Association Between Glycemic Gap and Mortality in Critically Ill Patients with Diabetes

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Research

Abstract

Objectives: Dysglycemia is pervasive and associated with poor outcomes in critically ill patients. Hyperglycemia, hypoglycemia and blood glucose fluctuation might all affect the outcomes, but appropriate level of blood glucose is uncertain especially in patients with diabetes regarding to the situation of glucose control before hospitalization. This study was aimed to investigate the effect of difference between mean blood glucose during ICU stay and level of blood glucose prior to admission to ICU upon outcomes of critically ill patients with diabetes.

Method: This retrospective study undertaken in a 24-bed intensive care unit(ICU). Patients with diabetes expected to stay for more than 24hs were enrolled, HbA1c was tested within 3 days after admission and converted to the A1C-derived average glucose (ADAG) by the equation: ADAG = [(HbA1c * 28.7) − 46.7] * 18^{-1}, arterial blood glucose measurements were fourth per day routinely during the first 7 days after admission, the mean glucose level(MGL) and SOFA (within 3 days, 5 days and 7days) were calculated for each person, GAP_{adm} and GAP_{mean} was calculated as admission blood glucose and MGL minus ADAG respectively, the incidence of moderate hypoglycemia(MH), severe hypoglycemia (SH), total dosage of glucocorticoids and average daily dosage of insulin within 7 days, duration of renal replacement therapy(RRT), ventilator-free hours and non-ICU stay days within 28 days were also collected. Patients enrolled were divided into survival group and non-survival group according to survival or not at 28-day, compare GAP_{adm} and GAP_{mean} between the two groups and explore the relationship between GAP and mortality in these critically ill patients.

Results: 431 patients were enrolled and divided into survival group (n=256) and non-survival group (n=175). It was shown that two groups had comparable level of HbA1c, the non-survivors had greater APACHE II, SOFA, GAP_{adm}, GAP_{mean-3}, GAP_{mean-5}, GAP_{mean-7} and higher MH and SH incidences. Less duration of ventilator-free, non-ICU stay and longer duration of RRT were recorded in non-survival group, of whom received less carbohydrates intake, higher insulin daily dosage and glucocorticoid dosage. GAP_{mean-5} had the greatest predictive power with AUC of 0.807(95%CI: 0.762-0.851), the cut-off value was 3.6mmol/L(sensitivity 77.7% and specificity 76.6%). The AUC was increased to 0.852(95%CI: 0.814-0.889) incorporated with $SOFA_5$ (NRI = 11.34%, P < 0.001).

Conclusion: Glycemic GAP between mean level of blood glucose especially MGL within 5 days after admission to ICU and A1C-derived average glucose was independently associated with 28-day mortality of critically ill patients with diabetes. The predictive power was optimized with addition of the top level of SOFA within 5 days.

Background

Metabolism disturbance of glucose is pervasive in critically ill patients, hyperglycemia and hypoglycemia are proved to be risk factors for adverse outcomes in the populations of acutely ill patients[1] [2]. Then we have got the consensus that glycemic fluctuation imposes much more harmful effects upon the outcomes than both hyperglycemia and hypoglycemia[3][4], so as the variability of blood glucose[5]. Nevertheless, this

seemingly unquestionable assertion had been doubted in some studies[6], it was more commonly proven in the non-DM cohort but not in the DM [7]. Paul E Marik suggests that hyperglycemia and insulin resistance in the setting of acute illnesses is an evolutionarily preserved adaptive responsiveness to the disorders, which was believed to be a beneficial host response that enhanced the host's chances of survival[8] [9]. Meanwhile, chronic pre-morbid hyperglycemia increases the risk of hypoglycemia and modifies the association between acute hypoglycemia and mortality[10].

Acute hyperglycemia in patients with diabetes could result from acute physiological stress, a high baseline blood glucose, or both, which make analysis difficult even misled. In a retrospective observational study measuring glycosylated hemoglobin (HbA1c) as a marker of premorbid glycaemia in the 3 months prior to intensive care unit(ICU) admission, authors believed that acute hyperglycemia was associated with a reduction rather than an increase in mortality in patients with 'insufficiently controlled' diabetes [11]. Furthermore, the glycemic gap-difference between admission blood glucose and A1C-derived average glucose (ADAG) levels has been used to evaluate the disease severity and predict the prognosis to explore the relationship between stress induced hyperglycemia (SIH) and mortality in critically ill patients with diabetes. It is confirmed that glycemic gap which is calculated by subtracting the ADAG from the admission blood glucose levels can depress the impact of chronic hyperglycemia on the disease severity assessment in patients with diabetes to some extent, the elevated glycemic gap can optimally improve the value of the assessment consequently [12].

However, we found the top level of blood glucose occurred within first 7 days mostly in preliminary experiment, which means the level of admission blood glucose could not refelect severity of SIH. The objective of the present research is in order to identify whether GAP_{mean} (glycemic gap-mean) defined as difference which is between the mean blood glucose level within the first 7 days after admission to ICU and ADAG is independently associated with mortality of critically ill patients with diabetes and to evaluate the predictive power on mortality comparing with GAP_{adm} (glycemic gap-admission, the difference between admission blood glucose and ADAG) and whether the predictive power will be improved by incoporating APACHE II or SOFA into GAP.

Methods

Study Design and Setting

We conducted a retrospective observational cohort study of consecutive patients with type 2 diabetes admitted to general ICU between June 1, 2016 and May 31,2019. Our department is a 24-bed general ICU of *Fu Xing Hospital, Capital Medical University* in Beijing. A mixed population of adult medical and surgical patients. The institutional review board for human investigation approved this study and waived the need for informed consent. The protocol was elaborately formulated by director, elaborately performed by all the staffs and closely supervised by a group of intensivists who were in charged to this study.

Cohort and Data Collection

Adult patients admitted to our ICU during the 3-year period of the study, of those with diagnosis of type 2 diabetes (in accordance with 1999 WHO diagnostic criteria for diabetes)estimated to stay over 24 hours without oral feeding were enrolled regardless of whether insulin or oral antidiabetic agents were prescribed previously. Patients were excluded based on the following criteria: 1) an admission diagnosis of diabetic ketoacidosis or hyperosmolar hyperglycemic state, 2) treatment with corticosteroids or admitted to ICU within 3 months before admission, 3) patients or their representatives refused to participate in the study or signed informed consent of withdrawing life-sustaining treatment within 28 days after the admission, 4)the level of HbA1c was not obtained and number of blood glucose value obtained was no more than 3 during the period of study.

The medical records of enrolled patients were reviewed for the following data: age, sex, body mass index(BMI), whether received regular insulin therapy before admission, primary disorders, underlying comorbidities, APACHE II score within first day and the highest SOFA (Sequential Organ Failure Assessment) score during the first 3, 5 and 7 days ($SOFA_{top3}$, $SOFA_{top5}$, $SOFA_{top7}$)after admission, laboratory data including arterial blood glucose level during the first 7 days, HbA1c levels measured within 24 hours after admission. Average daily amount of carbohydrates intake, average daily dosage of insulin (Novolin R) and total dosage of glucocorticoid (converted into dosage of Methylprednisolone) for the first 7 days were obtained.

Outcome indicators including duration of ventilator free days, renal replacement therapy (RRT) and non-ICU length of stay during 28 days, survived or not at 28-day after admission were recorded.

Data of Blood Glucose Level, HbA1c Value and Glycemic Gap

We tested arterial blood glucose level at least every 6 hours during first 7 days after admission using a blood-gas analyzer (GEM PRIMIER3000) equipped with current method. HbA1c was detected within the first 24 hours. MH was defined as blood glucose level at range of 2.2-3.3mmol/L, whereas SH defined as blood glucose level lower than 2.2mmol/L.

Parameters including mean glucose level during first 3 days(MGL-3), 5 days(MGL-5) and 7 days(MGL-7), the incidence of moderate hypoglycemia(MH) and severe hypoglycemia(SH) were calculated based on measurements of blood glucose level.

HbA1c levels were converted into A1C-derived average glucose (ADAG) to represent chronic average blood glucose levels using the following equation: A1C-derived average glucose (ADAG) = $[(HbA1c * 28.7) − 46.7] * 18^{−1}$. GAP_{adm} was calculated as admission blood glucose minus ADAG as follows: $GAP_{adm} = [$ admission BG − ADAG], $GAP_{mean−3}$ was calculated as MGL-3 minus ADAG as follows $GAP_{mean−3}= [$ MGL-3 − ADAG], $GAP_{mean−5}$ was $GAP_{mean−5}= [$ MGL-5 − ADAG] and $GAP_{mean−7}$ was $GAP_{mean−7}= [$ MGL-7 − ADAG].

Statistical Analysis

Consecutive data are expressed as mean and standard deviation, categorical data are expressed as frequencies (percentage). Analyses were performed by the 2-tailed Student t test and the Chi-square test or

Fisher exact test. Logistic regression models were built after screening statistically significant variables and plotted receiver operating characteristic (ROC) curves to analyze the discernibility of the predictive parameters, and the area under the ROC curve (AUC) and 95% confidence internal (CI) was calculated simultaneously to identify the relationship between the glycemic gap and 28-day mortality. Youden's index was applied to ascertain the preponderant value of glycemic gap as an independently predictive factor of 28-day mortality. Graphs were built using Medcalc, Version 19.6.1 and data analyzed using SPSS statistics, Version 24.0. P value of < 0.05 was considered statistically significant.

Results

Study Population and Baseline Characteristics

1938 patients were admitted to our general ICU during study period, 431 patients were enrolled, of which 175 (40.6%) died at 28-day after inclusion, based on which we separated patients into two groups-survival and non-survival (Fig. 1). Blood glucose samples with number of 11800 in total and 27.4 per capita were collected. Non-survivors tended to be older and to have higher APACHE II score and SOFA score comparing with survivors. The proportion of patients undergoing surgery in non-survivors was lower than that of survivors (Table 1).

Table 1
Baseline Characteristics of the Diabetic ICU Survivors and Non-survivors

	ICU Survivors (n = 256)	ICU Non-survivors (n = 175)	All Patients (n = 431)	P-Value
Sex (male),n (%)	152(59.4%)	92(52.6%)	244(56.6%)	0.167
Age (y)	81(70,85)	83(78,87)	81(74,86)	0.002*
BMI (Kg/m^2)	24.22(21.48,25.95)	24.03(21.64,26.08)	24.22(21.48,25.97)	0.657
APACHE II score	20(15,25)	25(19,32)	22(16,27)	0.000*
SOFA$_{top3}$	6(5,9)	11(8,13)	8(6,11)	0.000*
SOFA$_{top5}$	6(5,9)	11(9,14)	8(6,11)	0.000*
SOFA$_{top7}$	6(5,9)	10(9,14)	8(6,11)	0.000*
Surgical patients, n(%)	43(16.8%)	15(8.6%)	58(13.5%)	0.015*
Insulin therapy before ICU, n(%)	105(41.0%)	80(45.7%)	185(42.9%)	0.373
Reason for ICU admission, n(%)				
Sepsis	72(28.1%)	70(40.0%)	142(32.9%)	0.012*
Thoracic or respiratory disease	80(31.3%)	40(22.9%)	120(27.8%)	0.063
Cardiac and vascular disease	36(14.1%)	35(20.0%)	71(16.5%)	0.113
Neurologic disease	18(7.0%)	10(5.7%)	28(6.5%)	0.692
Renal dysfunction	13(5.1%)	4(2.3%)	17(3.9%)	0.207
Gastrointestinal disease	13(5.1%)	9(5.1%)	22(5.1%)	1.000
Hematological disease	0(0%)	2(1.1%)	2(0.5%)	0.164
Postoperatie care	16(6.3%)	1(0.6%)	17(3.9%)	0.002*
Other	8(3.1%)	4(2.3%)	12(2.8%)	0.769
Patient comorbidities				
Respiratory disease	58(22.7%)	42(24.0%)	100(23.21%)	0.816

APACHE II scores: Acute Physiology and Chronic Health Evaluation II score, SOFA: Sequential Organ Failure Assessment, SOFA$_{top}$: the top level of SOFA score.

*P < 0.05

	ICU Survivors (n = 256)	ICU Non-survivors (n = 175)	All Patients (n = 431)	P-Value
Cardiac and vascular disease	223(87.1%)	167(95.4%)	390(90.5%)	0.004*
Cerebrovascular disease	179(69.9%)	107(61.1%)	286(66.4%)	0.062
Chronic renal disease	95(37.1%)	83(47.4%)	178(41.3%)	0.037*
Gastrointestinal disease	17(6.6%)	15(8.6%)	32(7.4%)	0.460
Malignancy	54(21.1%)	28(16.0%)	82(19.0%)	0.212
APACHE II scores: Acute Physiology and Chronic Health Evaluation II score, SOFA: Sequential Organ Failure Assessment, SOFA$_{top}$: the top level of SOFA score.				
*P < 0.05				

Relevant Data of Blood Glucose Level

There were no significant differences in HbA1c value and ADAG between two groups, greater level of BG at admission, MGL-3, MGL-5 and MGL-7 were found in non-survivors, the incidence of MH and SH were more common among non-survivors who had higher GAP$_{adm}$, GAP$_{mean-3}$, GAP$_{mean-5}$ and GAP$_{mean-7}$ (P < 0.05, Table 2).

Table 2
Relevant Data of Plasma Glucose Levels and GAP

	ICU Survivors (n = 256)	ICU Non-survivors (n = 175)	All Patients (n = 431)	P-Value
BG at admission (mmol/L)	10.0(7.6,13.3)	11.5(8.7,14.9)	10.6(8.2,14.1)	0.005*
MGL-3 (mmol/L)	10.5(8.6,12.7)	12.7(10.8,14.7)	11.5(9.3,13.8)	0.000*
MGL-5 (mmol/L)	10.5(8.0,12.5)	12.6(11.2,14.3)	11.6(9.4,13.3)	0.000*
MGL-7 (mmol/L)	10.8(8.7,12.7)	12.8(11.2,14.4)	11.6(9.8,13.4)	0.000*
HbA1c (mmol/L)	6.9(6.1,7.7)	7.0(6.2,7.8)	6.9(6.3,7.8)	0.439
ADAG (mmol/L)	8.3(7.1,9.7)	8.6(7.3,9.8)	8.4(7.3,9.8)	0.454
GAPadm (mmol/L)	1.8(-0.6,4.3)	3.0(0.8,6.2)	2.3(-0.2,5.2)	0.001*
GAPmean-3 (mmol/L)	2.3(0.8,3.6)	4.3(2.8,5.4)	3.2(1.4,4.6)	0.000*
GAPmean-5 (mmol/L)	2.5(-0.4,3.5)	4.1(3.7,5.0)	3.4(1.4,4.2)	0.000*
GAPmean-7 (mmol/L)	2.6(1.1,3.5)	4.2(3.6,4.9)	3.3(1.9,4.3)	0.000*
Number of MH, n(%)	9(3.5%)	40(22.9%)	49(11.4%)	0.000*
Number of SH, n(%)	4(1.6%)	19(10.9%)	23(5.3%)	0.000*

BG: blood glucose, MGL: mean glucose level, ADAG: A1C-derived average glucose, GAP_{adm}: glycemic gap between blood glucose at admission and ADAG, GAP_{mean}: glycemic gap between MGL and ADAG, MH: moderate hypoglycemia, blood glucose:2.2-3.3mmol/L, SH: severe hypoglycemia, blood glucose: <2.2mmol/L

*P < 0.05

Therapy and Outcome Data

Non-survivors received less daily intake of carbohydrates and higher daily dosage of insulin (Novolin R) and accumulated dosage of glucocorticoid (converted into dosage of Methylprednisolone) during the first 7 days of admission.

Outcome indicators including ventilator-free hours and non-ICU stay days during 28 days were longer and duration of renal replacement therapy (RRT) shorter among non-survivors (P < 0.05, Table 3).

Table 3
Therapy and Outcome Data

	ICU Survivors (n = 256)	ICU Non-survivors (n = 175)	All Patients (n = 431)	P-Value
Carbohydrates intake (Kcal/kg)	158.33(132.59,174.25)	142.86(121.61,167.86)	151.79(126.43,172.14)	0.014*
Insulin daily dosage (u)	8(0,32)	17.1(2,33.3)	12(0.32.68)	0.009*
Glucocorticoid dosage (mg)	26.67(0,80)	53.33(0,213.33)	26.67(0,144)	0.000*
Duration of ventilator-free (h)	518(272.75,612)	1(0,30)	195(2,561)	0.000*
Duration of RRT (h)	0(0,0)	0(0,44)	0(0,10)	0.000*
Non-ICU stay (d)	13.5(0.25,21)	0(0,0)	0(0,16)	0.000*
MV: mechanical ventilation, RRT: renal replacement therapy				
*P < 0.05				

Predictors of 28-day Mortality

Variables related to the primary outcome were screened out during single factor analysis and logistic regression analysis revealed that $SOFA_{top5}$ and GAP_{mean-5} were independent risk factors for mortality at 28-day, AUC of GAP_{mean-5} was higher than that of $SOFA_{top5}$, which reflected the greater predictive power. GAP_{mean-3} and GAP_{mean-7} were removed from regression equation due to the collinearity with GAP_{mean-5} and lower discriminative power with smaller AUC comparing with GAP_{mean-5}. $SOFA_{top5}$ was kept, $SOFA_{top3}$ and $SOFA_{top7}$ were removed with the same reason as GAP_{mean-3} and GAP_{mean-7}.

The optimal cut-off value of GAP_{mean-5} to predict 28-day mortality was 3.6mmol/L (sorted by Youden index), which provided a sensitivity and specificity of 77.7% and 76.6%.

Table 4 showed the AUC of APACHE II, GAP and SOFA within 3, 5 and 7 days to predict the mortality of 28-day, GAP_{adm} incorporated with APACHE II, GAP_{mean-3} incorporated with $SOFA_{top3}$, GAP_{mean-5} incorporated with $SOFA_{top5}$ and GAP_{mean-7} incorporated with $SOFA_{top7}$ were performed as well, GAP_{mean-5} incorporated with $SOFA_{top5}$ was the best, which increased the predictive power with the AUC of 0.807(95%CI: 0.762−0.851) to 0.852(95%CI: 0.814−0.889) (NRI = 11.34%, P < 0.001).

Table 4
AUC and 95%CI of APACHE II, SOFA and GAP for prediction of 28-day mortality

	AUC	95%CI
APACHE II	0.678	0.626−0.731
$SOFA_{top3}$	0.773	0.728−0.819
$SOFA_{top5}$	0.796	0.752−0.839
$SOFA_{top7}$	0.786	0.741−0.831
GAP_{adm}	0.591	0.535−0.647
GAP_{mean-3}	0.749	0.701−0.797
GAP_{mean-5}	0.807	0.762−0.851
GAP_{mean-7}	0.795	0.750−0.840
GAP_{adm}+ APACHE II	0.683	0.631−0.736
GAP_{mean-3}+ $SOFA_{top3}$	0.819	0.778−0.861
GAP_{mean-5}+ $SOFA_{top5}$	0.852	0.814−0.889
GAP_{mean-7}+ $SOFA_{top7}$	0.850	0.813−0.888

Discussion

Stress-induced hyperglycemia(SIH) is a commonplace in critically ill patients from which they suffered such as sepsis, multiple trauma, major surgery, acute myocardial infarction (AMI) [13], burns and stroke[14], presenting secondary to elevated levels of counter-regulatory hormones (cortisol, catecholamines, glucagon, and growth hormone) and impaired response, which results in increased gluconeogenesis and decreased glycogenolysis. SIH occurs in individuals with and without a history of diabetes and is believed to be more closely related to increased risk of death in the patients without diabetes comparing with the hyperglycemia in the diabetes[16]. Moritoki, et al. reported that in patients with critical illness-associated hyperglycemia(CIAH) and 'adequately controlled' diabetes, acute hyperglycemia is associated with increased mortality, whereas in patients with 'insufficiently controlled' diabetes it is not[17]. There is the comparable conclusion that Krinsley[18] reached, which is that patients with diabetes may benefit from higher glucose target ranges than those without diabetes. We found higher level of mean blood glucose in non-survivors without significantly statistical association with 28-day mortality, higher average daily dosage of insulin and incidences of MH and SH were also recorded, this finding was consistent with previous studies and indicated that restraint of SIH was not definitely beneficial[9], patients with diabetes tend to be tolerant of prolonged hyperglycemia and might be adaptive to wider and individualized range of blood glucose[19].

Tight glucose control reduces the risk of microvascular complications, but the benefits are counterbalanced by higher risk of hypoglycemia, which is a frequent consequence of tight glucose control, particularly with the use of insulin-providing medications, counterbalance the benefits[20]. Hypoglycemia was confirmed repeatedly associated with ICU mortality regardless of whether the patients were diagnosed of diabetes, which could result in drastic fluctuation of blood glucose and induced more serious cellular impairment[21], that might be the reason why studies failed to replicate the benefit of tight glycemic control on ICU mortality[22], patients were more likely suffering poor outcomes[23]. The conclusion above impelled us to implement more rational and effective protocol to monitor and control blood glucose so as to avoid or balance the two extremes which were 'uncontrolled hyperglycemia' and 'over tightly controlled glucose[24].

Tangible proofs convinced researchers of the fact that hyperglycemia of critically ill patients could not totally attribute to stress response[25]. It makes researchers turn to the relationship between the degree of premorbid glycaemia and mortality, the admission blood glucose levels are especially proved associated with higher mortality[26]. Researchers had concluded that admission hyperglycemia could result from a combination of acute physiological stress or higher baseline blood glucose[27]. Quantification of the level of chronic glycemia in the critically ill patients provides important clinical information how severity critical illness-associated dysglycemia is[19]. Level of HbA1c represents premorbid chronic hyperglycemia before the admission and is not affected by stress or fasting status, it is inconsiderable within-day and day-to-day variations[28], HbA1c thus could be regarded as a parameter of identifying SIH and diabetic hyperglycemia[29] and routinely performed, further evidences showed the difference between blood glucose level at admission and ADAG was associated with adverse outcomes[30] [31]. Nonetheless, the study had witnessed the unparalleled predictive power of GAP_{mean} on 28-day mortality in critically ill patients with diabetes comparing with other parameters including GAP_{adm} based on blood glucose measurements. The results reminds us that different responses to standard glucose control in patients with chronic hyperglycemia and normoglycemia should be considered[19]. Farid Fawzy believed that elevated glycemic gap and APACHE-II score were associated with an increased ICU mortality and their incorporation could predict the mortality of critically ill patients effectively[32]. Date showed that GAP_{adm} with smaller AUC than previous studies, despite improvement attributed to incorporation of APACHE II, the AUC was lower than 0.70 yet. The reasons might refer to diverse reactivity among patients, severity and progression of the diseases, single point of blood glucose value could not reflect the reality and variation veritably and timly with numerous impacted factors and unforeseen circumstances, whereas the mean level of blood glucose during several days after admission to ICU might reflect more comprehensive information of the patients.

Treating patient and predicting mortality in the ICUs is always a challenge as well as great concern for physicians, the effect of this prediction is on various aspects of patient care[33]. Researchers believed that both SOFA and APACHE II had discriminative power of predicting mortality of critically ill patients with comparable sensitivity and specificity, APACHE II was better, the reason might be that most of patients admitted to the emergency department were shifted to the ICU without significant vital support[34]. Nevertheless, the validity of the APACHE II has been challenged because it does not take into account the treatment or the subsequent course of disorders after the first 24 hours admitted to ICU, the severity of

critically ill patients might not get top level at admission, the situation of patients may deteriorate after admission, recognition of evolving illness severity in ICU is invaluable. SOFA score is commonly used for assessing severity and predicting outcomes of critically ill patient[35], it has the potential advantages of assessing the intensity of organ failure and organ support during the patient's stay in ICU comparing with APACHE II[36]. Our data showed that the top level of SOFA during 3, 5 and 7 days after admission were related to mortality of critically ill patients definitely, furthermore, when we incorporated the top level of SOFA into GAP_{mean} within same period would provide more optimal predictive power on 28-day mortality. We believed that these parameters were mutual complementary, and the

predictive power was increased consequently.

Limitations

There are limitations in the study. First, this is a single-center study with a limited number of samples, thus selection bias may exist. Second, there remains controversy about strategy of controlling and target level of blood glucose. Insulin was administered through intravenous way continuously or subcutaneous way intermittently to achieve the target level of blood glucose which ranged from 8.0mmol/L to 10.0mmol/L during the study. Third, we did not exclusively analyze the impact on blood glucose the type of nutritional support or medication such as catecholamine, diuretic or antibiotics may have. It is necessary to carry out multi-center studies to increase sample size and balance the process of monitoring and controlling the level of blood glucose in the future, subgroup analysis of the effects of related medication and classifications of adverse outcome may be needed either.

Conclusions

In this study, an elevated glycemic gap between the mean blood glucose level in the first 7 days especially MGL within 5 days after admission to ICU and A1C-derived average glucose(ADAG) was independently associated with 28-day mortality in critically ill patients with diabetes significantly, the predictive power on mortality was superior to GAP_{adm} (the difference between admission blood glucose and ADAG). The predictive power was optimized with addition of the top level of SOFA within 5 days.

Declarations

Acknowledgments

Authors' contributions

RL and LJ designed the study. RL and BJ performed data collection. RL did data analysis and drafted the manuscript. LJ was in charge of overall direction and planning and contributed to reviewing and editing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consentto participate

This study was approved by institutional review board for human investigation and waived the need for informed consent, and patients' details were anonymized in a secure database of our department, informed consent was not obtained.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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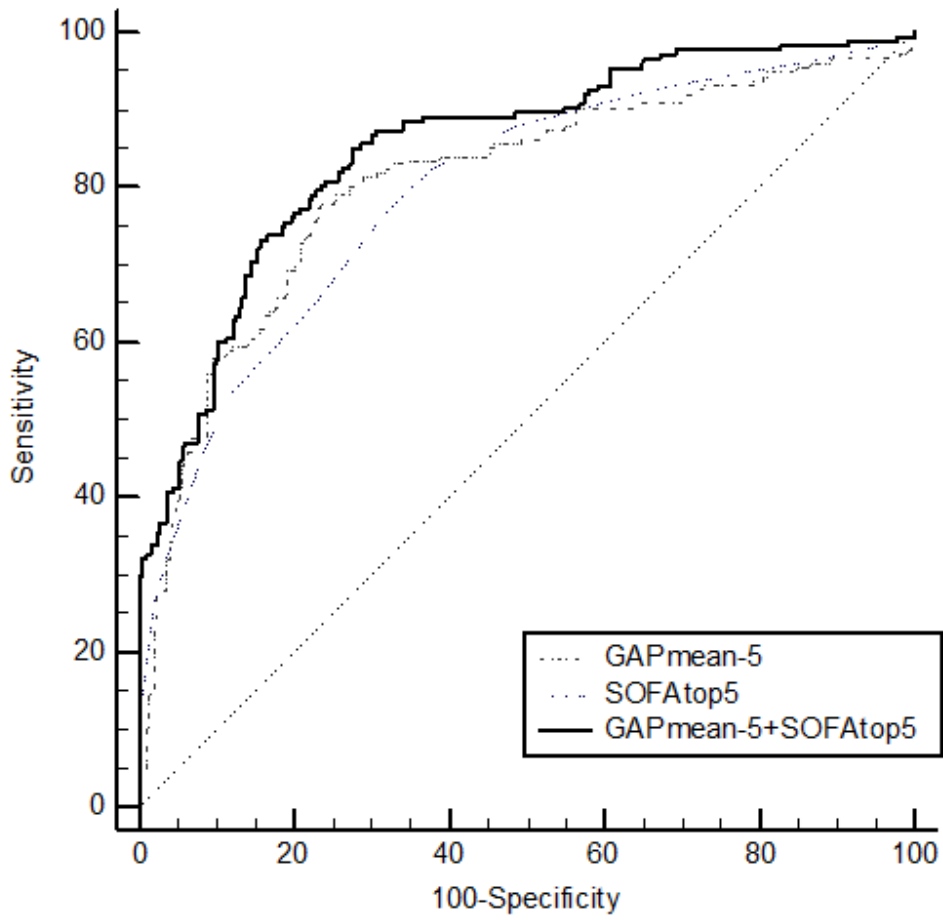
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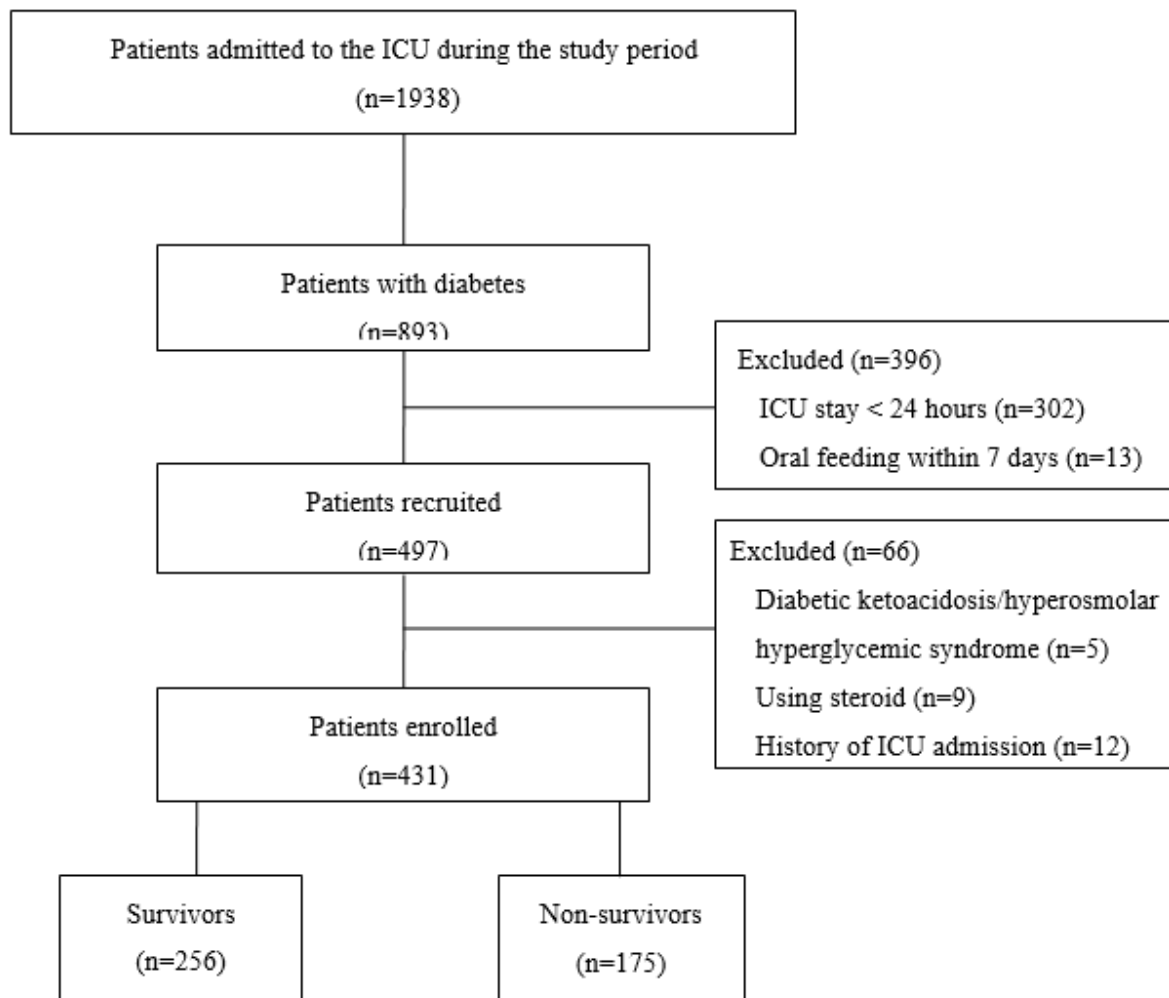
Figure 1

Flow chart of the study

Figure 2

ROC curves for GAP and SOFA score for predicting 28-day mortality