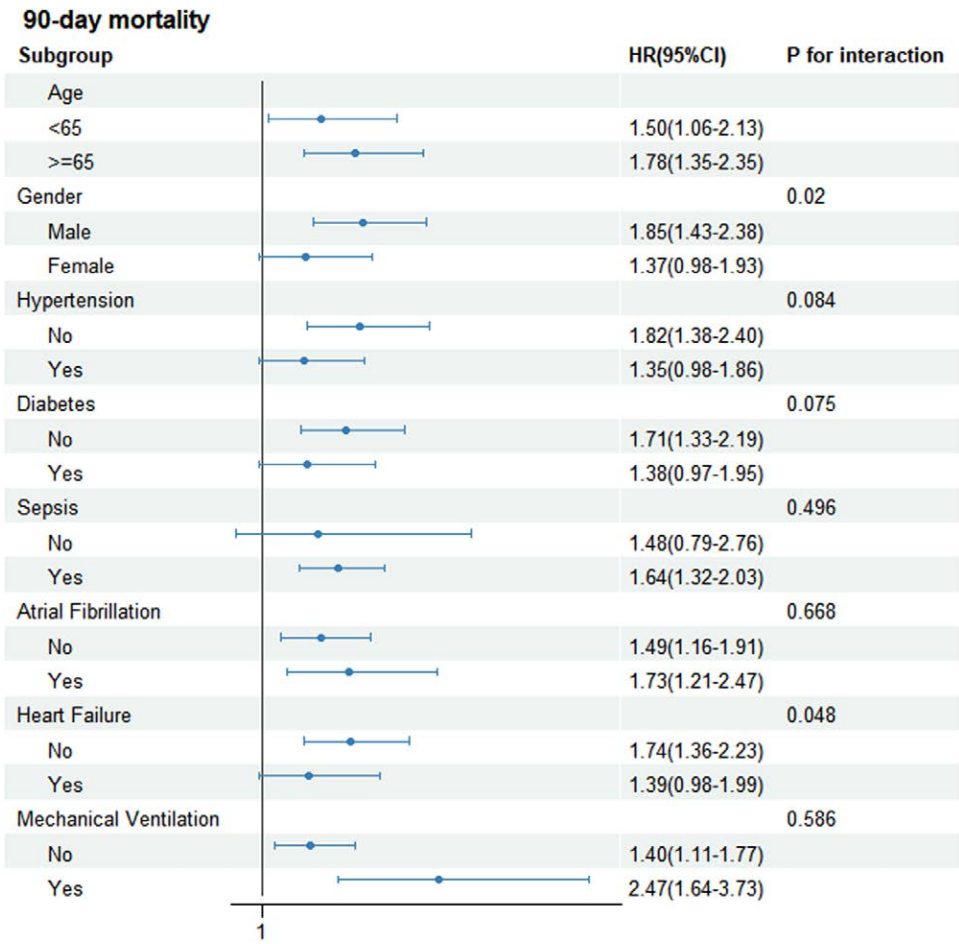

Figure 5. Subgroup analysis on association of ACAG with 90-d all-cause mortality in GIB patients. ACAG = albumin-corrected anion gap, GIB = gastrointestinal bleeding.

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