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Relationship between glycemic control and readmission rates in patients hospitalized with congestive heart failure during the implementation of hospital-wide initiatives

Kathleen M Dungan, MD[1], **Kwame Osei, MD**[1], **Haikady N Nagaraja, PhD**[2], **Dara Schuster, MD**[1], and **Philip Binkley, MD, MPH**[3]

[1]The Ohio State University Division of Endocrinology, Diabetes & Metabolism

[2]The Ohio State University Department of Statistics

[3]The Ohio State University Division of Cardiovascular Medicine and the Dorothy M. Davis Heart and Lung Research Institute

Abstract

Objective—To determine the relationship between inpatient glycemic control and hospital readmission in patients with congestive heart failure (CHF).

Methods—We used an electronic data collection tool to identify patients with a discharge diagnosis of CHF who underwent point-of-care glucose assessments. Time-weighted mean glucose (TWMG), HbA1c, and glycemic lability index (GLI) served as glycemic indicators, and readmission for CHF was determined at 30 and 30-90 days.

Results—748 patients were included in the analysis. After adjustment for significant covariates, increasing TWMG (OR 3.3, p=0.03) and HbA1c (OR 5.5, p=0.04) were independently associated with higher readmission for CHF at 30-90 days, but not at 30 days. Renal disease, African American race, and year of hospital admission were also significantly associated with readmission, but GLI was not. There was no difference in TWMG when analyzed according to race or renal status. There was a decrease in TWMG (p=0.004) and a trend for reduction in 30-90 day readmission rates (p=0.06) following hospital-wide interventions to improve glycemic control, but no difference in GLI or hypoglycemia.

Conclusions—Increasing glucose exposure, but not glycemic variability was associated with higher risk of 30-90 day CHF readmission. Prospective studies are needed to confirm or refute these results.

Keywords

diabetes; glucose; rehospitalization

INTRODUCTION

Mixed results from randomized controlled trials in the ICU (1-3) have triggered appeals for focused efforts to identify patient populations and disease states that are at increased risk of

Corresponding author: Kathleen M. Dungan, MD The Ohio State University Division of Endocrinology, Diabetes, and Metabolism 4th Floor McCampbell Hall 1581 Dodd Drive Columbus, OH 43210-1296 Phone (615)292-3800 Fax (614)292-1550 Kathleen.dungan@osumc.edu.

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hyperglycemia-mediated harm.(4) A large retrospective study demonstrated that the magnitude of the relationship between hyperglycemia and mortality is dependent upon the admission diagnosis, with cardiac patients generally showing the highest risk.(5) In the case of congestive heart failure (CHF), the relationship between in-hospital glycemic control and outcomes has been less well-defined.(6,7)

CHF poses an enormous medical, societal and financial burden in the U.S.,(8) and over 40% of patients with CHF have diabetes as a discharge diagnosis.(9) CHF is a common cause of hospital readmission, and the Medicare Payment Advisory Commission has recently recommended reduced reimbursement rates for patients having early rehospitalizations for CHF.(10) A systematic review reported inconsistencies in the literature regarding patient characteristics that predict readmission, such as history of diabetes.(11) In a large retrospective analysis of hospitalized CHF patients, diabetes was associated with increased readmission rates.(12) However, it is unclear whether this is due to glycemic control.

In the present study, we used a computerized data collection tool to determine whether measures of inpatient glycemic control are related to readmission rates in patients hospitalized with CHF. In addition, recent studies have identified an association between glycemic variability (GV) and ICU mortality,(13-14) and we examined whether GV is related to readmission rates in CHF patients. Finally, we investigated whether outcomes changed during the implementation of hospital-wide inpatient diabetes initiatives.

METHODS

Hospital admissions between January 1, 2005 and December 31, 2006 were searched using the Ohio State University's Information Warehouse, a computerized data analysis tool that validates, cleanses, and de-identifies patient information incorporated from multiple electronic sources. Patients with a primary discharge diagnosis of congestive heart failure (defined as an ICD-9 code of 428.0) were identified (N=1144). Only patients having a hospital LOS of less than 60 days and at least 2 point-of care (POC) glucose values in a given day were included in the final analysis. The purpose of this criterion was to capture a more clinically relevant population (only patients with known or suspected diabetes generally undergo bedside glucose monitoring). This criterion would also ensure that a minimum amount of data would be available for calculation of glycemic variability. Data collection and analysis from the Information Warehouse was approved by the Ohio State University's Institutional Review Board.

Glycemic Variables

The primary glucose variables of interest were total time weighted mean glucose (TWMG), calculated as the area under the curve for glucose using the trapezoidal rule divided by the total time in hours, and glucose lability index (GLI), also corrected for time. Time-weighting was performed because the interval between glucose measurements was non-uniform; time-weighting has been described previously.(3) Serum glucose values were excluded in order to maintain homogeneity in glucose methodology.(15)

GLI is a measure of glucose variability, determined by the sum of the square of the difference between successive glucose measurements divided by the difference in time between measurements:(16)

$$LI = \sum_{n=1}^{N} \frac{(BG_n - BG_{n+1})^2}{h_{n+1} - h_n}$$

GLI was chosen for this study due to its ease of use, ability to correct for heterogeneity in timing of glucose measurements, reflection of rapidity (as opposed to solely the magnitude) of glucose swings, and previous association with hospital outcomes that was superior to other measures of glycemic variability.(17)

Hypoglycemia was defined as proportion of patients with any BG <70 mg/dL, and Hemoglobin A1C (HbA1c) was available for a subset of patients.

Clinical Variables

The primary clinical outcome was readmission with CHF as the primary diagnosis code. Readmission was reported as the percentage of patients requiring readmission early (30 days) or between 30-90 days. Patients with less than 30 or 90 day readmission data were excluded from the 30 or 30-90 day analysis respectively. For patients with multiple admissions during the time period, glucose values were analyzed only for the index admission.

Secondary clinical variables included demographics (age, gender, race), and relevant comorbidities (determined using the top 3 diagnosis codes). An assessment of left ventricular ejection fraction (EF) was available for a subset of patients.

Analysis

Continuous variables are reported as mean +/− standard deviation (SD), with the exception of GLI, which was reported as median and interquartile range (IQR). Dichotomous variables are reported as sums and percentages. Continuous variables were compared using independent t-test and Fisher's exact test was utilized for the dichotomous variables. GLI was compared using the Wilcoxon rank-sum. Stepwise multiple logistic regression analyses were performed using 30-90 day readmission as the dependent variable and race, year of admission, discharge diagnosis of renal disease (ICD-9 codes 250.4, 403.x, 404.x, 584.x, 585.x, V45.1), and either TWMG or HbA1c as independent variables. The choice of dependent variables was based upon associations with readmission in univariable analysis. Odds ratios are reported as change in odds per unit for continuous variables and per category for dichotomous variables. TWMG and HbA1c were log-transformed to provide better dispersion of the data. Analyses were performed using JMP 6.0 software.

Our institution has implemented hospital-wide inpatient glycemic control initiatives, beginning in January of 2006, including practice guidelines, computerized order sets, a universal insulin drip guideline, prandial insulin based on carbohydrate intake, and hospital-wide education. Therefore, we further evaluated results by year of admission.

RESULTS

A total of 748 patients and 9,236 glucose measurements (mean 12.3 per patient) were included in the final analysis. The overall frequency of glucose monitoring was variable, with 94% having at least 1 reading/day but only 11% with >3 reading/day when averaged over the entire hospital stay. A summary of demographics and clinical information is detailed in table 1. The mean glucose was 137+/−44.7 mg/dL, and 34.9% of patients experienced hypoglycemia (BG <70 mg/dl). However, the frequency of hypoglycemia was 4.1% of all measurements, 80% of which were >50 mg/dl. Eleven percent of patients had diabetes listed as a second or third diagnosis code (250.x). Readmission by 30 and between 30-90 days occurred in 53 (7.4%) and 36 (4.7%) of patients respectively.

Readmission

TWMG and HbA1c were similar in patients that were or were not readmitted at 30 days (table 2). None of the other dependent variables were significantly associated with 30-day readmission. In patients that were readmitted between 30 and 90 days, TWMG was slightly higher than in those that were not readmitted (162 +/− 77.4 vs. to 137 +/−42.5 mg/dl), although this was not statistically significant (p=0.06). HbA1c was 8.3+/− 2.4 in patients readmitted between 30-90 days, compared to 7.5 +/− 1.9% in those who were not (p=0.09). Patients who were readmitted between 30 and 90 days were more likely to be AAs (58 vs. 39%, p=0.02) and have a billing code for renal disease (42% vs. 25%, p=0.02). TWMG did not differ between AAs and Caucasians (140 +/− 52 mg/dl vs. 136 +/− 39 mg/dl respectively, p=0.23) or between those who did or did not have renal disease (135 +/− 50 mg/dl vs. 138 +/−43 mg/dl respectively, p=0.53). Other comorbidities identified by hospital billing codes (table 1) were not associated with readmission (data not shown).

Since there were no significant univariable associations for 30 day readmission, stepwise logistic regression was performed for the 30-90 day readmission interval only. In the initial logistic regression model containing TWMG, it was determined that admission in 2005, renal disease and higher log-transformed TWMG were associated with significantly higher readmission rates (table 3). In the final model, the OR for log-transformed TWMG was 3.3 (p=0.03). In the model that contained HbA1c, admission in 2005, renal disease, AA race, and log-transformed HbA1c (OR 5.5, p=0.04) were all significant predictors.

Effect of Year of Admission

Following hospital-wide interventions that were implemented beginning in early 2006, there was a decrease in TWMG (from 142 +/−47 to 133 +/− 42 mg/dL, p=0.004, table 4). There was no difference in frequency of glucose monitoring, mortality, GLI, HbA1c, or rate of hypoglycemia. The mean EF was lower in 2006 compared to 2005 (28.7% vs. 34.7%, p=0.001). In addition, there was a nonsignificant reduction in 30-90 day readmission (7.1% to 3.5% from 2005 to 2006, p=0.06) but no difference in 30 day readmission.

DISCUSSION

The present study demonstrates that increased TWMG and HbA1c are associated with intermediate (30-90 days), but not short-term (<30 day) CHF readmission rates after adjustment for other important variables (table 4). This relationship was observed despite otherwise acceptable glycemic control.(18) It is possible that inpatient glycemic control is simply a surrogate for long-term glycemia (as determined by HbA1c), particularly since short-term readmission rates were unrelated to glycemia. Whether one concludes that inpatient or outpatient glycemic control is partly responsible for increased readmission rates, it is reasonable to assume that successful achievement of glycemic control in the hospital may facilitate sustained glycemic control post-discharge. Therefore, achievement of glycemic control is desirable regardless of the setting. However, prospective data are lacking in this regard. There was an estimated 2-fold increase in odds of readmission for every 1% increase in HbA1c. However, based on the data, we can not recommend a cut-off HbA1c for the individual patient since there is considerable overlap between those who were readmitted and those who were not readmitted. This highlights the importance of other contributing factors in addition to glycemic control.

Hyperglycemia is believed to play a role in the development of diabetic cardiomyopathy. (19) Limited evidence suggests that improvement in glycemic control may improve cardiac function by as early as 3 weeks, at least early in the disease (20). However, there are no data on patients with advanced CHF. Further, we identified no relationship between glycemic

control and early (30 day) readmission, suggesting that more time is required for a benefit, if any, to develop. Limited data from some (21,22), but not all (23), studies indicate that improved glycemic control is also associated with reduced readmission rates in unselected hospitalized patients, supporting a more generalized association with disease processes.

In contrast, our data do not show a relationship between glycemic variability (as measured by GLI) and CHF readmission rates. Other evidence (13,14) suggests that glycemic variability is associated with increased ICU mortality, a short-term outcome, but there are currently no studies that have reported the relationship between glycemic variability and hospital readmission. Of note, the frequency of capillary glucose assessments may have been insufficient to capture true glycemic variability.

Although the number of patients with a second or third diagnosis code for diabetes was lower than expected, the actual prevalence of diabetes is likely to be higher, because only patients with fingerstick glucose values were included in the analysis. Diagnosis codes for diabetes may be underrepresented in the hospital due to competing priorities for billing.(24) Identification of CHF using discharge diagnosis codes also underestimates the true prevalence, but the specificity is high.(25) Thus, the present sample likely truly represents patients who are hospitalized with heart failure. The role of renal disease (26) and race (27) in CHF rehospitalization is in agreement with other studies.

Finally, the data show that glycemic control improved over time in this study, without a significant increase in hypoglycemia. This was also associated with a trend for lower readmission rates. No systematic program specifically targeting CHF readmission rates was otherwise in place during the time of the study.

The major limitations of this study relate to its retrospective nature. We are unable to account for CHF readmissions to other hospitals, and a heterogeneous population with varying etiology of CHF and disease severity was included. Finally, there are no data regarding the details of interventions for heart failure or diabetes. Strengths of this study include the inclusion of all evaluable bedside glucose values as opposed to admission glucose only, and the time-weighted analysis, which accounts for heterogeneity in glucose sampling intervals. Finally, this is the first study to assess the relationship between inpatient glycemic control and CHF readmission rates. In summary, total glycemic exposure, but not glycemic variability, is related to higher intermediate-term CHF readmission rates. Prospective studies are needed to determine if patients with CHF would benefit from improved glycemic control.

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Table 1

Summary of Patient Characteristics

	Total (N=748)
Male	426 (57.0%)
Race	
Caucasian	438 (59.8%)
African American	295 (40.2%)
Age (mean years +/− SD)	65.8 +/−13.8
Ejection Fraction (%,mean +/−SD, N=360)	31.7 +/− 17.3
Readmission (30 day)	53 (7.4%)
Readmission (30-90 day)	36 (5.5%)
Expiration (Index hospitalization)	35 (4.7%)
Glycemic variable (mean +/− SD)	
TWMG (mg/dl)	137 +/−44.7
GLI $(mg/dl)^2/hr^*day^{-1}$	7.2 (2.4-19.3)
A1c (%, N=329)	7.58 +/− 1.96
Hypoglycemia (<70 mg/dl)	261 (34.9%)
Other Diagnosis Codes *	
Diabetes	83 (11%)
Renal disease	197 (26.3%)
Atrial arrhythmia	134 (17.9%)
Hypertension	109 (14.6%)
Valvular disorder	75 (10.0%)
CAD	67 (9.0%)
Pneumonia	46 (6.2%)
COPD	41 (5.5%)
AMI/ACS	38 (5.1%)

TWMG=time-weighted mean glucose, GLI=time-adjusted glycemic lability index.

* Second or third ICD-9 code groupings with a frequency ≥5%; ICD-9 codes: renal disease (250.4, 403.x, 404.x, 584.x, 585.x, V45.1), atrial arrhythmia (427.x), hypertension (401.x-403.x), diabetes mellitus (250.x), valvular disorder (396.x, 397.x, 424.x, 746.4, 996.02), Coronary artery disease (CAD, 396.x, 397.x 413.x, 414.x, 424.x, 746.4, 996.02), pneumonia (482.x, 486), Chronic obstructive lung disease with exacerbation (492.1), Acute myocardial infarction, acute coronary syndrome (AMI/ACS, 410.x, 411.x).

Table 2

Readmission

	Readmitted	Not Readmitted	p-value
30 Day			
Age	65.2 +/− 10.7	65.9 +/− 14.1	0.64
Gender (Male)	29 (55%)	375 (57%)	0.78
Race (African American)	28 (53%)	252 (39%)	0.06
TWMG	132 +/−33.5	138 +/− 45.8	0.18
GLI*	4.1 (1.8-13.6)	7.4 (2.5-20.3)	0.12
A1c	7.9 +/− 2.0	7.6 +/− 1.8	0.43
EF	28.1 +/− 17.1	32.6 +/− 17.5	0.18
Renal disease	16 (30%)	172 (26%)	0.52
Hypoglycemia	20 (35%)	232 (38%)	0.77
90 Day			
Age	62 +/− 12.7	66 +/− 13.9	0.08
Gender (Male)	20 (56%)	344 (56%)	>0.99
Race (African American)	21 (58%)	236 (39%)	0.02
TWMG	162 +/− 77.4	137 +/− 42.5	0.06
GLI*	12.3 (2.7-26.9)	6.8 (2.4-19.0)	0.12
HbA1c	8.3 +/− 2.4	7.5 +/− 1.9	0.09
Ejection fraction	35 +/− 19	32 +/− 17	0.48
Renal disease	15 (42%)	152 (25%)	0.02
Hypoglycemia	14 (39%)	217 (357%)	0.72

*Values reported as median (IQR) and differences analyzed using Wilcoxon Rank-sum; TWMG=time-weighted mean glucose, GLI=time-adjusted glycemic lability index

Table 3

Logistic Regression Model for Readmission at 30-90 day

	OR	P-Value
TWMG		
30-90 day (Initial Model)		
Year of Admission [2005 vs. 2006]	2.2	0.04
Renal disease	2.3	0.02
Log TWMG	3.1	0.03
Race (African American)	1.9	0.06
30-90 day (Final Model)		
Year of Admission [2005 vs. 2006]	2.2	0.04
Renal disease	2.5	0.01
Log TWMG	3.3	0.03
HbA1c		
30-90 day (Final Model)		
Year of Admission [2005 vs. 2006]	2.6	0.03
Renal disease	3.4	0.004
Log HbA1c	5.5	0.04
Race (African American)	2.3	0.049

TWMG=time-weighted mean glucose. OR for log HbA1c and log TWMG reported per unit change.

Table 4

Comparison of Glycemic Variables and Outcomes by Year

	2005	2006	P-value
Total	365	383	
TWMG (mg/dL) (+/− SD)	142 +/−47	133 +/− 42	0.004
GLI $(mg/dl)^2/hr*day_{-1}$) (median, IQR)	7.5 (2.4-21)	6.6 (2.3-17)	0.25
Hypoglycemia (N, %)	123 (34%)	138 (36%)	0.54
HbA1c (%, +/− SD)	7.7 +/− 1.9	7.5 +/− 2.0	0.29
Ejection fraction (%, +/− SD)	34.7 +/− 17.8	28.7 +/− 16.3	0.001
30-day Readmission (N, %)	30 (8.2%)	23 (6.6%)	0.48
30-90 day Readmission (N, %)	27 (7.1%)	10 (3.5%)	0.06
Mortality	17 (4.7%)	18 (4.7%)	>0.99

TWMG=time-weighted mean glucose, GLI=time-adjusted glycemic lability index