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The association of mean glucose level and glucose variability with intensive care unit mortality in patients with severe acute pancreatitis☆,☆☆

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Abstract

Purpose: The objective of this study was to retrospectively analyze the association of mean glucose level (MGL) and glycemic lability index (GLI; as a measure of glucose variability) with intensive care unit (ICU) mortality in patients with severe acute pancreatitis (SAP).

Materials and Methods: Paper-based medical records of patients with SAP who were admitted to the ICU of West China Hospital between July 1, 2005, and July 1, 2010, were analyzed. Glucose measurements, demographic characteristics, clinical features, data on the first and second 24-hour Acute Physiology and Chronic Health Evaluation (APACHE) II scores, and outcomes were obtained. Time-weighted glucose parameters were used. We statistically analyzed the relationship between these variables and both ICU and hospital mortality.

Results: A total of 294 patients with 34 796 glucose measurements were included in the final analysis. The time-weighted MGL was 9.31 ± 1.91 mmol/L, and the median of GLI was 55.27 $(mmol/L)^2$ h^{-1} wk^{-1}. Intensive care unit mortality was 43.5% and increased progressively as GLI increased, reaching 62.5% of patients with GLI above 115.89 $(mmol/L)^2$ h^{-1} wk^{-1}. The highest odds ratio for ICU death was found in patients with the highest quartile of GLI: odds ratio, 3.47 (95% confidence interval, 1.76-6.86; $P < .000$). No such relationship could be found with MGL. Glycemic lability index was better able to predict ICU death than was MGL (the area under the curves were 0.642 vs 0.561, respectively; z test was 2.677; $P = .0074$). The logistic regression analysis showed that GLI, the second 24-hour APACHE II score, and the number of organ failures upon ICU admission contributed independently to the risk of mortality.

Abbreviations: MGL, mean glucose level; GV, glucose variability; ICU, intensive care unit; SAP, severe acute pancreatitis; APACHE, Acute Physiology and Chronic Health Evaluation; GLI, glycemic lability index; CI, confidence interval; OR, odds ratio; SD, standard deviation; ROC, receiver operating characteristic curve; AUC, area under the curve.

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Conclusions: We observed that GLI was a better predictor of ICU and hospital mortality than was MGL. Together with the second 24-hour APACHE II score and the number of organ failures upon ICU admission, GLI is an independent predictor of mortality in patients with SAP.

1. Introduction

Critical illness is associated with numerous endocrine and metabolic disturbances including alterations in carbohydrate metabolism [1,2]. Hyperglycemia is common in severe illness, such as severe acute pancreatitis (SAP), regardless of whether the patient has diabetes, and hyperglycemia is associated with adverse outcomes [3-8]. Consequently, many studies on glucose control have emerged. A landmark study from Belgium involving a cohort of 1548 mechanically ventilated postoperative patients showed that intensive insulin therapy (targeted to a blood glucose level of 4.4-6.1 mmol/L) could accomplish a considerable reduction in morbidity and mortality [9]. However, the results of this study have not been replicated in other settings [10-14]. One explanation for these mixed results is that measures of glucose control other than the glucose concentration may also be of great importance. Mounting evidence shows that a wide glucose variability (GV) is an independent predictor of an increased risk of death [15], regardless of the glucose level [16]. Consequently, GV plays a key role in both the short- and long-term outcomes in critically ill patients [17-19], including patients with sepsis [20], severely burned patients [21], and other populations with a critical illness [22].

Because hyperglycemia is common in SAP, it is important to evaluate whether mean glucose level (MGL) or GV is a better predictor of increased mortality in this group of patients.

2. Materials and methods

2.1. Patients

A total of 452 patients with diagnosed SAP were admitted to the intensive care unit (ICU) of West China Hospital between July 1, 2005, and July 1, 2010. The study cohort consisted of patients with SAP who had an ICU stay lasting at least 3 days. Patients were excluded if they were younger than 18 years, had an onset of SAP more than 14 days on ICU admission, or were pregnant.

2.2. Design

We performed a retrospective study of a large cohort of patients with SAP in a 52-bed medical ICU in a teaching hospital (West China Hospital, Chengdu, China). Death from any cause during ICU stay was the primary outcome variable, and the secondary outcome measure was hospital mortality.

2.3. Data collection

Data on blood glucose measurements during the ICU stay, the number of organ failures upon ICU admission, the first and second 24-hour Acute Physiology and Chronic Health Evaluation (APACHE) II scores, demographic characteristics, clinical features, and outcomes were extracted from paper-based medical records. To maintain homogeneity in glucose methodology, only glucose values tested by a point-of-care glucose monitor (ACCU-CHEK Active; Roche Diagnostics GmbH, Mannheim, Germany) were included in this analysis. Glycemic lability index (GLI) was chosen for this study as a measure of GV because of its ease of use, its ability to correct for heterogeneity in the timing of glucose measurements, and its previous superior association with hospital outcomes compared with other methods of capturing GV [20], as demonstrated by Dungan et al [23]. Glycemic lability index is calculated as the squared difference between consecutive glucose measures per unit of actual time between those samples [24] (GLI = $E[\Delta\text{glucose (mmol/L)}]^2\ \text{h}^{-1}\ \text{wk}^{-1}$). Time weighting was performed to correct for nonuniform glucose sampling intervals, and all the glucose parameters in the paper were corrected for time. If a patient required readmission before hospital discharge, only the data and outcomes from the first admission were included in the analysis.

2.4. Statistical analysis

We compared baseline and outcome variables using the Student t test, χ^2 test, and Mann-Whitney U test, as appropriate. To define predisposing factors, the odds ratio (OR) and its 95% confidence interval (CI) were used as a binary parameter. We used the area under the receiver operating characteristic (ROC) curve to compare the ability of different glucose parameters to predict ICU and hospital death. Logistic regression models were created to analyze the independent effects of age, sex, GLI, MGL, first and second 24-hour APACHE II scores, and the number of organ failures on mortality. Results are presented as mean ± SD, number (percentage), or median (interquartile range), unless otherwise indicated. Statistical analysis was performed using the SPSS (Statistical Package for the Social Sciences, Chicago, Ill) 17.0 statistical software package. We compared ROC curves using MedCalc software (MedCalc Software bvba, Mariakerke,