

RESEARCH ARTICLE

How well do we need to control blood glucose before discharging DKA patients? A retrospective cohort study

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Purpose: To determine the ideal length of stay and glycemic control after resolution of acidosis in patients hospitalized for diabetic ketoacidosis, in order to reduce 30-day readmission. We hypothesized that both discharging patients within 24 hours of acidosis resolution and hyperglycemia at discharge are associated with higher probability of readmission.

Methods: We examined data from 208 consecutive patients hospitalized for diabetic ketoacidosis. Logistic regression was performed adjusting for age, blood glucose (BG) level at presentation, prior hospitalization within 30 days, season of current hospitalization, and length of hospital stay.

Results: Higher BG at discharge is associated with lower probability of readmission (odds ratio, 0.990; 95% CI, 0.983–0.996; $P=0.002$). Higher average BG over the 24 hours prior to discharge is also associated with lower readmission rate (odds ratio, 0.991; 95% CI, 0.982–1.000; $P=0.044$). The direction of the association remains the same even after these predictive variables are converted to categorical variables. In addition, discharge within 24 hours of acidosis resolution is not inferior to discharge after 24 hours of normalized BG (odds ratio, 0.431; 95% CI, 0.083–2.252; $P=0.318$).

Conclusion: Neither discharging patients within 24 hours of acidosis resolution nor hyperglycemia at discharge is associated with higher readmission rate. Randomized prospective studies are needed to confirm or refute our study.

Keywords: *diabetic ketoacidosis; readmission; risk factors; hospitalization; hyperglycemia; length of stay*

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According to American Diabetes Association guidelines, diabetic ketoacidosis (DKA) patients should be treated with continuous intravenous insulin infusion until acidosis resolves and should then be started with subcutaneous insulin (1). However, it does not mention how long patients should stay in the hospital after resolution of acidosis or how well blood glucose (BG) needs to be controlled before discharge. There has been no previous study that provided an answer to these questions, according to our literature search.

Ideally, patients would be discharged when they are less likely to be readmitted. Hyperglycemia is a sign of relative insufficiency of insulin as compared with its counter-regulating hormones, and this imbalance precipitates DKA (1). Hyperglycemia can also worsen the outcomes in diseases other than DKA (e.g., coronary artery or cerebral artery disease). Therefore, our hypothesis is that hyperglycemia at the time of discharge would be associated with a higher readmission rate. We also hypothesize that discharges after a 24-hour period of normalized BG level post acidosis resolution would be associated with a lower

readmission rate as compared with earlier discharges. In this study, readmission is defined as any hospital encounter (which includes emergency room visit, observation, or full admission) within 30 days of discharge. The cutoff number of 30 days is per guidelines of Centers for Medicare and Medicaid Services (2).

Methods

Study population: We examined 208 sequential patients who were treated for DKA during their hospitalizations in Unity Hospital from January 1, 2011, to July 15, 2014. Unity Hospital is a community hospital located in Rochester, New York. We have an insulin administration protocol in the hospital. Basal-bolus subcutaneous insulin regimen is initiated right after resolution of acidosis. It includes one dose of long acting insulin once a day and four doses of short acting insulin before each meal and at bedtime. This approach was shown to be associated with a lower rate of hypoglycemic events (3). BG is measured four times a day (before breakfast, lunch, and dinner; and one time at night around 9 PM) while patient is receiving

subcutaneous insulin. As a result, there are at least four measurements for each 24 hours. The data was collected by screening the diagnosis codes in our electronic medical records with an automatic data mining program (SQL Server® Management Studio 2008 R2 [version 10.50.1600.1]). For patients with more than one DKA admission in the study time period, we only included the first admission. We only included the first admission because some patients could have multiple readmissions during the study period. As a result, these readmissions would not be independent events. However, our statistical methods require that every admission is independent from each other. We excluded patients who died or started comfort care during the index hospitalization. We also excluded patients who had no BG data in the last 12 hours of hospitalization or less than four BG data points in the last 24 hours of hospitalization. We recorded information on admission date, discharge date, length of stay, age, BG at the time of presentation and discharge, average of the four measurements in the last 24 hours of hospital stay, hypoglycemia, hospitalization in Unity Hospital within 30 days prior to the index hospitalization, readmission to Unity Hospital within 30 days after discharge, and readmission diagnosis. We defined hypoglycemia as a BG less than 70 mg/dl because BG below 65–70 mg/dl leads to increased glucagon, epinephrine, and growth hormone secretion (4, 5).

Statistical analysis

We compared baseline characteristics among patients with or without readmission. We used *t*-test if the variable being compared is normally distributed or Mann–Whitney *U*-test if it is not normally distributed (Table 1).

Logistic regression analyses were performed with IBM SPSS Statistics 20 to assess the relationship between

readmission and two predictive variables 1) BG at the time of discharge, and 2) average BG in the 24 hours prior to discharge (Tables 2 and 3). The analyses were performed separately for these two variables to avoid collinearity. Confounding variables included in the analyses are 1) BG at presentation, 2) age, 3) prior hospitalization within 30 days of the index hospitalization, 4) season in which the patient was discharged, and 5) length of stay. The rationales for choosing these confounding variables are: 1) Higher initial BG may indicate more severe insulin resistance or non-compliance with treatment. We do not always have data for hemoglobin A1c. As a result, initial BG was chosen as a substitute. 2) Older patients are more likely to be admitted to the hospital, which is probably related to their comorbidities. 3) Patients with a recent hospital encounter are more likely to be readmitted, possibly due to their comorbidities and the severity of their diabetes. 4) Winter tends to be the peak season for admission in Unity Hospital based on our experience, partly due to a higher prevalence of upper respiratory tract viral infection. In this study, ‘winter’ is defined as the time period from November 1, to March 31. 5) Patients who stay in the hospital for a longer time tend to be the ones with more comorbidities or more severe diabetes, which also makes them susceptible to readmission. However, the increased length of stay would allow physicians more time to treat hyperglycemia and therefore they are more likely to be discharged with a normalized BG level.

Tests for collinearity were performed and no significant collinearity was found among all continuous variables. We also included interaction variables in the model to assess for interaction between the five confounding variables and each predictive variable. Backward regression analyses were performed and interactive variables were eliminated if the likelihood ratio test had a *P* value

Table 1. Comparing predictive and confounding variables between readmitted and non-readmitted group

Characteristics	Patients readmitted within 30 days <i>N</i> = 27	Patients not readmitted within 30 days <i>N</i> = 158	<i>P</i> value (2-sided)
Age, median (interquartile range)	55.0 (43.0, 70.0)	43.0 (29.8, 56.0)	0.002
Length of stay, median (interquartile range)	3.0 (2.0, 9.0)	2.0 (1.0, 5.0)	0.246
BG at presentation, median (interquartile range)	485.0 (314.0, 589.0)	456.5 (342.0, 544.0)	0.556
Percentage of patients discharged within 24 hours of subcutaneous insulin initiation	14.8% (4/27)	22.2% (35/158)	0.456
Percentage of patients discharged in winter	37.0% (10/27)	44.9% (71/158)	0.531
Percentage of patients with hospitalization 30 days prior to the index hospitalization	33.3% (9/27)	15.2% (24/158)	0.031
BG at discharge, mean (standard deviation)	184.7 (71.5)	231.8 (90.2)	0.011
Average BG over the last 24 hours prior to discharge, median (interquartile range)	185.0 (159.0, 228.0)	213.0 (170.5, 267.5)	0.048

None of the interactive variables was found to be statistically significant on likelihood ratio test and therefore they were all excluded. The variables in the final model are shown in Tables 2 and 3, with their odds ratio and *P* value.

Table 2. Analysis^a of risk factors for 30-day readmission with BG at discharge being the predictive variable (on Hosmer and Lemeshow test, $P = 0.758$)

Variable name	Odds ratio (95% confidence interval)	P value (2-sided)
BG at discharge	0.990 (0.983–0.996)	0.002
Age	1.044 (1.016–1.073)	0.002
Length of stay	0.995 (0.951–1.041)	0.833
Hospitalization 30 days prior to the index hospitalization	2.500 (0.889–7.027)	0.082
BG at presentation	1.001 (0.999–1.003)	0.486
Season of discharge (winter or not)	0.432 (0.163–1.143)	0.091

^aSix subjects with BG at discharge less than 70 mg/dl were excluded from the analysis.

equal or greater than 0.10. Hypoglycemia may lead to increased readmission, which makes a linear model (like logistic regression model) invalid. Therefore, subjects with BG at discharge less than 70 mg/dl were excluded ($N = 6$) when BG at discharge was the predictive variable under analysis.

We also converted the two predictive variables into categorical variables in order to reduce the impact of outliers. According to American Association of Clinical Endocrinologist and American Diabetes Association consensus, inpatient pre-meal BG target for non-critically ill patients is 70–140 mg/dl and BG target for critically ill patients is 140–180 mg/dl (6). In DKA diagnosis criteria, BG needs to be greater than 250 mg/dl (1). Therefore, we converted ‘BG at discharge’ to a four-category variable after excluding the six hypoglycemic observations; our categories were BGs of 70–139 mg/dl, 140–180 mg/dl, 181–250 mg/dl, and greater than 250 mg/dl. We also converted ‘average BG over the 24 hours prior to discharge’ to a five-category variable which includes the categories of 70–139 mg/dl, 140–180 mg/dl, 181–250 mg/dl, greater than 250 mg/dl, and discharge within 24 hours of subcutaneous insulin initiation (There is no hypoglycemic observation for average BG over the 24 hours prior to discharge). Regression analyses were performed again with these two categorical variables as the predictive variables (Tables 4 and 5).

Table 3. Analysis of risk factors for 30-day readmission with average BG over the 24 hours prior to discharge being the predictive variable (on Hosmer and Lemeshow test, $P = 0.554$)

Variable name	Odds ratio (95% confidence interval)	P value (2-sided)
Average BG over the 24 hours prior to discharge	0.991 (0.982–1.000)	0.044
Age	1.030 (1.001–1.060)	0.041
Length of stay	0.999 (0.960–1.039)	0.952
Hospitalization 30 days prior to the index hospitalization	2.639 (0.942–7.390)	0.065
BG at presentation	1.002 (0.999–1.002)	0.490
Season of discharge (winter or not)	0.497 (0.180–1.374)	0.178

The analyses results after the two predictive variables are converted to categorical variables are displayed in Tables 4 and 5.

Results

Out of the 208 patients, 21 were excluded due to missing or incomplete BG data, 1 patient was excluded because of death, and 1 patient was excluded due to initiation of comfort care during hospitalization. Within 30 days, 27 of 185 (14.6%) patients were readmitted. Based on the emergency room physician documentation, the readmissions were related to diabetes in 9 (33.3%) of the cases, with 4 DKA, 3 hyperglycemia, 2 hypoglycemia, and no hyperglycemic hyperosmolar syndrome; other admission diagnoses included altered mental status of unknown etiology, injury, fever, COPD exacerbation, colitis, fetal growth deficit, cellulitis, urinary tract infection, tremor, gout, pneumonia, decubitus ulcer, abdominal pain, and musculoskeletal pain.

Patients in the readmitted group are older than the ones in the non-readmitted group (55.0 years vs 43.0 years, $P = 0.002$). Patients in the readmitted group were more likely to have been hospitalized within 30 days prior to the index DKA visit (33.3% vs 15.2%, $P = 0.031$). Surprisingly, patients in the readmitted group had lower BG at discharge and lower last 24-hour average BG as compared with non-readmitted group (Table 1).

Discussion

Non-readmitted patients had higher mean of BG at discharge and higher median of last 24-hour average BG

Table 4. Analysis of risk factors for 30-day readmission with BG at discharge being a categorical variable (on Hosmer and Lemeshow test, $P=0.183$)

Variable name ^a	Odds ratio (95% confidence interval)	P value (2-sided)
BG at discharge (70–139)	Reference level	
BG at discharge (140–180)	1.095 (0.278–4.317)	0.897
BG at discharge (181–250)	0.455 (0.123–1.691)	0.240
BG at discharge (>250)	0.145 (0.035–0.612)	0.009
Age	1.044 (1.015–1.073)	0.002
Length of stay	0.994 (0.953–1.038)	0.789
Hospitalization within 30 days prior to index hospitalization	2.482 (0.875–7.039)	0.087
BG at presentation	1.001 (0.999–1.003)	0.503
Season of discharge (winter or not)	0.421 (0.158–1.123)	0.084

^aNumbers in the bracket indicate range of blood glucose level in that category, unit is mg/dl.

as compared with readmitted patients. In addition, after adjustment for confounders, both higher BG at discharge and higher 24-hour average BG prior to discharge were found to be associated with a lower readmission rate. The direction of the association remains the same even when we analyze them as categorical variables. Based on our literature search, there has been no previous study to support a protective effect of hyperglycemia on readmission. One explanation for the results is that physicians require tighter BG control prior to discharge if they predict that the patient is at higher risk for readmission. Unfortunately, these patients are still more likely to be readmitted than other patients due to their comorbidities. Although we tried to adjust the effect of comorbidities by using substitute markers including age, prior hospitalization, and length of stay, there is no accurate model to measure comorbidities. Another explanation for the result is that patients who were discharged at higher BG level made fewer errors in insulin administration at home, because they were more worried about recurrence of DKA. A previous study showed that 61% of hospitalized

DKA patients made errors in administering insulin to themselves (7). However, obtaining data on post discharge compliance is practically difficult.

Table 5 showed that discharge within 24 hours of acidosis resolution is not inferior to waiting for 24 hours of normalized average BG (70–139 mg/dl) ($P=0.318$), despite the fact that the median BG at discharge of the first group is greater than that of the second group (186.5 mg/dl vs 102.0 mg/dl, $P=0.000$ on Fisher's exact test). Again, this result could be due to selective earlier discharge of healthier or difference in patients' compliance with post-discharge treatment.

We also found that older age is associated with higher readmission rate. We found that the association between readmission and previous hospitalization within 30 days approached significance. However, there is no association between BG at presentation, length of stay, or season of discharge and subsequent readmission.

A limitation of the study is that we do not have data on readmission to other hospitals. There was no clear reason identified to explain why no data, or incomplete data,

Table 5. Analysis of risk factors for 30-day readmission with average BG over the 24 hours prior to discharge being a categorical variable (on Hosmer and Lemeshow test, $P=0.298$)

Variable name ^a	Odds ratio (95% confidence interval)	P value (2-sided)
Average BG over the 24 hours prior to discharge (70–139)	Reference level	
Average BG over the 24 hours prior to discharge (140–180)	0.567 (0.118–2.724)	0.478
Average BG over the 24 hours prior to discharge (181–250)	0.473 (0.113–1.984)	0.306
Average BG over the 24 hours prior to discharge (>250)	0.128 (0.019–0.865)	0.035
Discharged within 24 hours of subcutaneous insulin initiation	0.431 (0.083–2.252)	0.318
Age	1.035 (1.008–1.062)	0.010
Length of stay	0.995 (0.954–1.037)	0.802
Hospitalization within 30 days prior to the index hospitalization	2.029 (0.734–5.605)	0.173
BG at presentation	1.001 (0.999–1.002)	0.482
Season of discharge (winter or not)	0.568 (0.227–1.421)	0.227

^aNumbers in the bracket indicate range of blood glucose level in that category, unit is mg/dl.

were recorded for the 21 patients. However, there is no evidence to indicate that these 21 patients were more or less likely to be readmitted as compared with the study population (2/21 vs 27/185 in the study population, $P=0.745$ on Fisher's exact test). Finally, our study was retrospective and this limited our ability to adjust for confounders. For example, efficient communication between hospital and patient's primary care physician can potentially decrease readmission rate, but a confounder like this is difficult to adjust in a retrospective study. A prospective study in which subjects are discharged with different BG levels would provide the best evidence.

Conclusion

Hyperglycemia at the time of discharge was associated with a lower readmission rate. Discharge within 24 hours of acidosis resolution was not inferior to discharge after 24 hours of normalized average BG level. A randomized controlled trial in which subjects are discharged with different BG levels is needed to confirm or refute our study.

Disclosure

There is no conflict of interest to be disclosed.

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References

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 2009; 32: 1335–43.
2. 2012 inpatient prospective payment system rule. Centers for Medicare and Medicaid Services. Available from: <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program.html> [cited 19 June 2014].
3. Umpierrez GE, Jones S, Smiley D, Mulligan P, Keyler T, Temponi A, et al. Insulin analogs versus human insulin in the treatment of patients with diabetic ketoacidosis: A randomized controlled trial. *Diabetes Care* 2009; 32: 1164–9.
4. Schwartz NS, Clutter WE, Shah SD, Cryer PE. Glycemic thresholds for activation of glucose counterregulatory systems are higher than the threshold for symptoms. *J Clin Invest* 1987; 79: 777–81.
5. Mitrakou A, Ryan C, Veneman T, Mookan M, Jenssen T, Kiss I, et al. Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction. *Am J Physiol* 1991; 260: E67–74.
6. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, et al. American association of clinical endocrinologists and American diabetes association consensus statement on inpatient glycemic control. *Diabetes Care* 2009; 32: 1119–31.
7. Bagg W, Sathu A, Streat S, Braatvedt GD. Diabetic ketoacidosis in adults at Auckland Hospital, 1988–1996. *Aust N Z J Med* 1998; 28(5): 604–8.