Highest In-Hospital Glucose Measurements are Associated With Neurological Outcomes After Intracerebral Hemorrhage

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Background and Purpose: The relationship between in-hospital hyperglycemia and neurological outcome after intracerebral hemorrhage (ICH) is not well studied. *Methods:* We analyzed the relationships between pre-hospital and hospital variables including highest in-hospital glucose (HIHGLC) and discharge Glasgow Coma Scale (GCS), discharge Modified Rankin Scale (MRS) and 3-month MRS using a single-institution cohort of ICH patients between 2013 and 2015. *Results:* There were 106 patients in our sample. Mean HIHGLC was 154 ± 58 mg/dL for patients with discharge GCS of 15 and 180 ± 57 mg/dL for patients with GCS < 15; 146 ± 55 mg/dL for patients with discharge MRS 0-3 and 175 ± 58 mg/dL for patients with discharge MRS 4-6; and 149 ± 52 mg/dL for patients with 3-month MRS of 0-3 and 166 ± 61 mg/dL for patients with 3-month MRS of 4-6. On univariate analysis, discharge GCS was associated with HIHGLC ($P = .01$), age ($P = .006$), ICH volume ($P = .008$), and length of stay (LOS) ($P = .01$); discharge MRS was associated with HIHGLC ($P < .001$), age ($P < .001$), premorbid MRS ($P = .046$), ICH volume ($P < .001$), and LOS ($P < .001$); and 3-month MRS was associated with HIHGLC ($P = .006$), discharge MRS ($P < .001$), age ($P = .001$), sex ($P = .002$), ICH volume ($P = .03$), and length of stay ($P = .004$). On multivariate analysis, discharge GCS only had a significant relationship with ICH volume (odds ratio [OR] .949, .927-.971); discharge MRS had a significant relationship with age (OR 1.043, 1.009-1.079), premorbid MRS (OR 2.622, 1.144-6.011), and ICH volume (OR 1.047, 1.003-1.093); and 3-month MRS only had a significant relationship with age (OR 1.039, 1.010-1.069). *Conclusions:* The relationship between in-hospital hyperglycemia and neurological outcomes in ICH patients was meaningful on univariate, but not multivariate, analysis. Glucose control after ICH is important.

Search terms: Intracerebral hemorrhage—glucose—hyperglycemia—outcome

Introduction

Intracerebral hemorrhage (ICH) constitutes 10%-15% of strokes, with an incidence of 24.6 per 100,000 person years and a median fatality of 40% at 1 year.[1] Between 13% and 39% of patients are able to live independently 6 months after ICH[1] and 75%-80% of patients with ICH have permanent neurologic deficits.[2] As has been noted for the ischemic stroke population,[3,4] admission blood glucose in patients with ICH has been found to correlate with short-term[5-8] and long-term mortality[9-11] and 3-month Modified Rankin Scale (MRS).[12,13]

While admission blood glucose cannot be modified, in-hospital glucose can be controlled. Despite this, few studies have examined the relationship between in-hospital

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blood glucose and functional outcome in patients with ICH. Koga et al reported that higher blood glucose 24 and 72 hours after admission was associated with worse neurological outcome 3 months after ICH.[14] Qureshi et al showed that increasing blood glucose during the initial 72 hours after ICH was associated with worse neurological outcome at 3 months.[15] Wu et al found that increased variability of blood glucose over the first 7 days of hospital admission after ICH is associated with worse neurological outcome at 30 days.[16]

We sought to expand on the existing literature by examining the association of highest blood glucose during the entire hospital course (highest in-hospital glucose [HIHGLC]) and neurological outcome at discharge and 3 months after ICH. Identifying the relationship between HIHGLC and neurological outcome is important both to (1) provide more insight into the robustness of the relationship between blood glucose and outcome and (2) elucidate a potential in-hospital opportunity for intervention to improve outcome after ICH.

Methods

Patient Management

Patients admitted to our institution with ICH are managed according to our institutional ICH clinical guideline (see Appendix 1). Blood glucose is measured every 6 hours and subcutaneous insulin is administered as needed to target blood glucose of 100-180 mg/dL. If a patient has > 2 consecutive blood sugars of > 180 mg/dL, evidence of diabetic ketoacidosis, or hyperglycemic hyperosmolar nonketosis, use of an insulin drip is considered.

Data Collection

Data were extracted from Neurological Emergencies Outcomes at NYU, a combined retrospective (2013-2014) and prospective (2015) database that includes data on demographics, vital signs, labs, procedures, imaging results, and the clinical status of acute neurology patients at our institution. Patients with ICH who were admitted before November 2015 were included in this analysis. Three-month MRS was determined for prospective patients via telephone using the MRS structured interview.[17] Three-month MRS for retrospective patients and patients who could not be reached by telephone was determined through chart review by board-certified, MRS-trained neurologists. This project was approved by the institutional review board at NYU Langone Medical Center.

Statistics

Data were analyzed using SPSS Statistics 21 and MATLAB R2014b. Variables included in the analyses were age, sex, history of diabetes, premorbid MRS, highest in-hospital glucose (HIHGLC), ICH volume, intraventricular hemorrhage (IVH), ICH location, and length of stay in the hospital (LOS). Outcomes included discharge Glasgow Coma Scale (GCS), discharge MRS, and MRS 3 months after admission. Spearman correlations, Chi square tests, likelihood ratios, and Mann-Whitney U tests were used as appropriate for univariate analysis to assess the relationship between prehospital and hospital factors and outcome. A P value $< .05$ was considered to be statistically significant. Parameters that were significant on univariate analysis were included in multivariate regression analysis.

Results

Patients

There were 106 ICH patients in our sample, 83 (78%) of whom were entered into the database retrospectively and 23 (22%) of whom were entered into the database prospectively. See Table 1 for demographic data and Fig 1 for the breakdown of bleed etiology. The peak in-hospital glucose (HIHGLC) occurred on admission for only 33 patients (31%) and sometime after admission for 73 patients (69%). The mean HIHGLC was 165 ± 58 mg/dL. There were 18 patients (17%) with a history of diabetes and 6 (6%) who required an insulin drip for acute glycemic control. The 99 patients (93%) discharged alive had a median GCS of 15 (IQR = 13-15), a median discharge MRS of 4 (IQR = 2-5) and a median 3-month MRS of 3 (IQR = 2-4). Of the 22 prospective patients, contact was made with 14 (64%) for the 3-month MRS telephone interview. Of the 85 remaining patients, 69 (81%) were seen in our institution after discharge and their 3-month MRS was extrapolated based on data from the visit closest to

Table 1. *Characteristics of patient population*

Characteristic	Value
Number of patients	106
Male (%)	54 (51%)
Age, mean ± std. (years)	62 ± 19
History of diabetes, number (%)	18 (17%)
Premorbid MRS, median (IQR)	0 (0-1)
Admission GCS, median (IQR)	14 (11-15)
Admission NIHSS, median (IQR)	6 (2-15)
ICH Volume, mean ± std. (mm^3)	24 ± 21
Intraventicular hemorrhage, number %	40 (38%)
Highest in-hospital glucose, mean ± std. (mg/dL)	165 ± 58
Insulin drip required, number (%)	6 (6%)
Hospital Length of Stay, mean ± std. (days)	10 ± 8
Discharge GCS, median (IQR)	15 (13-15)
Discharge MRS, median (IQR)	4 (2-5)
3-month MRS, median (IQR)	3 (2-4)

IQR, interquartile range; ICH, intracerebral hemorrhage; GCS, Glasgow Coma Scale; MRS, modified Rankin Scale; NIHSS, NIH Stroke Scale; std., standard deviation.