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Admission Hyperglycemia and Other Risk Factors as Predictors of Hospital Mortality in a Medical ICU Population*

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Background: **Tight glycemic control is recommended for patients in the ICU, as hyperglycemia is associated with increased morbidity and mortality.**
Design: **Observational cohort of patients admitted to a 12-bed, inner-city, medical ICU (MICU).**
Subjects: **A total of 1,185 of 1,506 patients from July 1, 1999, to December 31, 2002, selected based on a diagnosis other than diabetic ketoacidosis or glycemia > 280 mg/dL or < 80 mg/dL.**
Purpose: **To determine if the highest serum glucose level within 24 h after ICU admission is associated with increased hospital mortality when adjusted for confounders.**
Measurements: **Age, gender, race, worst values within 24 h after ICU admission to construct the acute physiology and chronic health evaluation (APACHE) II score, and highest glucose within 24 h after ICU admission. Hospital mortality was the primary outcome. Admitting diagnosis, MICU length of stay (LOS), and hospital LOS were obtained. Glucose, albumin (n = 867), and lactic acid (n = 319) were stratified for analysis.**
Analysis: **Univariate analysis identified factors included in the multivariate model.**
Results: **Patients were predominantly African-American (79%) and men (56%; mean age, 49.2 years). The mean ICU admission highest glucose level was 139 ± 43.7 mg/dL (± SD). MICU LOS and hospital LOS were 6.2 days and 12.9 days, respectively, and 50% of patients received mechanical ventilation. MICU and hospital mortality were 18% and 20%, respectively; standardized mortality ratio was 66%. On univariate analysis, survivors (n = 945) and nonsurvivors (n = 240) showed APACHE II score, mechanical ventilation, hypoalbuminemia, lactic acidemia, and logistic organ dysfunction system score to be hospital mortality predictors; however, the highest admission serum glucose level was not. Logistic regression estimated APACHE II score/per point (odds ratio, 1.06; 95% confidence interval, 1.02 to 1.11), mechanical ventilation (odds ratio, 3.06; 95% confidence interval, 1.34 to 6.96), severe hypoalbuminemia (< 2 g/dL) [odds ratio, 2.98; 95% confidence interval, 1.3 to 7.02], and severe lactic acidemia (≥ 8 mmol/L) [odds ratio, 7.3; 95% confidence interval, 2.14 to 24.9], but not ICU admission hyperglycemia, to be associated with hospital mortality.**
Conclusions: **Conventional factors of disease severity, but not highest glucose value during the first 24 h after ICU admission, predict hospital mortality in an inner-city MICU.**
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Key words: diabetes; hospital mortality; hyperglycemia; ICU; insulin

Abbreviations: APACHE = acute physiology and chronic health evaluation; CABG = coronary artery bypass graft; LODS = logistic organ dysfunction system; LOS = length of stay; MICU = medical ICU; SICU = surgical ICU; SMR = standardized mortality ratio; TISS = therapeutic intervention scoring system

Hyperglycemia on hospital admission worsens clinical outcomes in patients with stroke, myocardial infarction, or coronary artery bypass graft (CABG) surgery, all of these populations with established lesions in critical vascular territories.[1–5] Our previous study,[6] unstratified for disease severity, found hyperglycemia in hospitalized patients irrespective of admitting diagnosis to be associated with increased mortality. Previous reports[7–16] suggested morbidity and survival to be directly affected by hospital course hyperglycemia in patients with or without diabetes, as well on those affected by stroke, myocardial infarction, or CABG; and such patients benefited from insulin therapy.

A European, open, randomized clinical trial[17] reported that in patients admitted to a surgical ICU (SICU) with prolonged ICU stay (> 5-day SICU length of stay [LOS]), ICU outcome can be im-

proved if near-normal glucose control is maintained with insulin therapy. Krinsley,[18] in a large observational study from a community teaching hospital with elderly patients admitted to a general ICU with a broader case-mix, confirmed these findings; he found increased mortality in patients with sustained hyperglycemia on multiple determinations.

Extrapolations of results obtained from SICUs to medical ICUs (MICUs) with different case-mix populations remains problematic.[19–24] The aim of this study was to explore whether hyperglycemia, as determined by the highest serum glucose level in the first 24 h after admission to the MICU, adversely affects hospital survival in a predominantly inner-city, African-American population. We also explored how blood glucose concentrations on ICU admission compare to traditional risk factors influencing hospital mortality.

Materials and Methods

Design

The study population is a single institution, prospective, concurrent, nonrandomized observational cohort of all patients consecutively admitted to the MICU at The Regional Medical Center (The MED), Memphis, TN.

Setting

Our MICU is a closed (staffed by intensivists and fellows of the Pulmonary Critical Care and Sleep Medicine Division, University of Tennessee Health Science Center), 12-bed unit in an urban, inner-city, county-owned, safety net hospital. The MICU generally does not service post-CABG, trauma, surgical, burn, or neurosurgical patients. The Institutional Review Board of the University of Tennessee Health Science Center approved the data collection used in the study and waived the need for informed consent.

Subjects

We obtained data on 1,506 adult patients admitted from July 1, 1999, to December 31, 2002. Exclusion criteria were an admitting diagnosis of diabetic ketoacidosis or extreme serum glucose levels, arbitrarily defined for the purpose of this analysis, as an ICU admission glucose level > 280 mg/dL or < 80 mg/dL. A total of 1,185 patients were subjects for this evaluation.

Purpose

To determine if the highest serum glucose level during the first 24 h of ICU admission is associated with increased hospital mortality, when adjusted for disease severity and other confounders (*ie*, serum albumin, lactic acidemia on ICU admission, or invasive mechanical ventilation use).[25–30]

Measurements

Baseline patient characteristics (age, gender, and race) were collected as well as elements of the acute physiology and chronic health evaluation (APACHE) II score, logistic organ dysfunction system (LODS), and therapeutic intervention scoring system (TISS).[31–33] The APACHE II score-derived risk of death during hospitalization was determined from the worst values obtained within 24 h of MICU admission, and was established according to the literature.[31] Hospital mortality was the primary outcome of interest. Serum or Accu-Chek (Roche Diagnostics; Indianapolis, IN) determinations, with its limitations, were assumed to be equivalent.[34] Other clinical variables obtained during the first 24 h of hospital admission were albumin and lactic acid levels. Utilization and duration of invasive mechanical ventilation, MICU LOS, hospital LOS, and MICU mortality were also recorded. Admitting diagnosis frequency distribution was tabulated (split at age 65 years). Glycemia strata were defined as euglycemic (80 to $<$ 120 mg/dL), mild hyperglycemia (120 to 159 mg/dL), moderate hyperglycemia (160 to 199 mg/dL), and severe hyperglycemia ($\geq$ 200 to $<$ 280 mg/dL). Albumin determination on ICU admission (n = 867) and lactic acid (n = 319) reflected practice behavior of residents, fellows, and attending physicians, rotating monthly over the study period. Albumin strata were defined as normal hypoalbuminemia ($\geq$ 3 g/dL), mild-to-moderate hypoalbuminemia ($<$ 3 but $\geq$ 2 g/dL), and severe hypoalbuminemia ($<$ 2 g/dL). Lactic acidemia strata were arbitrarily defined for study purposes as normal ($<$ 2 mmol/L), mild ($\geq$ 2 but $<$ 8 mmol/L), and severe ($\geq$ 8 mmol/L). Residents, fellows, and staff physicians were masked of the data recorded for the study. Data quality control was performed concurrently by one of the investigators (L.B.), who individually reviewed medical records for data extraction completeness and accuracy.

Analysis

Mean $\pm$ SD was calculated for continuous variables. Median values were determined for continuous variables with skewed distribution. Independent variables were initially selected based on clinical judgment and published literature. Univariate analyses among survivors (n = 945) and nonsurvivors (n = 240) were used to identify factors statistically associated with increased hospital mortality, and were included later in a multivariate modeling (if significance was $p \leq 0.1$ to avoid omitting influential predictors). Comparisons of continuous variables between groups were carried out using unpaired *t* test or one-way analysis of variance, when appropriate. The Mann-Whitney *U* test was used when data were skewed. For comparison of categorical variables, χ^2 analyses were performed. A two-tailed p value ≤ 0.05 was considered significant. A standardized mortality ratio (SMR) was calculated as the ratio of the hospital-observed mortality to the APACHE II score-predicted hospital mortality. Albumin, lactic acidemia, hyperglycemia strata, and the baseline clinical variables associ-

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ated with increased mortality by univariate analysis (mechanical ventilation, disease severity adjustment/APACHE II score) were entered as predictors into an adjustment-descriptive unconditional multiple logistic regression model to control for confounders and to determine their independent association with hospital mortality.[35,36] In highly correlated carriers, one variable was chosen to represent the domain. The interaction among age and glucose was explored. Forward stepwise variable inclusion was used to reach the final parsimoniously reduced model. Stratification of continuous variables provided the added advantage of giving odds effects that were concordant with the data rather than with the logarithmic distribution of the multivariate model. The odds ratios and 95% confidence intervals were determined for variables entered into the multiple logistic regression model. Statistical analysis was preformed using statistical software (StatView 5.0; SAS Institute; Cary, NC).

Results

The study population demographics, description, APACHE II score and predicted mortality, TISS, and LODS score (based on worst values obtained in the first 24 h of ICU stay) are listed in Table 1. The APACHE II-predicted mortality was higher than the observed hospital mortality (20.3%), with an SMR of 65.5%.

Admission diagnoses are listed in Table 2. We found 81.4% of our study population to be < 65 years old. The < 65-year-old group had more drug overdose- and other medical illness-related ICU admissions, whereas the ≥ 65-year-old group had more pulmonary-related admissions (*eg*, COPD, pneumonia) [Table 2]. Also, as expected, there were more combined cardio/cerebrovascular events in the ≥ 65 group (acute myocardial infarction, cerebrovascular accident/transient ischemic attack, cardiac arrest [25 of 221 patients, 11.3%; vs 6.1%; χ^2 p = 0.01]). A history of diabetes as a preexisting

Table 1—*Description of Study Patients Admitted to the MICU, July 1, 1999, to December 2002**

Characteristics	All (n = 1,185)
Age, yr	49.22 ± 16.6
Male gender	664 (56.1)
Race	
African-American	937 (79.1)
White	231 (19.5)
Hispanic	5 (< 1)
Asian	12 (< 1)
Mechanical ventilation	594 (50.1)
Duration of mechanical ventilation, d	6.1 ± 7.9 (3)
Glucose, mg/dL	139 ± 43.7 (128)
Albumin, g/dL	2.67 ± 0.8 (2.7)
Lactic acid, mmol/L	3.4 ± 3.8 (2.2)
APACHE II score	18.13 ± 9.7 (17)
APACHE II predicted mortality†	31 (23)
TISS score	28.4 ± 10.2 (27)
Initial LODS	5.48 ± 4.4 (5)
Worst LODS score	7.3 ± 5.4 (6)
ICU LOS, d	6.2 ± 7.7 (3)
Hospital LOS, d	12.9 ± 14.4 (8)
ICU mortality, %	209 (17.6)
Hospital mortality, %	240 (20.3)
SMR, %	65.5

*Data are presented as mean ± SD, No. (%), or mean ± SD (median) unless otherwise indicated.
†Data is presented as mean.

Table 2—*Primary Diagnosis Upon Admission to the MICU by Age (n = 1,185)**

Subgroup (%)	Age < 65 yr (n = 964)	Age ≥ 65 yr (n = 221)	p Value
Cardiopulmonary arrest (3.97)	34	13	0.15
Cardiac (12.3)	112	34	0.16
Myocardial infarction	16	6	
Congestive heart failure	33	13	
Intermediate syndrome	6	2	
Rhythm disturbance	5	6	
Hypertension	47	4	
Cardiogenic shock	0	2	
Miscellaneous	5	1	
Pulmonary (35.7)	330	93	0.03
ARDS/acute lung injury	75	25	
Pneumonia	131	36	
COPD	44	16	
Pulmonary embolism/ deep vein thrombosis	22	6	
Asthma	40	5	
Miscellaneous	18	5	
Anaphylactic shock/angioedema (0.3)	3	0	0.93
Septic shock/severe sepsis (13.1)	124	31	0.71
Nonurinary source	117	28	
Urosepsis	7	3	
Other medical diagnosis (16.6)	172	25	0.02
GI	122	18	
Liver	21	1	
Renal	3	1	
Miscellaneous	26	5	
Drug overdose/toxic/ delirium tremens (6.8)	78	3	< 0.001
Neurologic (9.5)	93	19	0.72
Intracerebral bleed	16	4	
Subarachnoid bleed	3	1	
Cerebrovascular accident/ transient ischemic attack	9	6	
Seizure	27	3	
Meningitis	11	0	
Miscellaneous	27	5	
General surgical/trauma (1.8)	18	3	0.81
Abdomen	6	0	
Thoracic	5	0	
Vascular	4	1	
Miscellaneous	3	2	

*Data are presented as No.

comorbidity (11.1% overall, n = 1,023) was obtained in 74 of 829 patients (8.93%) in the < 65-year-old group, vs 39 of 194 patients (20.1%) in the > 65-year-old group (χ^2 p = < 0.0001), but rates of preexisting diabetes were no different among survivors (88 of 819 patients; 10.75%) and nonsurvivors (25 of 204 patients; 12.3%) [χ^2 p = 0.6]. Glycemia distribution among the 964 patients < 65 years old were euglycemia (43.4%), mild (32.5%), moderate (13.9%), and severe (10.2%). Glycemia distribution among the 221 patients > 65 years old were euglycemia (31.7%), mild (36.7%), moderate (15.3%) and severe (16.3%) [χ^2 p = < 0.005].

We found APACHE II score, presence of invasive mechanical ventilation, hypoalbuminemia, lactic acidemia, and LODS score (initial and worst) are associated with increased hospital mortality. Glycemia on ICU admission was not associated with hospital mortality by univariate analysis (Table 3). As glycemia had a skewed distribution, stratification was performed to identify subsets—or trend effects—in the outcome of interest. Hypoalbuminemia and lactic acidemia were also analyzed and, as their effects may not be linearly distributed, stratification was carried out as described (Table 4).

We evaluated the relationship between age and glucose with hospital mortality. An interaction product ([age × glucose]/100) was univariate analyzed as a continuous variable. We found it to be associated (mean ± SD) with hospital mortality: alive, 68.4 ± 34.3; dead, 73.8 ± 38.3 (p = 0.035). Age ≥ 65 years showed a "trend" to significance by univariate analysis (p = 0.06), but age or interaction factor value as an independent predictor, however, were lost with multivariate adjustment. We also constructed an additional stratum of glycemia values in our population (> 280 to 600 mg/dL) and found 81 patients in this subgroup with a mean glycemia of 355.7 ± 82 (62 subjects were < 65 years old). In this subgroup, 62 patients (76.5%) survived and 19 patients died (23.5%), a nonsignificant statistical difference with the other glycemia strata (p = 0.46). In the < 65-year-old group, 47 of 62 patients (75.8%) survived vs 15 of 19 patients (78.9%) in the > 65-year-old group (p = 0.98). Given the limited subgroup events (deaths), the relationship of age/glucose strata and the additional glycemia strata were considered exploratory and were not included in the final multivariate model, as they do not provide robust estimates.

Multivariate analysis revealed that APACHE II score-derived severity of illness, presence of invasive mechanical ventilation, severe hypoalbuminemia, and severe lactic acidemia to be independently associated with hospital mortality; however, the highest glucose value during the first 24 h of MICU admission was not (Fig 1), with a log-likelihood reduction of < 1%. The final model was the most plausible construct with the lowest log-likelihood (from – 457.3 to – 116.2) and included five predictor variables (Table 5).

Table 3—*Univariate Analysis for Hospital Survival (ICU-Admitted Patients)

Characteristics	Survived (n = 945)	Deceased (n = 240)	p Value
Age, yr	48.8 ± 16.3	51 ± 17.8	0.06
Gender			
Male	534	130	
Female	411	110	0.51
Race			
African-American	741	196	
White	192	39	
Hispanic	4	1	
Asian	8	4	0.37
Mechanical ventilation			
Yes	398	196	
No	546	44	< 0.0001
Glucose, mg/dL	137.9 ± 42.6	143.1 ± 47.6	0.09
Albumin, g/dL	2.79 ± 0.85	2.23 ± 0.89	< 0.0001
Lactic acid, mmol/L	2.52 ± 2.1	6.11 ± 6	< 0.0001
APACHE II score (median)	15.8 (15)	27.4 (26)	< 0.0001
APACHE II predicted mortality, % (median)	24 (17)	59 (61)	< 0.0001
TISS score (median)	26.7 (26)	35.4 (36)	< 0.0001
Initial LODS score (median)	4.4 (4)	9.7 (9)	< 0.0001
Worst LODS score (median)	5.5 (5)	14.1 (15)	< 0.0001
ICU LOS, d	5.95 ± 7.2	6.9 ± 9.2	0.08
Duration of mechanical ventilation, d	6.14 ± 7.9	6.04 ± 8.12	0.88

*Data are presented as mean ± SD or % unless otherwise indicated.

Discussion

We found the APACHE II score-derived severity of illness, use of invasive mechanical ventilation, severe hypoalbuminemia, and severe lactic acidemia to be independent predictors of hospital mortality.[25–29,37] The highest blood glucose value during the first 24 h of admission to our MICU was not an independent predictor of hospital mortality.

In 2001, a large prospective, randomized controlled trial[17] from Leuven showed that near normalization of blood glucose using an intensive insulin protocol improved clinical outcomes in patients admitted to a SICU with an APACHE II score median of 9 (interquartile range, 7 to 13). In that study,[17] insulin was administered to maintain blood glucose levels from 80 to 110 mg/dL. This intervention reduced ICU mortality by 42% (number needed to treat of 10 patients in the subgroup with prolonged

Table 4—*Patient Characteristics by Albumin, Lactic Acid, Glucose Strata, and Hospital Mortality*

Stratified Variables	Mean ± SD (Median)	Survived, No. (%)	Deceased, No. (%)	p Value
Hypoalbuminemia (n = 867)				0.0001
None, ≥ 3 g/dL	3.6 ± 0.4 (3.5)	303 (89.4)	36 (10.6)	
Mild, < 3 but ≥ 2 g/dL	2.4 ± 0.3 (2.4)	259 (80.2)	64 (19.8)	
Severe, < 2 g/dL	1.5 ± 0.3 (1.6)	127 (61.9)	78 (38.1)	
Lactic acidemia (n = 319)				< 0.0001
None, < 2 mmol/L	1.28 ± 0.4 (1.3)	126 (87.5)	18 (12.5)	
Mild, ≥ 2 to < 8 mmol/L	3.55 ± 1.43 (3.1)	107 (74.3)	37 (25.7)	
Severe, ≤ 8 mmol/L	12.7 ± 5.8 (10.3)	7 (22.6)	24 (77.4)	
Hyperglycemia (n = 1,185)				0.24
Euglycemia, < 120 mg/dL	101.9 ± 10.5 (103)	395 (80.9)	93 (19.1)	
Mild, 120 to 159 mg/dL	137.1 ± 11.3 (136)	320 (81.2)	74 (18.8)	
Moderate, 160 to 199 mg/dL	176.2 ± 11.3 (174)	130 (77.4)	38 (22.6)	
Severe, 200 to < 280 mg/dL	231.6 ± 22.8 (228)	100 (74.1)	35 (25.9)	

SICU LOS, 29 patients for the overall trial) and reduced the risk of multiorgan failure, systemic infections, incidence of acute renal failure, blood transfusions, and need for prolonged mechanical ventilatory support.[17] Interventional studies[13–15,38–40] in the setting of acute coronary events and cardiac surgery have been associated with reduced mortality and with a significant reduction in deep sternal wound infections. Based in these observational and interventional studies[6,17,18,41–43] in selected populations, aggressive control of blood glucose is recommended for patients with critical illness.

Differences between our observational cohort (effectiveness study) and the results from previous efficacy studies can be explained by the fact that our patient population included inner-city, nonsurgical patients admitted to an MICU with higher APACHE II score and rates of established infections (Tables 1,

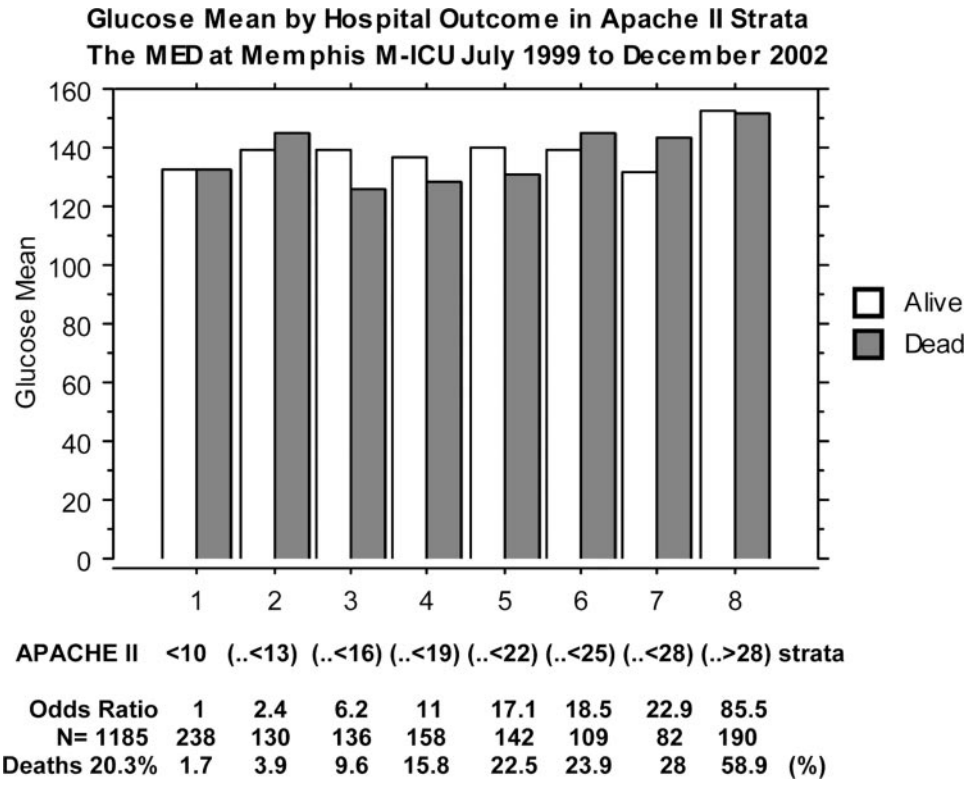

FIGURE 1. Glucose mean by hospital outcome in APACHE II strata. The MED = The Regional Medical Center, Memphis, TN.

Table 5—*Multiple Logistic Regression Analysis of Predictors of Hospital Mortality*

Associated Variables	Coefficient	SE	χ^2	p Value	OR (95% Confidence Interval)
Constant	− 4.038	0.61			
APACHE II score/per point	0.062	0.22	7.57	0.0059	1.06 (1.02–1.11)
Received mechanical ventilation	1.12	0.42	7.07	0.0079	3.06 (1.34–6.96)
Hypoalbuminemia					
Mild, < 3 but ≥ 2 g/dL	0.424	0.424	1.001	0.3171	1.53 (0.7–3.5)
Severe, < 2 g/dL	1.090	0.438	6.196	0.0128	2.98 (1.3–7.02)
Lactic acid					
Mild ≥ 2 < 8 mmol/L	0.41	0.38	1.16	0.28	1.5 (0.7—3.2)
Severe ≥ 8 mmol/L	1.99	0.63	10.05	0.0015	7.3 (2.14—24.9)
Hyperglycemia					
Mild, 120 to 159 mg/dL	− 0.25	0.41	0.37	0.54	0.78 (0.35–1.75)
Moderate, 160 to 199 mg/dL	0.17	0.47	0.13	0.72	1.18 (0.48–2.95)
Severe, 200 to 280 mg/dL	− 0.17	0.53	0.1	0.75	0.9 (0.3–2.4)

2). Furthermore, we analyzed hospital mortality, rather than ICU mortality, as the primary outcome. In addition, patients in our MICU are younger and had a significant shorter hospital LOS compared to those reported in the surgical ICU setting. The mean age of our patients was 49 ± 16 years, which is much younger than the previously reported, approximately 60 years in patients admitted to surgical or coronary care units. As ours is a younger population, the vascular complications in critical territories (*eg*, cerebral, cardiac, renal) may not have yet fully developed, which may further explain the differences seen with studies that observe an older population with different ICU-related problems (post-CABG, stroke, myocardial infarction).[11,13,16,38] Our short ICU LOS of 6.2 ± 7.7 days may have prevented us from detecting effects seen in patients with a longer LOS in the SICU. Thus, our findings do not contradict the findings of the Leuven group[17] but rather complements their concepts by providing a perspective of a population with different characteristic using an effectiveness study design. In the study[17] from Leuven, the maximal beneficial effect on mortality and complications were observed in patients with LOS > 5 days.

Although hyperglycemia is a frequent—almost universal—transient, stress-related finding in patients admitted to the ICU, the preponderance of these reports have set off intensivists toward early, tight-insulin-hyperglycemia control without a complete understanding of when (threshold), in whom (population), and how early (timing), this intervention should be started.[19,44–49] Such type of an approach will undoubtedly expose patients to the risk of hypoglycemia (as reported by Goldberg et al[50] in 12 of 52 patients [23%] for glycemia levels < 60 mg/dL; number needed to induce this glycemia level, 5 patients; 3 of 52 patients [5.8%] for levels < 40 mg/dL; number needed to induce this glycemia level, 18 patients]), difficult to recognize in a noncommunicative, sedated patients receiving mechanical ventilation.[17,51]

Insulin is an anti-inflammatory anabolic hormone that favorably affects sepsis mechanisms (suppresses tumor necrosis factor-α, interleukin-6, enhance interleukin, inhibitory κB, and endothelial nitric oxide production).[44–49] Based on our data and observations from others,[18,41,52,53] it is likely that the persistence of hyperglycemia, rather than the isolated admission glycemic response, may be what is associated with undesirable hospital mortality. Krinsley[18] reported a mortality benefit in an observational study with insulin-glycemia control in an MICU population that was older than ours with sustained hyperglycemia. It is likely that hyperglycemia secondary to a sustained inflammatory state—reflective of insulin resistance, not the insulin amount used—identifies patients at higher risk for septic-infectious complications and hospital mortality.[18,41,52–54]

Observational studies report experienced associations from different perspectives (populations), the truth being the integration of all those views. We previously reported that among 1,886 consecutive patients admitted to a community teaching hospital, 38% had hyperglycemia as defined at hospital admission, or in-hospital fasting glucose levels > 126 mg/dL (7 mmol/L), or two or more random glucose levels > 200 mg/dL (11.1 mmol/L). Patients with stress or newly diagnosed hyperglycemia were associated with higher in-hospital mortality rate (16%) compared to those patients with a history of diabetes (3%) or subjects with normoglycemia (1.7%).[6] The present study differs from our earlier study primarily on the definition of hyperglycemia as well as the cohort age and clinical acuity of illness. Furthermore, the present study is based on hyperglycemia present on initial (first-day highest) MICU admission day, whereas our earlier studies consisted of multiple

blood glucose determination during the entire hospital stay. A limitation of our study is our lack of information about the duration of diabetes or glycosylated hemoglobin A_1C on ICU admission, which may be an important confounder (associated with the variable of interest serum glucose and with the main outcome, *ie*, hospital mortality).[55] Other confounders not evaluated in this study were early enteral nutrition, use of glucocorticoids, and parenteral nutrition (rarely used in our ICU in the first 24 h), which are factors known to affect glucose levels in patients in the ICU. As such, our study is a descriptive evaluation of the effects on hospital mortality of admission hyperglycemia (first 24 h) adjusted by severity of illness and other cofactors. Ours is not an intervention trial to evaluate the benefits of insulin and/or glycemia control in the MICU.

Randomized clinical trials (randomized clinical trial/efficacy studies) are the "gold standard" for evaluating therapeutic interventions, as they prevent observer bias in controlled studies. The added effect of balancing confounders and providing comparable groups (good sample) is obtained 95% of the time (type I error 0.05). But observational studies in the ICU (effectiveness studies) are a powerful tool when total capture of the study population is achieved, as in our study; the universality provides the added effect of minimize observer bias (all information was equally collected, no intervention tested). They are robust estimates of established associations in real-world circumstances as they operate in the population base for the description. Care should be taken, however, in appreciating the population data set, source of the observations, to assess external validity and to prevent erroneous extrapolations. Our cohort included a young, inner-city, predominantly African-American MICU population, and our findings may not represent those of community hospitals with older patients, different comorbidities (myocardial infarction, strokes), and case-mix (SICU, post-CABG). In summary, hyperglycemia in the first 24 h of ICU admission did not predict hospital mortality in our predominantly young, African-American, inner-city MICU population.

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