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First plasma glucose value after urgent admission and in-hospital mortality in acutely decompensated heart failure

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ABSTRACT

Background: We used data from three <250-bed hospitals to test how plasma glucose (PG) values influenced in-hospital mortality (IHM) in acute heart failure in people without diabetes.
Methods and results: We identified 788 HF admissions (62% female; median age 83.3 years). 20.9% had chronic kidney disease, 7.7% cancer history, 24.7% acute renal failure and 29.7% concomitant infection. Mean first PG was 124.3 ± 32.4 mg/dl; 22.7% had stress hyperglycemia. Fifty-six people died (IHM = 7.1%). Women, older patients and people with infections showed higher PG values. People who died had higher PG values (136.3 ± 43.9 vs. 123.4 ± 31.2 mg/dl; $p = 0.029$). In a multivariate regression model with IHM as main outcome, the first PG (per mg/dl, odds ratio (OR): 1.01 [1.00–1.02]; $p = 0.045$), age (per year, OR: 1.06 [1.02–1.10]; $p = 0.003$) and acute renal failure (OR: 0.42 [0.24–0.74]; $p = 0.003$) remained significantly associated with IHM.
Conclusions: The first PG value predicted IHM in participants without diabetes after admission for heart failure.

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Background

The prevalence of hyperglycemia has been reported to be as high as 44% in the elderly patients hospitalized for heart failure.[1] Hyperglycemia leads to generation of reactive oxygen species, lipid peroxidation, cardiac myocyte death, nitric oxide suppression and increased risk of infection.[2]

For cardiovascular acute conditions other than heart failure, some authors have reported worse outcomes associated with higher plasma glucose values; these conditions include acute myocardial infarction,[3] dilated cardiomyopathy[4] and others. Nevertheless, there is conflicting evidence on how hyperglycemia influences in-hospital mortality during an episode of acutely decompensated heart failure. Whereas some previous work found no significant effect on mortality on behalf of hyperglycemia,[1] other authors have claimed that admission blood glucose levels are independent predictors of in-hospital mortality in acute heart failure.[5–7]

Although differences in the methodology might help explain the apparently divergent results, the deleterious role of stress hyperglycemia could paradoxically turn more relevant in the non-diabetic patients.[8] Also, the effects might vary between critically and non-critically ill populations or for different admission diagnoses.[6,9] Actually, most studies included people with and without diabetes and mainly focused on cases in the intensive care unit. These and other limitations preclude drawing more robust conclusions in alternative settings, such as general internal medicine wards. Thus, our aim was to provide additional evidence on how plasma glucose at admission influences survival only for those people without diabetes who are admitted for acutely decompensated heart failure to general internal medicine wards.

Abbreviations: PG, plasma glucose; IHM, in-hospital mortality; ED, Emergency Department; HF, heart failure; OR, odds ratio; MBDS, minimum basic data set; ICD-9-CM, International Classification Diseases-Ninth Revision, Clinical Modification.

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Patients and methods

We conducted this retrospective, observational study using data from three <250-bed community Hospitals (Sureste, Henares and Infanta Cristina Hospitals) located in the South-Eastern region of Madrid. The administrative data used for this study was reported to the Spanish National Hospital Database (MBDS, Minimum Basic Data Set).[10] The MBDS allows to link administrative and coding data with results for laboratory variables. We analyzed the data collected between January 1, 2010 and December 31, 2012 (3-year time period) only for patients older than 18 years.

We chose disease criteria according to the International Classification Diseases-Ninth Revision, Clinical Modification (ICD-9-CM),[11] which is used in the Spanish MBDS. We selected all diagnostic admissions of patients with heart failure (ICD-9-CM codes, 428.x, 402.01, 402.11, 402.91, 512), identified based on the first diagnosis field. We excluded those patients coded for acute myocardial infarction (ICD-9-CM codes 410.x).

We focused on the first plasma glucose value in the population without diabetes hospitalized for decompensated heart failure. To appropriately exclude people with diabetes, we firstly sought the ICD-9-CM diagnoses codes at discharge 249.x and 250.0–250.3. For a better ascertainment of the non-diabetes status, we removed all the cases who had a previous or current HbA1C determination over 6.5% (≈3% of the sample) and further thoroughly reviewed in a blinded way the medical charts of those participants with first plasma glucose values below 75 mg/dl or over 160 mg/dl; this way, we excluded other 24% of the cases. To evaluate the degree of misclassification of the diabetes status, we randomly selected two samples, each of them including 10% of the people whose first plasma glucose values at the Emergency Department were found to be in the range of 75–160 mg/dl; after reviewing these medical charts, we concluded that the probability of having true non-coded diabetes was less than 4% in both evaluations according to standard diabetes definitions. It was quite reassuring that all these patients with no formerly identified diabetes were milder cases, who were being treated with diet alone or diet plus metformin.

As covariates, we included any infection diagnosis (ICD-9-CM codes: 038, sepsis; 041, bacterial infection; 480.x–488.x, pneumonia and influenza; 590.x, 599.x and 601.x, urinary tract infection; 680.x–686.x, skin infections; 707.x, skin pressure ulcers); current or previous history of neoplasm (ICD-9-CM codes 140.x–239.x); acute renal failure (ICD-9-CM codes 584.x); and chronic kidney disease (ICD-9-CM codes 585.x).

The outcome of interest was in-hospital mortality, defined as the proportion of patients who died during admission.

Statistical analyses

We analyzed the association between first plasma glucose values and the other variables using non-parametric statistical tests (Mann–Whitney's *U* test) due to the non-Gaussian distribution of glucose values (as shown by Kolmogorov–Smirnov and Levene tests). We additionally studied the association between categorically distributed plasma glucose values and in-hospital mortality with a survival analysis and log-rank test.

We next evaluated the univariate associations between plasma glucose values and other potential confounding variables with in-hospital mortality. We then ran logistic regression analyses, using in-hospital mortality as a binary outcome, adding those factors that could potentially confound the association between plasma glucose and in-hospital mortality into the model, such as sex, age, a simultaneous diagnosis of infection, chronic kidney disease, acute renal failure and neoplasm history. In sensitivity analyses, we tested age (below vs. over median age) and plasma glucose values (distributed in tertiles) as categorical variables. We used SPSS software (Version 15.0, released 2006. Chicago, SPSS Inc.). We set nominal statistical significance at $p < 0.05$ (2-tailed).

Ethical aspects

We maintained data confidentiality at all times. The Ethics and Research Committee at the Hospital del Sureste approved the study protocol.

Results

We screened a total number of 12,632 admissions, of which 1478 were admitted for heart failure as the first diagnosis code (11.7%). After excluding 690 diabetes cases (46.7%), we analyzed 788 heart failure admissions (53.3%) in people without diabetes over a 3-year time period (Table 1). Women comprised over 62% of the study population and median age was 83.3 years old (interquartile range 76.9–88.0).

The mean first in-hospital plasma glucose value was 124.3 ± 32.4 mg/dl. We detected stress hyperglycemia (plasma glucose value over 140 mg/dl) in 22.7% of the cases ($N = 179$). On average, women showed higher plasma glucose values, 125.8 ± 32.6 vs. 121.9 ± 31.9 mg/dl (Table 2). People aged older than the median had higher plasma glucose values (128.6 ± 34.7 mg/dl vs. 120.3 ± 29.6). Also, patients who were coded for a diagnosis of infection had higher plasma glucose values (130.4 ± 35.4 vs. 121.7 ± 30.7 mg/dl).

Table 1
Differential characteristics of people without diabetes admitted for heart failure to the participating hospitals, 2010–2012.

	Sureste Hospital ($N = 273$)	Henares Hospital ($N = 285$)	Infanta Cristina Hospital ($N = 230$)	All hospitals combined ($N = 788$)
Female sex, *N* (%)	177 (64.8)	178 (62.5)	139 (60.4)	494 (62.7)
Age in years, median (IQR[a])	84.9 (79.9–88.1)	82.0 (75.5–87.0)	82.7 (74.4–88.3)	83.3 (76.9–88.0)
Chronic kidney disease, N (%)	55 (20.1)	66 (23.2)	44 (19.1)	165 (20.9)
Acute renal failure, *N* (%)	53 (19.4)	80 (28.1)	62 (27.0)	195 (24.7)
Cancer history, *N* (%)	16 (5.9)	16 (5.6)	20 (8.7)	61 (7.7)
Any diagnosis of infection, *N* (%)	68 (24.9)	123 (43.2)	43 (18.7)	234 (29.7)
Mean first glucose value, mg/dl (SD[b])	123.6 (28.0)	126.0 (35.6)	123.1 (33.1)	124.3 (32.4)
Length of hospital stay in days, median (IQR)	6.0 (5.0–10.0)	8.0 (6.0–12.0)	5.0 (3.0–8.0)	7.0 (5.0–10.0)
30-day readmission, *N* (%)	16 (5.9)	46 (16.1)	20 (8.7)	82 (10.4)
180-day readmission, *N* (%)	47 (17.2)	88 (30.9)	28 (12.2)	163 (20.7)
In-hospital mortality, *N* (%)	19 (7.0)	16 (5.6)	21 (9.1)	56 (7.1)

[a] IQR: interquartile range.
[b] SD: standard deviation.

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