Reducing Inpatient Hypoglycemia in the General Wards Using Real-time Continuous Glucose Monitoring: The Glucose Telemetry System, a Randomized Clinical Trial

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OBJECTIVE

Use of real-time continuous glucose monitoring (RT-CGM) systems in the inpatient setting is considered investigational. The objective of this study was to evaluate whether RT-CGM, using the glucose telemetry system (GTS), can prevent hypoglycemia in the general wards.

RESEARCH DESIGN AND METHODS

In a randomized clinical trial, insulin-treated patients with type 2 diabetes at high risk for hypoglycemia were recruited. Participants were randomized to RT-CGM/GTS or point-of-care (POC) blood glucose testing. The primary outcome was difference in inpatient hypoglycemia.

RESULTS

Seventy-two participants were included in this interim analysis, 36 in the RT-CGM/GTS group and 36 in the POC group. The RT-CGM/GTS group experienced fewer hypoglycemic events (<70 mg/dL) per patient (0.67 [95% CI 0.34–1.30] vs. 1.69 [1.11–2.58], $P = 0.024$), fewer clinically significant hypoglycemic events (<54 mg/dL) per patient (0.08 [0.03–0.26] vs. 0.75 [0.51–1.09], $P = 0.003$), and a lower percentage of time spent below range <70 mg/dL (0.40% [0.18–0.92%] vs. 1.88% [1.26–2.81%], $P = 0.002$) and <54 mg/dL (0.05% [0.01–0.43%] vs. 0.82% [0.47–1.43%], $P = 0.017$) compared with the POC group. No differences in nocturnal hypoglycemia, time in range 70–180 mg/dL, and time above range >180–250 mg/dL and >250 mg/dL were found between the groups. The RT-CGM/GTS group had no prolonged hypoglycemia compared with 0.20 episodes <54 mg/dL and 0.40 episodes <70 mg/dL per patient in the POC group.

CONCLUSIONS

RT-CGM/GTS can decrease hypoglycemia among hospitalized high-risk insulin-treated patients with type 2 diabetes.

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Several studies have shown that abnormal glucose control in the inpatient setting is associated with adverse clinical outcomes (1–6), leading to increased health care expenditure (7). Professional societies recommend insulin in inpatients with diabetes (8), which can predispose patients to hypoglycemia, a condition that is associated with increased morbidity and mortality (4,9,10).

Consequently, hospitals have carefully devised hypoglycemia prevention and treatment protocols to mitigate this risk. These protocols are based on using point-of-care (POC) glucose testing and, therefore, are inherently limited because of the infrequency by which POC is performed. In the noncritical care setting, where most patients are hospitalized, POC is recommended to be performed four to six times per day (8), leaving extended intervals of time where hypoglycemia may occur undetected. Hospitalized patients with diabetes may also experience altered mental status secondary to underlying medical conditions or medications with sedating properties, resulting in an inability to recognize and/or report symptoms of hypoglycemia to the nursing staff. Furthermore, busy hospital environments and increased nursing workload can lead to decreased patient monitoring and surveillance. Overall, these hospital-related factors place patients with diabetes at risk for undetected and severe prolonged episodes of hypoglycemia, which can lead to seizures, coma, arrhythmias, increased length of stay (LOS), or death (4,9,11).

Continuous glucose monitoring (CGM) represents an alternative method to monitor glucose values. Compared with POC, CGM systems measure glucose levels every few minutes, increasing surveillance during these otherwise extended time intervals. With the ability to set low glucose alerts, CGM systems can be used to prevent hypoglycemia. However, compared with the outpatient setting where CGM use is growing, use of CGM devices in the hospital setting is still considered investigational (12). This is partly due to the lack of proven benefits from randomized controlled clinical trials, especially in the noncritical setting. Another major limitation relates to current CGM system design, which is intended for outpatient use. In the inpatient setting, the CGM receiving device would need to be placed at or near the patient's bedside, posing a logistical challenge because nursing staff would need to frequently enter the patient's room to view the glucose values or hear the audible alerts (13). This would be an impractical method to monitor large numbers of hospitalized patients with diabetes.

To overcome this limitation, the glucose telemetry system (GTS) was developed where CGM glucose values are transmitted wirelessly from the bedside to a centralized monitor at the nursing station (14). The purpose of this clinical trial was to examine whether real-time (RT) CGM/GTS combined with a simplified hypoglycemia prevention protocol can reduce hypoglycemia in the noncritical care setting. This is the first randomized controlled clinical trial to explore the benefits of RT-CGM devices using GTS in patients with diabetes in this environment. In this article, we present results from a planned interim analysis conducted as required by the institutional review board (IRB) for safety monitoring, which included evaluating differences in hypoglycemia between the two groups. Similar to what has occurred with many trials nationally, the study was halted shortly after the interim analysis was completed because of safety concerns related to the COVID-19 pandemic, as per IRB and data safety monitoring board recommendations. In the context of this pandemic emergency, there has been increasing use of CGM devices in the hospital, even in the absence of efficacy data. Therefore, we decided to proceed with publishing our interim analysis results.

RESEARCH DESIGN AND METHODS

Patient Population

In this prospective, randomized controlled clinical trial, we enrolled hospitalized adult patients with type 2 diabetes who were at higher risk for development of inpatient hypoglycemia and were admitted to the general medicine service at the Baltimore Veterans Affairs (VA) Medical Center (14). All participants were receiving insulin as part of their outpatient diabetes medication regimen and had at least one or more risk factors for inpatient hypoglycemia (15–18): advanced age defined as $\geq$65 years; BMI $\leq$27 kg/m^2; total daily dose (TDD) of insulin $\geq$0.6 units/kg; a history of renal failure; liver failure; cerebrovascular accident; active malignancy; congestive heart failure; systemic infection; or a history of hypoglycemia during a recent hospitalization. Participants were recruited from the general medicine service at the Baltimore VA Medical Center if they had an expected LOS of $>$72 h. We excluded patients who did not have type 2 diabetes, were not on insulin as part of their outpatient diabetes regimen, or had significant hyperglycemia or diabetic ketoacidosis requiring continuous intravenous insulin infusion or intensive care unit (ICU) admission. Finally, we excluded pregnant patients and any individual incapable of independently comprehending the objectives and potential consequences of the study. The study was approved by the University of Maryland IRB and the VA Maryland Health Care System Research and Development Committee.

Study Procedures

After informed consent was obtained, eligible participants were stratified on the basis of their number of risk factors for inpatient hypoglycemia (two or fewer or three or more risk factors) and were randomized to either RT-CGM/GTS (intervention/unblinded group) or POC blood glucose testing (POC/standard-of-care/blinded group). After randomization, Dexcom G6 CGM systems (Dexcom, San Diego, CA) were placed by the study team members. Participants randomized to RT-CGM/GTS had an iPhone at the bedside that transmitted glucose values to an iPad at the nursing station. A detailed description of GTS has previously been published (14,19). In short, GTS consisted of three components: a Dexcom CGM device, an iPhone, and an iPad (14) (Supplementary Fig. 1). Using Dexcom software applications, glucose values were sent from the sensor/transmitter through Bluetooth to an iPhone located in the patient's room (serving as an intermitting routing device). These data were further transmitted, using a commercially available Internet network, to an iPad located at the nursing station. Both the iPhones and the iPads were supported by research funds; no personal devices were used in this study. In this group, low-glucose alerts were set to $<$85 mg/dL on the iPad at the nursing station. Similar to cardiac telemetry, nursing staff were educated to notify the patient's assigned nurse to initiate the hypoglycemia preventive action if he/she was unavailable when a glucose value $<$85 mg/dL was observed or an audible

alert was heard because it is impractical for the patient's assigned nurse to consistently remain near the iPad. Nursing staff were requested to obtain a POC for hypoglycemia alarms as permitted and to provide at least 15 g of carbohydrates (15–16 g using glucose tablets/glucose gel/juice) for impending hypoglycemia. Nurses were instructed to give another 15 g if inadequate response in the glucose value occurred. Although the focus of our study was to prevent hypoglycemia and not hyperglycemia, high-glucose alerts were set at 400 mg/dL because we believed that it would be unethical to turn the high alerts off.

Participants in the standard-of-care group used blinded CGM systems to collect CGM glucometric data. For this group, CGM alerts were turned off, and if the POC was <85 mg/dL, 15 g of carbohydrates (as described above) were given to the participant as a preventive measure for hypoglycemia.

In both groups, as per standard of care, if the POC was <70 mg/dL, the hypoglycemia treatment protocol was initiated. If the patient had hypoglycemia and was able to eat, nurses provided 15 g carbohydrates per os. If the patient was unable to swallow or eat or developed severe hypoglycemia, he/she was started on D50 (dose range 20–25 mL), and if there was no intravenous access, then glucagon 1 mg intramuscularly was suggested to be used. Nurses were also trained on the use of CGM devices, such as removal of sensors and transmitters as needed (before computed tomography scan or MRI).

All participants were managed with basal:bolus (glargine-aspart) insulin regimens during their inpatient stay. Insulin initiation and titration were performed per protocol or as clinically indicated (20,21). Participants who were treated with basal:bolus insulin regimens on an outpatient basis were initiated on 80% of their TDD. Participants not treated with basal:bolus regimens before admission were started on a weight-based insulin regimen, with a TDD of 0.4 units/kg/day if their prerandomization POC was ≤200 mg/dL and 0.5 units/kg/day if their blood glucose was between 201 and 400 mg/dL. The starting TDD was 0.3 units/kg/day in participants ≥70 years of age or with an admission serum creatinine of ≥2 mg/dL. Participants were given 50% of the TDD as insulin glargine and 50% as insulin aspart divided into three equal doses before meals. Participants in both groups also received rapid-acting insulin for correction of hyperglycemia, if needed (Supplementary Table 1). POC glucose testing was checked at least four times per day in both treatment groups, as recommended (8). Basal insulin dose adjustments were made daily on the basis of fasting POC morning values (Supplementary Table 2), and titration of prandial insulin was performed using the previous day's premeal POC, as clinically indicated. Insulin dose adjustments (increases or decreases) were performed on the basis of POC. In cases when hypoglycemia alerts were triggered in the RT-CGM/GTS group, insulin doses were decreased for patient safety.

Outcomes Measures

The purpose of this clinical trial was to examine whether RT-CGM/GTS combined with a simplified hypoglycemia prevention protocol can reduce hypoglycemia in the noncritical care inpatient setting. To evaluate clinical efficacy, we adapted CGM metrics proposed for ambulatory patients (22,23). The primary outcome was difference in hypoglycemic events per patient, defined as CGM glucose values <70 mg/dL for >15 min. Secondary outcomes were percentage of time spent in hypoglycemic range <70 mg/dL and hypoglycemic event rates (defined as number of hypoglycemic events/patient/day). Additional secondary outcomes included differences in clinically significant hypoglycemic events per patient (defined as CGM glucose values <54 mg/dL for >15 min) and percentage of time below range (TBR) <54 mg/dL. We also examined whether there was any difference in nocturnal hypoglycemic events per patient (defined as hypoglycemic events <70 mg/dL or clinically significant hypoglycemic events <54 mg/dL occurring between midnight and 6:00 A.M.) and prolonged episodes of hypoglycemia (defined as hypoglycemia <70 mg/dL or clinically significant hypoglycemia <54 mg/dL for >120 min). Although our trial was not focused on improving hyperglycemia, a secondary outcome was to evaluate whether there was increased hyperglycemia by preventing hypoglycemia. To evaluate this, we calculated the percentage of time above range (TAR) >180–250 mg/dL and TAR >250 mg/dL as well as time in range (TIR) 70–180 mg/dL (23). Finally, we examined whether there was any difference in insulin TDD, hospital LOS, and glucose variability (using the coefficient of variation [CV]) between the two groups.

Statistical Analysis

For the glycemic outcomes, both primary and secondary, comparison of data from the two groups began with a visual review (side-by-side box plots) of the distribution of values. If the data appeared reasonably normally distributed (e.g., CV outcome) an unpaired Student *t* test was used to determine whether the mean of the two groups was the same. For all the other glycemic outcome measures, we used either a Poisson regression (clinically significant hypoglycemic events <54 mg/dL per patient and nocturnal hypoglycemic events <70 mg/dL per patient) or quasi-Poisson regression if the residual deviance divided by the residual df was >1, indicating a zero-inflated distribution (hypoglycemic events <70 mg/dL per patient, nocturnal hypoglycemic events <54 mg/dL per patient, hypoglycemic events <70 mg/dL per patient per day, TBR <54 mg/dL, TBR <70 mg/dL, TIR 70–180 mg/dL, TAR >180–250 mg/dL, and TAR >250 mg/dL). Both regressions were performed using the R glm function. Comparisons of baseline characteristics, LOS, and insulin TDD per kilogram between the two groups of patients was performed using Pearson χ^2 tests for categorical variables and Student *t* tests for continuous variables. Nonparametric approach Wilcoxon rank sum tests for continuous variables were performed when normality of data or homogeneity of variance were violated. Fisher exact tests for categorical variables were performed when >20% of cells had expected frequencies <5. We used the Lan-DeMets α-spending method with two-sided symmetric O'Brien-Fleming boundaries (upper and lower boundaries 0.025) assuming two interim and one final analysis to define critical values for stopping the study. The second interim analysis boundaries were 3.73 and −3.73 (R bounds function from the ldbounds library). Analyses were performed using R version 3.6.0 statistical software. A two-tailed $P \leq 0.05$ indicated significance.

RESULTS

A total of 82 patients with type 2 diabetes consented to participate in this trial (Supplementary Fig. 2); 10 participants

were not included in the analysis, leaving 36 in each group for the final analysis. The clinical and demographic characteristics were similar, with no statistically significant differences between the two groups (Table 1). Overall, mean ± SD age was 68 ± 10 years, median (interquartile range [IQR]) BMI was 32.0 kg/m^2 (26.8–36.3), and participants were predominantly admitted for cardiovascular- (27.7%) or infectious (25.0%) disease–related conditions. Mean estimated glomerular filtration rate was 57.6 mL/min/1.73 m^2 in RT-CGM/GTS group and 67.7 mL/min/1.73 m^2 in the control group ($P = 0.82$). Participants had a long duration of diabetes (median [IQR] 18 years [11.5–25.5]), and the majority were managed before admission with basal:bolus insulin regimens either alone (43.1%) or in combination with per os and/or glucagon-like peptide 1 receptor agonists (20.8%). No patients received enteral nutrition, and seven received steroids (three in the RT-CGM/GTS group vs. four in the control group, *P* not significant).

For our primary outcome, participants in the RT-CGM/GTS group experienced 60.4% fewer hypoglycemic events (<70 mg/dL) compared with the POC group (0.67 events/patient [95% CI 0.34–1.30] vs. 1.69 events/patient [1.11–2.58], $P = 0.024$) (Fig. 1 and Table 2), with an absolute risk reduction of 1.02. In both groups, there were 1.18 hypoglycemic events/patient, with a total of 85 events (24 in the RT-CGM/GTS group and 61 in the POC group). There was a reduction in percentage of time in hypoglycemic range <70 mg/dL in the RT-CGM/GTS group compared with the POC group (0.40% [95% CI 0.18–0.92%] vs. 1.88% [1.26–2.81%], $P = 0.002$) (Fig. 2). The rate of hypoglycemic events was also lower in the intervention group than in the standard-of-care group (0.12 events/patient/day [95% CI 0.06–0.24] vs. 0.35 events/patient/day [0.23–0.54], $P = 0.011$).

The RT-CGM/GTS group experienced fewer clinically significant hypoglycemic events <54 mg/dL compared with the POC group (0.08 events/patient [95% CI 0.03–0.26] vs. 0.75 events/patient [0.51–1.09], $P = 0.003$). There was also a decrease in TBR <54 mg/dL for the intervention group compared with the control group (0.05% [95% CI 0.01–0.43%] vs. 0.82% [0.47–1.43%], $P = 0.017$). There were 21.3 min/day and 102.3 min/admission (using median LOS) saved

Table 1—Baseline characteristics of the participants who completed the study

Variable	Overall	RT-CGM/GTS group	POC group	*P* value
Participants, *n*	72	36	36	
Age (years)	68.0 ± 10	68.0 ± 9	68.0 ± 10	0.95
Race				0.62
Caucasian	26 (36.1)	14 (38.9)	12 (33.3)	
African American	46 (63.9)	22 (61.1)	24 (66.7)	
Male sex	67 (93.1)	34 (94.4)	33 (91.7)	1.00
Weight (kg)	99.4 (83.8–122.3)	98.8 (84.2–120.2)	100.3 (83.0–124.4)	0.94
BMI (kg/m^2)	32.0 (26.8–36.3)	31.2 (26.8–35.3)	32.6 (26.8–38.0)	0.55
HbA_{1c}				0.87
%	8.4 ± 1.8	8.3 ± 1.5	8.6 ± 2.1	
n	70	35	35	
Diabetes duration (years)	18 (11.5–25.5)	18 (13.5–28)	17.5 (10–25)	0.45
Outpatient diabetes regimen				0.72
Basal only	11 (15.3)	6 (16.7)	5 (13.9)	
Basal + oral or GLP-1RA	15 (20.8)	9 (25.0)	6 (16.7)	
Basal + MDI	31 (43.1)	15 (41.6)	16 (44.4)	
Basal + MDI + oral ± GLP-1RA	15 (20.8)	6 (16.7)	9 (25.0)	
Risk factors for hypoglycemia				0.80
≤2 risk factors	25 (34.7)	13 (36.1)	12 (33.3)	
≥3 risk factors	47 (65.3)	23 (63.9)	24 (66.7)	
Diabetes complications				
Retinopathy	35 (48.6)	19 (52.8)	16 (44.4)	0.48
Neuropathy	47 (65.3)	24 (66.7)	23 (63.9)	0.81
Nephropathy	50 (69.4)	25 (69.4)	25 (69.4)	1.00
CAD	25 (34.7)	16 (44.4)	9 (25.0)	0.08
CVA	17 (23.6)	10 (27.8)	7 (19.4)	0.41
Amputation history/PVD	20 (27.8)	12 (33.3)	8 (22.2)	0.29
Primary admission diagnosis				0.88
Cardiovascular	20 (27.7)	6 (16.6)	14 (38.9)	
Pulmonary	4 (5.6)	1 (2.8)	3 (8.3)	
Infectious disease	18 (25.0)	8 (22.2)	10 (27.8)	
Endocrinology	2 (2.8)	1 (2.8)	1 (2.8)	
Nephrology	8 (11.1)	5 (13.9)	3 (8.3)	
Neurology/musculoskeletal	13 (18.1)	9 (25.0)	4 (11.1)	
Gastroenterology	7 (9.7)	6 (16.7)	1 (2.8)	

Data are *n* (%), mean ± SD, or median (IQR). CAD, coronary artery disease; CVA, cerebrovascular accident; GLP-1RA, glucagon-like peptide 1 receptor agonist; MDI, multiple daily injections; PVD, peripheral vascular disease.

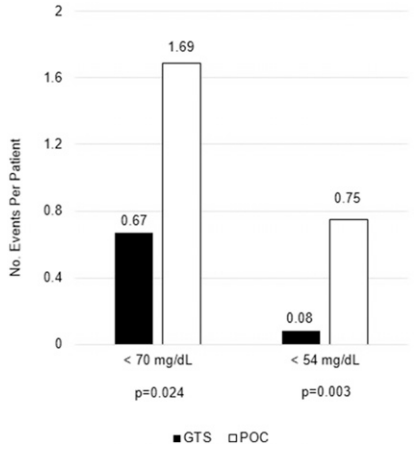

Figure 1—Hypoglycemic events per patient.

from hypoglycemia <70 mg/dL and 11.1 min/day and 53.2 min/admission saved from hypoglycemia <54 mg/dL. Notably, participants in the RT-CGM/GTS group had no prolonged hypoglycemic episodes <70 mg/dL or <54 mg/dL compared with participants in the POC group (0.2 episodes/patient <70 mg/dL and 0.4 episodes/patient <54 mg/dL). In contrast, there was no statistically significant difference in the number of nocturnal hypoglycemic events <70 mg/dL (0.19 [95% CI 0.09–0.41] vs. 0.33 [0.19–0.59], $P = 0.26$) or clinically significant nocturnal hypoglycemic events <54 mg/dL (0.03 [0.01–0.24] vs. 0.11 [0.04–0.33], $P = 0.26$) between the two groups.

The main purpose of our trial was reduction in hypoglycemia and not reduction in hyperglycemia, and insulin increases were made on the basis of POC versus CGM data. Therefore, we did not find any significant difference in TIR 70–180 mg/dL (59.12% [95% CI 52.47–66.61%] in the intervention group vs. 54.69% [47.96–62.37%] in the control group, $P = 0.39$), TAR >180–250 mg/dL (29.88% [26.11–34.19%] in the intervention group vs. 30.10% [26.11–34.70%] in the control group, $P = 0.94$), or TAR >250 mg/dL (10.60% [7.15–15.73%] in the intervention group vs. 13.33% [9.20–19.37%] in the control group, $P = 0.41$). There was no difference in glucose variability measured by CV (26.09% [24–28.19%] in the intervention group vs. 27.89% [25.41–30.36%] in the control group, $P = 0.28$) between the two groups. Mean glucose was 183.3 mg/dL and 180 mg/dL in the RT-CGM/GTS and control groups, respectively ($P = 0.69$).

Average POC tests per day was 4.26 in the RT-CGM/GTS group vs. 4.16 in the control group (P not significant). There were 80 preventive actions in the RT-CGM/GTS group vs. 15 in the control group ($P \leq 0.001$). Both groups had similar hospital LOS (median LOS 3.96 days [IQR 2.85–8.17] vs. 5.65 days [3.60–7.43], $P = 0.16$; mean LOS 6.78 ± 6.18 days vs. 6.02 ± 3.48 days in the intervention and control groups, respectively, $P = 0.32$) and received similar insulin doses during the hospitalization (mean TDD insulin 0.40 ± 0.31 units/kg in the intervention group vs. 0.49 ± 0.36 units/kg in the control group, $P = 0.28$). The study did not meet criteria for premature termination ($|z\text{-score}| > 2.41$).

CONCLUSIONS

In this randomized controlled trial, we explored whether the use of RT-CGM/GTS can decrease hypoglycemia among hospitalized high-risk patients with type 2 diabetes. Results from the interim analysis revealed that the RT-CGM/GTS intervention combined with a simplified hypoglycemia prevention protocol led to a decrease in inpatient hypoglycemia. Overall, RT-CGM/GTS led to an absolute risk reduction of 1.02 and a 60.4% relative risk reduction in inpatient hypoglycemic events (<70 mg/dL). Additionally, clinically significant hypoglycemic events (<54 mg/dL), hypoglycemic events per patient per day, percentages of time spent in hypoglycemia (<70 mg/dL and <54 mg/dL), and prolonged hypoglycemic events were also reduced.

Use of CGM devices lacks U.S. Food and Drug Administration approval for hospital use, and there is an absence of safety and efficacy evidence (24–26). For general medical wards, where the majority of patients with diabetes are hospitalized, few studies have been performed and were primarily observational in evaluating CGM accuracy (27–30). These studies revealed that CGM devices were more likely to detect hypoglycemia compared with POC. A limitation was the use of blinded CGM devices, where CGM glucose values were not viewable to providers or patients. As a result, interventions to prevent hypoglycemia could not be performed on the basis of the CGM data. Our study is the first large interventional randomized controlled clinical trial using RT-CGM systems in general wards with the goal of reducing inpatient hypoglycemia.

Our study focused on reducing inpatient hypoglycemia, which is associated with prolonged LOS, higher hospital charges, and increased risk for readmission and mortality (4,5,9,31). Severe hypoglycemic events have led institutions to

Table 2—Glycemic outcomes

	RT-CGM/GTS group ($n = 36$)	POC group ($n = 36$)	P value
Hypoglycemic events/patient			
<70 mg/dL	0.67 (0.34–1.30)	1.69 (1.11–2.58)	0.024
<54 mg/dL	0.08 (0.03–0.26)	0.75 (0.51–1.09)	0.003
Nocturnal hypoglycemic events/patient			
<70 mg/dL	0.19 (0.09–0.41)	0.33 (0.19–0.59)	0.26
<54 mg/dL	0.03 (0.01–0.24)	0.11 (0.04–0.33)	0.26
Hypoglycemic events (<70 mg/dL)/patient/day	0.12 (0.06–0.24)	0.35 (0.23–0.54)	0.011
TBR <70 mg/dL (%)	0.40 (0.18–0.92)	1.88 (1.26–2.81)	0.002
TBR <54 mg/dL (%)	0.05 (0.01–0.43)	0.82 (0.47–1.43)	0.017
TIR 70–180 mg/dL (%)	59.12 (52.47–66.61)	54.69 (47.96–62.37)	0.39
TAR >180–250 mg/dL (%)	29.88 (26.11–34.19)	30.10 (26.11–34.70)	0.94
TAR >250 mg/dL (%)	10.60 (7.15–15.73)	13.33 (9.20–19.37)	0.41
CV (%)	26.09 (24–28.19)	27.89 (25.41–30.36)	0.28

Data are mean (95% CI).

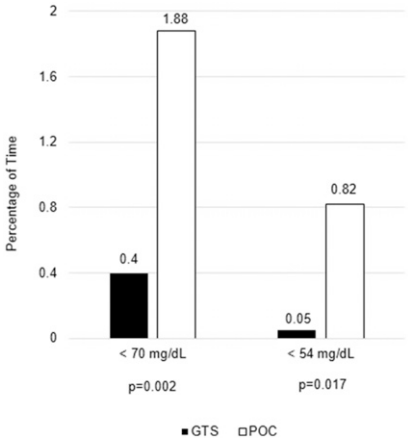

Figure 2—Percentage of TBR.

develop inpatient diabetes management teams to implement hospital protocols and procedures to reduce this risk (32). We believe that the proposed intervention of using RT-CGM/GTS, along with a simplified hypoglycemia prevention protocol, could serve as a useful tool to modify existing institutional hypoglycemia prevention protocols. A strength of our study was evaluating RT-CGM/GTS in the general wards, a setting where glucose monitoring is more limited (four to six times per day), in contrast to the ICU, where glucose values can be intensively monitored and checked hourly, if needed (19).

Results from this analysis did not reveal a reduction of nocturnal hypoglycemia with use of RT-CGM/GTS, a condition that can lead to severe hypoglycemic events (33). The lack of a statistically significant difference in nocturnal hypoglycemia may be attributable to the fact that a common cause of hypoglycemia in the hospital setting is meal interruptions (15). This is most likely to occur during the day when procedures or imaging studies are usually performed, when patients may receive prandial insulin and are unable to complete their meal. Additionally, we may have been underpowered to meet significance for nocturnal hypoglycemia. With a larger sample size, this trend of less nocturnal hypoglycemia in RT-CGM/GTS use may meet statistical significance.

There were no episodes of prolonged hypoglycemia in the RT-CGM/GTS group. This is not a surprising finding. For a participant monitored by RT-CGM/GTS to experience prolonged hypoglycemia, nursing staff would need to fail to respond to both the visual and the audible notifications on the iPad for >2 h.

Our study has some limitations. Although our study population included mainly male patients, we believe that our findings can be extrapolated because there are no known sex-specific differences in the incidence of inpatient hypoglycemia or in the prevention of hypoglycemia with CGM use. Additionally, we evaluated the use of the RT-CGM/GTS in patients considered to be high risk for inpatient hypoglycemia versus all admitted patients with diabetes. We focused on this subgroup of patients because we believe that this population would most likely benefit from the proposed hypoglycemia prevention interventions. We also did not evaluate whether use of RT-CGM/GTS can improve hyperglycemia. Because both groups had insulin increased on the basis of POC, it was not surprising that there was no improvement in normoglycemia or hyperglycemia. However, current ongoing studies will evaluate whether RT-CGM/GTS use can reduce hyperglycemia in the non-ICU setting (NCT03877068, ClinicalTrials.gov). Finally, we did not collect satisfaction surveys focusing on use of GTS; future studies are needed to evaluate nursing satisfaction.

Importantly, we did not observe increased TAR despite more hypoglycemia preventive actions in the RT-CGM/GTS group. This may be due to the minimal amount of carbohydrates used (i.e., 15 g for glucose between 70 and 85 mg/dL), which increases blood glucose sufficiently to prevent clinically significant hypoglycemia without causing significant hyperglycemia in patients with type 2 diabetes. Reduction in hypoglycemic events with GTS may be expected to reduce TAR as a result of decreased posthypoglycemic rebound hyperglycemia (secondary to counterregulatory hormones), a benefit that we did not observe in our study. Mechanistic studies are needed to evaluate this hypothesis.

Frequency of POC testing was consistent with recommendations (8). The nonsignificantly higher number in the RT-CGM/GTS group is likely secondary to POC testing following hypoglycemia alarms. This occurred 41 of 80 times after alarms were detected. Scheduled premeal/bedtime POC obtained immediately before the alarms were not accounted for, and in these cases, perhaps nurses were not compelled to repeat POC before intervening given the recent measurement. This study was conducted in a busy clinical environment and not in a research facility with the benefit of having an individual assigned nurse. Therefore, POC may have been bypassed to avoid delays in treating a symptomatic patient or when the busy workflow did not permit it (i.e., caring for another, more severely ill hospitalized patient or transporting a sick patient to radiology for imaging).

Our overall rate of hypoglycemic events per patient varies from prior reports (28–30). Previous studies included different hospitalized patient populations and likely used different insulin/hyper-/hypoglycemia protocols and different CGM systems. Studies conducted before the availability of the consensus guidelines (22,23) may have had differing requirements for minimum duration of hypoglycemia constituting an event, changing the overall number of events.

There were several steps in implementing GTS. Some examples are training nursing staff on GTS and providing technical support as needed, selecting a commercially available Internet network with consistent signal to ensure minimal interruption in glucose transmission between iPhone and iPad, and securing the devices with an antitheft iPad case at the nursing station and a locked safe box wired to a permanently affixed object at the bedside that contained the iPhone and portable battery.

Because of the COVID-19 pandemic, this trial halted shortly after the interim analysis was completed. We believe that widespread dissemination of these findings in the context of this health crisis could be important. During this emergency, providers have implemented inpatient use of CGM devices, which is still considered investigational. RT-CGM/GTS may be beneficial in this environment, although there is a lack of efficacy data about RT-CGM use in the hospital. In this article, we report that the use of RT-CGM devices through glucose telemetry can reduce inpatient hypoglycemia effectively. RT-CGM/GTS as a method of glucose monitoring could reduce the need for frequent entry of staff into patient rooms (typically four to six times daily to check POC). This would additionally reduce personal protective equipment utilization and decrease risk of exposure and

transmission between patients and hospital staff. Finally, by reducing time that nursing staff spend checking POC, the extra time could be reallocated to taking care of patients who have more emergent and critical needs. It is estimated that each POC test requires 5 min on average to perform (25,34). This benefit, which under normal circumstances would alleviate overburdened nursing staff, is now underscored as a result of the pandemic crisis.

In conclusion, RT-CGM/GTS combined with a simplified hypoglycemia prevention protocol can decrease hypoglycemia among insulin-treated patients with type 2 diabetes. Similar to cardiac telemetry, a system used for patients at high risk for arrhythmia, we believe that future RT-CGM systems could be used to monitor hospitalized patients with diabetes at high risk for hypoglycemia.

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Author Contributions. L.G.S. was involved with the operations of the clinical trial, reviewed the results, and wrote the manuscript. M.S., I.M., W.H.S., L.F.P., and G.E.U. made critical revisions to the manuscript for important intellectual content. Z.F. and J.D.S. performed the statistical analyses and made critical revisions to the manuscript for important intellectual content. E.K.S. conceived and designed the study, provided guidance for the statistical analysis, assisted with writing, and provided critical revisions to the manuscript. All authors approved the manuscript. E.K.S. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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