Discharge Glucose Is Not Associated With Short-Term Adverse Outcomes in Emergency Department Patients With Moderate to Severe Hyperglycemia

Brian E. Driver, MD*; Travis D. Olives, MD, MPH; Johanna E. Bischof, MD; Marcus R. Salmen, MD; James R. Miner, MD

*Corresponding Author. E-mail: briandriver@gmail.com, Twitter: @brian_driver.

Study objective: Hyperglycemia is frequently encountered in the emergency department (ED), and there is no consensus on optimal care before discharge. The importance of glucose reduction in the ED is unknown. We seek to determine whether an association exists between discharge glucose and 7-day adverse outcomes.

Methods: A cohort design with retrospective chart review was conducted at a high-volume urban ED. Patients were included if any glucose level was greater than or equal to 400 mg/dL and they were discharged from the ED. Generalized estimating equation models were created for the 7-day outcomes with a primary predictor of discharge glucose.

Results: The cohort consisted of 422 patients with 566 ED encounters. Mean arrival and discharge glucose were 491 mg/dL (SD 82 mg/dL) and 334 mg/dL (SD 101 mg/dL), respectively. In the 7-day follow-up period, 62 (13%) and 36 (7%) patients had a repeat ED visit for hyperglycemia and were hospitalized, respectively. Two patients had diabetic ketoacidosis. After adjustment for arrival glucose, whether a chemistry panel was obtained, amount of intravenous fluids administered, and amount of subcutaneous insulin administered, discharge glucose was not associated with repeat ED visit for hyperglycemia (adjusted odds ratio 0.997; 95% confidence interval 0.993 to 1.001) or hospitalization for any reason (adjusted odds ratio 0.998; 95% confidence interval 0.995 to 1.002).

Conclusion: ED discharge glucose in patients with moderate to severe hyperglycemia was not associated with 7-day outcomes of repeat ED visit for hyperglycemia or hospitalization. Attaining a specific glucose goal before discharge in patients with hyperglycemia may be less important than traditionally thought. [Ann Emerg Med. 2016;68:697-705.]

Please see page 698 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Hyperglycemia and diabetes-related emergency department (ED) visits are common, composing approximately 1% of ED encounters.[1] Moderate hyperglycemia with or without concomitant acute illness is frequently encountered in the ED. Although most patients presenting with moderate hyperglycemia do not have diabetic ketoacidosis[2] and are eligible for discharge after ED evaluation, approaches to caring for this common complaint are variable, without clear consensus.[3] There are no guidelines for ED care of hyperglycemia, and the care received by patients with hyperglycemia who are eventually discharged from the ED, and their short-term outcomes, have not previously been described, to our knowledge.

Importance

Prompt glycemic control in the ED is important for patients with hyperglycemia who are ill enough to warrant hospital admission,[4] and long-term proper glycemic control is crucial to decrease the risk of many associated chronic conditions such as cardiovascular disease, nephropathy, and retinopathy. Protocols that safely reduce glucose levels during an ED visit have been developed; it has been demonstrated that administering protocolized doses of insulin to ED patients with hyperglycemia more effectively reduces glucose levels than not providing insulin.[5] However, the importance of reducing glucose to achieve a specific glucose value for patients well enough to be discharged is not known. Although controlling hyperglycemia during a single ED visit could not reasonably be expected to affect

Editor's Capsule Summary

What is already known on this topic

Before the emergency department (ED) discharge of hyperglycemic diabetic patients, emergency physicians frequently attempt to reduce glucose level to below some arbitrary "safe" threshold such as 350 mg/dL.

What question this study addressed

Is the discharge glucose level associated with adverse outcomes at 7 days?

What this study adds to our knowledge

This retrospective analysis included 566 hyperglycemic patients with ED encounters leading to discharge, of whom 39% had final glucose levels ranging from 351 to 694 mg/dL. These higher discharge glucose levels were not associated with a greater risk of repeated ED visits, hospitalization, or other adverse outcomes.

How this is relevant to clinical practice

For diabetic patients with hyperglycemia, efforts to reduce glucose level during the ED visit itself appear to lack value, suggesting that management should instead focus on longer-term diabetic management.

any long-term outcome, ED glucose reduction, when carried out, is ostensibly performed to prevent short-term outcomes such as diabetic ketoacidosis, repeat ED visits, and hospitalization. If ED glycemic control, and thus the discharge glucose value, is not associated with short-term outcomes, then perhaps the most important intervention would be ensuring appropriate outpatient follow-up, with the goal to maintain long-term proper glycemic control.[6]

Goals of This Investigation

We therefore sought to describe the care received by ED patients with moderate to severe hyperglycemia who were eventually discharged from the ED, and their 7-day outcomes, including diabetic ketoacidosis, hyperosmolar hyperglycemic state, repeat ED visit for hyperglycemia, and hospitalization for any reason. Specifically, we sought to determine whether an association exists between discharge glucose and these 7-day outcomes.

MATERIALS AND METHODS

Study Design and Setting

This chart review study was set at an urban Level I trauma center with an average annual ED census of 100,000 visits. A comprehensive electronic medical record was used that tracks demographic information, laboratory values, medications, and fluids administered, as well as time stamps for a patient's flow through the ED. The institutional review board of Hennepin County Medical Center declared this to be exempt from review.

Selection of Participants

The electronic medical record was searched to find all patients aged 18 years or older who had a glucose value of greater than or equal to 400 mg/dL at any point during an ED encounter between January 1, 2010, and December 31, 2011. Patients were excluded if they were admitted to the hospital from the ED, if they had type 1 diabetes, and if the chief complaint was hypoglycemia. A patient was deemed to have type 1 diabetes if this diagnosis was specifically listed in his or her medical history. Patients who were noted to have diabetes mellitus, without mention of type, were not considered to have type 1 diabetes. Patients with type 1 diabetes were excluded because they typically have less insulin resistance and develop diabetic ketoacidosis at a higher rate than patients with type 2 diabetes.[7,8]

Outcome Measures

We described ED management, including arrival and discharge glucose values, diagnostic testing, treatment of hyperglycemia, length of stay, and whether iatrogenic hypoglycemia occurred. The main outcomes studied were the occurrence of diabetic ketoacidosis or hyperosmolar hyperglycemic state, repeat ED visit for hyperglycemia, or hospitalization for any reason within 7 days of the index ED encounter. The time frame of 7 days was chosen because the effect of treatments received for hyperglycemia in a single ED encounter, even allowing for time frames far exceeding the duration of rapid-acting insulin, could not be expected to last more than 7 days.

Data Collection and Processing

Data were collected from the electronic medical record through a comprehensive chart review of eligible ED encounters, including review of physician and nursing notes, laboratory values, medications and fluids administered, and follow-up information. Specific data points to collect were designated a priori. Four trained investigators (B.E.D., T.D.O., J.E.B., and M.R.S.) reviewed all eligible charts and entered data onto a standardized Excel spreadsheet (version 14.0; Microsoft, Redmond, WA). Abstractors first reviewed a standard set of 20 records to check for errors. They met periodically to review progress and ensure uniform variable definitions. In the event of conflicting data or disputes, 2 independent

reviewers came to a consensus after careful review of the patient chart. Missing data were left as such. Abstractors were not blinded to the study outcomes but did enter 7-day outcomes before other variables had been entered.

The following variables were extracted from the electronic medical record directly: age, sex, chief complaint, and ED length of stay. The following variables were abstracted by manual chart review: arrival glucose level, discharge glucose level, whether urinalysis or a basic chemistry panel test were obtained, whether ketonuria was present, total serum carbon dioxide level, serum anion gap, amount of intravenous fluids administered, amount of subcutaneous aspart or regular insulin administered, previous hemoglobin A_{1c} level (within 6 months), whether iatrogenic hypoglycemia occurred during the ED visit, whether discharge prescriptions for diabetes medication were ordered, and the occurrence of the 7-day outcomes of diabetic ketoacidosis or hyperosmolar hyperglycemic state, repeat ED visit for hyperglycemia, hospitalization for any reason, and death.

Arrival and discharge glucose levels were defined as the first and last glucose values obtained during an ED encounter, respectively. If a glucose level was recorded in the electronic medical record as "high," a value of 600 mg/dL was assigned because this is the maximum value detected by point-of-care glucose testing devices in our institution. If there was only 1 glucose value obtained during the ED encounter, the arrival and discharge glucose levels were assumed to be the same. Glucose reduction was defined as the arrival glucose level minus the discharge glucose level. Iatrogenic hypoglycemia was defined as any ED glucose value less than or equal to 60 mg/dL, or any ED glucose value less than or equal to 100 mg/dL, at which level the patient was documented by a nurse or provider to have symptomatic hypoglycemia and whose symptoms were relieved by food or dextrose administration. A discharge prescription was considered to be for diabetes for subcutaneous insulin of any type and the following oral medications: metformin, sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, and α-glucosidase inhibitors. Length of stay was defined as from the time the patient was roomed in the ED to the time the discharge order was placed by the physician.

Patients were assessed for a 7-day outcome if they were not lost to follow-up, which was defined as no encounters in our health system in the 30 days after the index ED visit. We assumed that patients with moderate to severe hyperglycemia would generally require a repeat visit in our health system within 30 days for ongoing care of diabetes and other comorbidities. If a patient had no encounter in our health system in 30 days, we assumed he or she came to our ED for a one-time acute care visit with follow-up in a different system; these patients were therefore considered to be lost to follow-up. To assess the occurrence of the 7-day outcomes, the chart was reviewed to determine whether the patient visited an outpatient clinic, visited the ED, or was hospitalized within 7 calendar days of the index ED visit. If there was a return visit, each encounter was examined to evaluate for diabetic ketoacidosis or hyperosmolar hyperglycemic state. Diabetic ketoacidosis was defined as a glucose level greater than 250 mg/dL, serum total carbon dioxide level less than or equal to 15 mEq/L, and the presence of urine or serum ketones.[9] Hyperosmolar hyperglycemic state was defined as glucose level greater than 600 mg/dL, pH level greater than 7.3, and concomitant mental status changes with a diagnosis of hyperosmolar hyperglycemic state documented in the ED, admission, or discharge notes.[9] A repeat ED visit was considered to be for hyperglycemia if the chief complaint was hyperglycemia or was polyuria, polydipsia, fatigue, blurry vision, or malaise with concomitant glucose level greater than 250 mg/dL. Repeat ED visits for unrelated problems (without symptoms of hyperglycemia), during which hyperglycemia was inadvertently discovered, were not considered to be a repeat ED visit for hyperglycemia. Hospitalization was defined as any admission to the hospital, including admission to the observation unit. Outcome data were abstracted by a second abstractor on a random selection of 20% of the charts to evaluate interobserver agreement.

Because patients could have visited other EDs and hospitals in the 7 days after the index ED encounter, countywide ambulance records were reviewed to determine whether any patient had an ambulance encounter to another ED during those 7 days. All ambulance encounters to other institutions were assumed to be ED visits for hyperglycemia that resulted in hospitalization.

Primary Data Analysis

The analysis of baseline characteristics and ED management of hyperglycemia in this patient population was descriptive; 95% confidence intervals (CIs) and standard deviations (SDs) are presented for categorical and continuous variables, respectively.

Analysis of 7-day outcomes was completed with generalized estimating equations with exchangeable correlation structure. Generalized estimating equations were used instead of multivariable logistic regression to account for patients who had more than 1 ED encounter for hyperglycemia during the study period. Independent variables deemed to be clinically useful and plausibly related to the 7-day outcomes were selected a priori. The primary predictor was discharge glucose level. The covariates of interest were arrival glucose level, whether a basic chemistry panel was obtained, amount of intravenous fluids

administered, and amount of subcutaneous aspart or regular insulin administered. Because anecdotal evidence suggests that ED interventions to treat hyperglycemia may reduce the risk of short-term adverse outcomes, intravenous fluid and insulin administered were included as covariates. The covariate of whether a basic chemistry panel was obtained was included because emergency physicians may order diagnostic testing more often for more ill-appearing patients. Laboratory values such as total carbon dioxide level, anion gap, or the presence of ketonuria were not included in this analysis because not all patients had such testing ordered.

Generalized estimating equation models were created for the outcomes of repeat ED visit for hyperglycemia and hospitalization for any reason. Similar analyses were planned for diabetic ketoacidosis and hyperosmolar hyperglycemic state but were unable to be performed because the number of outcome events was too small.

Additionally, a second model was constructed that was identical to the first, except that discharge glucose level was coded as a dichotomous (350-mg/dL threshold) rather than continuous variable, which was meant to replicate the clinical practice in which a patient is eligible for discharge only after reduction of the glucose level to below a specific threshold. The dichotomization of 350 mg/dL was selected because this is anecdotally a common treatment goal when treating moderate to severe hyperglycemia before discharge from the ED. Moreover, a post hoc analysis including age as a covariate was performed because older patients may be more likely to have repeat ED visits and hospitalizations after encounters for hyperglycemia. No a priori sample size calculations were completed.

Sensitivity Analyses

Sensitivity analyses were completed to attempt to account for the imperfect nature of the 7-day outcome analysis. It is almost certain that some patients sought care at other institutions. A finding that discharge glucose level is not associated with 7-day outcome could be erroneous because of systematic bias plausibly introduced by higher rates of ED visits to other hospitals by patients with higher discharge glucose values. To test whether this would have affected the outcomes of this investigation, 2 sensitivity analyses were performed.

In the first, it was assumed that patients with a discharge glucose level greater than 350 mg/dL who did not have any visit within 7 days (n=364) (Figure 1) had a 15% chance of a repeat ED visit for hyperglycemia and a 5% chance of hospitalization; outcomes for similar patients with a discharge glucose level less than or equal to 350 mg/dL did not change. Patients who were already known to have a repeat ED visit for hyperglycemia or hospitalization were still included, and their outcomes were not changed. The rates of 15% and 5% were chosen because they were on the higher end of what would be expected in this patient population. Furthermore, because the changes in outcomes were applied exclusively to patients with higher discharge glucose values, these rates should have adequately accounted for any potential systematic bias that could have been introduced by poorer follow-up rates for patients with higher discharge glucose values.

The second sensitivity analysis was identical to the first, except that patients who received insulin during the index ED encounter were assumed to have a discharge glucose level 20% lower than the recorded discharge glucose level to account for instances in which patients were discharged before the peak effect of the insulin. Fluid administration was not considered to be an effective glucose-lowering therapy, in accordance with results from a recent randomized trial.[10] This analysis attempted to use the "true" discharge glucose level in the model to account for the possibility that glucose-level reduction (and thereby discharge glucose level) was associated with a change in 7-day outcomes. In each sensitivity analysis, a new generalized estimating equation model was created with the same independent variables as above, with replacement of the respective variables from the sensitivity analysis calculations.

Furthermore, because the assumed rates of repeat ED visit for hyperglycemia and hospitalization were estimates without previous data to use for guidance, each sensitivity analysis was tested over a range of values. For patients with a discharge glucose level greater than 350 mg/dL, the chance of a repeat visit for hyperglycemia was tested in intervals of 1%, from 15% to 40%, and the chance of hospitalization was varied from 5% to 15%. At each interval, the sensitivity analysis was repeated 500 times. The threshold at which more than 5% of the iterations demonstrated an association between increasing discharge glucose level and an increasing risk for the respective outcomes is reported.

Stata (version 12.1; StataCorp, College Station, TX) and SAS (version 9.4; SAS Institute, Inc., Cary, NC) were used for data analysis.

RESULTS

Characteristics of Study Subjects

Of 706 encounters identified, 140 were excluded (135 because of type 1 diabetes mellitus; 5 with a chief complaint of hypoglycemia), leaving 566 ED encounters for analysis, with 422 unique patients, 244 (58%) of whom were men, with a mean age of 46.9 years (SD 12 years). Table 1 displays baseline data. The most common chief complaint was hyperglycemia (49% of patients). Mean arrival glucose level was 491 mg/dL (SD 82 mg/dL). For

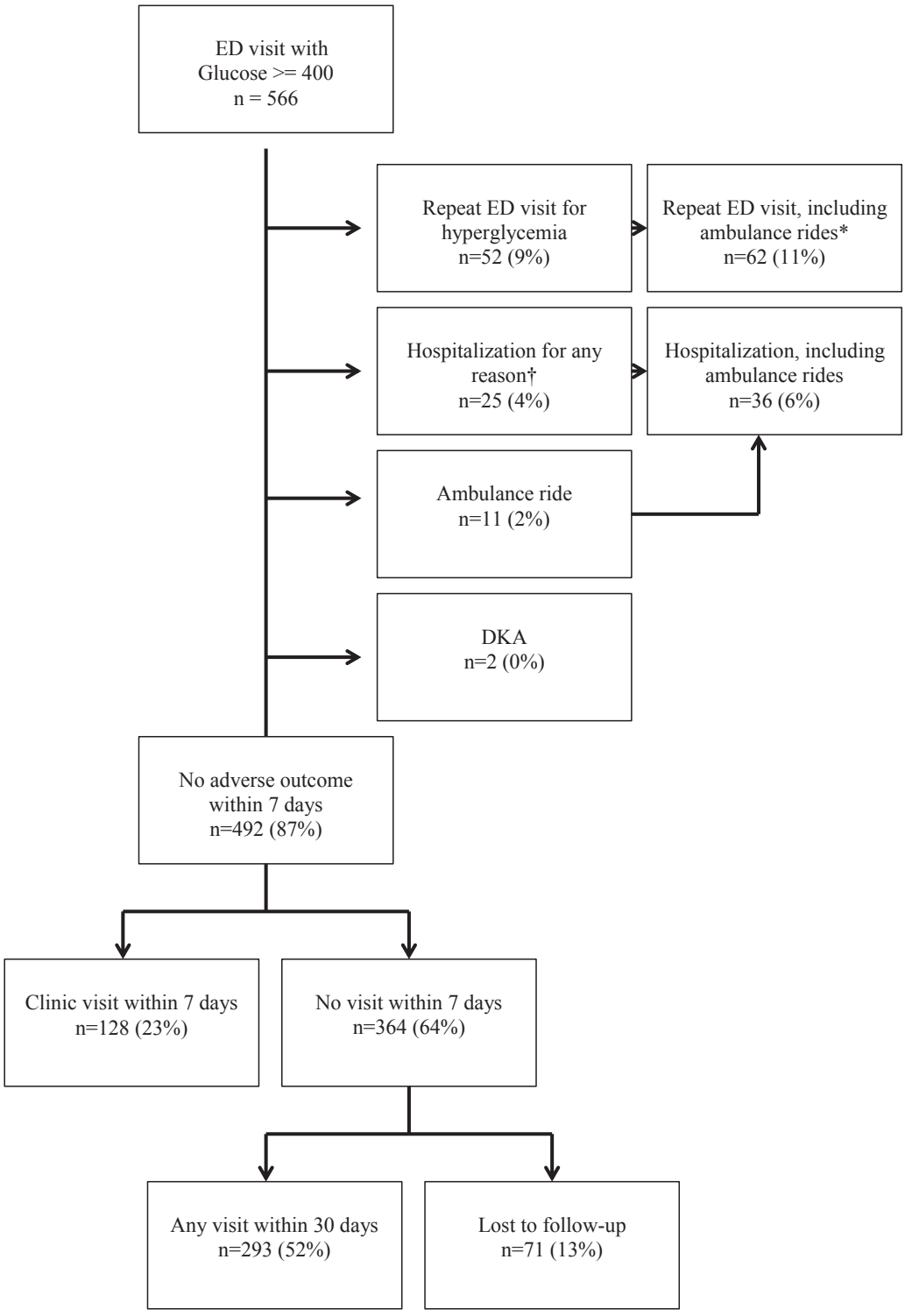

Figure 1. Flow diagram of study patients for 7-day outcomes and subsequent follow-up. *Of the 11 patients with an ambulance ride, 1 had a repeat ED visit for hyperglycemia in addition to the ambulance ride. †Of these 25 patients, 13 had a repeat ED visit for hyperglycemia. Both patients with DKA were hospitalized. *DKA*, Diabetic ketoacidosis.

the 446 patient encounters with a recent hemoglobin A_{1c} level available, glycemic control in the preceding months was poor, with a mean value of 10.7 mmol/mol (SD 2.8 mmol/mol). The management for moderate to severe hyperglycemia before discharge is presented in Table 2. In most encounters, laboratory studies were obtained, although in 89 (16%) neither a urinalysis nor basic chemistry panel was ordered. No patient had diabetic

Table 1. Baseline data.

	n = 566
Chief complaint, No. (%)	
Hyperglycemia	279 (49)
Alcohol intoxication	61 (11)
Abdominal pain	35 (6)
Abscess	22 (4)
Other	169 (30)
Arrival glucose level, mean (SD), mg/dL	491 (82)
Recent hemoglobin A_{1c} level, mean (SD), mmol/mol*	10.7 (2.8)

*A_{1c} data available for 446 patients.

ketoacidosis. Although a low bicarbonate level (≤15 mEq/L) and elevated anion gap level (>15 mEq/L) occurred in only 3 encounters (1%), in 85 encounters (23% of patients tested) ketonuria was observed. Glucose-lowering therapies were provided in most encounters. In 341 encounters (60%), both intravenous fluids and subcutaneous insulin were administered; in 70 (12%) neither was administered. Iatrogenic hypoglycemia occurred in 9 encounters (2%; 95% CI 0% to 3%). Mean glucose reduction and discharge glucose values were 157 mg/dL (SD 128 mg/dL) and 334 mg/dL (SD 101 mg/dL), respectively. Discharge glucose level ranged from 48 to 694 mg/dL; in 221 (39%) encounters, the discharge glucose level was greater than 350 mg/dL. The discharge glucose was greater than or equal to 600 mg/dL in 11 encounters; details can be found in Table E1 (available online at http://www.annemergmed.com). Glucose level was recorded in the electronic medical record as high and presumed to be 600 mg/dL for the arrival and discharge glucose levels of 74 (13%) and 9 (2%) encounters, respectively.

Main Results

Figure 1 displays the flow of study subjects. There were 71 (13%) encounters that were lost to follow-up, leaving 495 encounters for analysis of the primary outcome. Patients lost to follow-up had glucose values similar to those who were not. Mean arrival and discharge glucose values for patients lost and not lost to follow-up were 480 and 492 mg/dL, and 349 and 332 mg/dL, respectively.

The outcomes of return ED visit for hyperglycemia and hospitalization occurred in 62 (13%) and 36 (7%) encounters, respectively. Mean discharge glucose values for patients with and without a 7-day adverse outcome were 317 mg/dL (SD 96 mg/dL) and 336 mg/dL (SD 101 mg/dL), respectively, with a difference of –20 mg/dL (95% CI –45 to 6 mg/dL). The reasons for hospitalization are listed in Table E2 (available online at http://www.annemergmed.com). Diabetic ketoacidosis in follow-up was rare, occurring in 2 patients, and no patients were observed to have hyperosmolar hyperglycemic state. No deaths were observed. After adjusting for confounders with generalized estimating equation models, there was no association between discharge glucose level and either repeat ED visit for hyperglycemia (odds ratio 0.997; 95% CI 0.993 to 1.001) or hospitalization (odds ratio 0.998; 95% CI 0.995 to 1.002) in the 7 days after the index ED encounter. The outcomes by arrival and discharge glucose are presented in Figure 2. Interobserver agreement to ascertain the outcomes was excellent, with κ values of 0.96 and 0.86 for repeated ED visit for hyperglycemia and hospitalization, respectively.

The models for the 2 outcomes are displayed in Table 3. No covariate was associated with either outcome. Goodness of fit was estimated with quasi-likelihood under the independence model criterion, and both models had

Table 2. ED management of hyperglycemia.

	n = 566
Urinalysis obtained, No. (%; 95% CI)	367 (65; 61–69)
Urine ketones present, No. (% of obtained)	85 (23)
Basic chemistry obtained, No. (%; 95% CI)	414 (73; 69–77)
Intravenous fluid administered, No. (%; 95% CI)	448 (79; 76–82)
Amount of intravenous fluid administered, if received, mean (SD), L	2.1 (0.9)
Subcutaneous insulin administered, No. (%; 95% CI)	389 (69; 65–73)
Amount of subcutaneous insulin administered, if received, mean (SD), U	12.2 (7.0)
Glucose-level reduction, mean (SD), mg/dL	157 (128)
Discharge glucose level, mean (SD), mg/dL	334 (101)
Length of stay, mean (SD), min	276 (143)
Iatrogenic hypoglycemia, No. (%; 95% CI)	9 (2; 0–3)
Discharge prescription for diabetes medication, No. (%)	169 (30)

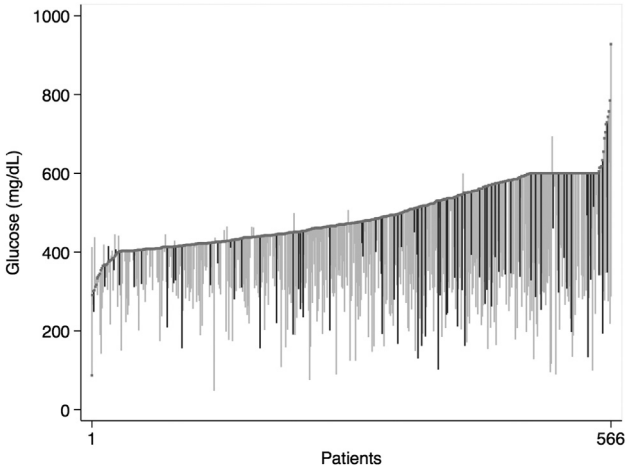

Figure 2. Arrival and discharge glucose values by outcome. The gray dot denotes the arrival glucose; the line connects arrival glucose level to discharge glucose level. Darker lines represent patients with a repeat ED visit for hyperglycemia or hospitalization for any reason within 7 days.

Table 3. Generalized estimating equation model results for 7-day outcomes.

	Seven-Day ED Visit for Hyperglycemia*		Seven-Day Hospitalization for Any Reason*	
Predictors	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Arrival glucose level, mg/dL	1.004	0.999–1.008	1.000	0.995–1.004
Discharge glucose level, mg/dL	0.997	0.993–1.001	0.998	0.995–1.002
Basic chemistry obtained	1.19	0.39–3.67	1.19	0.40–3.52
Intravenous fluids received, L	0.90	0.64–1.27	0.93	0.57–1.51
Insulin received, U	0.99	0.94–1.04	1.02	0.97–1.07

*This examines the 495 encounters not lost to follow-up.

satisfactory fitting; values for repeat ED visit for hyperglycemia and hospitalization were 384 and 271, respectively.

A secondary model was constructed with discharge glucose level as a dichotomous variable, with a threshold of 350 mg/dL. There was no association between a discharge glucose level of greater than 350 mg/dL and any 7-day outcome (Table 4).

When age was included as a covariate in post hoc analysis, there remained no association between discharge glucose level and 7-day adverse outcomes (Table E3, available online at http://www.annemergmed.com). In this model, the only variable associated with either outcome was arrival glucose level for return ED visit for hyperglycemia, with an odds ratio of 1.004, indicating that the odds ratio for a repeat ED visit for hyperglycemia increased to 1.49 and 2.22 for an increase in arrival glucose level of 100 and 200 mg/dL, respectively, assuming all other variables were held constant.

Results of the sensitivity analyses are presented in Tables E4 and E5 (available online at http://www.annemergmed.com). In both analyses, discharge glucose level had no association between either repeat ED visit for hyperglycemia or hospitalization. These analyses were repeated 500 times at each interval over a range of assumptions. For the first sensitivity analysis, an increasing discharge glucose level was associated with repeat ED visit for hyperglycemia and hospitalization for more than 5% of iterations when the increased chance of the outcome was 24% or higher and 10% or higher, respectively. The thresholds for the second sensitivity analysis were 37% or higher and 15% or higher, respectively.

LIMITATIONS

This investigation has several important limitations. First, this was a retrospective study and is subject to many inherent limitations. We attempted to mitigate this by adjusting for confounding variables, and guidelines for an unbiased chart review investigation were followed.[11,12] The outcomes chosen were objective and binary. Although outcome assessors were not blinded to the study outcomes, data for the outcome of interest were collected before other data points. To assess whether lack of blinding could have introduced bias into the outcome measurements, interobserver agreement was measured; κ values were excellent.

Second, the assessment of 7-day outcomes was imperfect owing to the fact that patients may seek care at more than 1 hospital. We first mitigated some of this bias by reviewing countywide ambulance data to determine whether any subjects had an ambulance ride to another institution; we assumed all ambulance rides were for hyperglycemia that resulted in a hospitalization. We then performed a sensitivity analysis that assumed encounters with a

Table 4. Generalized estimating equation model results for 7-day outcomes, with discharge glucose level as a dichotomous variable (350 mg/dL threshold).*

	Seven-Day ED Visit for Hyperglycemia		Seven-Day Hospitalization for Any Reason	
Predictors	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Arrival glucose level, mg/dL	1.004	0.999–1.008	1.000	0.995–1.004
Discharge glucose level >350 mg/dL	0.69	0.26–1.82	0.86	0.39–1.89
Basic chemistry obtained	1.29	0.39–4.24	1.25	0.41–3.83
Intravenous fluids received, L	0.92	0.65–1.30	0.95	0.59–1.52
Insulin received, U	0.99	0.94–1.04	1.02	0.97–1.07

*This model is identical to the primary model (Table 3), except that discharge glucose level is a dichotomous rather than continuous variable, which is meant to replicate the clinical practice in which a patient is eligible for discharge only after reduction of the glucose level to below a specific threshold.

discharge glucose level greater than 350 mg/dL had higher outcome rates to increase the chance of finding an association between increasing discharge glucose level and 7-day outcomes. Furthermore, in case the recorded discharge glucose level was not the actual one at discharge, we performed an additional sensitivity analysis identical to the first, except that if insulin was administered during the ED visit, the discharge glucose level was assumed to be 20% lower than the recorded value. This sought to increase the chance of finding an association between discharge glucose level and the 7-day outcomes if a higher discharge glucose level in untreated patients increased the risk of any outcome. Even after introducing bias to favor an association between increasing discharge glucose level and 7-day outcomes, we did not detect an association. These assumptions were varied across a range. If 24% and 10% or more additional patients with a discharge glucose level greater than 350 mg/dL had a repeat ED visit for hyperglycemia or hospitalization at another hospital, respectively, and no additional patients with a discharge glucose level less than or equal to 350 mg/dL had either outcome, then the results of this study would not be valid, although this is unlikely.

Third, some actual glucose values were unknown, instead resulting in the electronic medical record as "high." The upper limit of detection for point-of-care glucose-level meters in our ED is 600 mg/dL, and all readings of "high" were assumed to be 600 mg/dL. It was more common to observe this for arrival glucose values (13%) compared with discharge ones (2%). This limitation could therefore have affected the association of arrival glucose level to 7-day outcomes, but should not have significantly affected the primary analysis of discharge glucose level.

Fourth, if emergency physicians provided treatment only to patients who were intuitively deemed to require ED glucose reduction to avoid a short-term outcome, but did not provide treatment to patients deemed low risk for a short-term outcome regardless of glucose reduction, this would introduce bias against finding an association between discharge glucose level and 7-day outcomes. If, instead, emergency physicians generally decreased glucose values to an arbitrary threshold because this represented usual care, then no bias would be introduced. Because predicting who will have an adverse short-term outcome because of hyperglycemia is difficult, and because most patients well enough to be discharged after evaluation of hyperglycemia probably appear well on initial evaluation, it seems more likely that physicians did not systematically treat only those at higher risk of an adverse outcome.

Fifth, this investigation examined only patients who were eventually discharged directly from the ED. Thus, the results are not applicable to patients being admitted to the hospital with or because of hyperglycemia because this represents a different patient population.

DISCUSSION

To our knowledge, this is the first investigation describing ED treatments and associated outcomes for moderate to severe hyperglycemia in eventually discharged patients. We found no association between discharge glucose level and 7-day outcomes of repeat ED visit for hyperglycemia or hospitalization for any reason. Although conventional practice holds that the glucose level must be decreased in the ED to mitigate the risk of short-term adverse events, this practice is not supported by the results of this investigation. On multivariate analysis, no ED intervention was associated with short-term outcomes; therefore it is probable that baseline glycemic control and the attention paid to glycemic control in the days after the ED visit were important in modulating the risk for short-term adverse outcomes. ED efforts should probably be focused on factors that can improve outpatient glycemic control, such as ensuring an adequate supply of medications, supplies, and knowledge of medication use. Close outpatient follow-up to maintain glycemic control is also likely important.

The care received by patients with moderate to severe hyperglycemia was variable. Discharge glucose values spanned a wide range, and some patients received extensive laboratory evaluation and treatment, whereas others had none. This is more likely to represent a lack of consensus on how to best treat this patient population rather than selective treatment of only individuals deemed to be higher risk of short-term outcomes.

Most patients received intravenous fluids, which can be a time-consuming process. A recent small randomized trial that enrolled patients with hyperglycemia found no difference in glucose-level reduction with intravenous fluids compared with oral fluids; additionally, each arm had only a modest reduction in glucose with fluid administration (approximately 39 mg/dL glucose-level reduction per liter of oral or intravenous fluid given).[10]

Treatment for hyperglycemia was not without risk; 9 patients (2%) developed iatrogenic hypoglycemia during treatment of hyperglycemia. In this patient population, hypoglycemia is probably a more significant threat to life than hyperglycemia. Diabetic ketoacidosis was rarely observed in 7-day follow-up, which is consistent with low rates of diabetic ketoacidosis in patients with type 2 diabetes mellitus,[7,8] especially in a population that was selected to be safe for discharge after ED evaluation. It is not surprising that hyperosmolar hyperglycemic state was

not observed because this syndrome is more rare than diabetic ketoacidosis and usually develops during several days to weeks. Therefore, it may not be observed in a 7-day follow-up window.[9]

In summary, the ED discharge glucose level in patients with moderate to severe hyperglycemia was not associated with 7-day outcomes of repeat ED visit for hyperglycemia or hospitalization. Further studies should investigate the safety of minimizing ED treatments for moderate to severe hyperglycemia in patients who are well enough to be discharged. Although our study did not show an increased 7-day adverse outcome rate in patients with higher discharge glucose values, design limitations did not allow a safety assessment of avoiding treatment in moderate to severe ED hyperglycemia. In conclusion, attaining a specific glucose-level goal before discharge in patients with moderate to severe hyperglycemia may be less important than traditionally thought.

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Author affiliations: From the Department of Emergency Medicine, Hennepin County Medical Center, Minneapolis, MN.

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Table E1. ED and 7-day outcomes for patients with a discharge glucose level greater than or equal to 600 mg/dL.*

Chief Complaint	Arrival Glucose Level, mg/dL	Discharge Glucose Level, mg/dL	Fluids Administered, L	Insulin Administered, Units	Length of Stay, Minutes	Left Against Medical Advice	Repeat ED Visit for Hyperglycemia	Hospitalization	Lost to Follow-up
Hyperglycemia	600	600	0	10	41	No	Yes	No	No
Hyperglycemia	600	694	3	0	153	Yes	No	No	No
Back pain	546	600	0	0	230	Yes	No	No	No
Dental pain	600	600	0	0	107	Yes	No	No	No
Weakness	757	627	2	0	368	No	No	No	Yes
Foot pain	600	600	0	0	165	Yes	No	No	No
Hyperglycemia	600	600	0	0	224	Yes	No	No	No
Hyperglycemia	613	600	2	0	257	No	No	No	No
Dental pain	600	600	2	0	120	No	No	No	Yes
Cough	600	600	0	0	21	Yes	No	No	No
Hyperglycemia	600	600	0	0	84	No	No	No	Yes

*In this group, no patient had diabetic ketoacidosis, death, or an ambulance ride within 7 days from the index ED encounter. The patient with a discharge glucose level of 694 mg/dL was the only patient with a clinic visit within 7 days.

Table E2. Patients requiring hospitalization within 7 days of the index ED encounter.

Encounter*	Arrival Glucose Level, mg/dL	Discharge Glucose Level, mg/dL	Primary Diagnosis, Index ED Visit	Number of Days Between Index Encounter and Hospitalization	Admission Diagnosis	Discharge Diagnosis
1	423	316	Ankle fracture	3	Ankle fracture	Ankle fracture, ORIF
2†	536	245	Hyperglycemia	1	Hyperglycemia	Hyperglycemia
3	413	321	Asthma exacerbation	2	Asthma exacerbation	Asthma exacerbation
4	425	371	Hyperglycemia	1	Hyperglycemia	Chronic pancreatitis
5	582	346	Seizure	5	Community-acquired pneumonia	Community-acquired pneumonia
6†	560	336	Alcohol intoxication	5	Right hand pain	Right hand soft tissue infection
7	499	413	Abscess	2	Abscess	Abscess, status post incision and drainage
8	300	248	Gastroenteritis	2	Vomiting	Vomiting
9	415	412	Foot ulcer after burn	3	Foot ulcer after burn	Foot ulcer after burn, no debridement performed
10	573	387	Hyperglycemia	3	Chest pain	Chest pain, noncardiac
11	600	385	Alcohol intoxication	3	Altered mental status	Altered mental status as a result of alcohol and drug intoxication
12	444	220	Hyperglycemia	2	Hyperglycemia	Hyperglycemia
13	566	268	Hyperglycemia	1	Seizure	Pseudoseizure
14	496	167	Hyperglycemia	5	Diabetic ketoacidosis	Diabetic ketoacidosis
15	600	297	Hyperglycemia	6	Diabetic ketoacidosis	Diabetic ketoacidosis
16	414	328	Hyperglycemia	6	Chest pain	Chest pain, noncardiac
17	600	460	Leg edema caused by venous stasis	1	Hyperglycemia	Hyperglycemia
18‡	600	307	Seizure	7	Foot ulcer with cellulitis	Foot ulcer with cellulitis
19	403	311	Cavitary lung lesion	2	Pulmonary abscess	Pulmonary abscess
20	412	209	Abdominal pain	3	Pancreatitis	Hypertriglyceridemia with pancreatitis
21‡	451	255	Hyperglycemia	1	Hyperglycemia	Hyperglycemia
22	600	515	Hyperglycemia	6	Chest pain	NSTEMI
23	405	319	Hyperglycemia	1	Pneumonia	NSTEMI
24	518	186	Pneumonia	3	Pneumonia	Pneumonia
25†	484	400	Hyperglycemia	0	Lower extremity cellulitis	Lower extremity cellulitis

ORIF, Open reduction internal fixation; *NSTEMI*, non-ST-segment elevation myocardial infarction.
*The remaining 11 patients not accounted for in this table were assumed to have been admitted after an ambulance ride.
†Encounters 2, 6, and 25 were the same patient.
‡Encounters 18 and 21 were the same patient.

Table E3. Post hoc analysis: generalized estimating equation model, accounting for age.*

	Seven-Day ED Visit for Hyperglycemia		Seven-Day Hospitalization for Any Reason	
Predictors	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Arrival glucose level, mg/dL	1.004	1.000–1.008	1.000	0.995–1.004
Discharge glucose level, mg/dL	0.997	0.993–1.001	0.998	0.995–1.002
Basic chemistry obtained	1.19	0.39–3.68	1.19	0.40–3.51
Intravenous fluids received, L	0.90	0.63–1.30	0.93	0.58–1.51
Insulin received, U	0.99	0.94–1.04	1.02	0.97–1.06
Age, y	1.00	0.98–1.02	1.00	0.97–1.03

*This analysis is identical to the primary model (Table 3), except that age is included as a covariate to account for the possibility that increasing age increases the likelihood of a repeated visit for hyperglycemia or hospitalization.

Table E4. First sensitivity analysis.*

	Seven-Day ED Visit for Hyperglycemia		Seven-Day Hospitalization for Any Reason	
Predictors	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Arrival glucose level, mg/dL	1.004	1.000–1.008	1.002	0.998–1.006
Discharge glucose level, mg/dL	0.999	0.996–1.003	1.000	0.996–1.003
Basic chemistry obtained	0.89	0.41–1.94	1.04	0.38–2.84
Intravenous fluids received, L	0.89	0.66–1.18	0.94	0.61–1.46
Insulin received, U	0.97	0.93–1.02	1.01	0.96–1.05

*This sensitivity analysis includes all 567 encounters and attempts to account for instances in which patients sought care at another institution in the 7 days after the index ED encounter, with a bias that patients discharged with hyperglycemia would be more likely to have an adverse outcome. This analysis assumes that patients with a discharge glucose level greater than 350 mg/dL who had no visit within 7 days (n=364) (Figure 1) had a 15% chance of repeated ED visit for hyperglycemia and a 5% chance of hospitalization. Data for patients who were already known to have a repeat ED visit for hyperglycemia or hospitalization were unchanged in this analysis.

Table E5. Second sensitivity analysis.*

	Seven-Day ED Visit for Hyperglycemia		Seven-Day Hospitalization for Any Reason	
Predictors	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Arrival glucose level, mg/dL	1.003	0.999–1.007	1.000	0.996–1.004
Discharge glucose level, mg/dL	0.998	0.994–1.001	1.000	0.996–1.004
Basic chemistry obtained	1.01	0.42–2.45	1.47	0.49–4.37
Intravenous fluids received, L	0.83	0.60–1.13	0.86	0.55–1.35
Insulin received, U	0.98	0.94–1.03	1.01	0.96–1.06

*This sensitivity analysis is identical to the first (Table E4), except that patients who received insulin during the index ED encounter were assumed to have a discharge glucose level 20% lower than the recorded discharge glucose level to account for instances in which patients were discharged before the peak effect of the insulin.