Association of Glucose Concentrations at Hospital Discharge With Readmissions and Mortality: A Nationwide Cohort Study

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Context: Low blood glucose concentrations during the discharge day may affect 30-day readmission and posthospital discharge mortality rates.

Objective: To investigate whether patients with diabetes and low glucose values during the last day of hospitalization are at increased risk of readmission or mortality.

Design and Outcomes: Minimum point of care glucose values were collected during the last 24 hours of hospitalization. We used adjusted rates of 30-day readmission rate, 30-, 90-, and 180-day mortality rates, and combined 30-day readmission/mortality rate to identify minimum glucose thresholds above which patients can be safely discharged.

Patients and Setting: Nationwide cohort study including 843,978 admissions of patients with diabetes at the Veteran Affairs hospitals 14 years.

Results: The rate ratios (RRs) increased progressively for all five outcomes as the minimum glucose concentrations progressively decreased below the 90 to 99 mg/dL category, compared with the 100 to 109 mg/dL category: 30-day readmission RR, 1.01 to 1.45; 30-day readmission/mortality RR, 1.01 to 1.71; 30-day mortality RR, 0.99 to 5.82; 90-day mortality RR, 1.01 to 2.40; 180-day mortality RR, 1.03 to 1.91. Patients with diabetes experienced greater 30-day readmission rates, 30-, 90- and 180-day postdischarge mortality rates, and higher combined 30-day readmission/mortality rates, with glucose levels <92.9 mg/dL, <45.2 mg/dL, 65.8 mg/dL, 67.3 mg/dL, and <87.2 mg/dL, respectively.

Conclusion: Patients with diabetes who had hypoglycemia or near-normal glucose values during the last day of hospitalization had higher rates of 30-day readmission and postdischarge mortality. **(*J Clin Endocrinol Metab* 104: 3679–3691, 2019)**

Reducing hospital readmissions is a high priority for quality health care. The Centers for Medicare and Medicaid Services Readmissions Reduction Program penalizes hospitals with excessive 30-day readmission rates (1). Compared with patients without diabetes mellitus (DM), patients with DM have 40% higher rehospitalization

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Abbreviations: BMI, body mass index; CHF, congestive heart failure; DM, diabetes mellitus; POC, point-of-care; RR, rate ratio; VA, Veterans Affairs.

rates, with 30-day readmission rates reported to range between 14% and 26% (2–14). Notably, almost 30% of them experience two or more readmissions per year (15). In 2012 (16) and in 2017 (17), the cost of hospitalizations for patients with DM in the United States was ~$123 billion. Assuming a 20% readmission rate, the cost of 30-day readmissions is estimated to be ~$25 billion (11).

Studies have identified risk factors for readmissions among patients with DM (2–6, 11, 18–20), although little is known about the effect of glycemic control and the readmission risk. Hyperglycemia at admission or 24 hours before admission (18) and hypoglycemia at any point of the hospital stay (20) have been associated with increased 30-day readmission rates. Inpatient hypoglycemia at any time of the hospital stay among patients with and without DM is also associated with higher postdischarge mortality (21). Several studies have reported that patients with DM have increased mortality compared with patients without DM (21–24). In a recently published study that included hospitalized patients with and without diabetes, hypoglycemia was associated with increased short- and long-term mortality (24).

Most of the published studies have focused on the effect of glucose control at admission or during the hospital stay. Limited information, if any, is available on whether low blood glucose concentration during the day of hospital discharge (*i.e.*, the last 24 hours of hospitalization)—a potentially modifiable factor—is associated with adverse clinical outcomes, such as 30-day readmission and postdischarge mortality. The final day of hospitalization represents a unique period during the inpatient stay, when medications adjustments almost have been finalized, patients are able to tolerate a full diet, minimizing nutritional interruptions and abnormalities in glucose control, and the underlying conditions that necessitated hospitalization have been treated.

The purposes of this study were to examine the association of minimum glucose values in patients with DM during the last 24 hours of hospital stay and the risk of 30-day readmission and postdischarge mortality, and, more importantly, to investigate whether there is a specific lower glucose value threshold above which patients with DM can be safely discharged from the hospital without experiencing increased risk for either readmission or death.

Methods

Study overview and data sources

This nationwide cohort study used data obtained from the Veterans Affairs (VA) health system detailing the clinical course and outcomes of patients with DM admitted from 1 January 2000 to 31 December 2014 (25). The study period ended in 2014, which was the last full year that *International Classification of Diseases, Ninth Revision*, codes were used. We obtained the data from the VA Central Data Warehouse, a comprehensive national administrative database containing VA clinical, pharmacy, and utilization files. The VA Vital Status file provided dates of death (25). The study was approved by the University of Maryland Center Institutional Review Board and the Baltimore Veterans Administration Medical Research and Development Committee.

The cohort creation involved several steps, as previously described (25, 26) (Fig. 1). First, we identified all VA nationwide admissions (25) of patients with DM, defined by two or more International Classification of Diseases, Ninth Revision, codes during past 2 years from either inpatient stay or outpatient visits on separate days, and/or prescriptions for DM medications in the current year (26). We excluded hospitalizations to psychiatric or long-term care (n = 273,549) settings, admissions ending with a transfer to a non-VA hospital (n = 54,992), admissions with a length of stay ≥30 days (n = 34,006), and hospitalizations with death during admission

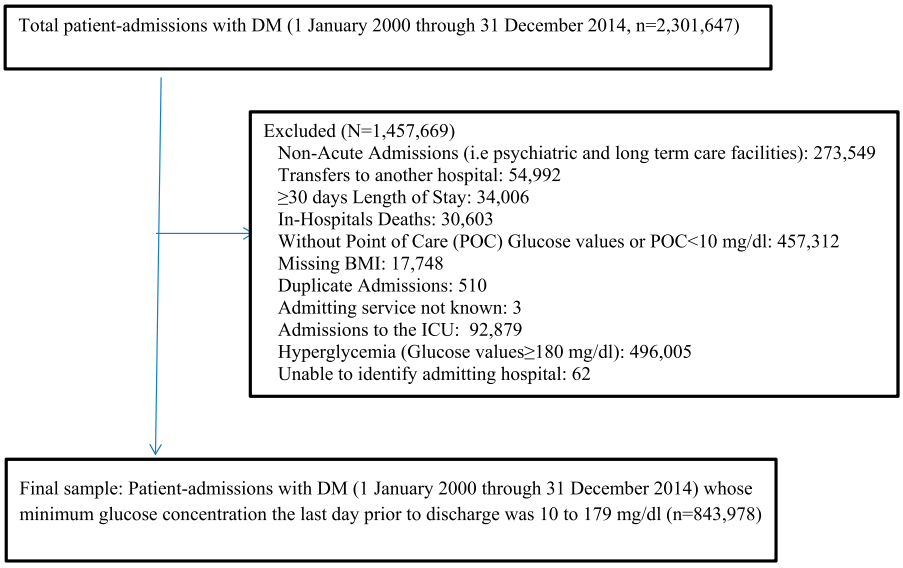

Figure 1. Study flow diagram. ICU, intensive care unit.

(n = 30,603) (25). We also excluded admissions during which point-of-care (POC) glucose concentrations were not reported and those with reported values <10 mg/dL (n = 457,312), admissions with missing body mass index (BMI; n = 17,748), or duplicate admissions (n = 510). We also excluded intensive care unit admissions, because this population of patients with DM is different from the patients with DM admitted to the general wards or noncritical care setting (n = 92,879) (27). We also excluded hospitalizations for which it was not possible to determine the admitting service (*i.e.*, medicine or surgery, n = 3) or the hospital that the patients were admitted (n = 62). Finally, because hyperglycemia may be associated with increased rate of readmission or postdischarge mortality, which was outside the scope of this report, we excluded subjects who were discharged with hyperglycemic values (average glucose level ≥180 mg/dL; n = 496,005). Our final cohort included 843,978 admissions.

Covariates

The independent variables that we studied included age, sex, BMI, income, admission source (whether patients were admitted from home or long-term care facilities), type of admitting service (medicine or surgery), DM medications received during the last 24 hours of their hospital stay (11, 25), and several different comorbid conditions as identified by Elixhauser *et al.* (28) (Table 1). We determined length of hospital stay by subtracting the discharge day and time from the admission day and time, to ascertain the last 24 hours of the hospitalization.

Outcomes and exposures

Our exposure of interest was minimum POC glucose concentration during the 24 hours before discharge. Hypoglycemia and severe hypoglycemia were defined as POC glucose values <70 mg/dL and <40 mg/dL, respectively (29). We studied five outcome measures: 30-day readmission; 30-, 90-, 180-day mortality; and a composite outcome of 30-day readmission or mortality (25, 30). We defined readmissions if they occurred within 30 days of the date of discharge from the index admission (25, 30). Because patients with DM are at risk for multiple admissions (15), limiting our cohort to include only the first readmission would have led us to exclude a substantial number of rehospitalizations. Readmissions >30 days after an index admission were considered as new index admissions, as previously described (25, 30). Mortality was defined as death that occurred 30, 90, or 180 days after initial discharge. The composite outcome of the 30-day readmission or mortality was defined as readmission or death within 30 days after discharge from the hospital.

Statistical methods

We used Poisson regression to compute adjusted rates of the five outcomes of interest. For each of the outcomes, event rates were computed for every 10-mg/dL glucose concentration categories reported on the last day of hospitalization. Overall, 17 glucose concentration categories were used for each of the five outcome measures. We used general estimating equations of Liang and Zeger (31, 32), with an exchangeable covariance structure to account for the serial autocorrelation of repeated admissions obtained from the same patient. Absolute events rates were adjusted to reflect the sample mean for each covariate and were generated as follows. For continuous variables, the mean of the variable was used in the adjustment. For categorical variables, the estimate was adjusted to reflect the prevalence of the variable in the population (*e.g.*, sex, 97% male). In addition to computing absolute event rates, we used linear contrasts to compute relative event rates. For these computations, 100 to 109 mg/dL was used as the reference category because this value is associated with lower rates of hospital complications and mortality (33).

From the list of collected covariates (Table 1), we selected those variables that were potential confounders of the association between glucose concentration and one or more of our five outcome measures. We defined a potential confounder as a covariate that, when added to the model (which included the 17 glucose-concentration categories), produced a ≥10% change in the association of the log event rate of one or more of the five outcome measures and at least three or more glucose concentration categories.

For each of our five outcome measures we performed two analyses: (1) an analysis including only the potential confounders selected as already described [age, BMI, and BMI^2 (calculated as BMI centered at 30 kg/m^2 and its square to decrease the collinearity between uncentered BMI and its square), admission source, admitting service, DM medications received on the last day of the hospitalization, and the presence of comorbidities, including congestive heart failure (CHF), liver disease, fluid or electrolyte disorders, hypertension, metastatic cancer, renal failure, solid tumor without metastasis, and myocardial infraction) and (2) an analysis including age, BMI, BMI^2, sex, admission source, admitting service, DM medications, and all the comorbidities (Table 1).

To determine if there was a glucose concentration below which the event rates in our five outcome measures increased, we fitted the adjusted event rates to a piecewise linear continuous regression (34, 35) in which each adjusted event rate was weighted by the inverse of the estimate's variance. The regressions assumed there would be two distinct linear relations between glucose concentration and each outcome (*i.e.*, relations that can be described by two lines having distinct intercepts and slopes, one describing the "normal glucose values" and the second the "lower glucose values"), and that the two linear relations met at a single glucose concentration referred to as the "knot." The analysis estimated multiple parameters including (1), the location of the knot, the glucose concentration at which two lines meet, one line describing the relation of glucose below the knot "lower glucose values" to outcome, the second line the relation above the knot "normal glucose values"; (2) the slope and intercept of the line in the range of the "lower glucose values"; and (3) the slope and intercept of the line in the range of the "normal glucose values." Statistical analyses were performed by using SAS software, version 9.4 (SAS Institute). A two-tailed $P < 0.05$ was considered statistically significant.

Results

The final cohort consisted of 843,978 admissions over 14 years of observation. The overall crude 30-day readmission rate was 17.3% and the 30-, 90-, and 180-day crude mortality rates were 2.3%, 6.0%, and 10%, respectively. Among the study cohort, 18.8% patients died or were readmitted within 30 days postdischarge. The mean (± SD) age of patients at admission was 66.8 ± 10.8 years,

Table 1. Characteristics of All Admissions of Patients With Diabetes

Variable	All Admissions (N = 843,978)	Without Hypoglycemia (n = 767,338)	With Hypoglycemia (n = 76,640)	*P*
Age, mean (SD), y	66.8 (10.8)	66.5 (10.8)	66.8 (10.8)	<0.001
Male sex	819,178 (97.0)	744,579 (97.0)	74,599 (94.3)	<0.001
BMI, median kg/m^2	29.7 (25.8—34.6)	29.8 (25.8–34.6)	28.8 (24.7–33.7)	<0.001
Income, median, USD	16,064 (8,962–31,322)	16,062 (8,961–31,321)	16,068 (9,000–31,234)	0.97
Length of stay, median, d	3.8 (2.0–6.8)	3.8 (2.0–6.8)	3.9 (2.0–7.0)	<0.001
Admission source				0.02
From home	799,047 (94.7)	726,416 (94.7)	72,631 (94.8)	
From other hospitals	21,236 (2.5)	19,414 (2.5)	1,822 (2.4)	
From nursing homes	23,695 (2.8)	21,508 (2.8)	2,187 (2.8)	
Admitting service				<0.001
Medicine	672,247 (79.7)	608,836 (79.3)	63,411 (82.7)	
Surgery	171,731 (20.3)	158,502 (20.7)	13,229 (17.3)	
DM medications				<0.001
Insulin	421978 (50.0)	380,170 (49.5)	41,808 (54.5)	
NIM	83,345 (9.9)	76,549 (10.0)	6,796 (8.9)	
Insulin and NIM	163,100 (19.3)	142,397 (18.6)	20,703 (27.0)	
None	175,555 (20.8)	168,222 (21.9)	7,333 (9.6)	
Comorbid conditions				
Alcohol abuse	40,247 (4.7)	37,034 (4.8)	3,213 (4.2)	<0.001
Blood loss anemia	7,577 (0.9)	6,939 (0.9)	638 (0.8)	0.04
Cardiac arrhythmia	197,147 (23.4)	180501 (23.5)	16646 (21.7)	<0.001
Congestive heart failure	193,926 (23.0)	173,863 (22.7)	20,063 (26.2)	<0.001
COPD	173,102 (20.5)	157,399 (20.5)	15,703 (20.5)	0.88
Coagulopathy	22,949 (2.7)	21,079 (2.8)	1,870 (2.4)	<0.001
Deficiency anemia	37,126 (4.4)	33,341(4.4)	3,785 (4.9)	<0.001
Depression	102,615 (12.2)	93,746 (12.2)	8,869 (11.6)	<0.001
Drug abuse	17,643 (2.1)	15,875 (2.1)	1,768 (2.3)	<0.001
Fluid-electrolyte disorder	134,572 (15.9)	120,206 (15.7)	14,366 (18.7)	<0.001
HIV/AIDS	3,840 (0.5)	3,463 (0.5)	377 (0.5)	0.11
Hypothyroidism	56,590 (6.7)	51,429 (6.7)	5,161 (6.7)	0.73
Hypertension				<0.001
Complicated	163,235 (19.3)	163,235 (18.8)	19,173 (25.0)	
Not complicated	450,213 (53.4)	413,430 (53.9)	36,783 (48.0)	
Liver disease	55,310 (6.6)	50,510 (6.6)	4,800 (6.3)	0.006
Lymphoma	9,503 (1.1)	8,729 (1.1)	774 (1.0)	0.001
Metastatic cancer	19,961 (2.4)	18,421 (2.4)	1,540 (2.0)	<0.001
Solid tumor, nonmetastatic	70,223 (8.3)	64,698 (8.4)	5,525 (7.2)	<0.001
Myocardial infarction	50,444 (6.0)	45,875 (6.0)	4,569 (6.0)	0.86
Neurologic disorder	36,510 (4.3)	33,433 (4.4)	3,077 (4.0)	<0.001
Paralysis	15,740 (1.9)	14,607 (1.9)	1,133 (1.5)	<0.001
Peptic ulcer disease	6,868 (0.8)	6,276 (0.8)	592 (0.8)	<0.001
Peripheral vascular disease	81,860 (9.7)	73,062 (9.5)	8,798 (11.5)	<0.001
Psychosis	21,301 (2.5)	19,494 (2.5)	1,807 (2.4)	0.002
Pulmonary circulatory disorder	25,732 (3.1)	23,401 (3.1)	2,331 (3.0)	0.91
Renal failure	184,784 (21.9)	162,963 (21.2)	21,821 (28.5)	<0.001
Rheumatologic diseases	10,538 (1.3)	9,528 (1.2)	1,010 (1.3)	0.07
Valvular disorder	40,473 (4.8)	37,043 (4.8)	3,430 (4.5)	<0.001

Data are reported as no. (%) or as median (25th, 75th percentile).

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; NIM, noninsulin medications.

with most of them admitted from home (94.7%) and hospitalized under medicine service (79.7%). The most common comorbid conditions were hypertension, either uncomplicated or complicated (53.4% and 19.3% respectively); cardiac arrhythmias (23.4%); CHF (23%); renal failure (21.9%); and chronic obstructive pulmonary disease (20.5%). Admissions with and without hypoglycemia (Table 1) differed significantly in several of the covariates that we examined; however, this is an effect that can be secondary to the large sample size of our cohort.

Most patients were discharged with minimum glucose values of 100 to 109 mg/dL (15.2%; Table 2). As the

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Table 2. Event Rates of the Five Outcomes, Allocated by Glucose Category, Obtained the Last 24 Hours of the Inpatient Stay[a]

Glucose Category (mg/dL)	No. of Admissions[b]	30-d Readmission		30-d Readmission or Mortality		30-d Mortality		90-d Mortality		180-d Mortality	
		No. of Events	Rate[c]	No. of Events	Rate[c]	No. of Events	Rate[c]	No. of Events	Rate[c]	No. of Events	Rate[c]
10–19	134	35	19.9 (13.9 to 28.4)	44	25.6 (19.2 to 34.2)	15	7.4 (4.7 to 11.6)	19	9.3 (6.3 to 13.8)	25	13.2 (9.5 to 18.2)
20–29	871	185	17.4 (15 to 20.3)	223	21.3 (18.8 to 24.2)	52	3.4 (2.7 to 4.4)	103	7.7 (6.5 to 9.2)	146	11.8 (10.3 to 13.5)
30–39	3661	797	18.3 (17 to 19.6)	896	20.7 (19.5 to 22.1)	148	2.5 (2.2 to 2.9)	348	6.6 (6.0 to 7.2)	551	11.1 (10.4 to 11.8)
40–49	11,032	2427	18.0 (17.3 to 18.8)	2663	20.0 (19.3 to 20.8)	355	2.0 (1.8 to 2.2)	924	5.8 (5.4 to 6.1)	1515	9.9 (9.5 to 10.4)
50–59	23,346	4832	16.9 (16.4 to 17.4)	5286	18.7 (18.2 to 19.2)	697	1.9 (1.7 to 2.0)	1689	5.0 (4.8 to 5.3)	2775	8.7 (8.4 to 9.0)
60–69	37,596	7278	15.8 (15.4 to 16.2)	7902	17.3 (17.0 to 17.7)	921	1.5 (1.4 to 1.6)	2469	4.6 (4.4 to 4.7)	4094	8.0 (7.7 to 8.2)
70–79	56,997	10,427	14.9 (14.6 to 15.2)	11261	16.3 (16.0 to 16.6)	1307	1.4 (1.3 to 1.5)	3478	4.2 (4.1 to 4.4)	5841	7.5 (7.3 to 7.6)
80–89	88,946	15,561	14.2 (14.0 to 14.5)	16840	15.5 (15.3 to 15.8)	1923	1.3 (1.2 to 1.4)	5350	4.1 (4.0 to 4.2)	9027	7.3 (7.2 to 7.5)
90–99	119,396	20,210	13.8 (13.6 to 14.0)	21920	15.1 (14.9 to 15.3)	2520	1.3 (1.2 to 1.3)	6936	3.9 (3.8 to 4.0)	11787	7.1 (7.0 to 7.2)
100–109	128,530	21,471	13.7 (13.5 to 13.9)	23312	15.0 (14.8 to 15.2)	2773	1.3 (1.2 to 1.3)	7417	3.9 (3.8 to 4.0)	12364	6.9 (6.8 to 7.0)
110–119	118,706	19,670	13.6 (13.4 to 13.8)	21527	15.0 (14.8 to 15.2)	2679	1.3 (1.3 to 1.4)	7035	3.9 (3.8 to 4.0)	11643	6.9 (6.8 to 7.0)
120–129	94,273	15,991	14.0 (13.8 to 14.2)	17447	15.4 (15.1 to 15.6)	2154	1.3 (1.2 to 1.4)	5555	3.9 (3.8 to 4.0)	9187	6.8 (6.7 to 6.9)
130–139	69,524	11,751	14.0 (13.8 to 14.3)	12948	15.6 (15.3 to 15.8)	1707	1.4 (1.3 to 1.5)	4163	3.9 (3.8 to 4.0)	6723	6.8 (6.6 to 6.9)
140–149	46,216	7665	13.9 (13.5 to 14.2)	8448	15.3 (15.0 to 15.7)	1146	1.4 (1.3 to 1.5)	2759	3.8 (3.7 to 4.0)	4369	6.5 (6.4 to 6.7)
150–159	26,262	4293	13.6 (13.2 to 14.1)	4798	15.3 (14.9 to 15.8)	699	1.5 (1.4 to 1.6)	1572	3.9 (3.7 to 4.0)	2430	6.4 (6.2 to 6.6)
160–169	12,776	2160	14.1 (13.5 to 14.7)	2389	15.7 (15.0 to 16.3)	323	1.4 (1.3 to 1.6)	724	3.7 (3.5 to 3.9)	1138	6.3 (6.1 to 6.6)
170–179	5,712	954	14.1 (13.2 to 15.1)	1055	15.8 (14.8 to 16.7)	132	1.4 (1.2 to 1.6)	266	3.2 (2.9 to 3.6)	410	5.3 (4.9 to 5.8)

[a]Adjusted for age, BMI, BMI^2, admission source, admitting service, diabetes medications, comorbidities (*i.e.*, cardiac arrhythmia, CHF, fluid or electrolyte disorder, hypertension, metastatic cancer, solid tumor without metastasis, renal failure, weight loss).

[b]The numbers of admissions are the same for each of the five outcomes.

[c]Reported as % (95% CI).

glucose concentrations became progressively lower than 100 mg/dL, the fraction of subjects who experienced an event (Table 2) and the relative rate generally increased for all five outcomes (Table 3). The results were almost similar even in in the fully adjusted model, where we adjusted for multiple covariates, among them all the comorbidities that we collected (Tables 4 and 5). Hypoglycemia and severe hypoglycemia during the last 24 hours of the inpatient stay was present in 9.1% and 0.6% of the admissions, respectively. The adjusted 30-day readmission rate; the combined 30-day readmission/mortality rate; and the 30-, 90-, and 180-day mortality rates were 18.5% (95% CI, 18.2% to 18.8%), 20.1% (95% CI, 19.8% to 20.4%), 1.8% (95% CI, 1.7% to 1.9%), 5.1% (95% CI, 4.9% to 5.2%), and 8.7% (95% CI, 8.5% to 8.9%) for admissions with hypoglycemia; and 20.3% (95% CI, 19.2% to 21.5%), 23.0% (95% CI, 21.8% to 24.2%), 2.8% (95% CI, 2.5% to 3.2%), 6.9% (95% CI, 6.3% to 7.5%), and 11.1% (95% CI, 10.4%% to 11.8%) for admissions with severe hypoglycemia, respectively. Admissions of patients with DM who had hypoglycemia during the last 24 hours of hospitalization had a 39% [rate ratio (RR), 1.39 (95% CI, 1.32 to 147)], 30% [RR, 1.30 (95% CI, 1.26 to 1.34)], and 27% [RR, 1.27 (95% CI, 1.24 to 1.30) higher rate of dying within 30, 90, and 180 days after discharge, respectively, compared with those who had glucose values between 100 and 109 mg/dL (Table 3). Furthermore, among those who experienced severe hypoglycemia, the rate was 124% [RR, 2.24 (95% CI, 1.96 to 2.57)], 81% [RR, 1.81 (95% CI, 1.66 to 1.97)], and 66% [RR, 1.66 (95% CI, 1.55 to 1.77)] higher. The rate of being readmitted in 30 days or experiencing either readmission or death in 30 days was 20% [RR, 1.20 (95% CI, 1.18 to 1.23)] and 22% [RR, 1.22 (95% CI, 1.20 to 1.24)] higher among patients with hypoglycemia and 32% [RR, 1.32 (95% CI, 1.24 to 1.40)] and 39% [1.39 (95% CI, 1.32 to 1.46)] among those in whom severe hypoglycemia developed.

For all the outcomes (Fig. 2), there was a progressive increase in the adjusted event rates (red circles with 95% CIs in Fig. 2) below the knot (determined by piecewise linear continuous regression), marking the point of intersection of the two lines (blue lines) smoothing the relation in the lower glucose values and normal glucose values. For all five outcome measures, the slope of the line below the knot obtained by fitting the adjusted event rates to a piecewise continuous regression was negative and statistically significant. For three of the five outcome measures, the slope above the knot was not statistically significantly different from zero (Table 6). For all five outcome measures, the slope below the knot was statistically significantly different from the slope above the knot (Table 6). Overall, the knots were located at 92.9 mg/dL for 30-day readmission rate, 45.2 mg/dL for 30-day mortality rate, 65.8 mg/dL for 90-day mortality rate, 67.3 mg/dL for 180-day mortality rate, and

Table 3. Event Rate Ratios of the Five Outcomes Allocated by Glucose Category, Obtained the Last 24 Hours of the Inpatient Stay[a]

Glucose Category (mg/dL)	30-d Readmission	30-d Readmission or Mortality	30-d Mortality	90-d Mortality	180-d Mortality
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
10–19	1.45 (1.02 to 2.08)	1.71 (1.28 to 2.28)	5.82 (3.69 to 9.18)	2.40 (1.62 to 3.55)	1.91 (1.39 to 2.63)
20–29	1.28 (1.10 to 1.49)	1.42 (1.25 to 1.62)	2.72 (2.11 to 3.50)	1.99 (1.68 to 2.36)	1.71 (1.49 to 1.96)
30–39	1.34 (1.24 to 1.44)	1.38 (1.30 to 1.48)	1.98 (1.69 to 2.32)	1.70 (1.55 to 1.86)	1.60 (1.50 to 1.72)
40–49	1.32 (1.26 to 1.38)	1.34 (1.29 to 1.39)	1.57 (1.42 to 1.74)	1.48 (1.40 to 1.57)	1.44 (1.38 to 1.50)
50–59	1.24 (1.20 to 1.28)	1.25 (1.21 to 1.29)	1.46 (1.35 to 1.58)	1.30 (1.24 to 1.36)	1.26 (1.22 to 1.30)
60–69	1.15 (1.12 to 1.19)	1.16 (1.13 to 1.19)	1.19 (1.11 to 1.28)	1.17 (1.13 to 1.22)	1.15 (1.12 to 1.19)
70–79	1.09 (1.06 to 1.12)	1.09 (1.06 to 1.11)	1.11 (1.04 to 1.18)	1.09 (1.05 to 1.12)	1.08 (1.05 to 1.11)
80–89	1.04 (1.02 to 1.06)	1.04 (1.02 to 1.06)	1.03 (0.97 to 1.08)	1.06 (1.03 to 1.09)	1.06 (1.04 to 1.09)
90–99	1.01 (0.99 to 1.03)	1.01 (0.99 to 1.03)	0.99 (0.94 to 1.04)	1.01 (0.98 to 1.04)	1.03 (1.01 to 1.05)
100–109	Referent	Referent	Referent	Referent	Referent
110–119	0.99 (0.97 to 1.01)	1.00 (0.98 to 1.02)	1.03 (0.98 to 1.08)	1.01 (0.98 to 1.04)	1.00 (0.98 to 1.02)
120–129	1.02 (1.00 to 1.05)	1.03 (1.01 to 1.05)	1.03 (0.97 to 1.08)	0.99 (0.96 to 1.02)	0.99 (0.97 to 1.01)
130–139	1.03 (1.00 to 1.05)	1.04 (1.02 to 1.06)	1.09 (1.03 to 1.16)	1.00 (0.97 to 1.04)	0.98 (0.96 to 1.00)
140–149	1.01 (0.99 to 1.04)	1.02 (1.00 to 1.05)	1.09 (1.02 to 1.16)	0.99 (0.95 to 1.03)	0.95 (0.92 to 0.98)
150–159	1.00 (0.96 to 1.03)	1.02 (0.99 to 1.06)	1.18 (1.09 to 1.27)	0.99 (0.95 to 1.04)	0.93 (0.90 to 0.96)
160–169	1.03 (0.98 to 1.08)	1.05 (1.00 to 1.09)	1.11 (1.00 to 1.24)	0.95 (0.89 to 1.01)	0.91 (0.87 to 0.95)
170–179	1.03 (0.96 to 1.11)	1.05 (0.99 to 1.12)	1.07 (0.91 to 1.25)	0.83 (0.75 to 0.91)	0.77 (0.72 to 0.84)
<70	1.20 (1.18 to 1.23)	1.22 (1.20 to 1.24)	1.39 (1.32 to 1.47)	1.30 (1.26 to 1.34)	1.27 (1.24 to 1.30)
<40	1.32 (1.24–1.40)	1.39 (1.32–1.46)	2.24 (1.96–2.57)	1.81 (1.66–1.97)	1.66 (1.55–1.77)

Abbreviation: RR, rate ratio.

[a] Adjusted for age, BMI, BMI^2, admission source, admitting service, diabetes medications, comorbidities (*i.e.*, cardiac arrhythmia, CHF, fluid or electrolyte disorder, hypertension, metastatic cancer, solid tumor without metastasis, renal failure, weight loss).

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Table 4. Event Rates of the Five Outcomes Allocated by Glucose Category, Obtained the Last 24 Hours of the Inpatient Stay[a]

Glucose Category (mg/dL)	No. of Admissions[b]	30-d Readmission		30-d Readmission or Mortality		30-d Mortality		90-d Mortality		180-d Mortality	
		Events	Rate	Events	Rate[c]	Events	Rate[c]	Events	Rate[c]	Events	Rate[c]
10–19	134	35	19.9 (13.9 to 28.4)	44	25.6 (19.2 to 34.1)	15	7.3 (4.7 to 11.4)	19	9.3 (6.3 to 13.7)	25	13.0 (9.5 to 17.9)
20–29	871	185	17.3 (14.9 to 20.2)	223	21.1 (18.6 to 24.0)	52	3.2 (2.5 to 4.1)	103	7.2 (6.1 to 8.6)	146	11.1 (9.7 to 12.7)
30–39	3661	797	18.2 (16.9 to 19.6)	896	20.6 (19.4 to 22.0)	148	2.4 (2.1 to 2.8)	348	6.4 (5.8 to 7.0)	551	10.7 (10.0 to 11.4)
40–49	11,032	2427	18.0 (17.2 to 18.7)	2663	19.9 (19.2 to 20.7)	355	1.9 (1.7 to 2.1)	924	5.6 (5.3 to 5.9)	1515	9.6 (9.2 to 10.1)
50–59	23,346	4832	16.9 (16.4 to 17.4)	5286	18.7 (18.2 to 19.2)	697	1.8 (1.6 to 1.9)	1689	4.8 (4.6 to 5.0)	2775	8.4 (8.1 to 8.7)
60–69	37,596	7278	15.7 (15.4 to 16.1)	7902	17.3 (16.9 to 17.7)	921	1.4 (1.4 to 1.5)	2469	4.4 (4.2 to 4.5)	4094	7.7 (7.5 to 7.9)
70–79	56,997	10,427	14.9 (14.6 to 15.2)	11261	16.2 (15.9 to 16.5)	1307	1.3 (1.3 to 1.4)	3478	4.0 (3.9 to 4.2)	5841	7.2 (7.1 to 7.4)
80–89	88,946	15,561	14.2 (13.9 to 14.4)	16840	15.5 (15.2 to 15.7)	1923	1.2 (1.2 to 1.3)	5350	4.0 (3.9 to 4.1)	9027	7.1 (7.0 to 7.2)
90–99	119,396	20,210	13.8 (13.6 to 14.0)	21920	15.0 (14.8 to 15.3)	2520	1.2 (1.1 to 1.2)	6936	3.8 (3.7 to 3.9)	11787	6.8 (6.7 to 7.0)
100–109	128,530	21,471	13.6 (13.4 to 13.8)	23312	14.9 (14.7 to 15.1)	2773	1.2 (1.2 to 1.3)	7417	3.7 (3.6 to 3.8)	12364	6.7 (6.6 to 6.8)
110–119	118,706	19,670	13.5 (13.3 to 13.7)	21527	14.9 (14.7 to 15.1)	2679	1.2 (1.2 to 1.3)	7035	3.7 (3.7 to 3.8)	11643	6.6 (6.5 to 6.8)
120–129	94,273	15,991	14.0 (13.7 to 14.2)	17447	15.3 (15.1 to 15.5)	2154	1.2 (1.2 to 1.3)	5555	3.7 (3.6 to 3.8)	9187	6.6 (6.5 to 6.7)
130–139	69,524	11,751	14.0 (13.7 to 14.3)	12948	15.5 (15.2 to 15.8)	1707	1.3 (1.3 to 1.4)	4163	3.7 (3.6 to 3.9)	6723	6.5 (6.4 to 6.7)
140–149	46,216	7665	13.8 (13.5 to 14.1)	8448	15.3 (14.9 to 15.6)	1146	1.3 (1.2 to 1.4)	2759	3.7 (3.6 to 3.8)	4369	6.3 (6.2 to 6.5)
150–159	26,262	4293	13.6 (13.1 to 14.0)	4798	15.2 (14.8 to 15.7)	699	1.4 (1.3 to 1.5)	1572	3.7 (3.5 to 3.8)	2430	6.1 (5.9 to 6.4)
160–169	12,776	2160	14.0 (13.4 to 14.7)	2389	15.6 (14.9 to 16.2)	323	1.3 (1.2 to 1.5)	724	3.5 (3.3 to 3.7)	1138	6.0 (5.7 to 6.3)
170–179	5712	954	14.0 (13.1 to 15.0)	1055	15.6 (14.7 to 16.6)	132	1.3 (1.1 to 1.5)	266	3.0 (2.7 to 3.3)	410	5.1 (4.7 to 5.5)

[a]Adjusted for age, BMI, BMI^2, sex, admission source, admitting service, diabetes medications, comorbidities [hypothyroidism, lymphoma, liver disease, paralysis, pulmonary circulatory disorder, renal failure, peripheral vascular disease, vascular disorder, cardiac arrhythmia, neurologic disorder, fluid or electrolyte disorder, deficiency anemia, alcohol abuse, drug abuse, depression, chronic obstructive pulmonary disease, psychoses, blood-loss anemia, coagulopathy, rheumatologic diseases (rheumatoid arthritis/collagen vascular disease), HIV/AIDS, peptic ulcer, CHF, metastatic cancer, solid tumor without metastasis, myocardial infarction].

[b]The numbers of admissions are the same for each of the five outcomes.

[c]Reported as % (95% CI).

Table 5. Event RRs of the Five Outcomes Allocated by Glucose Category, Obtained the Last 24 Hours of the Inpatient Stay[a]

Glucose Category (mg/dL)	30-d Readmission	30-d Readmission or Mortality	30-d Mortality	90-d Mortality	180-d Mortality
10–19	1.46 (1.02 to 2.08)	1.72 (1.29 to 2.29)	6.04 (3.86 to 9.47)	2.49 (1.70 to 3.66)	1.96 (1.42 to 2.69)
20–29	1.27 (1.09 to 1.48)	1.41 (1.24 to 1.61)	2.62 (2.03 to 3.39)	1.93 (1.62 to 2.30)	1.66 (1.45 to 1.91)
30–39	1.33 (1.24 to 1.44)	1.38 (1.30 to 1.48)	1.99 (1.70 to 2.34)	1.71 (1.56 to 1.87)	1.60 (1.50 to 1.72)
40–49	1.32 (1.26 to 1.38)	1.34 (1.29 to 1.39)	1.59 (1.43 to 1.77)	1.49 (1.41 to 1.59)	1.44 (1.38 to 1.51)
50–59	1.24 (1.20 to 1.28)	1.25 (1.21 to 1.29)	1.46 (1.35 to 1.58)	1.30 (1.24 to 1.36)	1.26 (1.21 to 1.30)
60–69	1.15 (1.12 to 1.19)	1.16 (1.13 to 1.19)	1.19 (1.11 to 1.28)	1.17 (1.13 to 1.22)	1.15 (1.12 to 1.19)
70–79	1.09 (1.06 to 1.12)	1.09 (1.06 to 1.11)	1.10 (1.04 to 1.17)	1.08 (1.05 to 1.12)	1.08 (1.05 to 1.11)
80–89	1.04 (1.02 to 1.06)	1.04 (1.02 to 1.06)	1.03 (0.97 to 1.09)	1.06 (1.03 to 1.09)	1.07 (1.04 to 1.09)
90–99	1.01 (0.99 to 1.03)	1.01 (0.99 to 1.03)	0.99 (0.94 to 1.04)	1.01 (0.98 to 1.04)	1.03 (1.01 to 1.05)
100–109	Referent	Referent	Referent	Referent	Referent
110–119	0.99 (0.97 to 1.01)	1.00 (0.98 to 1.02)	1.02 (0.97 to 1.08)	1.00 (0.98 to 1.03)	1.00 (0.98 to 1.02)
120–129	1.02 (1.00 to 1.05)	1.03 (1.01 to 1.05)	1.02 (0.97 to 1.08)	0.99 (0.96 to 1.02)	0.99 (0.97 to 1.01)
130–139	1.03 (1.00 to 1.05)	1.04 (1.02 to 1.06)	1.09 (1.03 to 1.16)	1.00 (0.97 to 1.04)	0.98 (0.96 to 1.00)
140–149	1.01 (0.99 to 1.04)	1.02 (1.00 to 1.05)	1.09 (1.02 to 1.16)	0.99 (0.95 to 1.02)	0.95 (0.92 to 0.97)
150–159	1.00 (0.96 to 1.03)	1.02 (0.99 to 1.05)	1.16 (1.08 to 1.26)	0.98 (0.94 to 1.03)	0.92 (0.89 to 0.95)
160–169	1.03 (0.98 to 1.08)	1.04 (1.00 to 1.09)	1.10 (0.99 to 1.22)	0.94 (0.88 to 1.00)	0.90 (0.86 to 0.95)
170–179	1.03 (0.96 to 1.10)	1.05 (0.99 to 1.11)	1.04 (0.89 to 1.23)	0.81 (0.73 to 0.90)	0.76 (0.71 to 0.82)

Data reported as RR (95% CI).

Abbreviation: RR, rate risk.

[a]Adjusted for age, BMI, BMI^2, sex, admission source, admitting service, diabetes medications, comorbidities [hypothyroidism, lymphoma, liver disease, paralysis, pulmonary circulatory disorder, renal failure, peripheral vascular disease, vascular disorder, cardiac arrhythmia, neurologic disorder, fluid or electrolyte disorder, deficiency anemia, alcohol abuse, drug abuse, depression, chronic obstructive pulmonary disease, psychoses, blood-loss anemia, coagulopathy, rheumatologic diseases (*i.e.*, rheumatoid arthritis/collagen vascular disease), HIV/AIDS, peptic ulcer, CHF, metastatic cancer, solid tumor without metastasis, myocardial infarction].

87.2 mg/dL for 30-day readmission or mortality rate. The location of the knots and the slopes in lower glucose values and normal glucose values were similar when we adjusted for multiple covariates (Fig. 3; Table 7).

Discussion

In this study, we evaluated the association of minimum glucose values during the last 24 hours of hospitalization with 30-day readmission and postdischarge mortality rates in patients with DM. We identified the following glucose thresholds ("knots"), below which there was an increased risk of one of the outcomes of interest developing: 92.9 mg/dL for 30-day readmission; 45.2 mg/dL, 65.8 mg/dL, and 67.3 for 30-, 90- and 180-day, respectively, for postdischarge mortality; and 87.2 mg/dL for the combined outcome of 30-day readmission or postdischarge mortality.

Hospital readmissions within 30 days have drawn national policy attention due to the increased cost of hospitalizations and concerns about poor quality of care, although the latter are debated (11, 30). In our cohort, the rate of readmission for patients with DM was 17.3%, consistent with previous reports (2–7, 9, 10, 18). Researchers have tried to identify risk factors for readmission in patients with DM (2–6, 11, 18–20). Previous studies have focused on the effect of glucose values at admission (18) or during the entire hospital stay (20), but not on glycemic control during the last day of hospitalization. In our analysis, even low to normal glucose values between 70 and 93 mg/dL were associated with a higher 30-day readmission rate. The reasons for the increased risk for readmission for this glucose category is unknown. We hypothesize that patients with DM with glucose levels close to the hypoglycemia range before discharge are more likely to have even lower glucose values after discharge. This hypothesis may be difficult to explore because hypoglycemic events can be transient, albeit sufficient enough to lead to severe adverse events (*e.g.*, falls, arrhythmias, seizures), resulting in hospital readmissions and increased mortality risk. Evidence from the Veterans Affairs Diabetes Trial, ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation), and ACCORD (Action to Control Cardiovascular Risk in Diabetes) trials showed an increased association of severe hypoglycemia with mortality, and major macrovascular and microvascular events (36–39). Our data suggest that in analogy to the outpatient setting, hospitalized patients with DM with glucose concentrations close to the hypoglycemia range are at risk for readmissions and complications after discharge.

Patients with DM have a higher risk of postdischarge mortality compared with patients without DM (21, 27, 40–44). The cause for increased mortality is

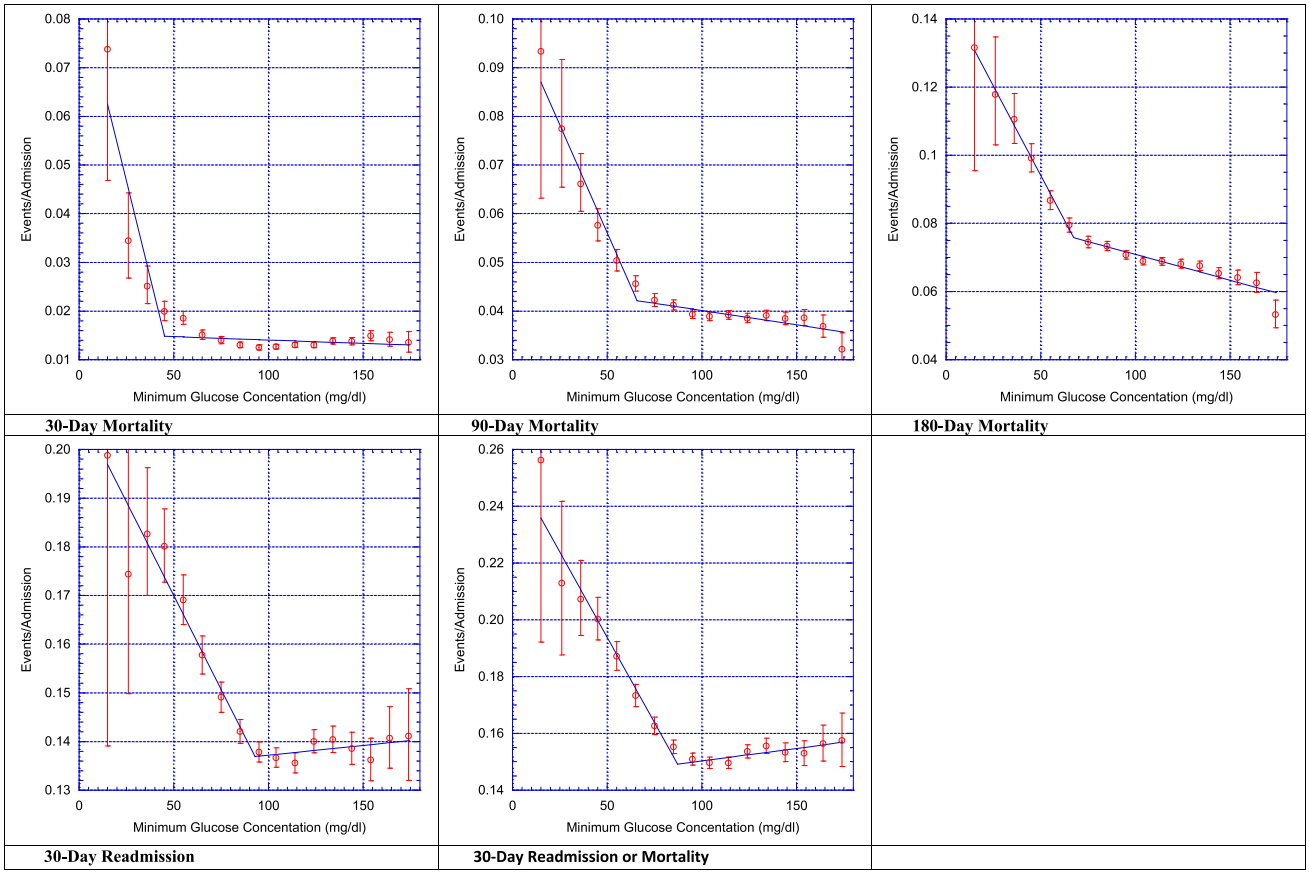

Figure 2. Relation of 17 glucose-concentration categories to mortality, readmission, and readmission or mortality rates. The red circles represent adjusted event rates; the red lines are 95% CIs. The blue lines are smoothed rates obtained by fitting the adjusted rates to a piecewise, continuous nonlinear regression with a single knot, resulting in two straight lines meeting at the knot. The knot can be interpreted as the glucose concentration separating normal glucose concentrations from hypoglycemia. The analyses are adjusted for age, BMI, BMI^2, admission source, admitting service, diabetes medications, comorbidities (*i.e.*, cardiac arrythmia, CHF, fluid or electrolyte disorder, hypertension, metastatic cancer, solid tumor without metastasis, renal failure, and weight loss).

multifactorial; patients with DM frequently have multiple comorbidities and are hospitalized with more severe medical conditions compared with individuals without DM. In addition, they are at risk for hypoglycemia, which is a well-known risk factor associated with adverse clinical outcomes. In our study, we showed that glucose values <67.3 mg/dL during the last 24 hours of the hospitalization were associated with increased risk of postdischarge mortality.

The prevalence of hypoglycemia after discharge is unknown and few studies have focused on the optimal glycemic management after hospitalization. A recent randomized clinical trial, hypoglycemia (<70 mg/dL) after hospitalization was reported in 22% of patients

Table 6. Slopes Above and Below the Knot From Piecewise Continuous Regression[a]

	Below Knot		Above Knot		Difference Between Slopes
Outcome	**Slope ($\times 10^{-4}$)**	***P***	**Slope ($\times 10^{-4}$)**	***P***	***P***
30-d readmission	−7.70	<0.001	0.01	0.97	<0.001
30-d readmission or mortality	−12.00	<0.001	0.88	0.38	<0.001
30-d mortality	−15.80	<0.001	−0.10	0.72	<0.001
90-d mortality	−8.8	<0.001	−0.60	0.02	<0.001
180-d mortality	−10.50	<0.001	−1.50	<0.001	<0.001

[a] Adjusted for age, BMI, BMI^2, admission source, admitting service, diabetes medications, comorbidities (*i.e.*, cardiac arrhythmia, congestive heart failure, fluid or electrolyte disorder, hypertension, metastatic cancer, solid tumor without metastasis, renal failure, weight loss).

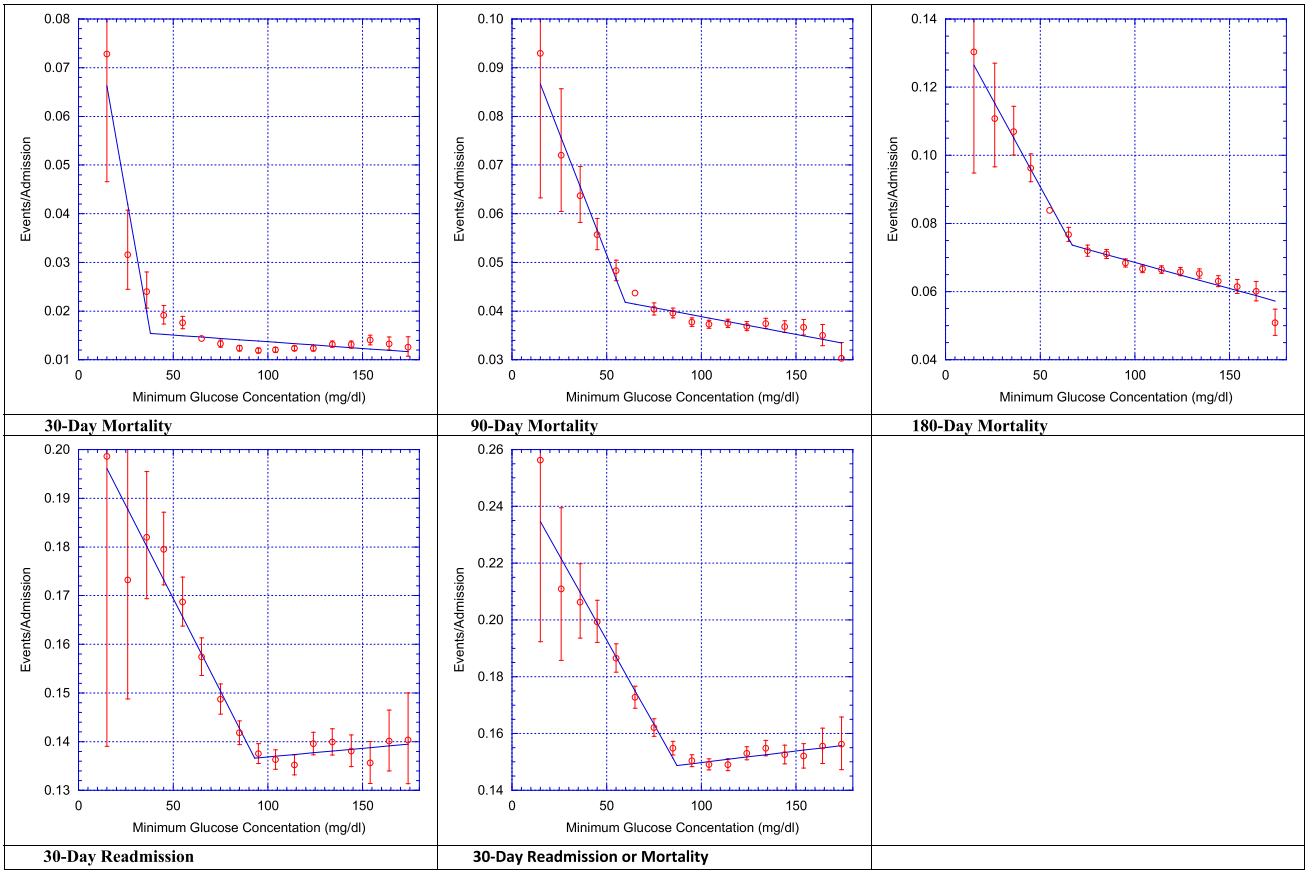

Figure 3. Relation of 17 glucose-concentration categories to mortality, readmission, and readmission or mortality rates. The red circles represent adjusted event rates; the red lines are 95% CIs. The blue lines are smoothed rates obtained by fitting the adjusted rates to a piecewise, continuous nonlinear regression with a single knot, resulting in two straight lines meeting at the knot. The knot can be interpreted as the glucose concentration separating normal glucose concentrations from hypoglycemia. The analyses are adjusted for age, BMI, BMI^2, sex, admission source, admitting service, diabetes medications, comorbidities [hypothyroidism, lymphoma, liver disease, paralysis, pulmonary circulatory disorder, renal failure, peripheral vascular disease, vascular disorder, cardiac arrhythmia, neurologic disorder, fluid or electrolyte disorder, deficiency anemia, alcohol abuse, drug abuse, depression, chronic obstructive pulmonary disease, psychoses, blood-loss anemia, coagulopathy, rheumatologic diseases (*i.e.*, rheumatoid arthritis/collagen vascular disease), HIV/AIDS, peptic ulcer, CHF, metastatic cancer, solid tumor without metastasis, myocardial infarction].

discharged with oral antidiabetic drug therapy, 30% taking oral antidiabetic drugs plus basal insulin, 44% taking basal-bolus insulin, and 25% taking basal insulin only (45). The transition of care from the inpatient to the outpatient setting is often challenging, leading to adverse events, poor glycemic control, increased emergency room visits, and higher hospital readmission rates and costs (45, 46). Clinical studies are lacking, and large

Table 7. Slopes Above and Below the Knot From Piecewise Continuous Regression Analysis[a]

	Below Knot		Above Knot		Difference Between Slopes
Outcome	**Slope ($\times 10^{-4}$)**	***P***	**Slope ($\times 10^{-4}$)**	***P***	***P***
30-d readmission	−7.60	<0.001	0.04	0.93	<0.001
30-d readmission or mortality	−11.90	<0.001	0.81	0.15	<0.001
30-d mortality	−22.10	<0.001	−0.30	0.17	<0.001
90-d mortality	−10.0	<0.001	−0.50	<0.001	<0.001
180-d mortality	−10.20	<0.001	−1.50	<0.001	<0.001

[a]Adjusted for age, BMI, BMI^2, sex, admission source, admitting service, diabetes medications, comorbidities [hypothyroidism, lymphoma, liver disease, paralysis, pulmonary circulatory disorder, renal failure, peripheral vascular disease, vascular disorder, cardiac arrhythmia, neurologic disorder, fluid or electrolyte disorder, deficiency anemia, alcohol abuse, drug abuse, depression, chronic obstructive pulmonary disease, psychoses, blood-loss anemia, coagulopathy, rheumatologic diseases (rheumatoid arthritis/collagen vascular disease), HIV/AIDS, peptic ulcer, CHF, metastatic cancer, solid tumor without metastasis, myocardial infarction].

randomized clinical trials are needed to evaluate the impact of improved glycemic control after discharge on clinical outcomes and the effectiveness of innovative strategies on the transition of care (45).

Our study has several strengths. To our knowledge, our cohort represents one of the largest studies that examined readmission rates and postdischarge mortality in patients with DM. In this study, we used national data to examine readmission rates in an integrated health system. Although we may have missed admissions and rehospitalizations to non-VA hospitals, we believe that analyzing data from the VA Health Care System, a "closed" health system where most veterans are admitted and readmitted, represents one of the most robust ways to examine readmission rates. Another strength of the study is the extensive Veterans Health Administration data sources that allowed us to include numerous covariates and risk factors (Table 1).

Our study has some limitations to consider when interpreting the results. Similar to previously published studies that used administrative data from the Veterans Affairs Health Care System, our analysis was restricted to a single health care system (25). Although we included in our analysis nationwide data from the VA hospitals, data on admissions and readmissions to non-VA hospitals were not obtained. Our study population, veterans admitted between 1 January 2000 and 31 December 2014, may be different from the general US population, because they were more likely to be male, elderly, and have chronic illness. Despite these differences, our ability to adjust for demographic data and an extensive list of comorbid conditions lead us to believe that our findings are applicable to the general population. Several studies have shown an increased risk of readmission and mortality in patients with DM compared with patients without DM (2–14, 21–24); therefore, we limited our analysis to patients/admissions with a diagnosis of diabetes. Therefore, our findings cannot be generalized and can only be applicable in this group of individuals. In addition, we did not try in this study to distinguish preventable readmissions from other readmissions. As previous publications have pointed out, although administrative data to determine preventability of readmissions have been used, preventability is subjective and using administrative data may not be the best method for this purpose (25, 47).

In conclusion, the results of this VA nationwide cohort study that included 843,978 admissions indicate that patients with DM, who had hypoglycemia or near-normal glucose values on the last day of their inpatient stay, were at a higher risk for 30-day readmission and postdischarge mortality. More specifically, glucose concentrations <92.9 mg/dL and 67.3 mg/dL had higher rates of 30-day readmissions and mortality, respectively; and glucose levels <87.2 mg/dL were associated with higher combined 30-day readmissions or mortality compared with patients with glucose levels >100 mg/dL.

Prospective studies need to be performed that will lead to alternative safest discharge planning. Potential approaches that may reduce the risk for readmission or death after discharge include delaying patient release from the hospital until normoglycemia is achieved, modifying outpatient DM medications or advise patients to perform frequent glucose monitoring or use continuous glucose-monitoring devices.

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