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Predicting Mortality of Critically Ill Patients by Blood Glucose Levels (*Diabetes Metab J* 2013;37:385-90)

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Critical illness is associated with a high risk for multiple organ failure and mortality. Hyperglycemia is common in critically ill patients and is related to adverse outcome. In the article entitled "Predicting mortality of critically ill patients by blood glucose levels," Park et al. [1] reported that blood glucose levels upon admission to intensive care unit (ICU) predicted clinical outcomes. This article merits much attention, because its findings remind clinicians that critically ill patients with dysglycemia upon ICU admission should be monitored and treated more closely. Although the authors did not assess the degrees of disease severity and length of stay, which could affect mortality, they clearly demonstrated that hyperglycemia (>300 mg/dL) at the time of ICU admission was associated with higher mortality rate among critically ill patients, regardless of the presence of diabetes mellitus (DM). In this study of 1,224 critically ill patients, they found that subjects whose blood glucose levels ranging between 100 and 199 mg/dL upon admission had the lowest mortality rate, revealing a J-curved relationship between glucose levels and mortality rates. This study is in line with previous reports stating that hyperglycemia during critical illness is strongly associated with increased mortality [2-5].

However, there remain a couple of intriguing queries to be addressed in this study. First, the relationship between hyperglycemia (>300 mg/dL) and mortality rate appears to be stronger in critically ill patients with DM when compared to those without. In contrast to these findings, some observational studies showed that mortality was much greater for hyperglycemic patients without DM in comparison to those with DM when average glucose levels during ICU stay were analyzed [5-7], suggesting that prior exposure to higher glucose levels in DM patients may weaken the association between hyperglycemia and mortality. The differences in study subjects and data collection of glucose levels might lead to these conflicting results.

Growing evidence suggests that hypoglycemia, as well as hyperglycemia, predicts morbidity and mortality in critically ill patients, although no causal relationship between glycemic statuses and mortality has been established. Egi et al. [8] have demonstrated a significant association between even mild hypoglycemia (<81 mg/dL) and mortality after adjustment for insulin therapy and other confounding factors in critically ill patients. In another study, hypoglycemia within the initial 24 hours of ICU admission has been found to be associated with an increased risk for mortality [9]. Moreover, a recent *post hoc* analysis of NICE-SUGAR study showed a dose-response relationship between hypoglycemia and mortality [10]. There are several plausible explanations for the association between hypoglycemia and adverse outcome in critically ill patients, while specific mechanisms remain elusive. Hypoglycemia might contribute to mortality by elevating systemic inflammatory response, sympathetic stimulation, and fatal cardiac arrhythmias. Furthermore, it is possible that hypoglycemia is a biomarker for severity of disease in critical illness [6].

In this study, the authors showed that patients (group 1, n=110) with glucose levels less than 100 mg/dL upon ICU admis-

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sion had higher mortality rate compared to those (group 2, n=799) with glucose levels ranging between 100 and 199 mg/dL, although there was no statistical difference. They also noted that a higher risk of hypoglycemia in group 1 might contribute to increased mortality. In this regard, it will be particularly interesting to further investigate the association between hypoglycemia (for example, <70 mg/dL) and mortality in this study. In addition, recent studies have shown that increased glycemic variability is independently associated with mortality in critical illness [9,11]. Thus, fluctuations in glucose levels appear to confer adverse biologic effects in critically ill patients.

Data from both observational and interventional studies suggest that dysglycemia such as hyperglycemia, hypoglycemia, or increased glycemic variability is independently related to increased mortality in critically ill patients. Therefore, it now seems important for clinicians to note that critical illness-related dysglycemia should be promptly recognized and appropriately managed in ICU.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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