Original Contribution

Comparison of two glycemic discharge goals in ED patients with hyperglycemia, a randomized trial

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ABSTRACT

Study objective: Hyperglycemia is commonly encountered in the ED; the importance of glucose reduction in patients well enough to be discharged is unknown.
Methods: We conducted a prospective, randomized trial of ED patients with hyperglycemia with a glucose value 400–600 mg/dL who were discharged from the ED, excluding those with type 1 diabetes mellitus. Patients were randomly assigned to a discharge glucose goal, <350 mg/dL (moderate control) or < 600 mg/dL (loose control). The primary outcome was ED length of stay.
Results: Among 110 enrolled patients, 57 were assigned to moderate and 53 to loose glycemic control. Median (IQR) length of stay was 211 min (177–288 min) for the moderate group and 216 min (151–269 min) for the loose group (difference, 17 min [95% CI −15 to 49 min]). ED length of stay for those with an actual discharge glucose <350 mg/dL was 29 min longer (95% CI −1 to 59 min). Repeat ED visits for hyperglycemia (7% vs 6%), hospitalization for hyperglycemia (0% vs 2%), and hospitalization for any reason (4% vs 8%) did not differ significantly between groups.
Conclusion: In the intention-to-treat analysis, ED length of stay and 7-day outcomes were not significantly different whether moderate or loose glycemic control was pursued. However, the length of stay for those with discharge glucose <350 mg/dL was approximately 29 min longer. ED glycemic control did not appear to be associated negative short-term outcomes. Glucose reduction in well-appearing ED patients may consume time and resources without conferring short- or long-term benefits.
Trial Registration: Clinicaltrials.gov NCT02478190

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1. Introduction

1.1. Background

Diabetes mellitus is a prevalent chronic disease in the U.S., and the incidence continues to increase [1]. Consequently, emergency physicians frequently care for patients with hyperglycemia in the Emergency Department (ED) [2]. Although some patients with hyperglycemia are critically ill with diabetic ketoacidosis or hyperosmolar hyperglycemic state, it is more common for patients with hyperglycemia, especially those with type 2 diabetes mellitus, to be considered for discharge from the ED after evaluation and treatment.

Despite the prevalence of hyperglycemia in the ED, there remains no consensus on the necessity of ED glucose reduction or other therapies for patients with hyperglycemia without a hyperglycemic emergency

or another illness necessitating hospital admission [3-5]. Some advocate admission to the hospital if the glucose is >400 mg/dL [6], others believe glucose reduction in the ED or admission to observation units is appropriate to facilitate glycemic control [7,8]; alternatively, retrospective data demonstrate that the discharge glucose value is not associated with short-term adverse events, suggesting it may be safe to discharge these patients directly from the ED. [9]

Long-term glycemic control is paramount to decrease the risk of diabetes-associated complications such as vascular disease, nephropathy, and retinopathy. However, the importance of glycemic control as an endpoint during any one ED encounter, which is unlikely to mitigate long-term diabetes-associated complications or to be associated with short-term adverse outcomes in patients well enough to be discharged [9], has not been well studied. It could be that, similar to ED patients with elevated blood pressure but without evidence of end organ injury [10], ED efforts should focus on appropriate outpatient pharmacologic therapy and close primary care follow-up. Additionally, glucose lowering therapies in the ED consume time and resources [11], and can occasionally cause iatrogenic hypoglycemia [9].

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1.2. Goals of the investigation

We sought to compare ED length of stay and 7-day outcomes between ED patients with hyperglycemia treated with a goal of moderate (<350 mg/dL) versus loose (<600 mg/dL) glycemic control, by conducting a randomized clinical trial. We hypothesized that ED length of stay would be at least 60 min shorter in the loose glycemic control group. We selected ED length of stay as the primary outcome as it is an important metric that is associated with quality of care and ED crowding and could be influenced by the amount of treatment received [12-16].

2. Materials and methods

2.1. Trial design and setting

We conducted a prospective, randomized clinical trial in the ED of an urban, county, academic Level 1 Trauma Center with approximately 100,000 annual ED visits. This ED does not have a standardized protocol for caring for patients with hyperglycemia or a streamlined process to assure primary care or endocrinologist follow-up.

The local institutional review board approved this study, and all patients provided written informed consent. The study was registered at Clinicaltrials.gov, NCT02478190.

2.2. Patient selection

Trained research associates screened consecutive adult (≥ 18 years old) ED patients. Patients were eligible if they had an ED glucose value of >400 mg/dL and < 600 mg/dL, the treating physician intended to discharge the patient at the end of the encounter, and the patient had a working phone and was willing to discuss their health status one week after enrollment. Patients were excluded if they had type 1 diabetes mellitus, had already received insulin in the ED, did not speak English, had diabetic ketoacidosis or were otherwise critically ill (in the opinion of the treating physician), were a prisoner or pregnant, or were unable to provide informed consent. To determine the type of diabetes, we asked both the patient and physician if the patient had type 1 or 2 diabetes. No laboratory studies were required before enrollment. Ketoacidosis, for the purpose of enrollment, was not formally defined; the treating physician determined whether the patient had diabetic ketoacidosis either by gestalt (i.e., without laboratory studies) or by review of laboratory results, though no serum bicarbonate or anion gap cutoffs were provided. A physician evaluation occurred prior to enrollment, but there was no stipulation as to when enrollment had to occur (e.g., before or after lab results returned, or within a specified time of being roomed in the ED); enrollment could occur at any point after the initial physician evaluation but before discharge, provided the patient met inclusion and exclusion criteria.

We selected the lower limit of the eligible glucose range because below this level most physicians in our ED are comfortable limiting ED interventions. Above this level there seemed to be equipoise in our practice; some physicians feel there is a need to lower the glucose value before discharge while others think this practice lacks value. The upper limit was selected because glucose values higher than 600 mg/dL cannot be detected by our point-of-care glucometers, which simply read "HIGH."

2.3. Randomization and trial procedures

Eligible patients were randomly assigned in a 1:1 ratio to either moderate or loose glucose control. Randomization was performed before the start of the trial with the use of a computer-generated assignment sequence in permuted blocks of varying sizes. In an attempt to balance the number of patients in each treatment group presenting to the ED primarily for hyperglycemia, the randomization had two strata:

those with a chief complaint of hyperglycemia, and those with any other chief complaint. Intervention assignments were placed inside a folded sheet of paper in sequentially-numbered, opaque envelopes; after enrollment, a research associate opened the next envelope in the appropriate strata to determine group allocation.

Patients in the moderate and loose glucose control groups had goal ED discharge glucose values of <350 mg/dL and <600 mg/dL, respectively. This trial stipulated only the goal discharge glucose; all other care of the patient was at the discretion of the treating physician. There was no required treatment protocol in either group. In the moderate control group, the treating physicians received a recommendation to provide 0.1–0.2 units/kg of insulin aspart or the patient's usual home dose of short-acting insulin. In both groups, the treating physicians were instructed that fluid therapy was not required; if hydration was indicated, either intravenous or oral hydration were acceptable. Physicians were reminded that a recent randomized trial demonstrated similar, and modest, glucose reduction when intravenous or oral fluids were administered for hyperglycemia (approximately 40 mg/dL reduction per L administered) [17]. The physician instruction sheets with prompts for each group are available in the Supplementary Appendix. At discharge, for patients not currently taking antihyperglycemic agents we recommended prescribing glipizide XL 10 mg daily [18].

The treating physicians were blinded to the study outcomes, but by virtue of the interventions, the treating physicians were not blinded to the group allocation. A point-of-care glucose was obtained shortly before discharge to measure ED discharge glucose. Patients who, contrary to the initial treatment plan, were admitted to the hospital from the ED after study enrollment were excluded from outcome analyses.

2.4. Measurements

A trained research associate recorded patient demographics and ED glucose values. The treating physician completed a structured data collection form to record baseline antihyperglycemic agents, the amount of oral rehydration provided in the ED, and any prescriptions provided at discharge.

A trained abstractor blinded to group assignment reviewed the medical record to record the time the patient was roomed in the ED, time of the ED discharge order, laboratory and radiology studies obtained and the results, type and amount of insulin administered, amount of intravenous fluids administered, whether iatrogenic hypoglycemia occurred, and the final ED diagnoses. Iatrogenic hypoglycemia was defined as any glucose value <60 mg/dL, a glucose value <100 mg/dL with symptoms of hypoglycemia that resolved with food/drink, or any administration of 50% dextrose (0.5 g/mL), glucagon, or dextrose gel/tabs.

A trained, blinded research associate called each patient 7–10 days after enrollment and asked whether they had visited an ED or been hospitalized in the 7 days following enrollment, and the related reason. An ED visit or hospitalization was considered to be related to hyperglycemia if the chief complaint of the visit was hyperglycemia, if the chief complaint was polyuria, polydipsia, fatigue, blurry vision, or malaise and the patient had a glucose >250 mg/dL, or if the final ED or hospital diagnoses contained hyperglycemia, diabetic ketoacidosis, or hyperosmolar hyperglycemic state. For patients we could not contact by phone, we checked the medical record at our institution to determine if repeat ED visits or hospitalizations occurred, and why; we also checked if they had a future encounter at our hospital after 7 days and if hospitalization or diabetic ketoacidosis was mentioned in note for the first encounter after the 7-day period. If we could not contact a patient and they had no future encounter in our institution, we did not assign any value to the 7-day outcomes.

2.5. Study outcomes

The primary outcome was ED length of stay, defined as the time elapsed between rooming the patient in the ED and placement of the

discharge order by the physician. Secondary outcomes included repeat ED visit for hyperglycemia, hospitalization for any reason except trauma, or repeat ED visit for any reason within 7 days, and iatrogenic hypoglycemia.

2.6. Data analysis

The study was powered to detect a 60 min absolute difference in length of stay between groups, which was thought to be a meaningful difference from the perspectives of both physicians and patients. Based on pilot data at our institution the standard deviation of length of stay was approximately 100 min; therefore, we anticipated that 45 patients per group would be required to detect this difference with 80% power using a two-sided alpha of 0.05. We intended to continue enrollment until 90 patients were reached in 7-day follow up.

We present baseline and ED management data by group assignment, using means, medians, or proportions as appropriate for the distribution of the data. The primary and secondary outcomes were compared by calculating the difference in median value or proportion between groups, and the associated 95% confidence interval (95% CI). Stata 15.1 (StataCorp, College Station, TX) was used for data analysis.

3. Results

3.1. Baseline characteristics and ED management

Between June 2015 and December 2017, we enrolled 130 patients (Fig. 1); 12 were admitted to the hospital and 8 withdrew during the encounter and were excluded (admission reasons listed in
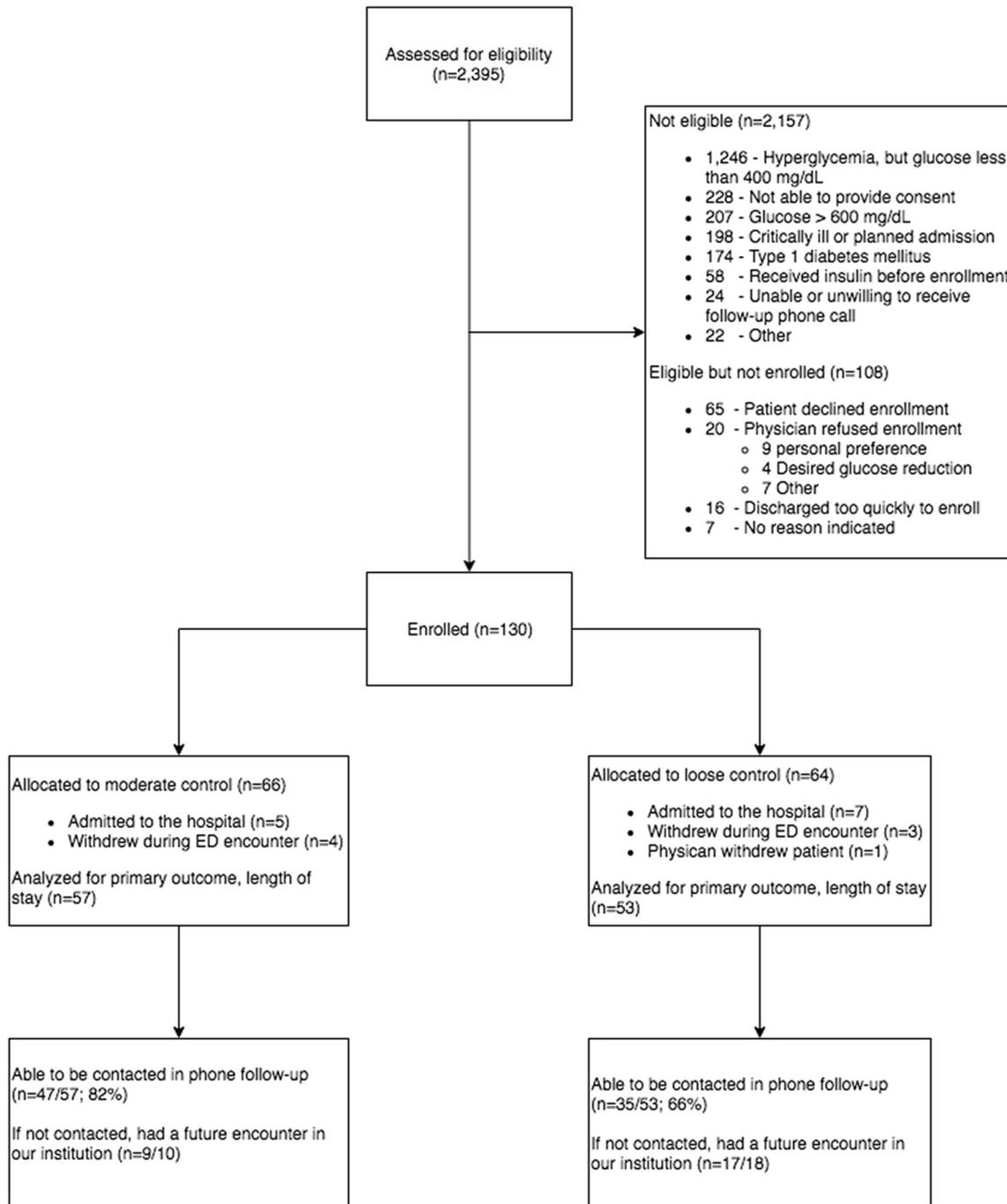

Fig. 1. This figure displays the flow of patients through the study. Those admitted to the hospital or withdrawn during the ED encounter were not analyzed for the primary outcome.

Table 1
Baseline characteristics.

Characteristic	Moderate control (N = 57)	Loose control (N = 53)
Age, mean ± SD - years	49 ± 12	49 ± 11
Male - no. (%)	39 (68)	27 (51)
Race/Ethnicity - no. (%)		
Black/African American	43 (75)	34 (64)
White/Caucasian	10 (18)	11 (21)
Native American	2 (4)	4 (8)
Hispanic	2 (4)	1 (2)
Other	0 (0)	3 (6)
Chief complaint - no. (%)		
High blood sugar	44 (77)	44 (83)
Blurry vision	3 (5)	1 (2)
Fatigue/Malaise	0 (0)	1 (2)
Polydipsia	1 (2)	0 (0)
Polyuria	3 (5)	1 (2)
Other	25 (44)	23 (43)
History of diabetes mellitus - no. (%)	54 (95)	49 (92)
Recent hemoglobin A1c, median (IQR)[b] - %	10.1 (7.1–12.5)	10.8 (8.9–13)
Baseline diabetes medications[c] - no. (%)		
Short-acting insulin	27 (47)	20 (38)
Long-acting insulin	25 (44)	30 (57)
Combination product of short & long insulin	3 (5)	4 (8)
Sulfonylurea	8 (14)	4 (8)
Metformin	28 (49)	19 (36)
Other	3 (5)	4 (8)
No baseline prescriptions	3 (5)	6 (11)
Elapsed time from ED rooming to enrollment, median (IQR) - min	63 (40–107)	69 (49–138)
Glucose at enrollment, median (IQR) - mg/dL	476 (438–512)	460 (429–528)

IQR: interquartile range; SD: standard deviation. [a]Patients could have more than one chief complaint.; [b]Hemoglobin A1c within 3 months of enrollment, available for 21 patients in each group.; [c]Patients could have more than one baseline medication.

Supplementary Table E1), leaving 110 patients for analysis; 57 were assigned to moderate control and 53 were assigned to loose control. Baseline characteristics are displayed in Table 1; median (interquartile range [IQR]) glucose at enrollment was 468 mg/dL (432–522 mg/dL) and most patients (80%) had a chief complaint of hyperglycemia. The time from being roomed to enrollment was 65 min (41–107 min) for moderate control and 69 min (49–138 min) for the loose control group, with a median difference of −8 min (95% CI −24 to 8 min).

ED management is presented in Table 2. Rates of blood, urine, and radiographic testing were similar between groups, as was the proportion receiving oral and intravenous fluid therapy. The moderate control group received insulin more frequently (79% vs 8%), had greater median glucose reduction (138 vs 39 mg/dL), and a lower median discharge glucose value (319 vs 429 mg/dL).

3.2. Primary outcome

The length of stay was similar in both groups; median (IQR) length of stay for the moderate and loose control groups was 211 min (177–288 min) and 216 min (151–269 min), respectively, with a median difference of 17 min (95% CI −15 to 49 min).

In a post hoc analysis, ED length of stay for those with an actual discharge glucose <350 mg/dL (including patients from both groups) was 29 min longer (95% CI −1 to 59 min) than those with a discharge glucose ≥350 mg/dL. In a second post hoc analysis, the ED length of stay after enrollment (elapsed time from enrollment to ED discharge) favored the loose control group, with a difference of 46 min (95% CI 18–72 min) (Table 3). For these analyses we calculated the difference between moderate control compared to loose control, therefore a positive value represents a higher value or point-estimate for the moderate control group. Combining patients from both groups, the median ED length of stay for those who received intravenous fluids was 52 min

longer (95% CI 16–85 min) than those who did not. Arrival and discharge glucose and ED length of stay are presented in Fig. 2.

3.3. Follow-up and secondary outcomes

We were able to contact 82 patients (75%) by phone in follow-up, 47 in the moderate control (82%) and 35 in the loose control group (66%). Of the 28 patients we could not contact, 26/28 were cared for in our institution again, and for these 26 no subsequent patient encounter mentioned hospitalization or diabetic ketoacidosis within 7 days of study enrollment.

Secondary outcomes were not significantly different between groups. Repeat ED visits for hyperglycemia were uncommon and no patient was observed to have diabetic ketoacidosis or hyperosmolar hyperglycemic state. Hospitalizations for other reasons were infrequent and not clearly related to hyperglycemia. Table 3 displays details of the secondary outcomes.

4. Limitations

In retrospect, the choice of length of stay as a primary outcome was not ideal. Length of stay is influenced by many factors, including

Table 2
ED management.

Parameter	Moderate control (N = 57)	Loose control (N = 53)
Laboratory and radiology testing obtained and results - no. (%)		
Urinalysis	39 (68)	33 (62)
Ketonuria	5/39 (13)	2/33 (6)
Chemistry panel	49 (86)	49 (92)
Total carbon dioxide, median (IQR) - mmol/L	25 (24–27)	25 (22–26)
Anion gap, median (IQR) - mmol/L	9 (7–10)	9 (7–10)
Venous blood gas	6 (11)	3 (6)
Complete blood count	29 (51)	20 (38)
Other laboratory tests	2 (4)	5 (10)
Radiograph	11 (19)	14 (26)
Computed tomography	3 (5)	3 (6)
ED treatments for hyperglycemia - no. (%)		
Oral rehydration	23 (41)	23 (47)
Amount, if administered, median (IQR) - L	0.5 (0.4–1)	0.25 (0.2–0.5)
Intravenous fluids	40 (70)	42 (79)
Amount, if administered, median (IQR) - L	1 (1–2)	1 (1–2)
Insulin administered, any	47 (82)	4 (8)
Insulin (aspart)	45 (79)	4 (8)
Amount, if administered, median (IQR) - units	10 (8–15)	10 (10–10)
Insulin (regular)	3 (5)	0 (0)
Insulin (glargine)	1 (2)	0 (0)
Discharge prescriptions for glycemic control[a] - no. (%)		
Any	20 (35)	9 (17)
Short-acting insulin	3 (5)	1 (2)
Long-acting insulin	8 (14)	5 (9)
Sulfonylurea	3 (5)	1 (2)
Metformin	13 (23)	1 (2)
Other[a]	0 (0)	2 (4)
Glucose reduction, median (IQR) - mg/dL	138 (83–204)	39 (0–113)
Discharge glucose, median (IQR; range) - mg/dL	319 (280–377; 117–579)	429 (365–465; 95–601)
Primary ED diagnosis[c] - no (%)		
Hyperglycemia	43 (75)	36 (68)
Other	14 (25)	17 (32)

ED: emergency department; IQR: interquartile range; L: liters. [a]Patients could have more than one discharge prescription. Other includes gliptins, meglitinides, thiazolidinediones, alpha-glucosidase inhibitors, and glucagon-like peptide-1 receptor agonists.; [b]There were 6 patients in the loose control group and 3 patients in the moderate control group who only had a single glucose measured. In these cases the single glucose value is counted as both the arrival and discharge glucose value.; [c]Patients may have had more than one ED diagnosis, but only the first diagnosis listed is displayed.

Table 3
Trial outcomes.

Outcome	Moderate control N = 57	Loose Control N = 53	Difference (95% CI)
ED length of stay, median (IQR) - min	211 (177–288)	216 (151–269)	17 (−15 to 49)
ED length of stay after enrollment, median (IQR) - min	154 (109–189)	101 (71–152)	46 (18–72)
Iatrogenic hypoglycemia during ED encounter - no. (%)[a]	0 (0)	1 (2)	-2% (−6 to 2%)
Outcomes within 7 days of the index encounter - no. (%; 95% CI)			
Repeat ED visit for hyperglycemia[b]	4 (7; 2–17)	3 (6; 1–16)	1% (−8 to 11%)
Repeat ED visit for any other reason[b]	4 (7; 2–17)	3 (6; 1–16)	1% (−8 to 11%)
Hospitalization for hyperglycemia, DKA, or HHS[c]	0 (0; 0–6)	1 (2; 0–10)	-2% (−6 to 2%)
Hospitalization for any other reason[d]	2 (4; 0–12)	4 (8; 2–18)	−4% (−13 to 5%)

This table displays the primary and secondary outcomes. We were able to assess secondary outcomes for all but 1 patient in each group. The difference column displays the difference of moderate control compared to loose control, therefore a positive value in this column indicates that the median value or proportion was higher for the moderate control group.
CI: confidence interval; DKA: diabetic ketoacidosis; ED: emergency department; HHS: hyperosmolar hyperglycemic state; IQR: interquartile range.

[a] One patient in the loose control group who received insulin had a glucose reduction from 548 mg/dL to 95 mg/dL, with symptoms of hypoglycemia that resolved with juice.
[b] This only includes ED visits that did not result in hospitalization.
[c] One patient was hospitalized for poor outpatient control of hyperglycemia. No patient had DKA or HHS.
[d] Reasons for hospitalization included chronic abdominal pain, suicide attempt (two patients; one of whom was in moderate control group), exacerbation of chronic obstructive pulmonary disease, hypertensive emergency (in moderate control group), and failure of outpatient management of facial cellulitis.

laboratory turnaround times [19], the number of elective surgery admissions, number of ED admissions, and hospital occupancy [20], among others. While length of stay is clearly important, and confounding factors may have been balanced by randomization, we feel that choosing length of stay as an outcome may have oversimplified ED goals of care for hyperglycemia and may have obscured other important differences between moderate and loose ED glycemic control, such as patient expectations and plans for future episodes of hyperglycemia, costs of care, and the emphasis of proper long-term glycemic control.

We were not able to contact all patients in follow-up, and more patients in the loose control group were missed in follow-up, though on chart review of those unable to be followed up by phone, there were no apparent short-term complications. Adverse events at 7-days were uncommon in both groups, consistent with prior data [9], but because of the relatively small sample size we cannot precisely estimate the difference in adverse events between groups.

5. Discussion

In this trial of ED patients with hyperglycemia, in the intention-to-treat analysis, ED length of stay and 7-day adverse outcomes were not significantly different whether a moderate or loose glucose control goal was utilized. However, ED length of stay for those with an actual discharge glucose <350 mg/dL (including patients from both groups) was 29 min longer than those with a discharge glucose ≥350 mg/dL. These data suggest that both moderate and loose control are acceptable practices for this patient population, and that reducing glucose values in well-appearing ED patients may consume time and resources without conferring short- or long-term benefits.

Because study outcomes were blinded, treating physicians could not systematically influence study outcomes, and the results demonstrate that no attempts were made in either group to shorten or prolong length of stay. In fact, contrary to the recommendations provided to treating physicians that fluid therapy was not required and is not particularly effective in glucose reduction [11,17], the vast majority (>70% in both groups) of patients received intravenous fluids, which is known to lengthen ED length of stay [11]. We underestimated the proclivity of physicians to provide fluid therapy, especially to patients with a higher discharge glucose goal. Had we restricted fluid therapy to the loose control group, it is possible we would have detected a difference in length of stay between groups. Additionally, available evidence suggests that oral and intravenous fluid both reduce glucose only by about 40 mg/dL per liter administered [11,17]; one could argue that fluid therapy in uncomplicated hyperglycemia should not be viewed as a method of glucose reduction and should be reserved for patients with hypovolemia.

Furthermore, we did not mandate that patients had to be enrolled within a certain time window after ED arrival. In retrospect, we should have; this would have eliminated the confounding of varying elapsed times between being roomed in the ED and study enrollment. In a post hoc analysis, the ED length of stay after enrollment (i.e., after the treatment strategy was determined), was shorter in the loose control group by 46 min. This indicates that ED management may be faster once a loose glycemic control strategy is decided upon, but because this is an unplanned analysis, this result can only be considered hypothesis generating.

In this patient population selected to be at low risk of hospital admission, a chemistry panel was obtained in 89% of patients. The utility of this practice has not been well studied. Zehtabchi et al. enrolled a convenience sample of patients with both type 1 and 2 diabetes mellitus, including patients with diabetic ketoacidosis and those being admitted to the hospital for other reasons, finding that 17% and 3% had hyper- and hypokalemia, respectively, and concluded that all patients with hyperglycemia require electrolyte testing [21]. However, the relevance of these data to a population of well-appearing patients with type 2 diabetes with a plan for discharge is unclear. This question remains unanswered and is a potential area of future study.
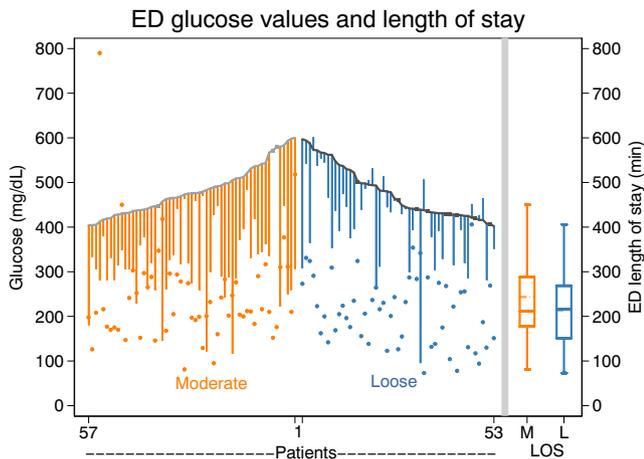

Fig. 2. Patients are presented by group, sorted in order of arrival glucose. Each patient is displayed as a line with a corresponding dot, matched vertically. The line connects arrival glucose to discharge glucose (those with only a single glucose value are displayed as a single square). The dots denote ED length of stay. On the right side of the graph, a box and whisker plot is displayed. M, moderate control group. L, loose control group. LOS, length of stay.

Although we cannot make an accurate comparison of 7-day adverse events between groups, true adverse outcomes such as diabetic ketoacidosis, hyperosmolar hyperglycemic state, or hospitalization for any reason, were uncommon in both groups and not clearly related to glycemic control. Consistent with prior literature [9], ED glycemic control does not appear to be closely associated with short-term adverse outcomes. It is probable that the glycemic control in the days following the ED encounter is much more important, highlighting the importance of ensuring this patient population has the correct medications, the knowledge required to correctly use them, and appropriate outpatient follow-up.

Diabetic ketoacidosis is uncommon in patients with type 2 diabetes [22,23], and is likely even more rare in patients who have an index ED visit with hyperglycemia and appear well enough to be discharged. Therefore, ED glucose reduction, it seems, should not be performed in this patient population with the goal to prevent short-term diabetic ketoacidosis. Although long-term, rather than short-term, glycemic control is paramount to prevent many diabetes-associated complications, there may be patient populations who could benefit from even short-term control in the ED, such as those with bacterial infections [24], those with hypovolemia from polyuria, or those with a history of epilepsy who present with a seizure [25]. However, this study supports the acceptability of loose glycemic control in ED patients well enough to be discharged who do not have a significant concomitant illness.

6. Conclusions

In summary, in the intention-to-treat analysis ED length of stay and 7-day outcomes for patients with type 2 diabetes and hyperglycemia were not significantly different whether a moderate (<350 mg/dL) or loose (<600 mg/dL) glycemic control goal was used. However, for those who achieved a discharge glucose <350 mg/dL, length of stay was approximately 29 min longer, compared to the remaining participants. ED glycemic control did not appear to be associated with a difference in negative short-term outcomes in this patient population. Glucose reduction in well-appearing ED patients may consume time and resources without conferring short- or long-term benefits.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2018.09.053.

Previous presentation

None.

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Author contributions

BD, LK, JC, and MP conceived and designed the investigation. BD and EF supervised the conduct of the study and data collection. BD and LK performed data analysis. JM provided departmental funding for the research infrastructure. BD drafted the article, and all authors contributed substantially to its revision. BD takes responsibility for the paper as a whole.

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