Normal Glucose Values Are Associated With a Lower Risk of Mortality in Hospitalized Patients

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OBJECTIVE — Hyperglycemia is a common condition in hospitalized patients. The aim of this study was to investigate the relationships between glycemia upon admission and mortality in a heterogeneous group of adult patients.

RESEARCH DESIGN AND METHODS — The 3-year records released from a general hospital were associated with a plasma glucose dataset of its general laboratory. A matched case-control study was implemented (3,338 case-control subject pairs). All-patient refined diagnosis–related groups and the relative risk of death were the matching criteria. A multivariate conditional logistic regression model was used to evaluate the associations between death and glycemia.

RESULTS — Higher in-hospital mortality was associated with hyperglycemia or hypoglycemia, whereas lower risk was observed for values between 78 and 101 mg/dl.

CONCLUSIONS — Our data confirm the relation between glycemia upon admission and mortality and suggest that slightly increased or decreased plasma glucose can be linked with increased mortality risk.

Diabetes Care **31:2209–2210, 2008**

Hyperglycemia is a common comorbid condition in hospitalized patients, independent of the diagnosis of diabetes, and is associated with adverse outcomes (1–4). Although there is strong evidence suggesting that tight glycemic control is intimately linked to an improved outcome in the intensive care unit (5), hyperglycemia in hospitalized patients is generally not considered a major therapeutic focus. It is important to determine target plasma glucose concentrations and glycemic thresholds associated with optimal benefits during hospitalization. The aim of this study was to investigate the relationship of plasma glucose on admission with in-hospital mortality and to identify the range of glycemic values associated with significant reductions of mortality risks in a heterogeneous group of hospitalized adult patients.

RESEARCH DESIGN AND METHODS

— Analyses included data released from 96,405 patients hospitalized for different pathologies at San Giovanni Battista Hospital of Turin, a large teaching general hospital excluding departments of ophthalmology, obstetrics and gynecology, and pediatrics and infectious diseases, between 1 October 2003 and 30 September 2006. For every patient, administrative records were linked with the laboratory measurements dataset of plasma glucose. Of the 96,405 admissions, 26,409 (27.4%) were excluded because plasma glucose was not measured upon admission to the hospital. From this cohort, a matched case-control study was implemented. Cases were defined as in-hospital deaths. All patients discharged alive were considered control subjects. Matching criteria were the all-patient refined diagnosis–related groups (APR-DRGs) and their relative risk of death (RISKD) (6). APR-DRGs are diagnosis-related groups–based severity measurement systems taking into consideration the principal diagnosis, age, interactions of multiple secondary diagnoses, and combinations of nonoperating procedures incorporated with the principal diagnosis of subjects. Among the 3,401 deaths, 63 records (62 with an APR-DRG 196, "Cardiac arrest, unexplained," and 1 with APR-DRG 130, "Respiratory system diagnosis with ventilator support 96+ hours") were excluded from the study because we could not find a surviving control subject. A total of 3,338 cases were thus matched with a random sample of control subjects within each matching stratum. This procedure led to a set of 6,676 patients perfectly balanced for APR and RISKD distribution. All plasma glucose measurements were determined in a central laboratory with a glucose analyzer (Roche/Hitachi Modular D analyser: ACN 767, Indianapolis, IN). We performed a multivariate conditional logistic regression model to evaluate the associations between in-hospital mortality and a set of variables including demographic characteristics (sex, age, marital status, and level of education) and clinical characteristics (type of admission, type of treatment, and plasma glucose on admission). APR-DRGs and RISKD, as matching variables, were not included in the model. All the covariates were inserted in the model without any formal selection. Plasma glucose measurements were added to the model as restricted cubic spline to investigate the association between in-hospital death and plasma glucose levels through a straight and smooth line outside the whole interval of values. Nonlinearity of the effects was eventually tested with a χ^2 type test. Values of plasma glucose minimizing the risk of death were determined using the inverse spline function, and 95% CIs were derived from bootstraps

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Received 11 April 2008 and accepted 11 August 2008.
Published ahead of print at http://care.diabetesjournals.org on 20 August 2008. DOI: 10.2337/dc08-0672.

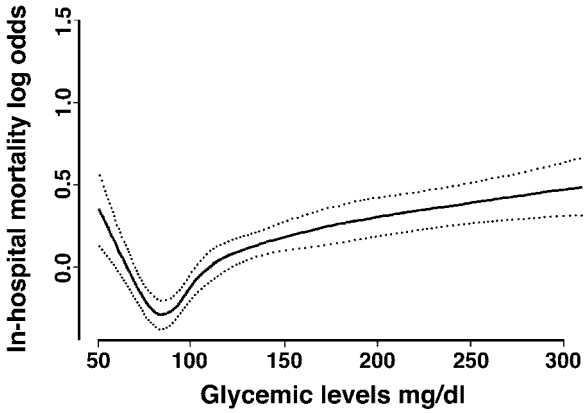

Figure 1—*Effect of plasma glucose values at admission in hospital (black line) on risk of in-hospital death (log odds) and 95% CIs (dotted lines) adjusted by sex, civil status, age, educational levels, type of admission, and type of treatment.*

with 1,000 runs. Data are reported as median and interquartile range and with 95% CIs whenever appropriate.

RESULTS — The whole population with plasma glucose available at admission presents 69,996 cases (mean 65 years of age [range 51–75]; 42% female; 5% dead). Within this group, we analyzed a cohort of 3,338 cases (dead) versus 3,338 control subjects (alive) (mean 70 years of age [59–78] vs. 73 years of age [63–80]; 40 vs. 42% female; and mean 99 mg/dl [82–128] vs. 107 mg/dl [85–144] plasma glucose on admission). The effect of plasma glucose adjusted by administration data was nonlinear, as described in Fig. 1. Accordingly, the minimal risk of in-hospital mortality was found at plasma glucose levels of mean 89 mg/dl (range 78–101). The adjusted odds ratio (OR) of deaths for plasma glucose on admission from 100 to 200 mg/dl is 1.32 (95% CI 1.22–1.43), whereas the OR for plasma glucose from 60 to 80 mg/dl is 1.06 (1.04–1.07).

CONCLUSIONS — A significant number of in-hospital patients display hyperglycemia, which can be the cause of admission or, more frequently, comorbidity. Previous reports (7–9) have pointed out the relationship between hyperglycemia and prognosis in critically ill patients. The main novelty of the present study is that even moderate glucose elevations or reductions are associated with increased in-hospital mortality in this heterogeneous population. In this study, we have analyzed a large cohort of patients hospitalized for multiple pathologies with a nested case-control study. Furthermore, our observations strongly suggest that, independently of the cause of hospitalization, a patient with an optimal plasma glucose measure between 78 and 101 mg/dl displays lower risk of death. Interestingly, this optimal glycemic range is closely related to normoglycemic values as defined by criteria of the American Diabetes Association (10). The main limitation of this study is its retrospective nature. The retrospective design prevents concluding whether hypo- or hyperglycemia was a cause of increased mortality or just a marker of increased risks of mortality, although we do observe a strong association between hospital mortality and glycemic levels. Other limitations are *1*) missing data for 27.4% of all admitted patients (this data gap could be the consequence of the use of point-of-care procedures)—in any case, within this group, the mortality rate was only 3.5%; *2*) some specialties were excluded from the study because they were allocated to other hospitals; *3*) we do not know the duration of hypo- or hyperglycemia; and *4*) hypoglycemic values could result from diabetes therapy or critical diseases. However, these data confirm the importance of glycemic value upon hospital admission (11). Lowest hospital mortality rates were observed among patients with plasma glucose concentrations between 78 and 101 mg/dl, and even a moderate variation below or above these cutoff values may increase mortality in a heterogeneous group of patients.

Acknowledgments — The study was supported by the Compagnia di San Paolo and by a grant from the Piedmont Region Ricerca Sanitaria Finalizzata.

We would like to acknowledge Dr. David H. St-Pierre for revising this manuscript.

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