

Glucose Control, Diabetes Status, and Mortality in Critically Ill Patients: The Continuum From Intensive Care Unit Admission to Hospital Discharge

James S. Krinsley, MD; Paula Maurer, RN; Sharon Holewinski, RN, MS; Roy Hayes, MS; Douglas McComsey, BS; Guillermo E. Umpierrez, MD, CDE; and Stanley A. Nasraway, MD

Abstract

Objective: To describe the relationships among glycemic control, diabetes mellitus (DM) status, and mortality in critically ill patients from intensive care unit (ICU) admission to hospital discharge.

Patients and Methods: This is a retrospective investigation of 6387 ICU patients with 5 or more blood glucose (BG) tests and 4462 ICU survivors admitted to 2 academic medical centers from July 1, 2010, through December 31, 2014. We studied the relationships among mean BG level, hypoglycemia (BG level <70 mg/dL [to convert to mmol/L, multiply by 0.0555]), high glucose variability (coefficient of variation $\geq 20\%$), DM status, and mortality.

Results: The ICU mortality for patients without DM with ICU mean BG levels of 80 to less than 110, 110 to less than 140, 140 to less than 180, and at least 180 mg/dL was 4.50%, 7.30%, 12.16%, and 32.82%, respectively. Floor mortality for patients without DM with these BG ranges was 2.74%, 2.64%, 7.88%, and 5.66%, respectively. The ICU and floor mean BG levels of 80 to less than 110 and 110 to less than 140 mg/dL were independently associated with reduced ICU and floor mortality compared with mean BG levels of 140 to less than 180 mg/dL in patients without DM (odds ratio [OR] [95% CI]: 0.43 (0.28-0.66), 0.62 (0.45-0.85), 0.41 (0.23-0.75), and 0.40 (0.25-0.63), respectively) but not in patients with DM. Both ICU and floor hypoglycemia and increased glucose variability were strongly associated with ICU and floor mortality in patients without DM, and less so in those with DM. The independent association of dysglycemia occurring in either setting with mortality was cumulative in patients without DM.

Conclusion: These findings support the importance of glucose control across the entire trajectory of hospitalization in critically ill patients and suggest that the BG target of 140 to less than 180 mg/dL is not appropriate for patients without DM. The optimal BG target for patients with DM remains uncertain.

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A large body of literature has found that dysglycemia—hyperglycemia, hypoglycemia, and increased glucose variability—is independently associated with mortality in critically ill patients.¹⁻⁷ This association is stronger for patients without diabetes (DM) than it is for patients with DM.⁸⁻¹⁴

Few studies have reported on the relationships of these domains of glycemic control to mortality, or other important clinical outcomes, in non-critically ill hospitalized patients.¹⁵ Hyperglycemia is strongly associated with mortality and morbidity, especially postoperative infection,

in patients with DM undergoing cardiovascular surgery.^{16,17} Other investigations have reported an association of hyperglycemia with adverse outcomes in patients admitted to general medical wards with community-acquired pneumonia¹⁸ and exacerbations of chronic obstructive pulmonary disease.¹⁹ Hypoglycemia has been associated with increased hospital length of stay, complications, and mortality in non-critically ill patients with DM.²⁰⁻²² Finally, glucose variability has been associated with deleterious outcomes in various populations in non-intensive care unit (ICU) settings.²³⁻²⁵



From the Division of Critical Care, Department of Medicine, Stamford Hospital, Columbia University College of Physicians and Surgeons, Stamford, CT (J.S.K.); Medical Decision Network, Charlottesville, VA (P.M., D.M.); Department of Nursing (S.H.) and Department of

Affiliations continued at the end of this article.

The transition from the ICU to general floor care has major implications for glucose management of the hospitalized patient. The higher nurse to patient ratio in the ICU facilitates greater frequency of blood glucose (BG) measurement and the implementation of protocols using intravenous insulin infusions to treat hyperglycemia. This stands in contrast to the lesser resources available on the wards for glycemic control. Limited data exist evaluating the changes in glucose metrics that occur in patients after discharge from the ICU to the general wards.²⁶ Although major emphasis has been placed on glycemic control in the ICU, glycemic control has not been as rigorously studied or pursued in hospitalized patients cared for outside of the ICU. No studies to date have reported on glucose control metrics spanning the entire trajectory of hospitalization, from ICU admission to hospital discharge of ICU survivors. We hypothesized that dysglycemia—hyperglycemia, hypoglycemia, and increased glucose variability—occurring in both settings, the ICU as well as the floors after ICU discharge, is independently associated with mortality. To test this hypothesis, we performed a 2-center cohort investigation of critically ill patients and their continuum of glycemic control from the ICU through to hospital discharge.

MATERIALS AND METHODS

Patients and Settings

This is a retrospective analysis of patients admitted to ICUs at Tufts Medical Center in Boston, Massachusetts, a tertiary medical center, and Stamford Hospital in Stamford, Connecticut, a university-affiliated teaching hospital, from July 1, 2010, through December 31, 2014. Patients at Tufts Medical Center were admitted to the medical and surgical ICUs, each a 10-bed unit. Patients at Stamford Hospital were admitted to the 16-bed mixed medical-surgical ICU. A total of 10,619 patients were admitted to the ICUs during this period. The study exclusion criteria included readmission to the ICU during the same hospitalization, an admitting diagnosis of diabetic ketoacidosis or hyperosmolar hyperglycemic state, and fewer than 5 BG tests during ICU care (Supplemental Table 1, available online at

<http://www.mayoclinicproceedings.org>). The 2 remaining cohorts consisted of 6387 ICU patients and the 4462 ICU survivors with at least 1 BG test after ICU discharge. Diabetes status was determined prospectively at the time of ICU admission based on all available clinical information obtained from patients, surrogates, and the electronic medical record.

The 2 ICUs at Tufts Medical Center were organized using a closed model, with intensivist-led multidisciplinary teams providing patient care. The Stamford ICU had a hybrid organization, with mandatory consultation required from a critical care physician and care provided by an intensivist-led multidisciplinary team. The nurse to patient ratio was 1:2 or 1:1 in both ICUs depending on patient acuity. In contrast, the nurse to patient ratio on the general medical and surgical wards ranged from 1:4 to 1:8. Hospitalists or non-hospital-based private physicians provided medical care to the patients, often with the assistance of medical and surgical house staff or mid-level practitioners (physician assistants or nurse practitioners).

Glucose Control and Metrics

At Tufts Medical Center, the BG target was 100 to 150 mg/dL (to convert to mmol/L, multiply by 0.0555) in the medical ICU and 95 to 135 mg/dL in the surgical ICU. The BG target in the Stamford Hospital ICU was 90 to 120 mg/dL. These targets were identical for patients with and without DM. Nurses used point-of-care devices to monitor BG levels; most measurements were made using glucose meters, testing primarily arterial or central venous blood when in the ICU; capillary point-of-care testing was the main source of measurement for patients on the ward. Paper-based protocols guided insulin therapy, and the frequency of monitoring ranged from hourly to every 4 to 6 hours based on the nurses' assessment of clinical need. In contrast, glucose control on the general floors was not standardized. Instead, the attending physician was responsible for writing glycemic control orders, including insulin orders and point-of-care testing. In both institutions, physicians had access to electronic order sets, specifically including basal-bolus—prandial insulin administration; neither institution used a

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