CLINICAL

Prognostic Factors of Mortality Among Patients With Severe Hyperglycemia

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ABSTRACT

Objectives

Severe hyperglycemia is associated with increased morbidity and mortality in a variety of patients. We undertook this study to identify prognostic factors of mortality among patients experiencing severe hyperglycemia in the emergency department (ED).

Study Design

Longitudinal observation study.

Methods

We recruited patients who visited the ED with blood glucose levels higher than 500 mg/dL between July 2008 and September 2010. The primary outcome was death from any cause within 90 days. Outcome analysis was first performed with Pearson's χ^2 test. Any characteristic with suspected significance (P <.1) was then used in a univariate Cox regression model. The variables found to be statistically significant were then subjected to multivariate analysis for further investigation.

Results

Among 733 patients with severe hyperglycemia, the 90-day mortality rate was 14.6% (n = 107). Independent prognostic factors for increasing 90-day mortality included elevated absolute neutrophil count (hazard ratio [HR], 7.34), elevated C-reactive protein (HR, 4.48), elevated blood urea nitrogen (HR, 3.04), elevated respiratory rate (HR, 2.91), decreasing body temperature (HR, 2.68), decreasing systolic blood pressure (HR, 2.65), elevated potassium (HR, 2.54), decreasing blood glucose (HR, 2.46), elevated creatinine (HR, 2.40), elevated white blood cell count (HR, 2.30), and elevated ratio of blood urea nitrogen to creatinine (HR, 2.23).

Conclusions

The 90-day mortality rate among patients with severe hyperglycemia in the ED was 14.6%. Sepsis, renal impairment with electrolyte imbalance, and lower blood pressure were independent prognostic factors.

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Severe hyperglycemia is associated with increased morbidity and mortality in a variety of groups of patients.[1-3] The numerous precipitating factors in the development of severe hyperglycemia include infection,[4-8] poor compliance with antidiabetes therapy,[4,7,9] myocardial infarction (MI),[6,9] cerebrovascular accidents,[6,9] other medical conditions,[7] and medication side effects. Many observational studies have shown a consistent relationship between blood glucose levels and adverse clinical outcomes, even in patients without established diabetes.[1,2,10] Hyperglycemia is associated with many undesirable effects, including worse outcomes for strokes,[11] increased likelihood of death or severe disability from subarachnoid hemorrhage,[12] adverse events such as ST segment elevation MI,[10] and morbidity after colectomy for cancer.[13]

The death rates from severe hyperglycemia for adults in the United States and Taiwan have gradually declined.[6,7] The prognostic concomitant factors for mortality include altered mental status on admission,[14] pneumonia, older age, stroke, MI,[6] and high urea plasma levels.[15] The cause of death is often related to concomitant life-threatening illnesses, rather than directly due to metabolic complications of hyperglycemia or ketoacidosis.[4,5] Successful treatment of these serious complications requires improving tissue perfusion; correcting hyperglycemia, hyperosmolality, and electrolyte imbalances; and identifying and treating comorbid precipitating events.[4,5]

The association between hyperglycemia and worse outcomes often reflects the severity of an illness, but hyperglycemia itself may also contribute to the burden of the disease. To our knowledge, few studies have addressed the presentation of and prognostic factors associated with hyperglycemia in the emergency department (ED). We executed this study to identify prognostic factors for mortality among patients with severe hyperglycemia in the ED.

METHODS

Study Participants

We reviewed charts and selected patients who visited the ED in Taipei Veterans General Hospital between July

1, 2008, and September 30, 2010, enrolling patients who had blood glucose levels higher than 500 mg/dL. Exclusion criteria included being aged less than 30 years or more than 99 years, and surviving less than 24 hours after arrival. We reviewed the charts and analyzed data from routine examinations in the ED, including vital signs, a complete blood count, and serum biochemical analysis. A total of 781 patients came to the ED with blood glucose higher than 500 mg/dL; twenty-five patients were excluded due to the age restrictions, and 23 patients were excluded due to a survival time of less than 24 hours. A total of 733 patients were thus enrolled for analysis (**Figure 1**).

Baseline Examination

Through medical records, we obtained the following data: age, gender, day arrived at ED, blood glucose, body temperature, systolic blood pressure (SBP), pulse rate, white blood cell count, absolute neutrophil count, hemoglobin, hematocrit, platelets, C-reactive protein, blood urea nitrogen, creatinine, sodium, potassium, and alanine aminotransferase. We also evaluated the ratio of blood urea nitrogen to creatinine, and effective serum osmolality, which we calculated with the following formula: 2[measured Na^+ (mEq/l)]+ glucose (mg/dL)/18.[4] The participants were divided into 5 equal-sized groups (quintiles) for each parameter in order to evaluate its impact on prognosis. Baseline characteristics were expressed as mean ± SD, median, and the 20th to 80th percentile interquintile (range). Admission rates and intensive care unit (ICU) hospitalization rates were also recorded.

Main Outcome Measures

The main outcome measure was death from any cause within 90 days.[16] Information on date of death was obtained from the Department of Health, Executive Yuan, ROC (Taiwan).

Statistical Analysis

To compare clinical characteristics among groups by mortality, we performed independent unpaired *t* tests or the Mann-Whitney U test for continuous variables, based on whether the variables had a normal distribution. Pearson's χ^2 test was used for categorical data. We used independent *t* tests to compare age, blood glucose levels, body temperature, respiratory rate, SBP, pulse rate, hemoglobin, hematocrit, creatinine, ratio of blood urea nitrogen to creatinine, effective serum osmolarity, and sodium and potassium levels; then we presented the results as mean ± SD. We used the Mann-Whitney *U* test to compare white blood cell counts, absolute neutrophil counts, platelets, C-reactive protein, blood urea nitrogen, and alanine aminotransferase, and we expressed the results as medians with interquintile ranges due to their nonnormal distribution.

We calculated 90-day mortality rates associated with each parameter by dividing patients into 5 groups according to a basic characteristics scale, as mentioned above. Outcome analysis was performed with the Pearson's χ^2 test, and if significance (P <.1) was suspected, a univariable Cox regression model was then used. We presumed every group was compared with the group with the lowest mortality rate. The results were expressed as hazard ratios with 95% CI. The data were all shown as forest plots. The variables that were statistically significant were then subjected to multivariate analysis to investigate whether they still had statistical significance.

The following models were used to identify potential confounders of the relationship between mortality and the parameter in question: 1) unadjusted, 2) adjusted for gender and age, and 3) adjusted for all other parameters, including age, sex, blood glucose, body temperature, respiratory rate, SBP, pulse rate, white blood cell count, absolute neutrophil count, hemoglobin, hematocrit, platelets, C-reactive protein, blood urea nitrogen, creatinine, sodium, potassium, and alanine aminotransferase. The ratio of blood urea nitrogen to creatinine was not adjusted for when considering blood urea nitrogen and creatinine as separate variables in Model 3. Similarly, effective osmolality was not adjusted for sodium and blood glucose in Model 3. We performed analyses with SPSS for Windows version 18.0 (SPSS, Inc, Chicago, Illinois). Statistical significance was considered as P <.05. The study had approval from the institutional review board of Taipei Veterans General Hospital.

RESULTS

Study Participants and Baseline Characteristics

We enrolled 733 patients for analysis, of which 494 (67.4%) were men. The mean age at baseline was 68.5 ± 15.4 years, mean blood glucose level was 691.5 ± 204.5 mg/dL, C-reactive protein level was 7.0 ± 9.6 mg/dL, blood urea nitrogen level was 46.2 ± 34.1 mg/dL, creatinine level was 2.6 ± 2.1 mg/dL, sodium level was 132.3 ± 8.7 mmol/L, and potassium level was 4.6 ± 1.0 mmol/L. The baseline clinical characteristics of our study subjects are shown in the **eAppendix Table** (available at **www.ajmc.com**).

Mortality

With 107 patients dying within 90 days of visiting the ED, the 90-day mortality rate was 14.6%. The causes of death are shown in Table 1. Causes of death among these patients with severe hyperglycemia were broadly similar to those expected in Taiwan; however, the proportion of patients in our study dying from pneumonia, infections, and diabetes was higher compared with expected values. Table 2 reveals the baseline clinical characteristics of our study subjects according to their survival status. Deceased subjects had higher admission rates (95.3% vs 85.9%) and more ICU admissions (58.9% vs 24.4%). The deceased subjects also tended to be older (72.2 ± 13.7 years vs 67.9 ± 15.6 years) and to have higher respiratory rates (22.5 ± 5.5 breaths per minute vs 20.4 ± 3.6 breaths per minute), white blood cell counts (12,700/cumm vs 9900/cumm), C-reactive protein (8.0 mg/dL vs 1.51 mg/dL), blood urea nitrogen (48.0 mg/dL vs 34.0 mg/dL), serum creatinine (3.05 ± 2.02 mg/dL vs 2.50 ± 2.12 mg/dL), and serum sodium (134.7 ± 11.5 mmol/L vs 131.9 ± 8.1 mmol/L). However, the subjects who died had lower blood glucose levels (651.8 ± 151.7 mg/dL vs 698.3 ± 211.6 mg/dL), lower systolic BP (128.2 ± 38.9 mm Hg vs 141.4 ± 35.4 mm Hg), and lower hemoglobin levels (11.6 ± 2.9 g/dL vs 12.6 ± 2.7 g/dL).

Dividing the patients into 5 equal groups for each parameter, we compared those who survived with those who did not, using Pearson's χ^2 test. The baseline characteristics, including blood glucose, body temperature, respiratory rate, SBP, pulse rate, white blood cell count, absolute neutrophil count, hemoglobin, C-reactive protein, blood urea nitrogen, creatinine, ratio of blood urea nitrogen to creatinine, effective osmolality, and sodium and potassium levels, were entered in the survival analysis, with the exception of platelet and alanine aminotransferase due to their nonsignificance ($P = .111$ and .609, respectively).

Survival Analysis

The parameters entered for survival analysis were first used in univariable Cox regression models. The results are expressed as hazard ratios with 95% CI and all are shown in the forest plot (Figure 2). We found significantly higher mortality rates among patients with blood glucose either between 542 mg/dL and 595 mg/dL or between 595 mg/dL and 677 mg/dL; body temperature lower than 36°C or higher than 37.4°C; respiratory rates exceeding 22 breaths per minute; SBP of lower than 110 mm Hg or between 110 mm Hg and 128 mm Hg; white blood cell count between 11,800/cumm and 15,900/cumm, or more than 15,900/cumm; absolute neutrophil count between 9721/cumm and 13,846/cumm, or more than 13,846/cumm; C-reactive protein between 4.20 mg/dL and 13.20 mg/dL, or more than 13.20 mg/dL; blood urea nitrogen between 43 mg/dL and 68 mg/dL or more than 68 mg/dL; creatinine between 2.27 mg/dL and 3.31 mg/dL, or more than 3.31 mg/dL; sodium levels above 137 mg/dL; and potassium levels above 5.2 mg/dL.

We subjected the statistically significant variables to multivariate analysis, adjusting for age and sex in Model 2, and then adjusted for the other parameters in Model 3. Finally, factors that were independent prognostic factors of 90-day mortality included blood glucose between 542 mg/dL and 677 mg/dL; body temperature lower than 36°C; respiratory rate greater than 22 breaths per minute; SBP lower than 110 mm Hg; white blood cell counts between 11,800/cumm and 15,900/cumm; absolute neutrophil counts of 9721/cumm or higher; C-reactive protein of 4.20 mg/dL or higher; blood urea nitrogen of 43 mg/dL or higher; creatinine of 2.27 mg/dL or higher; and potassium of more than 5.2 mg/dL (Table 3).

DISCUSSION

Patients in the 90-day mortality group were older and more likely to have sepsis, including more leukocytosis and elevated C-reactive protein; more azotemia and hypotension were also noted. Both hyperthermia and hypothermia increased the mortality rate, but hyperthermia was nonsignificant. Lower blood pressure (BP) and reduced hemoglobin, as well as elevated respiratory rate, white blood cell count, absolute neutrophil count, C-reactive protein, blood urea nitrogen, creatinine, blood urea nitrogen-creatinine ratio, and potassium were related to elevated mortality rate. Increasing pulse rate, sodium, and osmolality were also related to higher mortality rate but were not statistically significant. Lower BP and reduced hemoglobin were related to higher mortality. However, elevated blood glucose (>500 mg/dL) was associated with decreasing mortality rate among these extremely hyperglycemic patients.

Some studies have previously addressed mortality associated with hyperglycemia. Chung et al showed that the crude mortality rate associated with hyperglycemia crises was 17.7% and increased significantly with age. The strongest predictor of mortality in that study was change of mental status.[14] The factors predictive of mortality in a study by Ogbera et al were sepsis, foot ulceration,

newly diagnosed diabetes mellitus, hypokalemia, and older age.[17] Anthanont et al found a mortality rate of 8.4%, observing that infections and noncompliance with treatment were the 2 most common factors precipitating mortality. The most common etiology of death was infection, and serum sodium levels on admission were an independent risk factor.[8] In general, the mortality in hyperglycemic crises was near 15%, increasing substantially with aging and the presence of concomitant life-threatening illnesses.[9] In our study, the mortality rate was 14.6%, which was essentially the same as in previous reports.

Stress hyperglycemia is common among patients in critical condition. Some studies have found that infection is the most common precipitating factor in the development of severe hyperglycemia,[8-12] and is the leading cause of death in these patients.[10,12,17] Patients in our study also showed an excess of death from infectious disease (Table 1), with sepsis defined as infection combined with a systemic inflammatory response syndrome. Patients commonly presented with fever or hypothermia, tachycardia, tachypnea, hyperglycemia in the absence of diabetes, altered mental status, leukocytosis or leucopenia, elevated C-reactive protein and procalcitonin, arterial hypotension, and hypoxemia.[18,19] Our study found that several factors compatible with a diagnosis of sepsis were also independent risk factors in 90-day mortality, including hypothermia, tachycardia, tachypnea, leukocytosis, and elevated C-reactive protein. Thus, it seems that sepsis is an important contributing factor to mortality associated with hyperglycemia, and absolute neutrophil count (HR, 7.34; 95% CI, 1.93-27.96) was the best predictive factor.

Dehydration is an important characteristic of hyperglycemia hyperosmolality states and was found to be prognostic of mortality in medical admissions.[8,20,21] Patients with hyperglycemia have osmotic diuresis, which results in high effective serum osmolality.[8,13] Methods to evaluate dehydration include BP, osmolality, and ratio of blood urea nitrogen to creatinine.[22] Patients with hypotension in the ED have poorer prognoses than patients with normal BP,[23,24] and our study similarly found the mortality rate increased with decreasing SBP (**Figure 2d**). Among patients whose SBP was lower than 110 mm Hg, the hazard ratio for mortality was 3.167 when compared with those who had SBP above 168 mm Hg. The elevated BP is a physical response resulting from stimulation of the sympathetic system when stress is presented. We did not have data about serial BP readings in the ED; future studies should consider this. Elevated blood urea nitrogen, elevated creatinine, and elevated blood urea nitrogen to creatinine ratio were all independent risk factors of 90-day mortality. It might not be necessary to calculate the ratio of blood urea nitrogen to creatinine in order to evaluate the degree of dehydration. Osmolality was not a prognostic factor in our study.

Electrolyte imbalance was a prognostic factor for 90-day mortality, and significantly elevated or decreased serum levels often are associated with increased mortality. When severe hyperglycemia occurs, the hyponatremia does not reflect true plasma hypoosmolality; the initial hyperosmolality produced by severe hyperglycemia causes an osmotic shift of water from intracellular fluid to extracellular fluid, which in turn produces a dilutional decrease in serum sodium levels. Mild hyponatremia indicates the patient has the ability to compensate for the osmolality change caused by hyperglycemia, and among our study patients, hyponatremia did not increase mortality. Hypernatremia significantly increased mortality, however, which may be explained by patients losing the ability to compensate for the osmolality and severe dehydration. We also found that hyperkalemia (potassium level above 5.2 mmol/L) was prognostic of mortality. The most common etiologies of hyperkalemia in the ED included renal failure, status of cardiopulmonary resuscitation, and severe metabolic acidosis. Hypokalemia was associated with a nonstatistically significant increase in mortality (HR, 1.847; 95% CI, 0.932-3.661), a finding that may call for further study to prove or disprove the concept.

Our results revealed that the nadir of mortality rate was in the second highest, rather than the highest, blood glucose group, so higher blood glucose levels did not indicate higher mortality rates, per se. Hyperglycemia may serve not only as a risk factor, but also as a risk marker of underlying disease, which may play a more important role in eventual mortality than the severity of the hyperglycemia. Therefore, our data suggests that clinicians should do more examinations to determine the cause of hyperglycemia and treat that, rather than treating the single value of blood glucose.

Limitations

First, this is a retrospective study done in only 1 medical center, so it may not apply universally. Second, as the data were from ED reports, we could not be certain how the underlying diseases influenced mortality. Third, some factors that predict mortality rate, including lactate and blood gas levels[25] were not included in our study because they were not part of a routine examination in our ED. The advantages of our study include the fact that the study population was larger than in previous studies[11,12,14,15] and showed clear cutoffs for each parameter.

However, all of the parameters we enrolled were determined by the routine examinations in the ED. Further studies may be designed as prospective ones and could include greater study populations to better evaluate the prognostic factors.

CONCLUSIONS

Severe hyperglycemia is an important indicator in diabetes, and the 90-day mortality rate among patients with severe hyperglycemia in our ED was nearly 15%. We found age combined with hyperglycemia, sepsis, renal impairment with electrolyte imbalance, and lower BP were independent prognostic factors.

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Take-Away Points

Severe hyperglycemia is associated with increased morbidity and mortality in a variety of patients. We recruited patients who visited the emergency department (ED) with blood glucose levels higher than 500 mg/dL to identify prognostic factors of mortality.

- Our study found the 90-day mortality rate associated with severe hyperglycemia in the ED was 14.6%.
- Patients in the mortality group were older and more likely to have an electrolyte imbalance. Both low and high body temperature indicated increased mortality rates.
- However, higher blood glucose levels did not indicate higher mortality rates among these extremely hyperglycemic patients.

Table 1. Causes of Death Within 90 Days of Visiting the Emergency Department (N = 107)

Cause of death	n	%	% Expected[a]
Pneumonia	12	11.2	6.0
Other infection	8	7.5	3.9
Heart disease	11	10.3	10.9
Hypertensive disease	5	4.7	3.0
Cerebrovascular diseases	7	6.5	7.1
Diabetes	19	17.8	6.0
Malignancy	28	26.2	28.0
Esophageal and stomach	5		
Colon and rectum	4		
Lung and bronchus	5		
Liver	4		
Pancreas	3		
Breast	3		
Other	4		
Liver (cirrhosis)	7	6.5	3.4
Kidney (ESRD)	3	2.8	2.9
Accident	3	2.8	4.4
Other	4	3.7	

[a]From Taiwan Mortality Statistics 2011.
ESRD indicates end-stage renal disease.

Table 2. Baseline Characteristics of Patients According to Outcome

	Alive 90 Days After ED	Deceased Within 90 Days	*P*
Number	626	107	
Age (years)	67.9 ± 15.6[a]	72.2 ± 13.7[a]	.004
Male sex, n (%)	430 (68.7%)[b]	64 (59.9%)[b]	.070
Workday: weekend ED visit	467:159	78:29	.709
Blood glucose (mg/dL)	698.3 ± 211.6[a]	651.8 ± 151.7[a]	.007
Admission rate (%)	85.9	95.3	.007
ICU rate (%)	24.4	58.9	<.001
Body temperature (°C)	36.7 ± 1.0[a]	37.0 ± 1.4[a]	.056
RR (breaths per minute)	20.4 ± 3.6[a]	22.5 ± 5.5[a]	<.001
SBP (mm Hg)	141.4 ± 35.4[a]	128.2 ± 38.9[a]	<.001
PR (beats per minute)	97.9 ± 22.4[a]	102.5 ± 27.1[a]	.069
WBC count (/cumm)	9900 (6700-15,200)[b]	12,700 (8400-19,300)[b]	<.001
ANC (/cumm)	7845 (4882-13,167)[b]	10,898 (5825-17,295)[b]	<.001
Hb (g/dL)	12.6 ± 2.7[a]	11.6 ± 2.9[a]	<.001
Hct (%)	37.2 ± 7.7[a]	34.3 ± 8.2[a]	<.001
PLT (/cumm)	225,000 (158,000-307,000)[b]	226,000 (123,000-298,000)[b]	.157
CRP (mg/dL)	1.51 (0.26-10.89)[b]	8.0 (1.48-23.12)[b]	<.001
BUN (mg/dL)	34.0 (19-65)[b]	48.0 (27-81.4)[b]	<.001
Cre (mg/dL)	2.50 ± 2.12[a]	3.05 ± 2.02[a]	.013
BUN/cre ratio	19.0 ± 9.36[a]	21.4 ± 19.0[a]	.046
Osmolality	302.6 ± 19.0[a]	305.7 ± 24.1[a]	.211
Na (mmol/L)	131.9 ± 8.1[a]	134.7 ± 11.5[a]	.015
K (mmol/L)	4.6 ± 0.9[a]	4.7 ± 1.2[a]	.202
ALT (U/L)	23 (15-40)[b]	24.5 (15-58)[b]	.307

ALT indicates alanine aminotransferase; ANC, absolute neutrophil count; BT, body temperature; BUN, blood urea nitrogen; Cre, creatinine; CRP, C-reactive protein; ED, emergency department; Hb, hemoglobin; Hct, hematocrit; ICU, intensive care unit; K, potassium; Na, sodium; PLT, platelets; PR, pulse rate; RR, respiratory rate; SBP, systolic blood pressure; WBC, white blood cell.
[a]Mean ± SD.
[b]Mean (95 %).

Table 3. Relative Risk for Characteristics Associated With Mortality Among Patients With Severe Hyperglycemia in the Emergency Department

Characteristic	Relative Risk (95% CI)[a]		
	Model 1	Model 2	Model 3
Blood glucose, 2nd vs 4th quintile	1.95 (1.02-3.72)	1.82 (0.95-3.50)	2.46 (1.22-4.94)
Blood glucose, 3rd vs 4th quintile	2.14 (1.13-4.06)	1.99 (1.04-3.78)	2.05 (1.02-4.11)
Body temperature, 1st vs 2nd quintile	3.46 (1.74-6.88)	3.53 (1.77-7.02)	2.68 (1.30-5.51)
Body temperature, 5th vs 2nd quintile	4.25 (2.14-8.43)	3.94 (1.97-7.88)	1.95 (0.93-4.11)
Respiratory rate, 5th vs 2nd quintile	3.97 (1.66-9.52)	3.88 (1.62-9.31)	2.91 (1.19-7.14)
SBP, 1st vs 5th quintile	3.17 (1.55-6.48)	3.25 (1.59-6.64)	2.65 (1.23-5.71)
SBP, 2nd vs 5th quintile	2.26 (1.07-4.77)	2.38 (1.13-5.05)	1.91 (0.85-4.28)
Pulse rate, 5th vs 2nd quintile	2.65 (1.34-5.22)	2.68 (1.35-5.31)	1.42 (0.68-2.94)
WBC count, 4th vs 2nd quintile	2.59 (1.36-4.95)	2.54 (1.33-4.85)	2.30 (1.10-4.80)
WBC count, 5th vs 2nd quintile	2.87 (1.51-5.44)	2.76 (1.45-5.24)	1.62 (0.77-3.42)
ANC, 4th vs 2nd quintile	4.63 (2.14-9.99)	4.40 (2.04-9.52)	5.66 (2.17-14.74)
ANC, 5th vs 2nd quintile	4.80 (2.22-10.38)	4.41 (2.03-9.58)	7.34 (1.93-27.96)
Hb, 1st vs 5th quintile	2.38 (1.25-4.55)	1.99 (1.03-3.85)	1.31 (0.64-2.70)
Platelets, 1st vs 2nd quintile	2.22 (1.20-4.11)	2.30 (1.24-4.27)	2.15 (1.05-4.41)
CRP, 4th vs 1st quintile	3.85 (1.83-8.11)	3.49 (1.65-7.35)	2.90 (1.25-6.75)
CRP, 5th vs 1st quintile	5.51 (2.68-11.33)	5.35 (2.59-11.04)	4.48 (1.97-10.21)
BUN, 4th vs 1st quintile	3.16 (1.58-6.30)	2.73 (1.35-5.53)	3.04 (1.32-7.00)
BUN, 5th vs 1st quintile	3.25 (1.64-6.45)	2.70 (1.34-5.45)	2.76 (1.17-6.48)
Cre, 4th vs 2nd quintile	2.55 (1.30-5.00)	2.38 (1.21-4.68)	2.39 (1.13-5.02)
Cre, 5th vs 2nd quintile	2.90 (1.50-5.64)	2.76 (1.42-5.37)	2.41 (1.13-5.12)
BUN/cre ratio, 4th vs 2nd quintile	2.73 (1.36-5.49)	2.31 (1.09-4.91)	2.19 (1.02-4.73)
BUN/cre ratio, 5th vs 2nd quintile	2.99 (1.50-5.95)	2.68 (1.28-5.58)	2.23 (1.07-4.66)
Osmolality, 5th vs 3rd quintile	2.28 (1.23-4.22)	2.02 (1.08-3.76)	0.99 (0.48-2.04)
Na, 5th vs 2nd quintile	2.40 (1.38-4.18)	2.12 (1.21-3.71)	1. 60 (0.86-3.00)
K, 5th vs 4th quintile	2.37 (1.21-4.65)	2.26 (1.15-4.42)	2.54 (1.22-5.31)

ANC indicates absolute neutrophil count; BUN, blood urea nitrogen; Cre, creatine; CRP, C-reactive protein; Hb, hemoglobin; Hct, hematocrit; K, potassium; Na, sodium; SBP, systolic blood presssure; WBC, white blood cell.
Model 1: Univariate analysis.
Model 2: Adjusted for age and sex.
Model 3: Adjusted for age, sex, blood glucose, body temperature, respiratory rate, systolic blood pressure, pulse rate, alanine aminotransferase, platelets, ANC, BUN, Cre, CRP, Hb, K, Na, WBC.

Figure 1. Flow Diagram of the Study Population

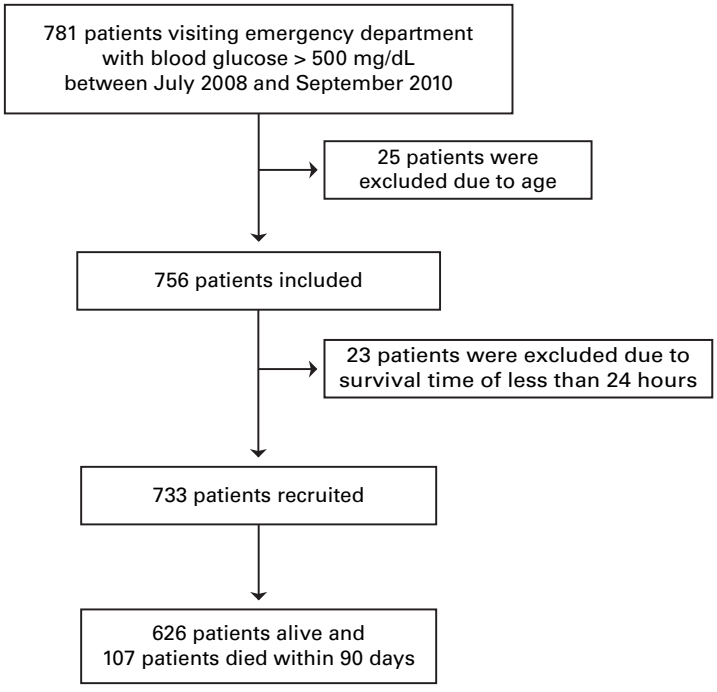


Figure 2. The Hazard Ratios of 90-Day Mortality Rate Associated With Each Parameter

ANC indicates absolute neutrophil count; BUN, blood urea nitrogen; Cre, creatine; CRP, C-reactive protein; SBP, systolic blood presssure; WBC, white blood cell.
The quintile column shows the cut-off values for each group. The hazard ratios with 95% CIs are presented without adjustment.

Figure 2a.

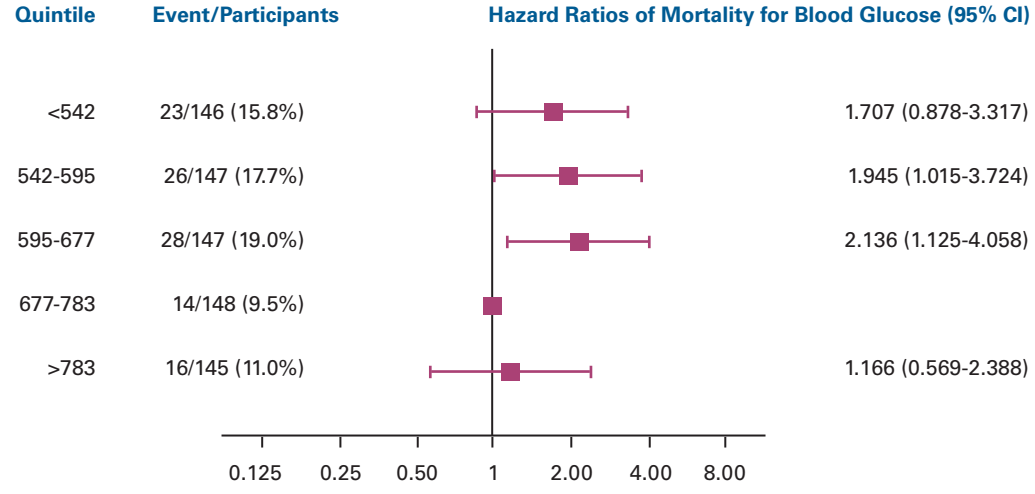


Figure 2b.

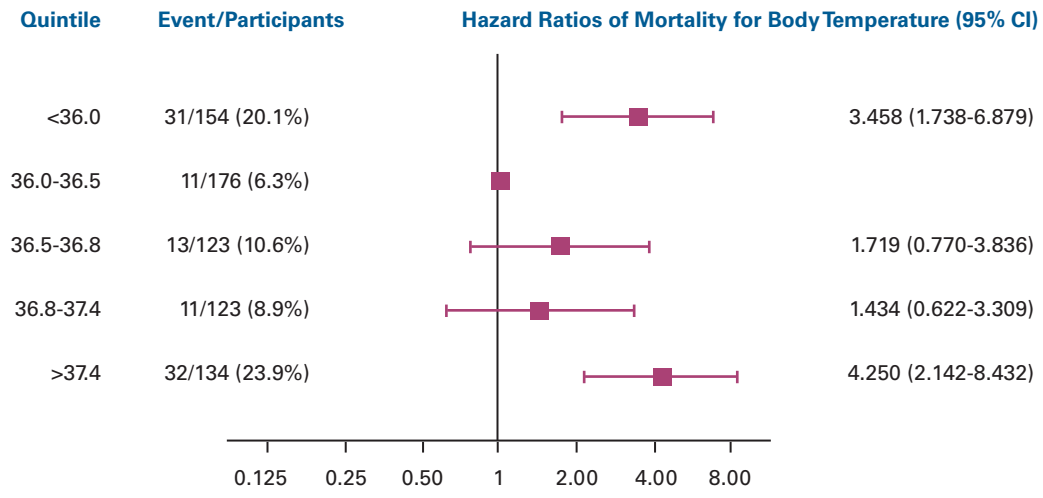


Figure 2c.

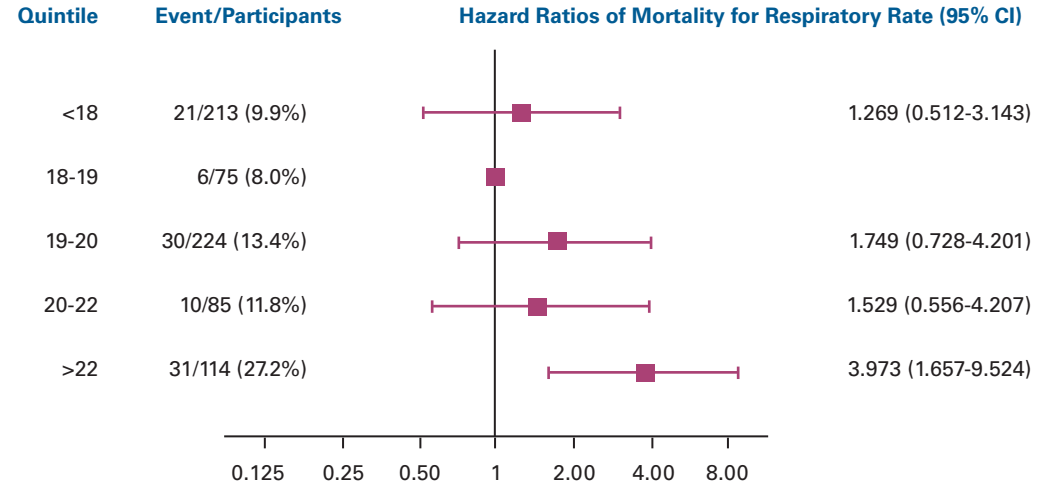


Figure 2d.

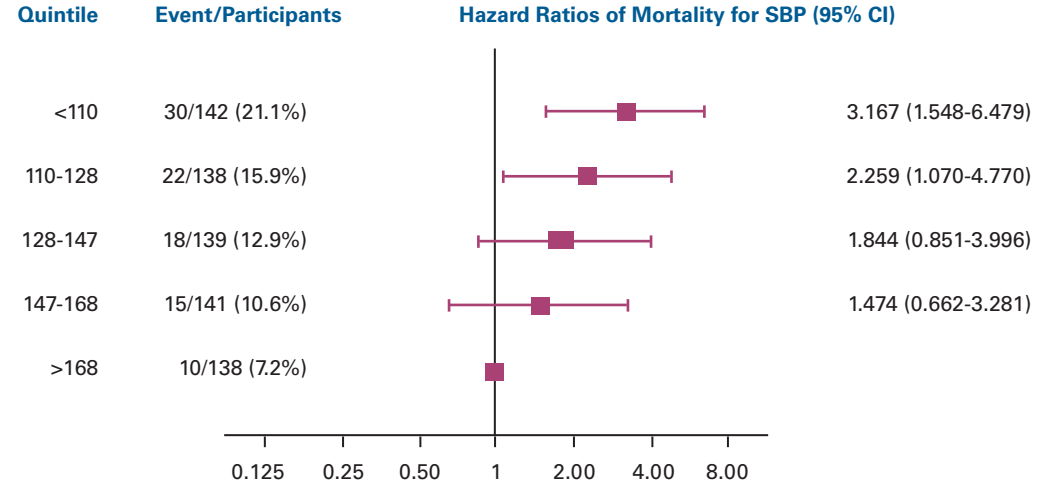


Figure 2e.

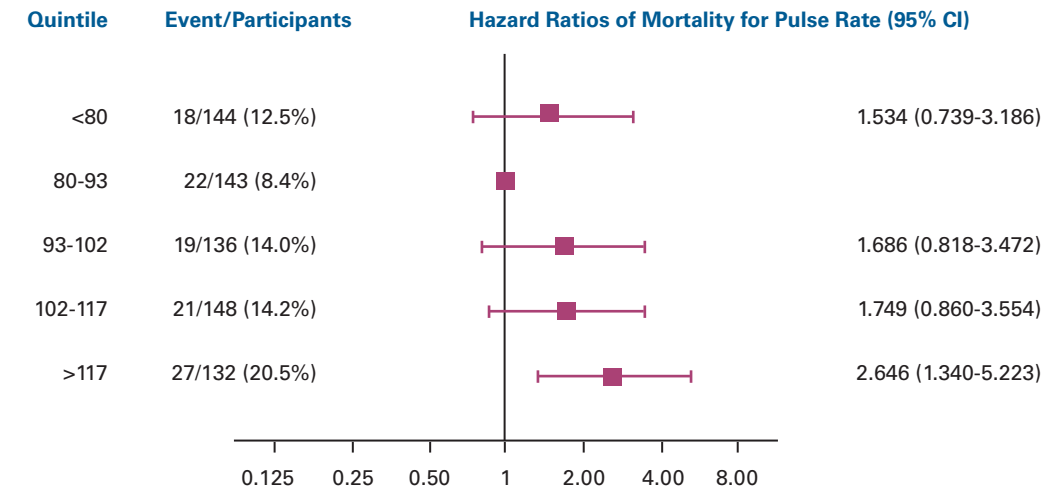


Figure 2f.

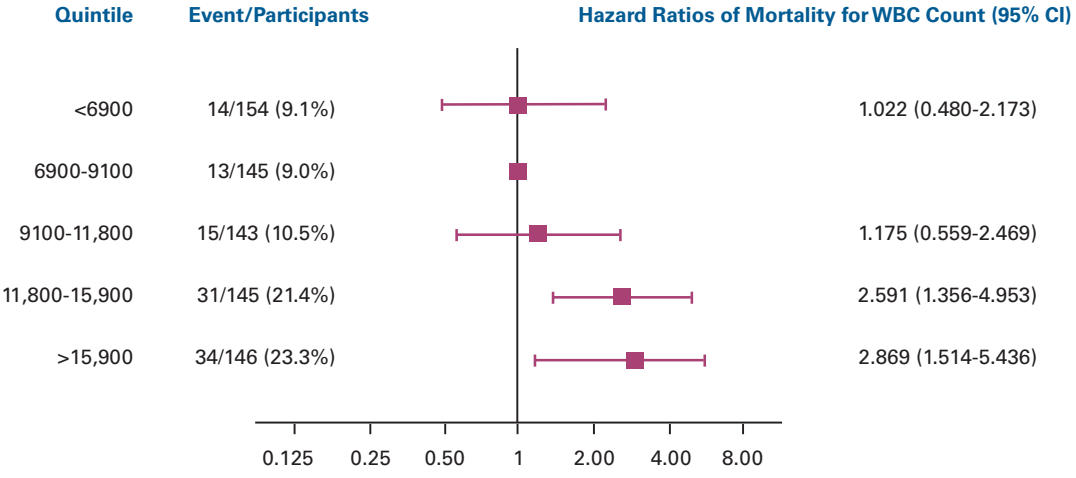


Figure 2g.

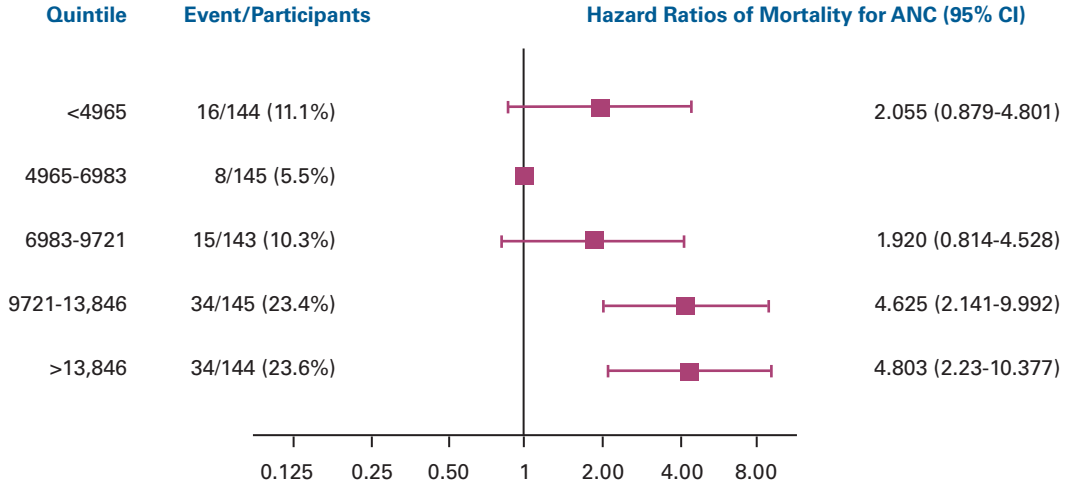


Figure 2h.

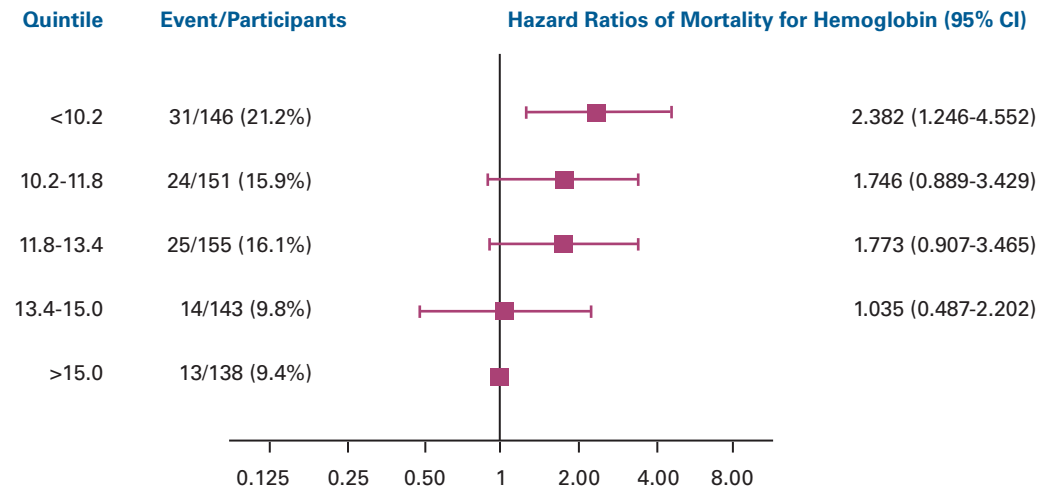


Figure 2i.

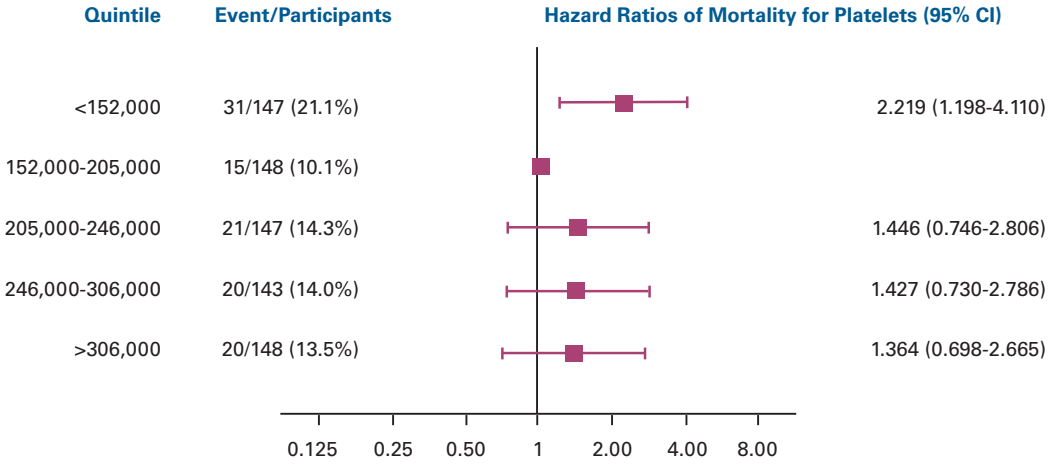


Figure 2j.

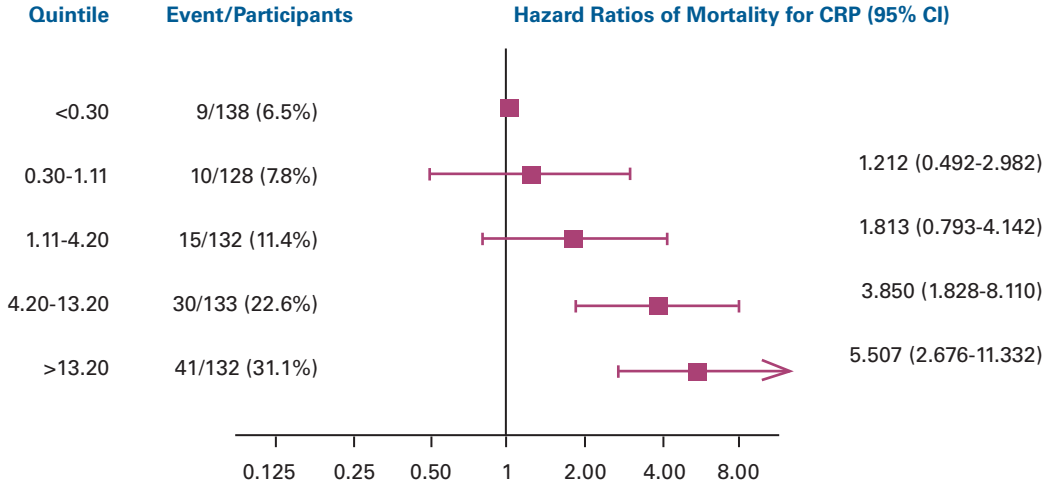


Figure 2k.

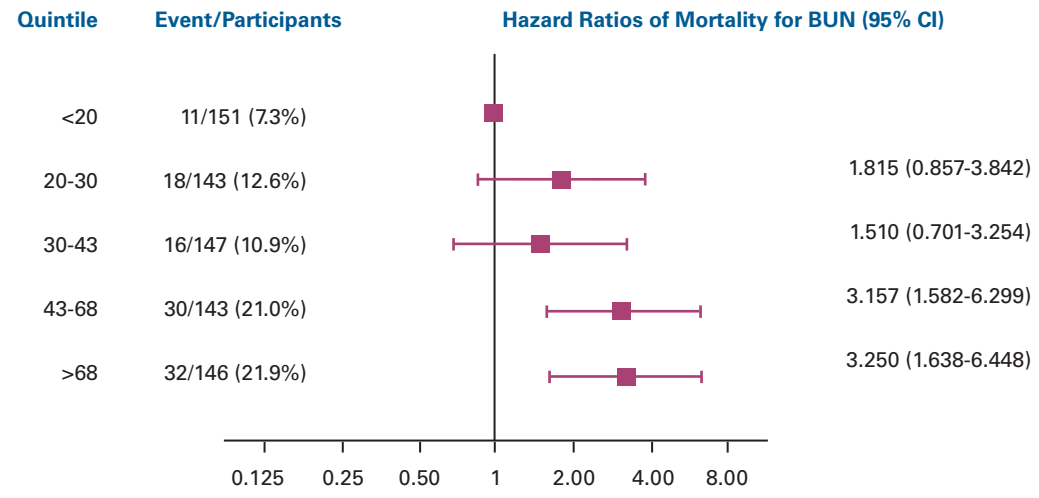


Figure 2l.

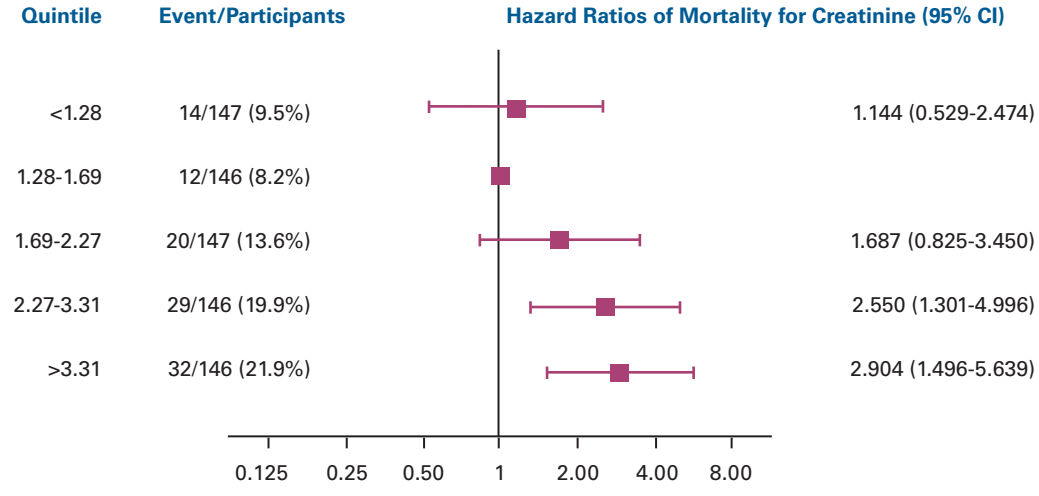


Figure 2m.

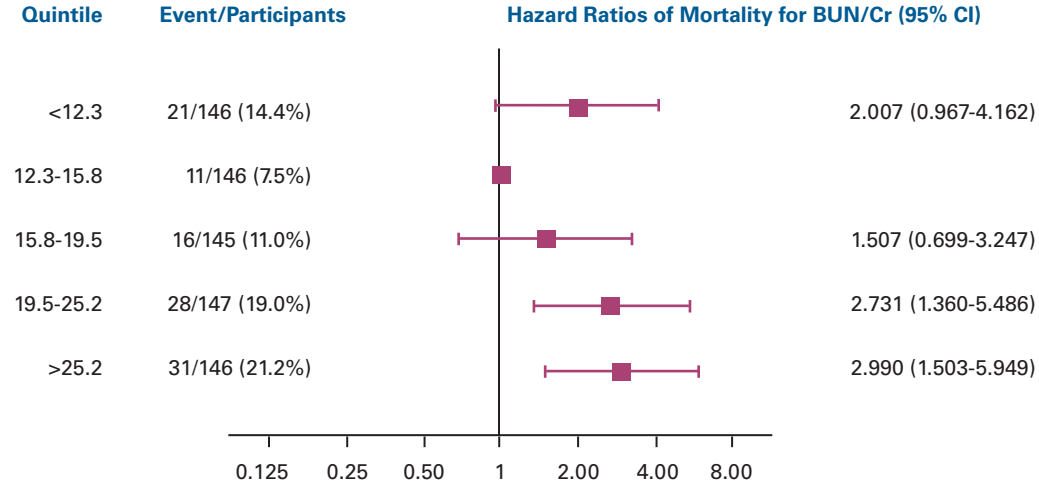


Figure 2n.

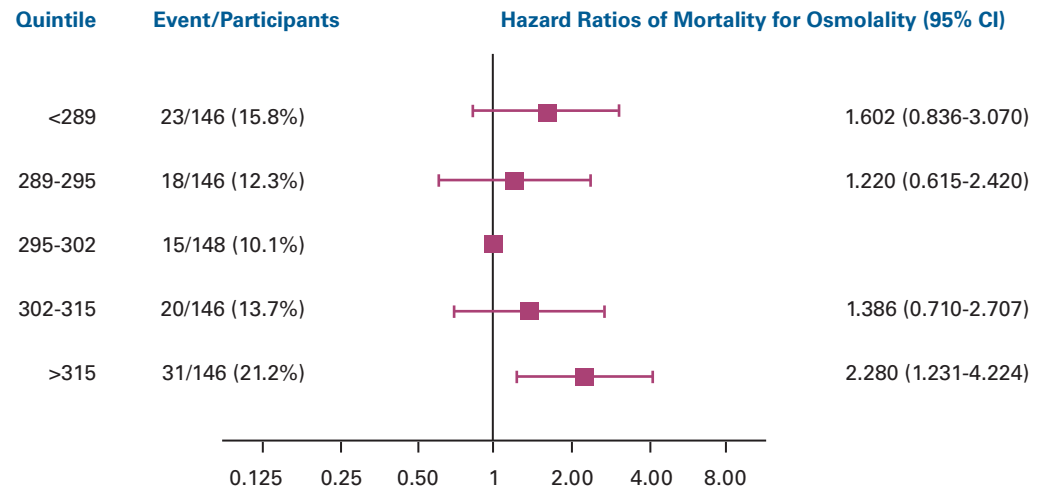


Figure 2o.

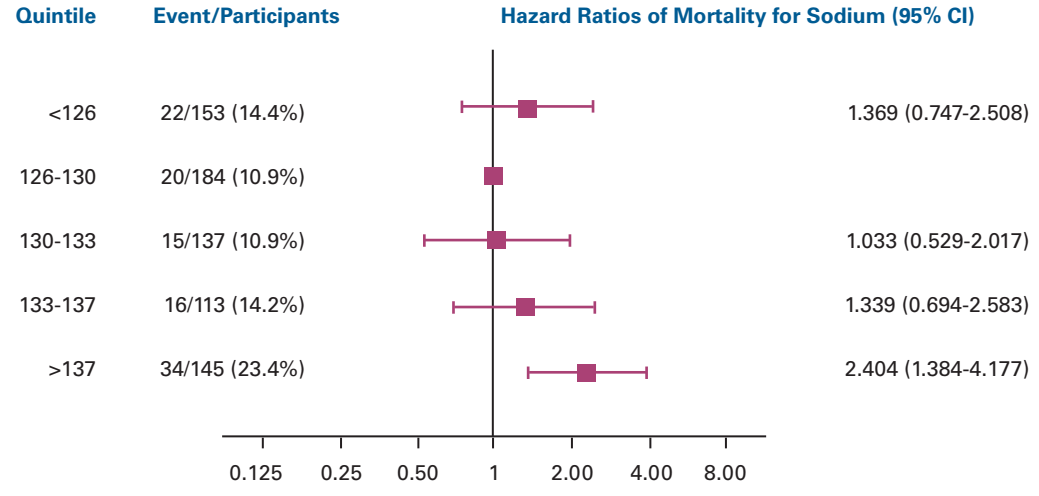
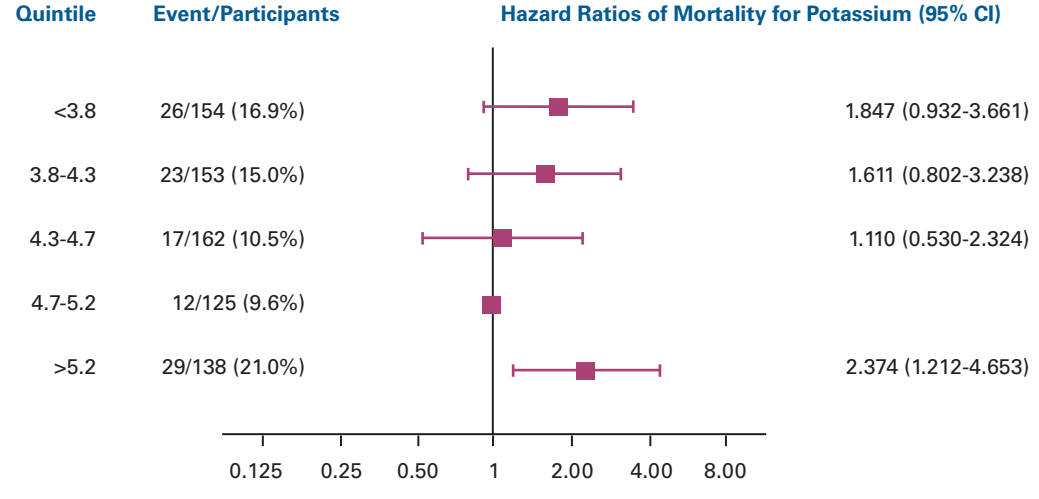


Figure 2p.



eAppendix Table. Baseline Clinical and Biochemical Characteristics of All Subjects

	Mean ± SD	Median	20th-80th percentile (range)
Age (years)	68.5 ± 15.4	72	53.8-82
Blood glucose (mg/dL)	691.5 ± 204.5	632	542-783
BT (°C)	36.7 ± 1.1	36.6	36.0-37.4
RR (breaths per minute)	20.7 ± 4.0	20	18-22
SBP (mm Hg)	139.6 ± 36.2	138	110-168
PR (beats per minute)	98.6 ± 23.1	97	80-117
WBC count (/cumm)	11,800 ± 6300	10,300	6900-15,800
ANC (/cumm)	9777 ± 6019	8296	4965-13,846
Hb (g/dL)	12.5 ± 2.7	12.6	10.2-15.0
Hct (%)	36.8 ± 7.9	37.1	30.1-43.6
PLT (/cumm)	233,000 ± 104,000	225,000	152,000-306,000
CRP (mg/dL)	7.0 ± 9.6	2.0	0.3-13.2
BUN (mg/dL)	46.2 ± 34.1	36	20-68
Cre (mg/dL)	2.6 ± 2.1	1.9	1.3-3.3
BUN/cre ratio	19.4 ± 9.8	17.6	12.3-25.3
Osmolality	303.1 ± 19.9	298.3	289.0-314.6
Na (mmol/L)	132.3 ± 8.7	131	126-137
K (mmol/L)	4.6 ± 1.0	4.5	3.8-5.2
ALT (U/L)	46.2 ± 135.2	23	15-41

ALT indicates alanine aminotransferase; ANC, absolute neutrophil count; BT, body temperature; BUN, blood urea nitrogen; Cre, creatine; CRP, C-reactive protein; Hb, hemoglobin; Hct, hematocrit; K, potassium; Na, sodium; PLT, platelets; PR, pulse rate; RR, respiratory rate; SBP, systolic blood pressure; WBC, white blood cell.