Real-time continuous glucose monitoring-guided glucose management in inpatients with diabetes receiving short-term continuous subcutaneous insulin infusion: a randomized clinical trial

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Summary

Background The use of real-time continuous glucose monitoring (rtCGM) technology remains largely investigational in the hospital setting. The current study aimed to evaluate the effectiveness of rtCGM in inpatients with diabetes who were treated with short-term continuous subcutaneous insulin infusion (CSII).

Methods In this randomized, parallel controlled trial conducted on the endocrinology wards in a tertiary hospital located in Shanghai, adults with type 1 and type 2 diabetes who required short-term CSII during hospitalization were randomly assigned (1:1) to receive either rtCGM-based glucose monitoring and management program or point-of-care (POC) standard of care (8 times/day) with blinded CGM. Primary outcome measure was the difference in the percentage of time within the target glucose range of 3.9–10 mmol/L (TIR, %). This study was registered at www.chictr.org.cn (ChiCTR2300068933).

Findings Among the 475 randomized participants (237 in the rtCGM group and 238 in the POC group), the mean age of was 60 ± 13 years, and the mean baseline glycated hemoglobin level was 9.4 ± 1.8%. The CGM-recorded mean TIR was 71.1 ± 15.8% in the rtCGM group and 62.9 ± 18.9% in the POC group, with a mean difference of 8.2% (95% confidence interval [CI]: 5.1–11.4%, P < 0.001). The mean time above range >10 mmol/L was significantly lower in the rtCGM group than in the POC group (28.3 ± 15.8% vs. 36.6 ± 19.0%, P < 0.001), whereas there was no significant between-group difference in the time below range <3.9 mmol/L (P = 0.11). Moreover, the time to reach target glucose was significantly shorter in the rtCGM group than in the POC group (2.0 [1.0–4.0] days vs. 4.0 [2.0–5.0] days, P < 0.001). There were no serious adverse events in both groups.

Interpretation In patients with diabetes who received short-term CSII during hospitalization, the rtCGM program resulted in better glucose control than the POC standard of care, without increasing the risk of hypoglycemia.

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Keywords: Real-time continuous glucose monitoring; Diabetes; Hospital; Randomized clinical study

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Research in context

Evidence before this study

Despite broad-based evidence supporting the use of continuous glucose monitoring (CGM) to improve glucose outcomes in outpatients, the technology remains largely investigational in the hospital setting. We searched PubMed and Web of Science, with the terms "continuous glucose monitoring", "diabetes" and "hospital", without any date or language restrictions. Three previous inpatient studies have investigated the use of real-time CGM (rtCGM) in patients with diabetes in non-critical care. The largest of these randomized controlled trials was done in 185 adult inpatients and found a significant reduction of recurrent hypoglycemic events in patients using rtCGM. However, no significant difference in time in range 3.9–10.0 mmol/L (%), a core CGM metric recommended by international guidelines and consensuses, has been found between the groups in previous studies. In addition, our search did not yield any previous studies that used real-time continuous glucose monitoring in inpatients with diabetes receiving short-term continuous subcutaneous insulin infusion (CSII).

Added value of this study

In this randomized clinical trial involving 475 hospitalized patients with diabetes who received CSII, we established a structured rtCGM program by incorporating data platforms, standardized insulin protocol and a specialized team, and found that TIR was 8.2% (equal to 118 min/day) higher among participants assigned to the rtCGM program than among those assigned to the usual point-of-care (POC) method. Furthermore, the use of rtCGM led to significant reductions in time above range, glycemia risk index and mean sensor glucose. These values were achieved without increasing time below range.

Implications of all the available evidence

In patients with type 1 and type 2 diabetes who were receiving CSII during hospitalization, the implementation of rtCGM program could result in better glucose control compared with the capillary POC standard of care, without increasing the risk of hypoglycemia.

Introduction

The burden of diabetes is increasing globally, as is the proportion of people with diabetes in hospitals.[1] Dysglycemia during hospitalization is a widely recognized marker of poor prognosis and is associated with prolonged length of stay and higher healthcare costs.[1,2] However, professional societies' recommendations of target glucose concentrations are not currently attainable by many healthcare institutions.[3,4]

Besides, due to the limited medical resources and insufficient self-management, a considerable gap exists between international guidelines' recommendations and actual clinical practice for the treatment of patients with type 1 diabetes in China.[5,6] For example, it was reported that 45% of people with type 1 diabetes use two premixed insulin injections/day in China, and the median frequency of self-monitoring blood glucose was 3.0 days/week.[5] Therefore, hospitalization for short-term intensive insulin therapy (STII) with a continuous subcutaneous insulin infusion (CSII) regimen[7–9] and intensified diabetes education is common in China.[10] Moreover, STII is also a generally preferred treatment option for people with uncontrolled type 2 diabetes in China and is recommended by the Chinese Diabetes Society,[10–12] which was based on evidence of its potential benefits in β-cell recovery and diabetes remission.[13–15] In such patients, in-hospital glucose management is even more challenging, which has spurred the development of more effective and safe management strategies.

Bedside point-of-care (POC) is the standard of care to assess glucose levels in the hospital. However, POC is recommended to be performed at specific time points, leaving large intervals of time unmonitored whereby hyper/hypoglycemia may occur undetected.[16] In contrast, real-time continuous glucose monitoring (rtCGM) offers a more complete glycemic profile by automatically sending glucose values every few minutes, and provides the important feature of high/low glucose alerts. Interest in the use of CGM in the hospital setting has been growing since the beginning of the COVID-19 pandemic in 2020, when the U.S. Food and Drug Administration (FDA) issued a non-objection statement for the expanded use of certain noninvasive remote monitoring devices.[17,18] Recently, focusing on the use of CGM in the hospital, the Diabetes Technology Society hosted the annual Virtual Hospital Diabetes Meeting and released a relevant consensus statement.[19,20]

However, the use of CGM has not been formally FDA-approved for the hospital setting, partly due to a paucity of inpatient experience and data. Despite broad-based evidence supporting the use of CGM to improve glucose outcomes in outpatients,[21,22] the technology remains largely investigational in the hospital setting. Another major barrier relates to the effective integration of CGM within clinical workflows for the hospital setting. Therefore, in the current study, we: (1) established a structured rtCGM program by incorporating data platforms, standardized insulin protocol and a specialized team; (2) conducted a randomized clinical

trial comparing glucose outcomes by POC standard of care and by rtCGM program in hospitalized patients with diabetes receiving short-term CSII.

Methods

Study design and participants

In this single-center, randomized controlled trial, participants were recruited from patients admitted to the inpatient wards at the Department of Endocrinology and Metabolism, Shanghai Sixth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, China. Inclusion criteria included: (1) an age of 18 years or older; (2) type 1 and type 2 diabetes by clinical history; (3) hyperglycemia necessitating insulin therapy during hospitalization, as determined by endocrinologists following clinical guidelines.[10] Exclusion criteria were: (1) pregnancy or breast-feeding; (2) significant hyperglycemia requiring continuous intravenous insulin infusion, including diabetic ketoacidosis and hyperosmolar hyperglycemic states; (3) current users of rtCGM or intermittently scanned CGM; (4) unable to tolerate tape adhesive or with serious skin diseases around sensor placement area; (5) expected to require surgery, MRI procedures or admission to the ICU during hospitalization; (6) mental disorders. Of note, since the CSII regimens during hospitalization were adjusted by clinicians instead of patients themselves in our study, we did not exclude those who had used CSII before the enrollment. The study was in accordance with the Helsinki Declaration principles, and approved by the Research Ethics Committees of Shanghai Sixth People's Hospital. Informed consent was obtained from all participants. This study was registered at www.chictr.org.cn (registration number ChiCTR2300068933).

rtCGM program

The workflow of the structured rtCGM program is depicted in Supplementary Fig. S1. At first, a rtCGM-based glucose telemetry system was established, incorporating Guardian™ Connect CGM devices equipped with Guardian Sensor 3 glucose sensors (Medtronic Inc, Northridge, CA), a ward-wide wireless local area network and Bluetooth routers, and specific data platforms exhibited at the clinician and nursing station. The data transmission procedure of this system was as follows: First, the glucose data obtained from the CGM sensors was transmitted via Bluetooth to the Bluetooth routers installed in each ward; subsequently, using password-protected local area network, glucose data were then wirelessly transmitted to electronic devices located at clinician and nursing station; finally, through specific data platforms developed by Medtronic, the CGM graphs, real-time glucose values and trends were displayed on these devices (including large-screen monitors, tablets, and multifunctional mobile workstations), along with high/low glucose alerts.

A specialized team from the Department of Endocrinology and Metabolism was built to implement the rtCGM program. In addition to bedside nurses and attending physicians, a CGM-dedicated advanced practice nurse was trained to closely monitor CGM charts and alerts, as well as to supervise the implementation of related medical orders according to a standard insulin protocol. Moreover, a senior endocrinology specialist who was highly experienced with CGM analysis and interpretation was available to provide guidance for clinical practice as needed.

Study procedures

Participants were allocated randomly from a computer-generated sequence to either the rtCGM or POC group in a 1:1 ratio, using the block randomization method. According to the guideline and consensus statement in China,[10–12] all participants were treated with CSII[7–9] for short-term intensive insulin therapy[13–15] during hospitalization, to target a glucose range between 3.9 and 10.0 mmol/L. Participants in the rtCGM group were monitored and managed by the rtCGM program. Of note, because CGM was not formally approved for hospital use, participants in the rtCGM group were still monitored via the hospital's standard POC protocol (8 times/day: before and after three meals, before bedtime and at 3:00 am). Participants in the POC group wore blinded CGMs with glucose management based on POC testing (8 times/day). Insulin doses were adjusted according to a standardized protocol (Supplementary Table S1). CGM data in both groups were collected for up to 7 days or until hospital discharge.

In addition, hypoglycemia alerts of the rtCGM system were set at 3.9 mmol/L (70 mg/dL). Following alerts, nursing staff were instructed to conduct a confirmatory POC testing and respond to clinical hypoglycemia according to the hospital's standardized protocol immediately. Hyperglycemia alerts were set at 16.7 mmol/L (300 mg/dL)[23] and the bedside clinician determined if insulin dose adjustment was necessary (Supplementary Table S1).

Hypoglycemic frequency and associated symptoms before hospitalization were assessed using the Clarke Questionnaire and Gold Score.[24] On the first day of hospital admission, all participants underwent a physical examination to measure blood pressure, weight and height as previously described.[25] Fasting venous blood samples were drawn on the second day after admission. Total cholesterol (TC), triglycerides (TG), and glycated hemoglobin (HbA1c) were measured as previously described.[25] Throughout the study, the participants chose standard hospital meals at usual mealtimes, according to local practice. The participants were unrestricted in their usual activity on the wards.

Outcomes

The primary outcome was the difference in the percentage of time within the target glucose range of 3.9–10.0 mmol/L (70–180 mg/dL) (TIR, %), as measured by CGM during hospitalization for up to 7 days or until hospital discharge. Secondary outcomes were the difference in the percentage of time spent above 10.0 mmol/L (180 mg/dL), above 13.9 mmol/L (250 mg/dL), below 3.9 mmol/L (70 mg/dL), below 3.0 mmol/L (54 mg/dL); mean sensor glucose; glycemia risk index[26]; coefficient of variation, and standard deviation of mean glucose. Primary outcome and secondary outcomes were also calculated for the overnight period (00:00 h to 05:59 h) and daytime period (06:00 h to 23:59 h)[27] as exploratory analyses. Additionally, the primary outcome was also examined in five subgroups stratified by baseline age, sex, body mass index (BMI), type of diabetes, HbA1c and diabetes duration.

Post hoc outcomes included the time in tight range (3.9–7.8 mmol/L [70–140 mg/dL]), total daily insulin dose (units/kg/day), total daily basal insulin dose (units/kg/day), total prandial insulin dose (units/kg/day), length of hospital stay (days) and time taken to achieve target glucose (days), with a maximum allowed time of 7 days. Specifically, target glucose was defined as CGM-recorded TIR 3.9–10.0 mmol/L (70–180 mg/dL) more than 70%.[27]

Furthermore, safety outcomes included diabetic ketoacidosis, severe hypoglycemia (defined as an event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions), and serious adverse events regardless of causality.

Statistical analysis

A difference of ≥5% in TIR is generally considered as a clinically meaningful difference.[27,28] A sample size of 432 for the 1:1 randomization was calculated to have 80% power to detect a difference in the mean TIR between treatment groups, assuming a population difference of 5%, a standard deviation of 18.5% (based on updated data from INDIGO study[25]), and a two-sided α level of 0.05. Assuming a dropout rate of 10%, 480 individuals were required for enrollment.

R version 4.0.3 was used for the statistical analysis. Participant data were analyzed according to their randomization assignment. The analysis data set included all participants, except those deemed to not have type 1 diabetes or type 2 diabetes after randomization. Data normality was evaluated by using a Shapiro–Wilk test and visual inspection of Q–Q plot. Continuous variables were presented as means ± standard deviations or medians (interquartile ranges), and categorical variables as *n* (%). We used the unpaired t-tests to compare normally distributed variables and the Mann–Whitney U tests for highly skewed variables. Categorical variables were compared using χ^2 tests. Additionally, we assessed the interaction between the treatment effect on the primary outcome and baseline factors by including interaction terms in the analysis of covariance models. A P value < 0.05 (two-tailed) was considered statistically significant.

Ethics approval and consent to participate

The study and the analysis plan were approved by the Research Ethics Committees of Shanghai Sixth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. We have obtained informed consent from all participants.

Role of the funding sources

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Participants

Between March 2023 and July 2023, 518 participants were screened, of whom 36 did not proceed to the randomization, and 7 participants determined after randomization to have specific types of diabetes due to other causes (after full examination during hospitalization) were excluded from analyses. Of the remaining 475 randomized participants, 237 were assigned to the rtCGM group and 238 to the POC group. The flow of participants through the study is shown in Supplementary Fig. S2.

The clinical characteristics of the study population are presented in Table 1. 286 (60.2%) participants were male. Mean age was 60 ± 13 years. Mean HbA1c level was 9.4 ± 1.8%. The rtCGM and POC groups had similar demographic and clinical characteristics, with respect to sex, age, body mass index, duration of diabetes, HbA1c level, Clarke hypoglycemia score and outpatient diabetes regimen. In addition, the comparison of participants characteristics between type 1 diabetes and type 2 diabetes are presented in Supplementary Table S2.

Glucose outcomes

The study duration, defined as the period from the first sensor reading until the last sensor reading, was similar between groups (6.7 ± 0.8 days vs. 6.7 ± 0.7 days, P = 0.84, Table 2). The overall mean absolute relative deviation (MARD) was 7.3% by comparing the matched CGM and POC glucose data, where CGM glucose was matched to reference (POC) glucose closest by time (n = 11,249 matched glucose pairs). The 24-h sensor glucose measurements are shown in Fig. 1a. The mean TIR was significantly higher in the rtCGM group (71.1 ± 15.8%) than in the POC group (62.9 ± 18.9%), with a mean difference of 8.2% (95% confidence interval [CI]: 5.1–11.4%, P < 0.001) (Table 2, Fig. 1b).

	Total (*n* = 475)	rtCGM group (*n* = 237)	POC group (*n* = 238)	P value
Age, years	60 ± 13	60 ± 13	60 ± 12	0.79
Sex, *n* (%)				0.18
Male	286 (60.2%)	135 (57.0%)	151 (63.4%)	
Female	189 (39.8%)	102 (43.0%)	87 (36.6%)	
Diabetes type, *n* (%)				0.34
Type 1 diabetes	45 (9.5%)	26 (11.0%)	19 (8.0%)	
Type 2 diabetes	430 (90.5%)	211 (89.0%)	219 (92.0%)	
Diabetes duration, years	13.7 ± 9.4	13.0 ± 8.8	14.4 ± 9.9	0.11
Systolic blood pressure, mmHg	138 ± 18	139 ± 18	137 ± 18	0.10
Diastolic blood pressure, mmHg	82 ± 11	82 ± 11	82 ± 11	0.53
BMI, kg/m^2	24.4 ± 3.6	24.4 ± 3.8	24.5 ± 3.4	0.66
Total cholesterol, mmol/L	4.6 ± 1.2	4.7 ± 1.3	4.6 ± 1.2	0.25
Triglycerides, mmol/L	1.2 (0.8–2.0)	1.2 (0.8–1.8)	1.3 (0.8–2.1)	0.12
Serum creatinine, μmol/L	67 (55–78)	65 (55–78)	69 (56–80)	0.11
HbA1c, %	9.4 ± 1.8	9.3 ± 1.8	9.4 ± 1.9	0.52
HbA1c, mmol/mol	79.1 ± 20.0	78.5 ± 19.2	79.7 ± 20.7	0.52
Glycated albumin, %	26.1 ± 7.5	25.8 ± 7.3	26.5 ± 7.7	0.29
Awareness of hypoglycemia				
Clarke score[a]	0.5 ± 1.0	0.6 ± 1.1	0.4 ± 1.0	0.25
Gold score[b]	1.2 ± 0.6	1.2 ± 0.6	1.2 ± 0.5	0.33
Outpatient diabetes regimen, n (%)				0.66
No drug	41 (8.6%)	19 (8.0%)	22 (9.2%)	
OAD only	135 (28.4%)	72 (30.4%)	63 (26.5%)	
Insulin only	92 (19.4%)	41 (17.3%)	51 (21.4%)	
OAD plus insulin	172 (36.2%)	89 (37.6%)	83 (34.9%)	
GLP-1 receptor agonists only	4 (0.8%)	3 (1.3%)	1 (0.4%)	
GLP-1 receptor agonists plus insulin	6 (1.3%)	2 (0.8%)	4 (1.7%)	
Other	25 (5.3%)	11 (4.6%)	14 (5.9%)	

Data are expressed as mean ± SD, *n* (%) or median (IQR). rtCGM, real-time continuous glucose monitoring; POC, point-of-care; BMI, body mass index; HbA1c, glycated hemoglobin; OAD, oral anti-diabetes medication; GLP-1, glucagon-like peptide-1. [a]Clarke scores range from 0 to 7, with higher scores indicating impaired awareness of hypoglycemia. [b]Gold scores range from 1 to 7, with higher scores indicating impaired awareness of hypoglycemia.

Table 1: **Characteristics of the study population.**

Furthermore, the mean TIRs for both the overnight period (00:00 h to 05:59 h) and the daytime period (06:00 h to 23:59 h) were also higher in the rtCGM group than in the POC group (overnight difference: 6.7 [3.3–10.1], P < 0.001; daytime difference: 8.8 [5.4–12.3], P < 0.001; Fig. 1b and Supplementary Table S3). When further analyzed by hour, participants in the rtCGM group exhibited consistently higher hourly mean TIRs compared with those in the POC group (Supplementary Fig. S3). Subgroup analyses suggested no significant heterogeneity in the treatment effect across baseline age, sex, body mass index, type of diabetes, HbA1c level and diabetes duration (all P for interaction > 0.05, Fig. 2).

The mean time above range was significantly lower in the rtCGM group than in the POC group (>10.0 mmol/L: 28.3 ± 15.8% vs. 36.6 ± 19.0%, P < 0.001; >13.9 mmol/L: 5.9 ± 7.0 vs. 9.6 ± 9.7, P < 0.001). There was no significant between-group difference in the time below range (<3.9 mmol/L: 0.0 (0.0–1.0) vs. 0.0 (0.0–0.0), P = 0.11; <3.0 mmol/L: 0.0 (0.0–0.0) vs. 0.0 (0.0–0.0), P = 0.95). The subgroup analyses regarding time above range and time below range showed no heterogeneity (Supplementary Fig. S4): time above ranges were significantly lower in the rtCGM group compared to the POC group in all examined subgroups except for participants with BMI ≥ 28 kg/m2, type 1 diabetes and diabetes duration ≤12 years, but all P for interaction were >0.05; and there was no difference between the groups in any subpopulation for time below range (all P for interaction > 0.05). Meanwhile, the mean glycemia risk index, mean sensor glucose and time in tight range (3.9–7.8 mmol/L) were significantly improved in the rtCGM group than in the POC group (both P < 0.001). With respect to glucose variability, standard deviation of mean glucose was significantly lower in the rtCGM group than in the POC group (P = 0.007), but there was no significant between-group difference in the coefficient of variation (P = 0.67). Similar results were observed when secondary outcomes during the overnight and daytime periods were compared between groups (Supplementary Table S3).

	rtCGM group (*n* = 237)	POC group (*n* = 238)	Mean difference (95% CI)	P value
Number of days CGM worn, days	6.7 ± 0.8	6.7 ± 0.7		0.84
Primary outcome				
Time in range (3.9–10.0 mmol/L [70–180 mg/dL]), %	71.1 ± 15.8	62.9 ± 18.9	8.2 (5.1–11.4)	<0.001
Secondary outcomes				
Other time in ranges measures, %				
Time above range (>10.0 mmol/L [>180 mg/dL])	28.3 ± 15.8	36.6 ± 19.0	−8.3 (−11.4 to −5.1)	<0.001
Time above range (>13.9 mmol/L [>250 mg/dL])	5.9 ± 7.0	9.6 ± 9.7	−3.8 (−5.3 to −2.2)	<0.001
Time below range (<3.9 mmol/L [<70 mg/dL])	0.0 (0.0–1.0)	0.0 (0.0–0.0)		0.11
Time below range (<3.0 mmol/L [<54 mg/dL])	0.0 (0.0–0.0)	0.0 (0.0–0.0)		0.95
Mean sensor glucose, mmol/L	8.8 ± 1.2	9.5 ± 1.5	−0.7 (−0.9 to −0.5)	<0.001
Glycemia risk index	28.9 ± 17.9	38.3 ± 22.0	−9.5 (−13.1 to −5.8)	<0.001
Coefficient of variation, %	29.0 ± 6.2	28.7 ± 5.9	0.2 (−0.9 to 1.3)	0.67
SD of mean glucose, mmol/L	2.6 ± 0.7	2.7 ± 0.7	−0.2 (−0.3 to −0.05)	0.007
Post hoc outcomes				
Time in tight range (3.9–7.8 mmol/L [70–140 mg/dL]), %	43.0 ± 17.7	35.1 ± 18.6	8.0 (4.7–11.3)	<0.001
Total daily insulin dose, units/kg/day	0.49 ± 0.12	0.51 ± 0.13	−0.02 (−0.05 to 0.00)	0.04
Total daily basal insulin dose, units/kg/day	0.23 ± 0.07	0.24 ± 0.07	−0.01 (−0.02 to 0.00)	0.09
Total daily prandial insulin dose, units/kg/day	0.26 ± 0.07	0.28 ± 0.08	−0.01 (−0.03 to 0.00)	0.07
Length of hospital stay, days	8.0 (8.0–9.0)	8.0 (7.2–9.0)		0.70
Time to reach target glucose, days	2.0 (1.0–4.0)	4.0 (2.0–5.0)		<0.001

Data are expressed as mean ± SD or median (IQR). rtCGM, real-time continuous glucose monitoring; POC, point-of-care; SD, standard deviation.

Table 2: **Outcomes.**

Other outcomes and adverse events

The total daily insulin dose was 0.49 ± 0.12 units/kg/day in the rtCGM group and 0.51 ± 0.13 units/kg/day in the POC group, with a borderline significant difference (P = 0.04). Although there was no significant between-group difference in the length of hospital stay (P = 0.70), the time to reach target glucose was significantly shorter in the rtCGM group than in the POC group (2.0 [1.0–4.0] days vs. 4.0 [2.0–5.0] days, P < 0.001).

No severe hypoglycemia or diabetic ketoacidosis was reported during the study. There were no serious adverse events in both groups.

Discussion

In this trial involving 475 hospitalized patients with diabetes who received CSII, we found that the rtCGM program resulted in significantly better glucose control compared with the capillary POC standard of care. TIR was 8.2% (equal to 118 min/day) higher among participants assigned to the rtCGM program than among those assigned to the usual POC method. Furthermore, the use of rtCGM led to significant reductions in time above range, glycemia risk index and mean sensor glucose. These values were achieved without increasing time below range.

It was suggested that short-term intensive insulin therapy (STII) led to improved outcomes, even in people with type 2 diabetes. Evidence from multicenter randomized controlled trials and meta-analyses showed that STII induces restoration of β-cell dysfunction by effectively reducing glucotoxicity, and drug-free diabetes remission for over 1 year was observed in half of patients with newly diagnosed type 2 diabetes who received STII.[13–15,29] However, the risk of hypoglycemia remains a primary concern for many healthcare professionals, hence many practitioners are reluctant to encourage this therapy.[30] Whereas in China, SIIT has now been recommended by the guideline from the Chinese Diabetes Society for patients with poorly controlled diabetes, including those with newly diagnosed type 2 diabetes presenting significant hyperglycemia, and those with persistent poor glucose levels despite ongoing oral agents and/or insulin for over 3 months, etc.[10–12] In addition, CSII is recommended as the preferred option for patients requiring STII,[10–12] based on evidence indicating that CSII achieves better glucose control and shorter hospital stays compared to multiple daily injections.[7–9] Currently, STII with a CSII regimen has been widely adopted and routinely implemented in endocrinology wards of many hospitals across China, including our wards. In the present study, we found that the rtCGM program compared with the POC standard of care resulted in better glucose control without an increased risk of hypoglycemia for patients with diabetes requiring CSII during hospitalization. Interestingly, the time to reach target glucose was 2 days in the rtCGM group, which was significantly shorter than that in the POC group. We speculate that rtCGM may assist healthcare professionals in more quickly and

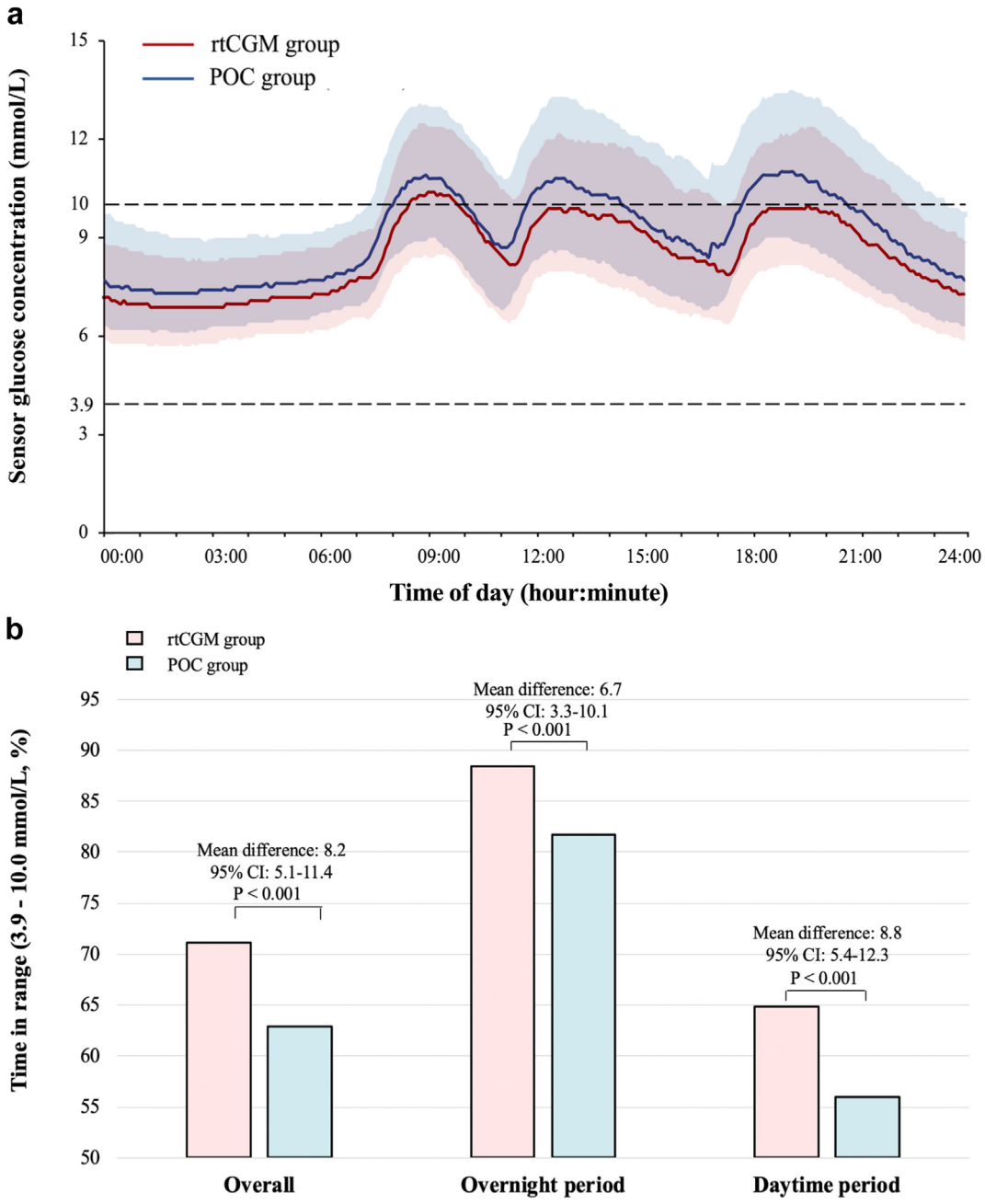

Fig. 1: **Glucose control in the rtCGM group and the POC group.** (a) Median (IQR) sensor glucose concentrations in the two groups. The values are reported during a 24-h period from midnight to midnight. (b) Mean difference (95% CI) in time in ranges between the two groups. Abbreviation: rtCGM, real-time continuous glucose monitoring; POC, point-of-care; IQR, interquartile range.

accurately grasping patients' glucose patterns, enabling more rational clinical decisions regarding insulin adjustments, thereby achieving better glucose control.

To date, only a handful of studies have discussed the use of CGM in the hospital,[23,31–34] and our finding expands the results of prior randomized controlled trials. Our trial had a larger sample size, had a longer follow-up period and established a structured rtCGM-based program incorporating a specialized team. The latter is important for the successful implementation of rtCGM in the hospital, as well as maximizing the expected utility.[34] Based on the above-mentioned strengths, the present study found a significant increase in TIR 3.9–10.0 mmol/L in the rtCGM group compared with

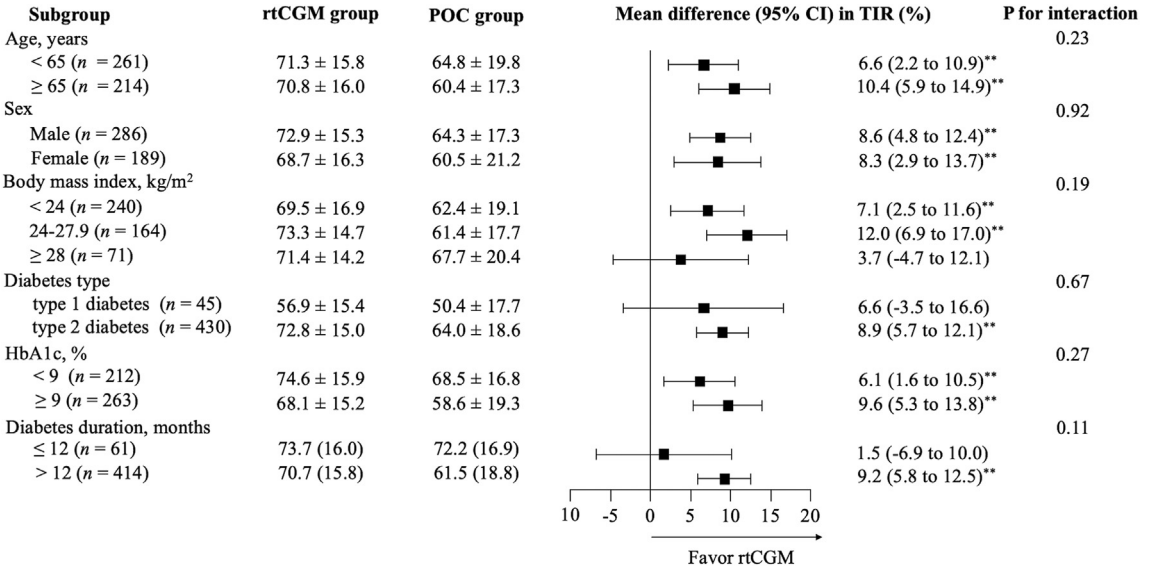

***Fig. 2:* Subgroup analyses for time in range (3.9–10.0 mmol/L, %).** **P < 0.01. Abbreviation: rtCGM, real-time continuous glucose monitoring; POC, point-of-care; TIR, time in range; HbA1c, glycated hemoglobin.

the POC group, which has not been detected in previous studies.[31–33] The improvements in TIR were generally consistent across baseline age, sex, BMI, diabetes type, and glycated hemoglobin levels, as well as during both overnight and daytime periods (Of note, although non-significant differences in TIR were observed among participants with BMI ≥ 28 kg/m^2, type 1 diabetes and diabetes duration ≤12 years, these subgroup results should be interpreted with caution given the relatively small sample size [n = 45∼71]). TIR 3.9–10.0 mmol/L is a core CGM metric recommended by international guidelines and consensuses as an important clinical target and outcome measurement.[19,27,35] The discrepancy between the current and previous studies might relate to the differences in study population, design, and sample size. For instance, a randomized controlled trial involving 110 patients with type 2 diabetes[31] found that the use of rtCGM increased TIR 3.9–13.9 mmol/L, but not TIR 3.9–10.0 mmol/L, however, the CGM sensors were worn for 48 h; an interim analysis of a randomized trial (n = 72)[32] reported that rtCGM can decrease hypoglycemia in high-risk hospitalized patients with diabetes, which was supported by another randomized controlled trial (n = 185) showing a significant reduction of recurrent hypoglycemic events with rtCGM,[33] however, there were no significant differences in TIR in both trials. Therefore, the current study complements significant evidence supporting the use of rtCGM for improving hyperglycemia in the hospital.

Of note, POC testing was performed up to 8 times per day in the current study. Although this monitoring frequency is quite common in endocrinology specialty wards in China, it should be recognized that for hospitalized individuals with diabetes who are eating, 4 times/day (before meals and at bedtime) is the recommended schedule for POC testing.[36] Despite this, the use of rtCGM still achieved improvements in glucose outcomes compared to the POC standard of care. Hence, it is reasonable to infer that rtCGM may yield even greater improvement in glucose outcomes in hospitalized diabetes with lower POC monitoring frequencies. In addition, it is important to note that rtCGM group also received the POC protocol, which could be a potential bias.

The CGM system used in the current study provides prospective real-time glucose measurements to be transmitted directly to a central clinician/nursing station, in which the established hospital network was stable throughout the study. It has the potential for hospital-wide use and is enable to integrate with automated insulin dosing (AID) systems, which deserve future research. However, the cost-effectiveness of rtCGM system remains a key issue for its broader implementation in the hospital. Nevertheless, the costs of the devices themselves and having a CGM support team may be offset by improved glucose control, reduced nursing hours, and decreased hospitalization costs.[19,37] Of note, although length of hospital stay did not differ between the groups, we observe a significant reduction in time to reach target glucose among participants using rtCGM. In the future, it might be interesting to collect data of β-cell function after therapy to evaluate the change of reversing glucose toxicity, which may provide some inspiration for the desirable discharge timing under the use of rtCGM. Moreover, when using rtCGM in the hospital, the frequency of

POC monitoring should be rationally reduced to establish a more cost-effective model. Finally, comprehensive cost-effectiveness analyses considering the above-mentioned factors and hospital outcomes are warranted for the update of relevant reimbursement policies.

Furthermore, further work is required to standardize the settings of rtCGM alerts in the hospital. In the first step, a future comparison between the rtCGM system with alerts on and with alerts off could further elucidate if alerts are the main reason for the better outcomes in rtCGM users, or rather the fact that sensor values are available in real-time. In addition, given the lack of evidence regarding the optimal threshold and timing for predictive alerts in the hospital setting, we only activated the threshold alerts in our study, whereas the predictive alerts remained inactive. While these predictive alerts have the potential to further reduce the risk of clinical hyper/hypoglycemia by providing additional time for interventions before its onset,[38] which needs to be addressed in future studies.

Our trial also has some limitations. First, as a single-center study conducted in a large tertiary care hospital, the findings should be confirmed in multicenter clinical trials. Second, the current study only included those admitted to endocrinology specialty wards, therefore whether the data could be extrapolated to hospital glucose management across different ICU and non-ICU settings remains to be discussed. Third, in light of the eligibility criteria, the results may not apply to individuals with gestational diabetes mellitus or specific types of diabetes due to other causes. Fourth, the CGM sensors can only monitor for up to 7 days. Fifth, we did not record the exact time between dysglycemia occurrence and intervention, as well as the number of interventions per group. Finally, we did not collect satisfaction surveys from clinician and nursing, as well as patient-reported outcome and experience measures satisfaction.[39]

In conclusion, in patients with type 1 and type 2 diabetes who were receiving CSII during hospitalization, we found that the use of rtCGM resulted in better glucose control than the POC standard of care. In addition, improved glucose control was achieved without increasing the risk of hypoglycemia. Further work is required to determine the cost-effectiveness of the rtCGM system, as well as standardize the settings of rtCGM alerts in the hospital.

Contributors

J.Z. and J.L. designed the study. W.L., W.Z., S.W., L.W, Y.B. and Y.W. contributed to the conduction of the study. Y.W., M.W., J.N. and J.Y. collected the data. Y.W. cleaned the data. Y.W. and J.L. performed statistical analysis and wrote the draft of the manuscript. J.G. and X.Y. provided advices for the research protocol, statistical analysis plan and data analyses. J.L. and J.Z. reviewed and edited the manuscript. All authors read and approved the final manuscript.

Data sharing statement

Restrictions apply to the availability of data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. Data are however available from the authors upon reasonable request.

Declaration of interests

All the authors have no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101067.

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