Serum Lactate/Albumin as a Predictor of In-Hospital Mortality in ICU Pancreatitis Patients: an Analysis of the MIMIC-III Database

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Research Article

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Abstract

Background: Acute pancreatitis (AP) is a common serious illness, and is characterized by rapid deterioration and a high mortality rate. Several biomarkers can evaluate and guide the treatment of acute pancreatitis, but there is currently no consensus on which markers are the most effective, simple, and economical for treating early-onset AP. In this study, we used the MIMIC III database to conduct a retrospective study on the relationship between early lactate/albumin (LAC/ALB), in-hospital mortality, and complication rates in patients with acute pancreatitis in the ICU.

Methods: Basic data and indicators of laboratory tests, hospital deaths, and hospitalization days of acute pancreatitis patients were extracted from the database, after which the relationship between LAC/ALB and hospital mortality, ICU hospitalization days, and organ failure were evaluated using a t-test, a rank-sum test, a chi-square test or Fisher’s exact probability method, and a Cox proportional hazard model.

Results: 894 patients met the requirements and were selected from the MIMIC III database. They were subsequently grouped according to the lower limit ratio of the LAC/ALB normal value of 0.7. The group with LAC/ALB>0.7 showed higher hospital mortality rates, and the Lac, Inr, nitrogen, blood sugar, AKI incidence, Tbil, Sapsii score, and Sofa scores were all higher than the group with LAC/ALB<0.7. A multivariate Cox regression analysis model was used to explore the relationship between LAC/ALB levels and inpatient mortality. After including different adjustment variables, we determined that LAC/ALB is a risk factor for in-hospital death. The results of the subgroup analysis of LAC/ALB levels and mortality of hospitalized patients indicate that higher levels of LAC/ALB are risk factors for in-hospital deaths in patients with acute pancreatitis.

Background

AP is a common serious illness characterized by rapid progression and high mortality, and can easily lead to multiple organ failure (MODS). The current treatment for acute pancreatitis primarily includes fasting, gastrointestinal decompression, acid-inhibiting pancreatin, fluid resuscitation, early and minimally invasive drainage, organ function support, and surgery [1]. If not effectively treated in its early stage, AP will often develop into severe acute pancreatitis (SAP). Pancreatitis patients admitted to the ICU have a poor prognosis and high mortality [2]. The Acute Physiology and Chronic Health Score (APACHE II) Ranson score is used to predict acute pancreatitis, however, its use in clinical practice is limited due to the difficult calculations and several parameters needed [3]. Therefore, it is particularly important to find fast, simple, and accurate predictive indicators.

Lac is an important indicator of organ tissue perfusion. During hypoxia and tissue hypoperfusion, lactate dehydrogenase will reduce the degradation of pyruvate, leading to the accumulation of lactic acid [4]. Previous studies have demonstrated that hyperlactic acidemia is closely related to prognostic outcomes in critically ill patients [5-7]. Additionally, elevated levels of lactate are an independent risk factor for poor prognosis in patients with pancreatitis [8]. However, using only lactic acid as a disease prognostic
indicator produces unreliable results. For example, the blood lactic acid clearance rate in patients with liver dysfunction often decreases. Serum albumin (ALB) is the main protein in human plasma and plays an important role in nutrition, anti-inflammatory, anti-oxidation, and anabolic metabolism in the human body. Hypoproteinemia is also associated with high mortality in ICU patients with sepsis.

Similarly, ALB is closely related to MODS occurrence in the pancreatitis model. ALB levels are typically affected by different factors. Critically ill patients in the ICU are typically in a state of stress, and their poor nutritional status and negative nitrogen balances usually lead to low ALB levels. Early fluid resuscitation could also reduce ALB levels, meaning there could be errors if only ALB levels are used as a predictor. It has been reported that LAC/ALB can effectively predict the in-hospital mortality and prognosis of patients with sepsis better than Lac and Alb alone. The higher the LAC/ALB ratio of early patients, the higher the possibility of MODS in sepsis patients. Based on previous studies, LAC/ALB could be able to assess and predict the condition of patients with acute pancreatitis. Our goal is to use the LAC/ALB ratio to predict the in-hospital mortality rate and MODS of patients with acute pancreatitis.

**Methods**

**Data source.** Data were obtained from a public and free clinical data database, the Multiparameter Intelligent Monitoring in Intensive Care III (MIMIC III, V1.4), which includes 46,520 patients admitted to Beth Israel Deaconess Medical Center in Boston from 2001 to 2012. The database primarily records the basic information of hospitalized patients, including vital signs, laboratory tests, water intake and discharge, and treatment measures. The database diagnoses and classifies patients according to the International Classification of Diseases, Ninth Revision (ICD-9). We completed the National Institutes of Health's web-based course and passed the Protecting Human Research Participants exam. Our research was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology (Cambridge, MA). The study was reviewed by the Ethics Committee of the Affiliated Hospital of Nantong University, and no further ethics approval was required.

**Population Selection Criteria.** A total of 961 patients participated, all of whom were diagnosed with acute pancreatitis based on the ICD-9 code. Based on their first hospitalization record, we excluded patients younger than 18 years old and hospitalized in the ICU for less than 24 hours. In the end, 894 patients were selected for this study.

**Data extraction and management.** PostgresSQL (version 9.6) was used to extract data from the MIMIC-III database. Basic patient information includes age, gender, vital signs, laboratory test results, scoring system, underlying diseases, and organ support methods. Underlying diseases primarily include cholelithiasis, chronic obstructive pulmonary disease (COPD), coronary heart disease, hypertension, and diabetes. In addition, laboratory test data were also extracted, including ALB, blood amylase, blood creatinine, hemoglobin, Lac, platelets, nitrogen, total bile, triglycerides, and glucose. Vital signs include
heart rate, systolic blood pressure, diastolic blood pressure, pulse, respiratory rate, and body temperature. The scoring system primarily includes simplified acute physiological score (Sapsii) and continuous organ dysfunction score (SOFA). Other selected items include whether to use ventilator mechanical ventilation, whether to use hypertensive drugs, and whether it is complicated by acute kidney injury (AKI).

**Statistical Analysis.** The mean ± standard deviation was used when continuous variables followed a normal distribution, otherwise, the median (minimum, maximum) was used; the categorical variable data is indicated by frequency (percentage). When comparing between groups, a t-test was used if continuous variables meet the normal distribution, and the rank-sum test was used if continuous variables do not follow a normal distribution. The chi-square test or Fisher's exact probability method was used for categorical variables. The KM method was used to draw the survival curve, and the log-rank test was used to compare whether the LAC/ALB stratification is statistically different. Cox proportional-hazards model was used to evaluate the relationship between LAC/ALB and hospital mortality, with LAC/ALB<0.7 serving as the reference group. In the crude model, no covariates were included; Model I was adjusted by age and gender; Model II was based on model I and also incorporated laboratory tests, vital signs, Sofa, and Sapsii scores, whether to use blood pressure drugs, concurrent AKI, and combined underlying diseases as covariates. The regression results of the Cox proportional-hazards model are expressed by an HR value and a 95% confidence interval. In the subgroup analysis, a hierarchical exploration was performed for each index to identify interactions between LAC/ALB and each index. All statistical analyses were performed with Stata 16.0 software. The hypothesis test was performed on both sides, with \( p<0.05 \) representing a significant statistical difference.

**Results**

**Baseline characteristics and outcomes**

In this study, we observed and summarized the baseline characteristics, vital signs, laboratory test results, organ function, and prognosis of 894 patients (Figure 1 and Table 1). The patients were divided into two groups according to their LAC/ALB levels: groups<0.7 and \( \geq 0.7 \) groups. Of the patients, 499 were males and 395 were females with average ages of 63.81±1.86 years old and 68.40±2.34 years old, respectively. There were no significant differences between gender and age groups. The levels of Lac, Inr, Nitrogen, Tbil, and Glucose and the scores of Sapsii and Sofa in the LAC/ALB\( \geq 0.7 \) group were both higher than in the <0.7 group. Compared with the LAC/ALB<0.7 group, patients in the LAC/ALB\( \geq 0.7 \) group were more likely to have AKI during hospitalization (22.25% VS 15.63%, \( p=0.011 \)), while the hospital mortality rate was also significantly higher (23.65% VS 8.14%, \( p<0.001 \)). However, there was no significant difference in ICU hospitalization time between the two groups.

**High LAC/ALB ratio is an independent prognostic predictor in pancreatitis patients**
As shown in Figure 2, the influence of the LAC/ALB ratio on the prognosis of patients with acute pancreatitis was explored by analyzing the survival rate. The median survival and 95CI in the LAC/ALB<0.7 group and ≥0.7 group were 80 (50, 95) days and 56 (47, 67) days, respectively, indicating that patients with high LAC/ALB ratios have higher mortality. Additionally, we also performed a multivariate Cox regression analysis on the baseline variables (Table 2). We analyzed LAC/ALB levels using continuous variables and categorical variables (classified based on whether it was less than 0.7) and explored the relationship between LAC/ALB levels and the mortality rate of hospitalized patients. In the crude model, no adjustment variable was added, and the continuous variable results demonstrated that the HR and its 95% CI value were [2.181 (1.935, 2.457)]. For categorical variables, the LAC/ALB<0.7 group was used as a reference, while the HR and 95% CI value of the LAC/ALB≥0.7 group is [2.641 (1.808, 3.857)]. We adjusted model I by age and gender and the result was the same as in the crude model. The continuous variable results demonstrated that HR and its 95% CI value was [2.285 (2.021, 2.584)]. For the categorical variable, the <0.7 group was used as a reference, while the HR and its 95% CI value in the ≥0.7 group is [2.684 (1.838, 3.920)]. We adjusted model II based on model I by including Tbil, Plates, Amy, Nitrogen, Triglycerides, Hbg, Hematocrit, Creatinine, Glucose, Sysbp, Diasbp, Pulsrate, Resprate, Temperature, SpO2, Sofa, Sapsii, Inr, Ventdurate, Hyperensort use, and AKI. The continuous variable results demonstrated that its HR and its 95% CI value was [2.016 (1.700, 2.390)], while the categorical variables results demonstrated that the HR and its 95% CI value of LAC/ALB≥0.7 group were [1.575 (1.026, 2.416)]. These all indicate that higher LAC/ALB levels are risk factors for death in hospitalized patients.

**Subgroup analysis**

The subgroup analysis of LAC/ALB levels and the mortality of hospitalized patients are shown in Table 3. No interactions were observed in each stratification (p=0.212~0.911). The results from the subgroups of Tbil, INR, Platelet, Amy, Hbg, Creatinine, Glucose, SBP, DBP, Heart rate, Respiratory rate, Temperature, SpO2, SOFA, SAPSII, and Ventdurate all demonstrated that higher levels of LAC/ALB are risk factors for death in hospitalized patients (p<0.05).

**Discussion**

AP is characterized by severe symptoms, rapid clinical progression, and high mortality rates. If effective treatment is not available in the early stages, MODS will be particularly acute in the severe AP stage[16]. It is particularly important to identify indicators that can assess the severity of AP patients during the early stages. Current early-identification methods for high-risk patients are high-resolution[17] and modified Marshall scoring systems[18], but a positive result is typically not noticed before the disease progresses. According to current research, C-reactive protein (CRP)[19], procalcitonin (PCT)[20], changes in serum lactic acid levels[21], and the product value of serum albumin and prothrombin[22] have all been used as predictors of AP severity. However, the sample size of previous studies was small, or using a single indicator was inaccurate. Therefore, we need to find other fast, accurate, and cheap methods of
identifying AP in its early stages. The results of our study assessing 894 AP patients supplies additional evidence.

Lac and Alb are economical and convenient laboratory indicators that are easy to clinically obtain. However, their individual use is complicated by many clinical factors. The upper limit of the normal value of Lac is 2.5mmol/L, and the lower limit of the normal value of Alb is 3.5mg/L. This ratio is used for grouping. Our results demonstrated that there is no statistical difference in age and gender between the two groups ($p=0.1227$, $p=0.964$). Based on the $t$-test results, there were significant differences between the two groups in INR and platelet count ($p=0.0122$, $p<0.0001$). Previous studies confirmed that the increased vascular permeability of SAP patients formed an embolization of the blood vessels between the pancreatic acinarls, and initiated the exogenous coagulation pathway through the tissue factor pathway, while platelet aggregation initiated the endogenous coagulation pathway by the overactivation of two coagulation pathways, eventually leading to hyperfibrinolysis [23]. The decline of platelets could be caused by the significant accumulation of PLT due to endothelial damage and the destruction of platelets by a large number of inflammatory factors in the blood circulation. Abdominal hemorrhage in patients with pancreatitis caused by coagulation dysfunction is another primary cause of death [24]. We found that patients with LAC/ALB>0.7 had higher blood glucose levels. When SAP attacks, pancreatic islet cells are destroyed and insulin secretion is reduced. Stress factors such as hypotension and shock can cause the excessive pancreatic release of glucose-increasing hormones such as glucagon and glucocorticoids. This can also lead to increased blood glucose stress. For example, during the early study of diabetes, it was generally believed that the greater the blood glucose fluctuations, the more serious the pancreatic exudation and necrosis, which would lead to higher mortality rates. However, recent clinical studies have demonstrated that when the body’s blood sugar control is poor, the risk of infection increases, inflammatory mediators are released, and pancreatic infection and exudation increase, which aggravates severe AP patients and significantly increases patient mortality [25]. The level of urea nitrogen was significantly different between the two groups ($p=0.0027$). As a common indicator for evaluating kidney function, higher urea nitrogen levels are related to peripancreatic exudation and necrosis. The level of urea nitrogen is largely affected by changes in blood vessel volume; therefore, levels of urea nitrogen upon admission could indicate that the patient has potential intravascular volume exhaustion and prerenal azotemia, increasing the risk of complications and mortality if it is not treated early [26]. Our research results confirmed that patients with elevated urea nitrogen are more likely to develop AKI. Additionally, patients in the LAC/ALB group >0.7 have fast heart rates, low blood pressure, and high breathing rate, all of which could be related to SIRS as the condition worsens. The ability of the SOFA score and SAPII score to evaluate disease severity has been confirmed in sepsis and pancreatitis patients [27]. In our study, we found that symptoms in patients with hyperlactic acid and hypoproteinemia were more serious. Our results were subjected to a Chi-square test, $t$-test, Cox proportional hazard model, and subgroup analysis have effectively confirmed that LAC/ALB>0.7 is an independent risk factor for in-hospital death in ICU patients with AP.
Our research indicates that the hospital mortality rate of an AP patient admitted to the ICU will be reduced if special attention is paid to serum lactic acid levels during early fluid resuscitation, the perfusion of organs and tissues, and maintaining a suitable blood pressure level. Hypoalbuminemia should be paid special attention during fluid resuscitation. Our follow-up studies will further confirm whether active albumin infusion and enhanced nutritional support will reduce the mortality of patients with pancreatitis.

This study has several limitations. First, patients selected for a retrospective study could be biased. For example, AP of pancreatitis according to the ICD_9 code might not be the primary reason for their hospital admission. Second, the database in this study is a single-center study, and additional cases should be considered from other medical centers to confirm our results. Third, there is a lack of follow-up on patient outcomes.

**Conclusion**

Pancreatitis progresses rapidly and mortality is higher in patients admitted to ICU. In this study, early Lac/Alb was found to be an independent risk factor for pancreatitis in ICU, suggesting that attention should be paid to serum albumin levels during early fluid resuscitation.

**Declarations**

**Acknowledgements**

Not applicable.

**Authors’ contributions**

BP collected the data, designed the study, and wrote the paper. SHL and WYP followed the study, and wrote the paper. CXL collected the data. LY followed the study and critically revised the paper. All authors read and approved the final manuscript.

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**Availability of data and materials**

The data set supporting the results of this article are included within the article.

**Ethics approval and consent to participate**

Data were obtained from a public and free clinical data database, the Multiparameter Intelligent Monitoring in Intensive Care III (MIMIC III, V1.4). We completed the National Institutes of Health’s web-based course and passed the Protecting Human Research Participants exam(NO.37333883). Our
research was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center and the Massachusetts Institute of Technology (Cambridge, MA). The study was reviewed by the Ethics Committee of the Affiliated Hospital of Nantong University, and no further ethics approval was required.

Not applicable.

**Competing interests**

The authors read and approved the final manuscript.

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Tables

Table 1 Baseline characteristics, vital signs, laboratory parameters and outcomes of patients with Acute pancreatitis
| Characteristics | <0.7 (n=467) | ≥0.7 (n=427) | t/Z/c² value | P value |
|-----------------|--------------|--------------|--------------|--------|
| Age, years      | 63.81±1.86   | 68.40±2.34   | 1.5450       | 0.1227 |
| Gender, n(%)    |              |              |              |        |
| Female          | 206 (44.11)  | 189 (44.26)  | 0.0021       | 0.964  |
| Male            | 261 (55.89)  | 238 (55.74)  |              |        |
| Comorbidities   |              |              |              |        |
| Diabetes, n(%)  |              |              |              |        |
| Yes             | 119 (25.48)  | 105 (24.59)  | 0.0944       | 0.75   |
| No              | 348 (74.52)  | 322 (75.41)  |              |        |
| Cholecystitis, n(%) |          |              |              |        |
| Yes             | 83 (17.77)   | 74 (17.33)   | 0.0302       | 0.862  |
| No              | 384 (82.33)  | 353 (82.67)  |              |        |
| COPD, n(%)      |              |              |              |        |
| Yes             | 51 (10.92)   | 30 (7.03)    | 4.1070       | 0.043  |
| No              | 416 (89.08)  | 397 (92.97)  |              |        |
| Coronary, n(%)  |              |              |              |        |
| Yes             | 82 (17.56)   | 78 (18.27)   | 0.0761       | 0.783  |
| No              | 385 (82.44)  | 349 (91.73)  |              |        |
| Hypertension, n(%) |            |              |              |        |
| Yes             | 334 (49.48)  | 100 (45.66)  | 0.9657       | 0.326  |
| No              | 341 (50.52)  | 119 (54.34)  |              |        |
| Laboratory parameters |        |              |              |        |
| Alb (g/dL)      | 3.14±0.02    | 2.83±0.30    | 7.7105       | <0.0001|
| Amy (IU/L)      | 225.10±12.22 | 218.39±11.08 | 0.4048       | 0.6857 |
| Creatinine (mg/dL) | 1.51±0.07   | 1.60±0.07    | 0.8786       | 0.3799 |
| Hbg (g/dL)      | 10.32±0.12   | 10.34±0.14   | 0.0974       | 0.9225 |
| Hematocrit (%)  | 31.07±0.18   | 31.16±0.19   | 0.3347       | 0.7379 |
|                  | Value 1    | Value 2    | Value 3    | Value 4    |
|------------------|------------|------------|------------|------------|
| Lac (mmol/L)     | 1.46±0.02  | 3.68±0.15  | 17091      | <0.0001    |
| Lac_Alb_ratio    | 0.47±0.01  | 1.38±0.05  | 20.5034    | <0.0001    |
| Inr              | 1.38±0.02  | 1.65±0.11  | 2.5100     | 0.0122     |
| Nitrogen (mg/dL) | 25.78±0.87 | 29.74±1.00 | 3.0102     | 0.0027     |
| Plates           | 291.53±6.52| 248.09±6.84| 4.5973     | <0.0001    |
| Tbil (mg/dL)     | 1.56±0.15  | 3.05±0.23  | 5.5334     | <0.0001    |
| Triglycerides (mg/dL) | 206.57±14.81 | 228.40±20.88 | 0.8760 | 0.3814 |
| Glucose (mmol/L) | 135.23±1.74| 142.87±2.26| 2.7073     | 0.0069     |
| Vital sighs     |            |            |            |            |
| Heartrate, bpm  | 92.62±0.78 | 95.00±0.84 | 2.0927     | 0.0367     |
| Sysbp, mmHg     | 125.03±0.82| 119.38±0.86| 4.7568     | <0.0001    |
| Diasbp, mmHg    | 65.12±0.57 | 63.45±0.60 | 2.2095     | 0.0427     |
| Pulsrate, bpm   | 82.19±0.56 | 80.10±0.58 | 2.5748     | 0.0102     |
| Resprate, bpm   | 20.29±0.20 | 20.87±0.21 | 2.0354     | 0.0421     |
| Temperature, °C | 37.11±0.03 | 36.93±0.03 | 4.1225     | <0.0001    |
| SpO2,           | 96.78±0.08 | 96.46±0.16 | 1.8283     | 0.0678     |
| Score system     |            |            |            |            |
| Sofa scores      | 4.44±0.14  | 6.02±0.21  | 6.3966     | <0.0001    |
| Sapsii scores    | 32.75±0.59 | 41.06±0.88 | 7.9714     | <0.0001    |
| Outcome          |            |            |            |            |
| ICU day, days    | 3 (1, 97)  | 3 (1, 79)  | 0.346      | 0.7295     |
| Hospital expire, n(%) |          |            |            |            |
| Yes              | 38 (8.14)  | 101 (23.65) | 40.8978    | <0.001     |
| No               | 429 (91.86)| 326 (76.35) |          |            |
| Hypertension, n(%) |            |            |            |            |
| Yes              | 244 (52.25)| 190 (44.50) | 5.3660     | 0.021      |
| No               | 223 (47.75)| 237 (55.50) |          |            |
| AKI, n(%)        |            |            |            |            |
| Yes              | 73 (15.63)| 95 (22.25)  | 6.3988     | 0.011      |
| Variable            | Crude model | Model I | Model II |
|---------------------|-------------|---------|----------|
|                     | HR (95% CIs)| P value | HR (95% CIs)| P value | HR (95% CIs)| P value |
| Hospital expired    |             |         |           |         |           |         |
| LAC/ALB &           | 2.181 (1.935, 2.457) | <0.001 | 2.285 (2.021, 2.584) | <0.001 | 2.016 (1.700, 2.390) | <0.001 |
| (Dichotomous)       |             |         |           |         |           |         |
| <0.7                | 1.0 (ref)   | -       | 1.0 (ref) | -       | 1.0 (ref) | -       |
| ≥0.7                | 2.641 (1.808, 3.857) | <0.001 | 2.684 (1.838, 3.920) | <0.001 | 1.601 (1.042, 2.458) | 0.032 |

HR: hazard ratio; CI: confidence interval. Models were derived from Cox proportional hazards regression models. Crude model adjusted for: none. Model I adjusted for : age and gender. Model II adjusted for: Tbil, Plates, Amy, Nitrogen, Triglycerides, Hbg, Hematocrit, Creatinine, Glucose, Sysbp, Diasbp, Pulsrate, Resprate, Temperature, SpO2, Sofa, Sapsii, Inr, Ventdurate, Hyperensort use, AKI.

**Table 3** Subgroup analysis of the associations between LAC/ALB ratio and hospital expire.
| Characteristic          | No. of patients | HR (95% CIs)           | P value | P for interaction |
|------------------------|-----------------|------------------------|---------|-------------------|
| Total bilirubin (mg/dL)|                 |                        | 0.700   |                   |
| <1.0                   | 468             | 2.415 (1.248, 4.677)   | 0.009   |                   |
| ≥1.0                   | 423             | 2.196 (1.374, 3.510)   | 0.001   |                   |
| INR                    |                 |                        | 0.878   |                   |
| <1.4                   | 560             | 2.247 (1.289, 3.915)   | 0.004   |                   |
| ≥1.4                   | 331             | 2.321 (1.338, 4.024)   | 0.003   |                   |
| Platelet (10^9/L)      |                 |                        | 0.664   |                   |
| <226                   | 368             | 2.587 (1.553, 4.308)   | <0.001  |                   |
| ≥226                   | 523             | 2.010 (1.121, 3.605)   | 0.019   |                   |
| Amy                    |                 |                        | 0.911   |                   |
| <100                   | 251             | 2.854 (1.199, 6.795)   | 0.018   |                   |
| ≥100                   | 640             | 2.599 (1.706, 3.962)   | <0.001  |                   |
| Nitrogen               |                 |                        | 0.529   |                   |
| <21                    | 430             | 2.152 (0.891, 5.198)   | 0.088   |                   |
| ≥21                    | 461             | 2.563 (1.672, 3.930)   | <0.001  |                   |
| Triglycerides          |                 |                        | 0.193   |                   |
| <150                   | 317             | 1.598 (0.834, 3.062)   | 0.158   |                   |
| ≥150                   | 574             | 3.257 (2.035, 5.215)   | <0.001  |                   |
| Hbg (g/dl)             |                 |                        | 0.762   |                   |
| <12                    | 374             | 2.885 (1.628, 5.112)   | <0.001  |                   |
| ≥12                    | 517             | 2.600 (1.557, 4.340)   | <0.001  |                   |
| Hematocrit (%)         |                 |                        | /       | /                 |
| <40.0                  | 870             | 2.501 (1.708, 2.663)   | <0.001  |                   |
| ≥40.0                  | 21              | /                      | /       | /                 |
| Creatinine (mg/dL)     |                 |                        | 0.521   |                   |
| <1.4                   | 608             | 2.106 (1.208, 3.671)   | <0.001  |                   |
| ≥1.4                   | 283             | 2.758 (1.626, 4.677)   | <0.001  |                   |
| Glucose (mg/dL)        |                 |                        | 0.371   |                   |
|                           | Count | Mean (95% CI) | p         |
|---------------------------|-------|---------------|-----------|
| **SBP (mmHg)**            |       |               |           |
| <134                      | 462   | 2.108 (1.219, 3.645) | 0.008    |
| ≥134                      | 429   | 3.191 (1.862, 5.468)  | <0.001   |
| **DBP (mmHg)**            |       |               |           |
| <114                      | 336   | 2.754 (1.612, 4.704)  | <0.001   |
| ≥114                      | 555   | 1.964 (1.123, 3.434)  | 0.018    |
| **Heart rate (beats/min)**|       |               |           |
| <87                       | 329   | 2.623 (1.432, 4.802)  | 0.002    |
| ≥87                       | 562   | 2.763 (1.692, 4.514)  | <0.001   |
| **Respiratory rate (beats/min)**| | | |
| <19                       | 345   | 3.100 (1.346, 7.144)  | 0.008    |
| ≥19                       | 546   | 2.406 (1.570, 3.687)  | <0.001   |
| **Temperature (℃)**      |       |               |           |
| <36.8                     | 351   | 2.494 (1.402, 4.438)  | 0.002    |
| ≥36.8                     | 540   | 2.462 (1.480, 4.093)  | 0.001    |
| **SPO2 (%)**              |       |               |           |
| <97                       | 451   | 3.373 (2.093, 5.436)  | <0.001   |
| ≥97                       | 440   | 2.004 (1.075, 3.735)  | 0.029    |
| **SOFA (score)**          |       |               |           |
| <5                        | 448   | 2.318 (1.054, 5.100)  | 0.037    |
| ≥5                        | 443   | 2.354 (1.513, 3.662)  | <0.001   |
| **SAPSII score**          |       |               |           |
| <39                       | 539   | 2.303 (1.145, 4.634)  | 0.019    |
| ≥39                       | 352   | 2.183 (1.362, 3.501)  | 0.001    |
| **Hyperensort use**       |       |               |           |
| Yes                       | 673   | 2.725 (1.581, 3.697)  | <0.001   |
| No                        | 218   | 1.692 (0.972, 2.946)  | 0.063    |
|                           |       |               |           |
|                           |       |               | 0.458    |
|                           |       |               | 0.343    |
|                           |       |               | 0.935    |
|                           |       |               | 0.524    |
|                           |       |               | 0.977    |
|                           |       |               | 0.212    |
|                           |       |               | 0.947    |
|                           |       |               | 0.858    |
|                           |       |               | 0.234    |
|                                |       |                  |          |
|--------------------------------|-------|------------------|----------|
| Ventdurate                     |  0.742|                  |          |
| Yes                            |  442 | 2.464 (1.596, 3.802) | <0.001  |
| No                             |  449 | 3.302 (1.469, 7.424) | 0.004   |
| Diabetes                       |  0.551|                  |          |
| Yes                            |  223 | 3.344 (1.627, 6.872) | 0.001   |
| No                             |  668 | 2.443 (1.563, 3.817) | <0.001  |
| AKI                            |  0.302|                  |          |
| Yes                            |  167 | 1.930 (1.043, 3.571) | 0.036   |
| No                             |  724 | 2.876 (1.778, 4.655) | <0.001  |

SOFA: sequential organ failure assessment; SAPSII: simplified acute physiology score II. AKI: acute kidney injury.

**Figures**
Figure 1

See image above for figure legend

Figure 2
<p>See image above for figure legend</p>