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ORIGINAL RESEARCH

Serum Anion Gap is Associated with Risk of All-Cause Mortality in Critically Ill Patients with Acute Myocardial Infarction

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Purpose: Anion gap (AG) is a valuable and easily obtained clinical tool for differentially diagnosis of acid-base disorders. Current understanding of the prognostic impact of AG on mortality after acute myocardial infarction (AMI) is limited. We aimed to investigate whether AG is a predictor of short-term and long-term all-cause mortality after AMI.

Patients and Methods: We examined 1806 patients diagnosed with AMI in intensive care unit from the Medical Information Mart for Intensive Care III (MIMIC-III) database. We analyzed the association of AG with 30-day, 180-day and 1-year all-cause mortality on a continuous scale and in categories, using multivariable Cox regression. We utilized restricted cubic splines to evaluate the linearity between hazard ratio (HR) and AG concentrations.

Results: AG was associated with a higher risk of 30-day, 180-day and 1-year all-cause mortality, with adjusted HRs of 1.083 (95% CI 1.051 to 1.117), 1.077 (95% CI 1.049 to 1.105), and 1.074 (95% CI 1.047 to 1.101), respectively. The results were consistent in subgroup analyses. The association between AG and all-cause mortality was linear for 180-day and 1-year mortality, and near linear for 30-day mortality, as higher concentrations were associated with high all-cause mortality. When stratified according to quartiles, AG was associated with 30-day mortality (HR[95% CI]: second quartile, 2.243[1.273, 3.955]; third quartile, 3.026[1.763, 5.194]; top quartile, 4.402[2.573, 7.531]), 180-day mortality (HR[95% CI]: second quartile, 1.719[1.118, 2.645]; third quartile, 2.362[1.575, 3.542]; top quartile, 3.116[2.077, 4.676]), and 1-year mortality (HR[95% CI]: second quartile, 1.700[1.143, 2.528]; third quartile, 2.239[1.536, 3.264]; top quartile, 2.876[1.969, 4.201]) using bottom quartile as reference.

Conclusion: We firstly demonstrated that higher AG was significantly associated with increased 30-day, 180-day and 1-year all-cause mortality in AMI patients. AG as an easily obtained marker is of strong and reliable predictive value for AMI mortality during follow-up.

Keywords: acute myocardial infarction, anion gap, all-cause mortality

Introduction

Acute coronary syndrome (ACS) is the leading cause of death worldwide. As an acute manifestation of ACS, acute myocardial infarction (AMI) incidence has been declined during the past few decades.[1] However, it still remains one of the top causes of disease burden especially in middle- and low-income countries.[2,3] Thus, increasing emphasis has been put on identifying the risk factors for mortality to guide risk stratification and treatment after AMI. In clinical practice, easily obtained predictors to determine prognosis are warranted.

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Anion gap (AG), most frequently calculated as the sum of serum chloride and bicarbonate concentrations subtracted from the sum of sodium and potassium concentrations, represents the differences between unmeasured anions and cations.[4] AG is a valuable and simple-to-use clinical tool for differentially diagnosis of complex acid-base disorders,[5] which has been used for over half a century. Other than reflecting acid-base balance, more recent studies have shown the prognostic values of AG in general population and for various diseases.[6,7] AG is predictive of mortality in non-selected elderly population.[8] And a positive association between AG and inflammation markers, such as leukocyte count and C-reactive protein, has been demonstrated in general population.[9] In acute kidney injury[10] and advanced chronic kidney disease,[11] higher AG was associated with increased risk for death over a long-term follow-up. In cerebrovascular disease, AG also showed predictive values for short-term mortality in patients after cerebral infarction.[12] Furthermore, in coronary artery disease, higher AG was related to worse clinical type and mortality.[13] In AMI patients, AG was found to be associated with increased in-hospital mortality,[14] suggesting AG may be of importance for predicting cardiovascular mortality and risk stratification.

However, to our knowledge, there are no studies addressing the relationship between AG and AMI mortality during follow-up. Herein, the present study seeks to investigate the predictive value of AG for 30-day, 180-day and 1-year all-cause mortality in AMI patients.

Methods

Database

We conducted a retrospective analysis utilizing the Medical Information Mart for Intensive Care III (MIMIC-III) database.[15] The MIMIC database is comprised of deidentified and well-defined health-related data associated with patients admitted to intensive care units (ICU) of the Beth Israel Deaconess Medical Center (Boston, Massachusetts) between 2001 and 2012. It contains records of demographics, hourly vital signs, laboratory results, treatment, medications, mortality and other related clinical variables from 58,976 admissions of 46,520 patients. The access for author (CX) to the MIMIC database was approved (certification ID: 43375338). The use of database has been approved by Institutional Review Boards of the Massachusetts Institute of Technology (Cambridge, MA, USA). Since patients were deidentified and MIMIC database does not contain protected information, a waiver of informed consent was granted by the ethical committee. Additional ethical approval from our institution was waived by our institutional ethics committee.

Data Extraction and Outcomes

Data was extracted by structured query language (SQL).[16] After including only first admissions of patients to ICU, we identified a total of 1877 AMI patients who were older than 18 years old. AMI was diagnosed based on International Classification of Diseases, Ninth Revision (ICD-9) codes. Of these, 48 patients without lab results of sodium, 18 without results of potassium, and 5 without results of bicarbonates were excluded. Thus, we recruited 1806 AMI patients in our final study cohort. The following variables were extracted: age, sex, weight on admission, mean heart rate during the first 24h of ICU stay, serum creatinine, blood urea nitrogen (BUN), hemoglobin, platelet, white blood cells (WBC), sodium, potassium, chloride, bicarbonate, Sequential Organ Failure Assessment (SOFA) score and Simplified Acute Physiology Score II (SAPS II) on ICU admission. AG was calculated as: AG (mmol/L) = [sodium(mmol/L) + potassium(mmol/L)] − [chloride (mmol/L) + bicarbonate (mmol/L)].[4] The AG range in healthy individuals is 8–16 mmol/L with an average of 12 mmol/L. Lower AG level is most commonly due to laboratory error while elevated AG usually indicates metabolic acidosis.[5] The comorbidities of hypertension, atrial fibrillation (AF), congestive heart failure (CHF), diabetes, chronic renal disease and cardiogenic shock (CS) were identified based on ICD-9 codes. Sepsis was diagnosed according to the Angus criteria.[17] Acute kidney injury (AKI) was defined according to Kidney Disease Improving Global Outcomes (KDIGO) definition.[18] The outcomes in this study include 30-day all-cause mortality, 180-day all-cause mortality and 1-year all-cause mortality.

Statistical Analysis

Patients were stratified based on quartiles of AG. Continuous variables were described as mean ± standard deviation (SD) and categorical variables were expressed as numeral and percentage. The Kolmogorov–Smirnov tests were conducted to test the normal distribution of continuous variables. The comparisons among AG quartiles were performed using One-way ANOVA or Kruskal–Wallis test as appropriate. And chi-square tests were performed to evaluate the categorical variables.

Cox hazard regression models were conducted to examine the association between AG and 30-day, 180-day and 1-year outcomes. AG was modeled as continuous variable or categorical variable according to quartiles. Age, sex, SOFA score, creatinine, BUN, platelet, WBC, hemoglobin, mean heart rate, SAPS II score and comorbidities of hypertension, AF, CHF, diabetes and renal disease were entered into the final model. The results were presented as hazard ratios (HRs) with 95% confidence intervals (CI), and using AG <12mmol/L as reference for categorical AG. Risk-adjusted survival plot were performed to depict the survival rate across AG quartiles adjusted for the covariates above.

Restricted cubic spline (RCS) models with 3 knots were constructed to model AG as a continuous variable to assess for linearity visually. The RCS plots displaying the association between the hazards of mortality and AG was adjusted for the covariates in the Cox hazards regression model, using the 12mmol/L of AG as the reference.

Sensitivity analyses were performed for patients defined by age, sex, hypertension, AF, CHF and diabetes. Similarly, the adjusted HRs and 95% CIs of mortality were estimated. And the interactions between subgroups and AG were tested by including the interaction terms in the Cox model.

Missing data were <0.5% for all variables included in the Cox model, including mean heart rate (8 missing), hemoglobin (4 missing), platelet (1 missing), and WBC (1 missing). Missing data were imputed to the median of the non-missing values. All the statistical analyses were carried out using R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed P-value <0.05 was considered to be statistically significant.

Results

Baseline Characteristics

In this study, 1806 patients with AMI were enrolled, including 1184 (65.6%) male and 622 (34.4%) female. Baseline characteristics of patients stratified by quartiles of AG are shown in Table 1. Patients in the top quartile of AG were older with an average age of 69.9. As AG increased, patients were more likely to have higher heart rate, creatinine, BUN, platelet, WBC, SOFA score and SAPS II score, especially in the fourth quartile. Moreover, patients with higher AG had increased rates of AF, CHF, diabetes, chronic renal disease, and CS, but lower rates of hypertension. AMI patients with increased level of AG quartiles also suffered higher 30-day ($p < 0.001$), 180-day ($p < 0.001$) and 1-year ($p < 0.001$) all-cause mortality.

The Association of Anion Gap with AMI Mortality

In the unadjusted Cox hazard regression model (Table 2), AG (continuous) was significantly associated with the increased risk of 30-day (HR 1.198, 95% CI 1.173 to 1.225), 180-day (HR 1.192, 95% CI 1.169 to 1.216) and 1-year (HR 1.189, 95% CI 1.166 to 1.212) mortality. After further adjustment, the associations were slightly attenuated but remained significant, with a HR of 1.083 (95% CI 1.051 to 1.117) for 30-day mortality, a HR of 1.077 (95% CI 1.049 to 1.105) for 180-day mortality, and a HR of 1.074 (95% CI 1.047 to 1.101) for 1-year mortality in the final model (Table 2).

To further investigate the relationship between AG and mortality, the relative hazards depending on AG level are shown in Figure 1. In the adjusted restricted cubic spline model, the association between AG level and 30-day mortality was near linear (Figure 1A, p for nonlinear = 0.049). Similarly (Figure 1B and C), the restricted cubic splines for 180-day and 1-year all-cause mortality showed linearity (p for nonlinear = 0.078 and 0.092, respectively).

Given the above results showing linear association between HR and AG level, subsequently, associations of AG as a categorical variable and mortality were analyzed and presented in Table 3. In comparison with the reference level of less than 12mmol/L, the top quartile of AG was associated with increased risk for mortality in the unadjusted model (p for trend <0.001 for all), with a HR of 10.086 (95% CI 6.189 to 16.437) for 30-day mortality, a HR of 7.036 (95% CI 4.911 to 10.088) for 180-day mortality, and a HR of 6.622 (95% CI 4.740 to 9.251) for 1-year mortality. Further adjustments in the final model did not significantly change the results (Table 3 and Figure 2), showing HRs of 4.402 (95% CI 2.573 to 7.531), 3.116 (95% CI 2.077 to 4.676) and 2.876 (95% CI 1.969 to 4.201) for those three outcomes in the top quartile, respectively. Furthermore, the survival plot depicted increased risk for 30-day, 180-day and 1-year all-cause mortality in higher AG quartile after adjustment (Figure 2).

Subgroup Analysis

In the subgroup analysis (Figure 3) conducted for age, sex, and comorbidities of hypertension, AF, CHF, diabetes, AKI and sepsis, the results remained generally similar

Table 1 Baseline Characteristics of AMI Patients According to AG

	AG (mmol/L)				
Characteristics	**Quartile 1 <12.0**	**Quartile 2 ≥12.0,<14.1**	**Quartile 3 ≥14.1,<16.7**	**Quartile 4 ≥16.7**	**p-value**
Number of patients	443	446	463	454	-
Age(years)	67.1±13.0	66.5±14.5	67.66±14.7	69.9±14.5	0.001
Male, n(%)	297(67.0)	291(65.2)	313(67.6)	283(62.3)	0.334
Weight(kg)	80.28±17.00	82.32±18.93	81.84±20.45	80.32±22.16	0.102
Mean heart rate(bpm)	79.81±14.23	79.22±13.69	80.82±14.13	86.28±16.91	<0.001
Creatinine(mg/dL)	0.89±0.41	0.98±0.46	1.15±0.70	1.96±1.82	<0.001
BUN(mg/dL)	16.99±8.02	19.23±10.04	22.21±12.71	34.72±23.64	<0.001
Hemoglobin(g/dL)	11.28±2.13	12.15±1.96	12.09±2.04	11.88±2.29	<0.001
Platelet($\times 10^9$/L)	210.78±98.11	225.64±79.26	237.40±91.71	244.87±104.83	<0.001
WBC($\times 10^9$/L)	11.52±5.08	11.50±4.05	12.45±4.82	15.21±6.81	<0.001
Sodium(mmol/L)	136.89±4.14	138.20±3.43	137.90±3.78	138.04±4.73	<0.001
Potassium(mmol/L)	4.15±0.69	4.12±0.64	4.22±0.65	4.37±0.87	<0.001
Chloride(mmol/L)	106.38±5.00	105.02±4.56	103.96±4.39	103.30±5.62	<0.001
Bicarbonate(mmol/L)	25.09±3.36	24.32±3.12	22.97±3.15	19.44±4.46	<0.001
SOFA score	3.17±2.76	2.81±2.61	3.21±2.75	5.65±3.75	<0.001
SAPS II score	32.08±12.13	30.46±12.26	32.50±13.50	43.95±16.90	<0.001
Hypertension, n(%)	244(55.1)	232(52.0)	229(49.5)	168(37.0)	<0.001
AF, n(%)	102(23.0)	110(24.7)	103(22.2)	148(32.6)	0.001
CHF, n(%)	114(25.7)	161(36.1)	182(39.3)	247(54.4)	<0.001
Diabetes, n(%)	96(21.7)	100(22.4)	114(24.6)	155(34.1)	<0.001
Chronic renal disease, n(%)	20(4.5)	23(5.2)	36(7.8)	52(11.5)	<0.001
CS, n(%)	29(6.5)	61(13.7)	71(15.3)	142(31.3)	<0.001
30-day mortality, n(%)	18(4.1)	40(9.0)	58(12.5)	154(33.9)	<0.001
180-day mortality, n(%)	35(7.9)	57(12.8)	84(18.1)	198(43.6)	<0.001
1-year mortality, n(%)	41(9.3)	68(15.2)	95(20.5)	214(47.1)	<0.001

Abbreviations: BUN, blood urea nitrogen; WBC, white blood cell; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II; AF, atrial fibrillation; CHF, congestive heart failure; CS, cardiogenic shock.

Table 2 Hazard Ratio of AG (Continuous) for Mortality

	30-Day Mortality		180-Day Mortality		1-Year Mortality	
	HR (95% CI)	**P value**	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Unadjusted	1.198 (1.173,1.225)	<0.001	1.192 (1.169,1.216)	<0.001	1.189 (1.166,1.212)	<0.001
Model 1	1.190 (1.164,1.216)	<0.001	1.181 (1.158,1.205)	<0.001	1.178 (1.155,1.201)	<0.001
Model 2	1.108 (1.076,1.141)	<0.001	1.098 (1.070,1.126)	<0.001	1.093 (1.066,1.120)	<0.001
Model 3	1.083 (1.051,1.117)	<0.001	1.077 (1.049,1.105)	<0.001	1.074 (1.047,1.101)	<0.001

Notes: Model 1: adjusted for age and sex; Model 2: adjusted for model 1 plus SOFA score, creatinine, blood urea nitrogen, platelet, white blood cell, hemoglobin, and heart rate; Model 3: adjusted for model 2 plus hypertension, atrial fibrillation, congestive heart failure, diabetes, renal disease, cardiogenic shock and SAPS II score.
Abbreviations: HR, hazard ratio; CI, confidence interval; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II.

for the association between AG and mortality. And no significant interactions were observed.

Discussion

In this retrospective study of 1806 patients with AMI in ICU, we found that AG was significantly associated with increased 30-day, 180-day and 1-year all-cause mortality. The associations were independent of other cardiovascular risk factors, and were robust across subgroup analyses, indicating the predictive implications in clinical practice of AG. Moreover, a linear association between AG and 180-day and 1-year all-cause mortality were observed. To the best of our knowledge, this is the first study to investigate the association between AG and short-term and long-term AMI mortality during follow-up.

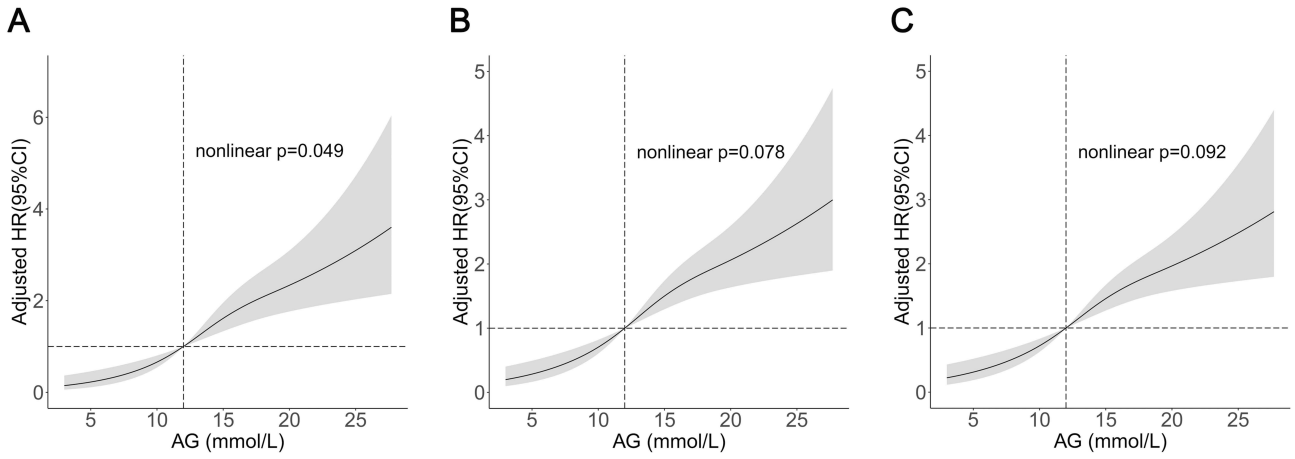

Figure 1 Associations between AG on a continuous scale and adjusted-risk of mortality in AMI patients. Hazard ratio (line) and 95% confidence interval (grey area) from adjusted Cox regression for 30-day mortality (**A**), 180-day mortality (**B**) and 1-year mortality (**C**). 12mmo/L of AG concentration were used as reference. Cox regression was adjusted for Age, sex, SOFA score, creatinine, BUN, platelet, WBC, hemoglobin, mean heart rate, SAPS II score and comorbidities of hypertension, AF, CHF, diabetes and renal disease as Model 3 described in Tables 2 and 3.
Abbreviations: AG, anion gap; HR, hazard ratio.

Recently, a study of patients admitted to coronary care units with a broad array of cardiovascular diseases has discovered a predictive role of AG for in-hospital mortality.[19] Another previous study of 733 individuals with AMI reported a significant association between high AG and increased risk of in-hospital death, with an odds ratio of 4.2 (95% CI 2.3 to 7.5) in comparison with low AG after multivariable adjustments.[14] In the present study, we studied AG on a continuous scale and further categorized individuals in larger groups based on AG quartiles. The association between AG on a continuous scale and all-cause mortality was linear, as higher concentrations were associated with increased all-cause mortality. Moreover, the second to fourth quartile of AG were associated with increased risk of death in 30-day, 180-day and 1-year follow-up. The association attenuated but remain significant even after adjustment for potential cardiovascular risk factors and comorbidities. These findings suggest that AG is a novel risk factor for AMI mortality independent of conventional cardiovascular risk factors. Our finding expands on the association of AG to all-cause death in AMI, indicating the predictive value of AG during follow-up.

Several risk factors are related to AG concentration. Higher AG has been independently associated with insulin-resistance[20] and lower cardiorespiratory fitness in general population.[21] Besides, although AG was not associated with severity of coronary artery stenosis, it is reported that higher AG related to worse cardiac function in coronary artery disease.[13] Furthermore, AG has been associated with outcomes of other critical illness like acute kidney injury,[10] advanced chronic kidney disease,[11] sepsis,[6] and cerebral infarction.[12] The evidence including the current study indicates that AG is a more general and reliable risk factor for cardiovascular and non-cardiovascular diseases, suggesting the clinical implications of this easily obtained predictor for prognosis.

The close association of AG to all-cause death in AMI might be explained by the relationship of AG to inflammation. A large study of 4525 healthy participants indicated increasing levels of leukocyte count and C-reactive protein with higher AG concentrations, even after various confounding factors were taken into account.[9] In our study, WBC increased with elevated AG. However, the association between AG and death remained significant after adjustment for WBC, and we were not able to adjust for other inflammation markers due to lack of information. Thus, inflammation may attribute to the hazard ratios, at least partly, in the current study. Furthermore, the major disorder that leads to the elevation of AG is metabolic acidosis, in which case increased AG is generally due to excessive production of organic acid such as lactate, β-hydroxybutyrate and acetoacetate.[5] It has been reported that two hours after symptom onset, most AMI patients had elevated lactate levels.[22] Many studies focusing on critically ill patients have reported that increased lactate level is a powerful predictor for short-term and long-term mortality in a spectrum of diseases,[23,24] including myocardial infarction.[25] On the other hand, β-hydroxybutyrate

Table 3 Hazard Ratio of AG (Quartile) for Mortality

AG, mmol/L	Unadjusted		Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
30-day mortality								
<12.0	1.0 (ref)		1.0 (ref)		1.0 (ref)		1.0 (ref)	
≥12.0,<14.1	2.248(1.289, 3.920)	0.004	2.236(1.282,3.900)	0.005	2.424(1.380,4.256)	0.002	2.243(1.273,3.955)	0.005
≥14.1,<16.7	3.211(1.892,5.449)	<0.001	3.162(1.863,5.366)	<0.001	3.054(1.785,5.224)	<0.001	3.026(1.763,5.194)	<0.001
≥16.7	10.086(6.189,16.437)	<0.001	9.287(5.694,15.146)	<0.001	5.090(3.017,8.586)	<0.001	4.402(2.573,7.531)	<0.001
P for trend	<0.001		<0.001		<0.001		<0.001	
180-day mortality								
<12.0	1.0 (ref)		1.0 (ref)		1.0 (ref)		1.0 (ref)	
≥12.0,<14.1	1.662(1.091,2.531)	0.018	1.647(1.081,2.510)	<0.001	1.877(1.224,2.880)	0.004	1.719(1.118,2.645)	0.014
≥14.1,<16.7	2.418(1.630,3.587)	<0.001	2.388(1.609,3.542)	<0.001	2.376(1.588,3.553)	<0.001	2.362(1.575,3.542)	<0.001
≥16.7	7.036(4.911,10.088)	<0.001	6.468(4.511,9.273)	<0.001	3.674(2.476,5.452)	<0.001	3.116(2.077,4.676)	<0.001
P for trend	<0.001		<0.001		<0.001		<0.001	
1-year mortality								
<12.0	1.0 (ref)		1.0 (ref)		1.0 (ref)		1.0 (ref)	
≥12.0,<14.1	1.696(1.151,2.498)	0.008	1.647(1.136,2.467)	<0.001	1.873(1.262,2.778)	0.002	1.700(1.143,2.528)	0.009
≥14.1,<16.7	2.342(1.623,3.377)	<0.001	2.315(1.605,3.339)	<0.001	2.265(1.558,3.294)	<0.001	2.239(1.536,3.264)	<0.001
≥16.7	6.622(4.740,9.251)	<0.001	6.098(4.362,8.525)	<0.001	3.398(2.349,4.915)	<0.001	2.876(1.969,4.201)	<0.001
P for trend	<0.001		<0.001		<0.001		<0.001	

Notes: Model 1: adjusted for age and sex; Model 2: adjusted for model 1 plus SOFA score, creatinine, blood urea nitrogen, platelet, white blood cell, hemoglobin, and heart rate; Model 3: adjusted for model 2 plus hypertension, atrial fibrillation, congestive heart failure, diabetes, renal disease, cardiogenic shock and SAPS II score.

Abbreviations: HR, hazard ratio; CI, confidence interval; SOFA, sequential organ failure assessment; SAPS II, simplified acute physiology score II.

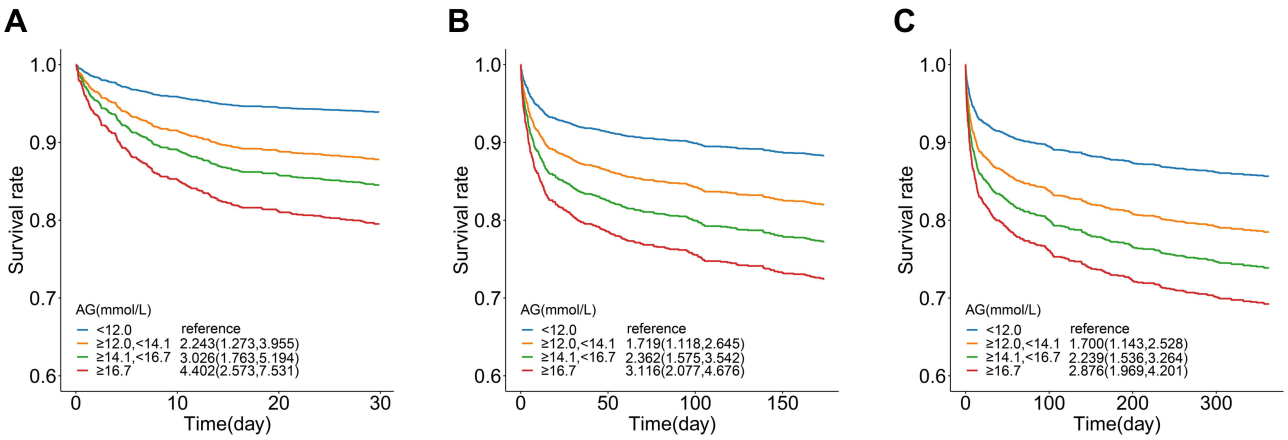

Figure 2 Adjusted survival rate by quartiles of AG. Risk-adjusted survival plots for 30-day mortality (**A**), 180-day mortality (**B**) and 1-year mortality (**C**). Cox regression was adjusted for age, sex, SOFA score, creatinine, BUN, platelet, WBC, hemoglobin, mean heart rate, SAPS II score and comorbidities of hypertension, AF, CHF, diabetes and renal disease as Model 3 described in Tables 2 and 3. The HRs and 95% CI were presented using the bottom quartile as reference.
Abbreviation: AG, anion gap.

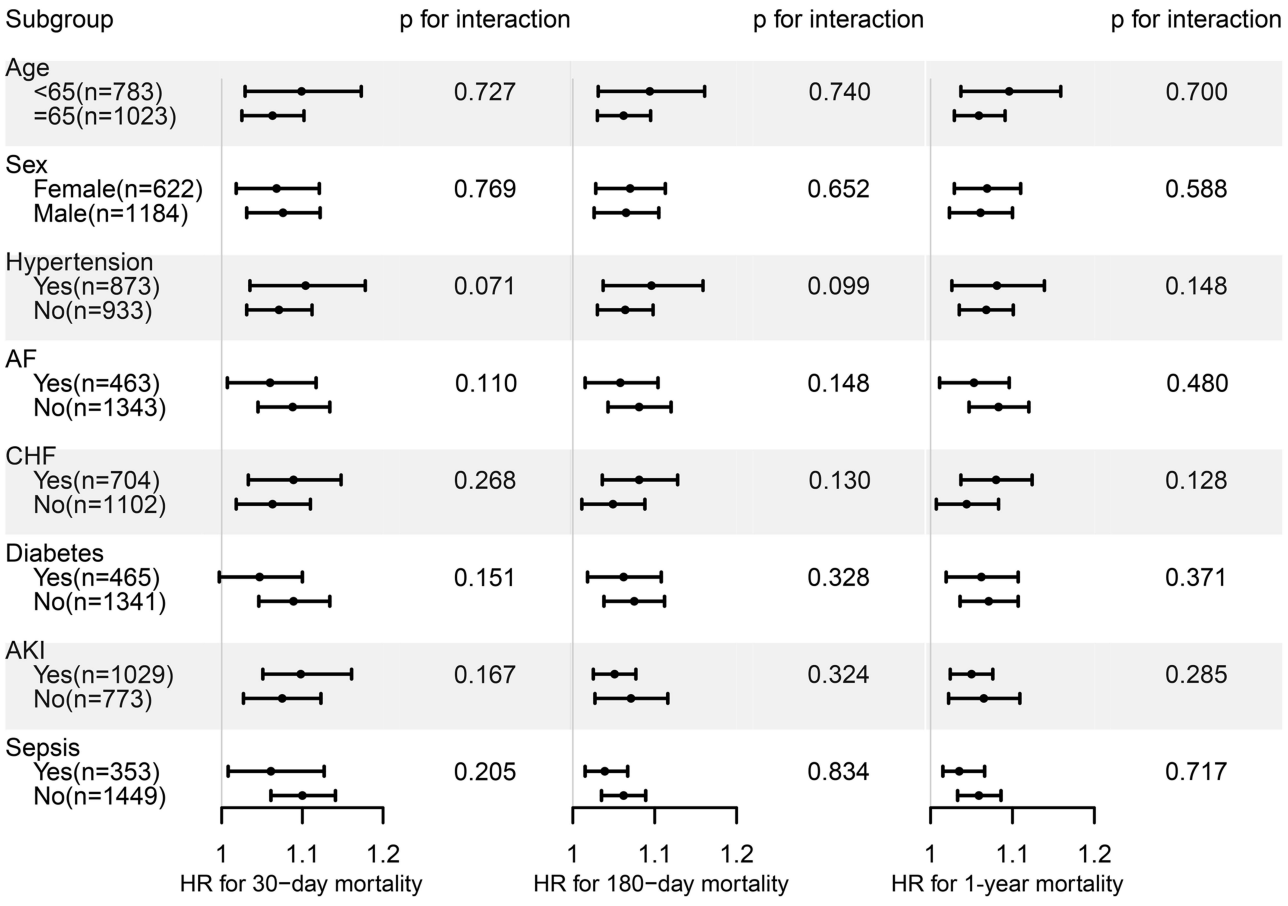

Figure 3 Associations between AG and risk of death in subgroups. Forest plot and adjusted hazard ratios with 95% CI for 30-day, 180-day and 1-year mortality.
Abbreviations: AF, atrial fibrillation; CHF, congestive heart failure; AKI, acute kidney injury.

and acetoacetate represent the two main ketone bodies.[26] A study showed that ketoacidosis associated to higher in-hospital mortality of ST-elevation myocardial infarction. Hence, organic acids that lead to elevated AG could also relate to the mechanisms by which AG increased risk of mortality.

The current study has several strengths. First, this is the first study to demonstrate the predictive value of AG

on AMI mortality during follow-up. We have relatively large number of recruited individuals from a well-characterized database, and information on both short-term and long-term mortality. Second, to test the consistency of our results, we utilized both continuous scale and categories based on AG concentrations. And we also conducted subgroup analyses which obtained comparable results. Third, we performed restricted cubic splines to evaluate linearity, reflecting the efficient predictive role of increased AG levels. Our study adds to the understanding of AG-AMI outcome associations, which provides important information to determine AMI prognosis for clinicians. Further study to develop predictive scoring system for AMI mortality prediction using AG is warranted.

Our study also has some limitations. First, as this study was observational, we could not determine the causal effect of AG on AMI all-cause mortality. Second, although we included important risk factors in our multivariable models like lab tests, comorbidities and clinical assessment scores, residual confounding factors cannot be eliminated completely. Other relevant factors like lactate, cardiac function, and myocardial injury markers need to be taken into account in further studies. Moreover, we only have the information about AG during hospitalization, so we were not able to distinguish between acute and chronic AG elevation, which may have affected outcomes to a different extent.

Conclusion

In summary, we firstly found higher AG was significantly associated with increased 30-day, 180-day and 1-year all-cause mortality in AMI patients. AG, as an easily obtained and inexpensive marker, is of reliable predictive value for AMI all-cause mortality during follow-up.

Abbreviations

ACS, acute coronary syndrome; AMI, acute myocardial infarction; AG, anion gap; ICU, intensive care units; SQL, structured query language; BUN, blood urea nitrogen; WBC, white blood cells; SOFA, Sequential Organ Failure Assessment; SOFA II, Simplified Acute Physiology Score II; AF, atrial fibrillation; CHF, congestive heart failure; AKI, acute kidney injury; RCS, restricted cubic spline.

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Disclosure

All authors report no conflicts of interest for this work.

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