Cardiovascular Diabetology

RESEARCH

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Use of an insulin titration protocol based on continuous glucose monitoring in postoperative cardiac surgery patients with type 2 diabetes and prediabetes: a randomized controlled trial

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Abstract

Background Maintaining optimal glucose control is critical for postoperative care cardiac surgery patients. Continuous glucose monitoring (CGM) in this setting remains understudied. We evaluated the efficacy of CGM with a specialized titration protocol in cardiac surgery patients with type 2 diabetes (T2D) and prediabetes.

Methods In this randomized-controlled trial, 54 cardiac surgery patients were randomized one day post-surgery, with 27 CGM and 25 point-of-care (POC) patients completing the study. The CGM group used Dexcom G6 with a CGM-specialized titration protocol, while the POC group used standard monitoring with blinded CGM. The primary outcome was time-in-range (TIR) 100–180 mg/dL for 7 days post-surgery. Secondary outcomes included various glycemic metrics and surgical outcomes. Multiple comparison adjustments were performed using false-discovery-rate (FDR).

Results Thirty-one (59.6%) had diabetes and 21 (40.4%) had prediabetes. While TIR 100–180 mg/dL showed no difference (74.7% vs. 71.6%, FDR-adjusted $p=0.376$), the CGM group demonstrated improvements in TIR 70–180 mg/dL (83.8% vs. 75.8%, FDR-adjusted $p=0.026$), time-in-tight-range (TITR) 100–140 mg/dL (46.3% vs. 36.3%, FDR-adjusted $p=0.018$), and TITR 70–140 mg/dL (55.3% vs. 40.5%, FDR-adjusted $p=0.003$). Both groups maintained very low rates of time below range (< 70 mg/dL: 0.03% vs. 0.18%, FDR-adjusted $p=0.109$). The CGM group showed lower postoperative atrial fibrillation (AF) (18.8% vs. 55.6%, FDR-adjusted $p=0.04999$).

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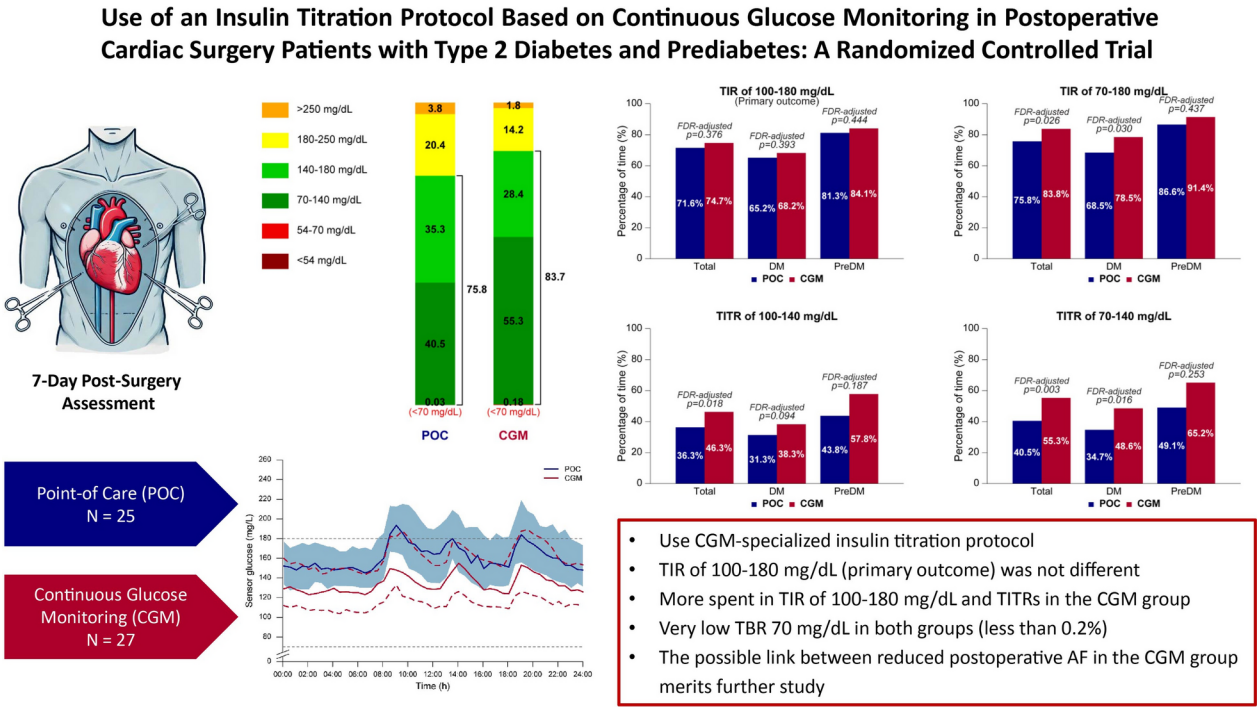
Conclusion While the primary outcome was not achieved, CGM with a specialized titration protocol demonstrated safe glycemic control with improvements in TIR 70–180 mg/dL and TITRs in cardiac surgery patients with T2D and prediabetes. The observed reduction in postoperative AF warrants further investigation.

Trial Registration ClinicalTrials.gov NCT06275971

Keywords Continuous glucose monitoring, CGM, Cardiac surgery, Time in range, Atrial fibrillation, Type 2 diabetes, Prediabetes

Graphical Abstract



Research Insight

What is currently known about this topic?

- Glucose dysregulation increases complications in cardiac surgery.
- Point-of-care monitoring misses many hypo/hyperglycemic events.
- Prior studies with standard protocols showed no time-in-range 70–180 mg/dL improvement with CGM.

What is the key research question?

- Can CGM with specialized protocol improve outcomes in post-cardiac surgery patients with diabetes and prediabetes?

What is new?

- First trial shows CGM improves glycemic control safely in cardiac surgery.
- Novel protocol achieved 83.8% vs 75.8% time-in-range 70–180 mg/dL without hypoglycemia increasement.
- CGM reduced post-op atrial fibrillation (18.8% vs. 55.6%).

How might this study influence clinical practice?

- CGM may enable safer glucose control in cardiac surgery, but needs validation in larger trials.

Background

Cardiovascular disease (CVD) is a major complication and leading cause of death in patients with diabetes, with significant risk beginning even in the prediabetic stage. Studies show individuals with prediabetes have a 15% higher risk of CVD compared to those with normal glucose tolerance [1, 2]. Notably, patients with diabetes face higher mortality risks and adverse outcomes during cardiac surgery compared to those with normal glucose levels [3, 4]. Also, recent evidence suggests prediabetes

independently increases risks of postoperative complications in cardiac surgery as well as in non-cardiac surgery [5, 6].

Perioperative hyper- or hypoglycemia leads to increased rates of surgical site infections, prolonged hospital stays, postoperative myocardial infarction, atrial fibrillation (AF), and higher mortality rates, even in patients without diagnosed diabetes [7–10]. Research has demonstrated that perioperative mean glucose levels, rather than HbA1c, more strongly influence post-surgical or procedural outcomes [8, 11, 12]. Consequently, current guidelines strongly recommend avoiding both hypo and hyperglycemia during the perioperative period [13, 14].

While achieving target glycemic levels during hospitalization requires frequent monitoring, point-of-care (POC) glucose testing has significant limitations. Studies show POC misses 31% of hyperglycemic and 86.7% of hypoglycemic episodes in hospitalized patients [15, 16]. Even in intensive care unit (ICU) settings with POC monitoring, significant hypoglycemic events below 70 mg/dL occur in 8–9% of patients, despite targeting levels ≥ 100 mg/dL [17].

Continuous glucose monitoring (CGM) offers advantages by providing real-time glucose data with numerical and graphical displays of current levels and trends. The system alerts users to actual or impending hyper- and hypoglycemia, enabling timely intervention [18]. Though initial concerns existed regarding CGM accuracy in hospitalized patients due to hypoxia, interstitial acidosis, catecholamine or vasopressin use, edema, and unstable hemodynamics, multiple studies have validated CGM's acceptable accuracy for hospitalized and perioperative use [19–21].

However, no interventional studies have examined CGM use specifically in cardiac surgery patients. While some randomized controlled trials (RCT) have compared CGM to POC in hospitalized patients, these were limited to stable patients in general wards and non-perioperative settings [22–25]. Additionally, these studies employed traditional POC-based protocols rather than CGM-optimized approaches, not utilizing features like trend arrows or postprandial correction injections. This limited utilization may explain their suboptimal results for time in range (TIR) of 70–180 mg/dL [22–25].

To address these knowledge gaps, we conducted an RCT evaluating real-time CGM (RT-CGM) in cardiac surgery patients with type 2 diabetes (T2D) and prediabetes, implementing a CGM-specialized in-hospital titration protocol. This study aims to provide insights into CGM's potential benefits for perioperative glycemic management in this high-risk patient population.

Methods

Trial oversight and study participants

We conducted a single-center, randomized, prospective, open-label study from November 2022 to April 2024 at Kangbuk Samsung Hospital (Institutional Review Board approval: KBSMC 2022-07-006; ClinicalTrials.gov: NCT06275971). We recruited participants scheduled for elective cardiac surgery who were > 18 years of age with T2D or prediabetes, confirmed by 75 g-oral glucose tolerance test (75 g-OGTT). Patients with high surgical severity, defined as Society of Thoracic Surgeons (STS) score ≥ 8 or European System for Cardiac Operative Risk Evaluation (EuroSCORE) ≥ 15 ", were excluded [26, 27]. Detailed in/exclusion criteria are provided in Additional file 1: Table S1.

Study design

After obtaining informed consent and baseline testing, participants wore Dexcom G6 CGM on their upper arms one or two days before surgery, linked to both smartphone and blinded receiver. All participants discontinued anti-diabetic medications and switched to insulin-only management, upon admission to the surgery ward. Prior to randomization, glycemic control relied on POC testing or arterial blood, not CGM data.

The morning after surgery, patients were randomized 1:1 to treatment or control groups, stratified by diabetes/prediabetes status. An independent statistician generated the randomization sequence using permuted blocks (size 4 or 6) using Stata version 17.0. The sequence was maintained by an uninvolved third party. In the control group, we removed the unblinded smartphone and retained only the blinded receiver, while the CGM group maintained both devices to prevent potential data loss from the smartphone. The CGM group's glycemic control was managed with alarms set at 100–180 mg/dL, with POC tests twice daily (and calibration when glucose levels differed by > 20% at ≥ 100 mg/dL, and by > 20 mg/dL at < 100 mg/dL. The calibration rule was set arbitrarily, with the cut-off value adopted from the accuracy standard of the 20/20 agreement rate [28].

CGM was removed 7 days post-surgery, with all data analyzed from the blinded receiver. Patients with < 70% available CGM data during the 7-day study period were withdrawn. We maintained standardized nursing workload with ratios of 1:2 in ICU and 1:8 in general ward, which are our hospital's routine practice, throughout the study. Endocrinologists remotely managed multiple daily insulin injections (MDI) insulin titration daily for both groups via electronic health records, with additional use of the CGM (Dexcom Clarity) interface for the CGM group, using preset algorithmic orders for correction doses. The surgical team independently determined IV-to-MDI transition timing based on post-operative

recovery, regardless of glycemic control or CGM assignment. Patients received standardized hospital meals totaling 25–30 kilocalories/kilogram ideal body weight at consistent times, with no carbohydrate counting in the insulin protocol.

Titration protocol

We implemented a modified protocol incorporating CGM-specific adjustments based on existing non-CGM based protocols [29, 30]. All patients received IV insulin during fasting and continuous feeding periods, transitioning to MDI when intermittent meals resumed. In the control group, during IV insulin administration, POC testing was performed every 2–4 h, with a target range of 100–180 mg/dL. For the MDI period, POC testing was performed four times a day (every pre-meal and bedtime), and basal insulin was adjusted daily based on fasting glucose (target 100–140 mg/dL) by changing doses by 20%, while prandial insulin doses comprised a base dose plus a correction dose determined by a correction scale according to pre-prandial glucose level.

The CGM group followed similar protocols and targets but benefited from continuous monitoring and trend data. During IV insulin periods, sensor glucose was checked every 2–4 h, and trend arrows were utilized in addition to current glucose levels. For the MDI period, sensor glucose was routinely checked seven times a day (every pre-meal, 2 h post-meal, and bedtime). Basal insulin titration was guided by the nighttime CGM graph (11 PM to 5 AM in our hospital), not just by single fasting glucose level. Additional post-meal corrections were calculated and applied using a formula incorporating current glucose, trend arrows, and pre-meal insulin dose. Detailed protocols are provided in the Additional file 2.

Outcomes and clinical variables

The primary outcome was time in range (TIR) 100–180 mg/dL of sensor glucose for 7 days starting one day after surgery. The target was adopted from the current guideline for hospitalized patients without CGM [31]. Prespecified secondary glycemic outcomes included TIR 70–180 mg/dL, time in tight range (TITR) 100–140 mg/dL, time below range (TBR, < 54 mg/dL, < 70 mg/dL), time above range (TAR, > 180 mg/dL, > 250 mg/dL), mean glucose, standard deviation, and coefficient of variance (%CV). Although no CGM study has revealed TITR for cardiac surgery, since tight target (< 140 mg/dL) of cardiac surgery patients in non-CGM studies showed better outcomes and TITR 70–140 mg/dL has been regarded as a key outcome in recent CGM clinical trials, it was additionally analyzed as an exploratory secondary outcome. [32–34]

For surgical outcomes, we analyzed AF, pneumonia, wound infection, continuous renal replacement therapy (CRRT), symptomatic cerebrovascular accident (CVA), changes in serum C-reactive protein (CRP) level between baseline and peak within 1 week after surgery, and length of hospital stay, ICU stay, and mortality after surgery up to 30 days. As exploratory outcomes, we examined insulin dosage, TIR and TITRs across study days, and performed subgroup analyses according to diabetes and prediabetes status, and IV insulin and MDI period.

As baseline data, fasting and 2-h C-peptide levels were collected during 75 g-OGTT at the time of enrollment. The CKD-EPI equation was used to calculate estimated glomerular filtration rate. STS score and EuroSCORE were calculated based on clinical data and echocardiography findings [26, 27]. The baseline laboratory data was collected as the latest data within 2 weeks before the surgery day. CGM applied period (from one or 2 days before the surgery day to the one day before surgery day) was analyzed as baseline CGM data.

Sample size and power calculation

Based on previous research comparing POC and CGM in hospitalized patients, we calculated a required sample size of 26 per group (TIR difference 5.5%, SD 7%, 2-sided $\alpha = 0.05$, power 0.8) [22]. Accounting for 30% dropout, we initially targeted 34 patients per group. However, as we experienced only two dropouts, we concluded enrollment at 54 patients, which satisfied the required sample size from our power calculation.

Statistical analysis

We conducted modified intention-to-treat (ITT) analysis as main analyses, excluding participants with < 70% CGM data or major protocol violations, with additional ITT sensitivity analyses including dropouts. We used ANCOVA for continuous outcomes and logistic regression for binary outcomes, with multiplicity adjusted using false discovery rate (FDR) based on outcome categories. FDR adjustment was not applied for the analyses across study days. For surgical outcomes, we excluded participants with pre-existing conditions at baseline. As covariates, we adjusted for diabetes and prediabetes status, baseline A1c, baseline TIR 70–180 mg/dL, and postoperative day (POD) of MDI transition due to between-group imbalance observed. For three participants with missing baseline CGM data, we performed imputation using mean values of baseline TIR 70–180 mg/dL for corresponding subgroups. We performed analyses using R version 4.1.2, with statistical significance at $P < 0.05$.

Results

Study population

Of 57 screened patients, 54 were randomized to CGM (n = 27) or POC (n = 27) groups. After two POC group dropouts, 52 patients were included in modified ITT

analyses (Fig. 1). Mean age was 63.8 ± 10.8 years, with HbA1c of 6.3 ± 1.3% (45.1 ± 13.9 mmol/mol)(Table 1). The cohort included 31 (59.6%) diabetes and 21 (40.4%) prediabetes patients with the mean HbA1c of 6.7 ± 1.5% and 5.6 ± 0.4%, respectively (Tables S2 and S3). Newly diagnosed diabetes was identified in 11 (21.2%) patients, with 5 (20.0%) in the POC group and 6 (22.2%) in the CGM group. Baseline characteristics were similar between groups except for POD of MDI transition, with more CGM group patients transitioning after POD 4 (Table 1). Baseline characteristics by diabetes status and ITT analysis are shown in Additional file 1: Tables S2–S4.

Glycemic outcomes

Baseline TIR 70–180 mg/dL was 72.4 ± 26.3% and 68.8 ± 23.6% for POC and CGM groups. The primary outcome, TIR 100–180 mg/dL for the 7-day post-surgery period, showed no significant difference between POC and CGM groups (71.6 ± 17.8% vs. 74.7 ± 12.0%; adjusted difference [adj. diff.] 3.5% [95% CI − 3.4 to 10.3], $P = 0.313$, FDR-adjusted $P = 0.376$) (Table 2 and Fig. 2A).

Several secondary glycemic outcomes improved in the CGM group. TIR 70–180 mg/dL was higher (75.8 ± 18.9% vs. 83.8 ± 10.6%; adj. diff. 8.9% [95% CI 1.9 to 15.6], FDR-adjusted $P = 0.026$). TITR 100–140 mg/dL and 70–140 mg/dL also improved (36.3 ± 19.0% vs. 46.3 ± 15.4%; adj. diff. 11.4% [95% CI 3.5 to 19.4], FDR-adjusted $P = 0.018$ and 40.5 ± 22.5% vs. 55.3 ± 15.3%; adj. diff. 16.8% [95% CI 7.5 to 26.0], FDR-adjusted $P = 0.003$, respectively) (Table 2 and Fig. 2B–D). Cumulative distributions and proportions of TIRs and TITRs are presented in Fig. 3 and Additional file 1: Figure S1, respectively. TIR 70–180 mg/dL and TITRs began to show improvement in the CGM group from day 2 of the study period, though not consistently across all days (Additional File 1: Figure S2).

TAR > 180 mg/dL and mean glucose were lower in the CGM group. Both groups showed minimal TBR < 70 mg/dL (0.18 ± 0.39% vs. 0.03 ± 0.11%, FDR-adjusted $P = 0.109$) and < 54 mg/dL (0.00 ± 0.02% vs. 0.01 ± 0.04%, FDR-adjusted $P = 0.420$). CV was higher in the CGM group (22.0 ± 6.2% vs. 25.0 ± 5.9%, FDR-adjusted $P = 0.029$), while SD remained similar (35.3 ± 13.8 mg/dL vs. 36.2 ± 10.6 mg/dL, FDR-adjusted $P = 0.733$) (Table 2). Ambulatory glucose profiles according to the POC and CGM groups are presented in Additional file 1: Figure S3A. As sensitivity analyses, ITT analyses showed similar results presented in Additional file 1: Table S5.

Subgroup analyses

In patients with diabetes, TIR 100–180 mg/dL showed no difference between groups (65.2 ± 17.2% vs. 68.2 ± 10.4%; FDR-adjusted $P = 0.393$). However, TIR 70–180 mg/dL (68.5 ± 17.9% vs. 78.5 ± 9.1%; adj. diff. 12.4% [95% CI 2.9 to 21.8], FDR-adjusted $P = 0.030$) and TITR 70–140 mg/dL were improved in the CGM group (Fig. 2, Additional

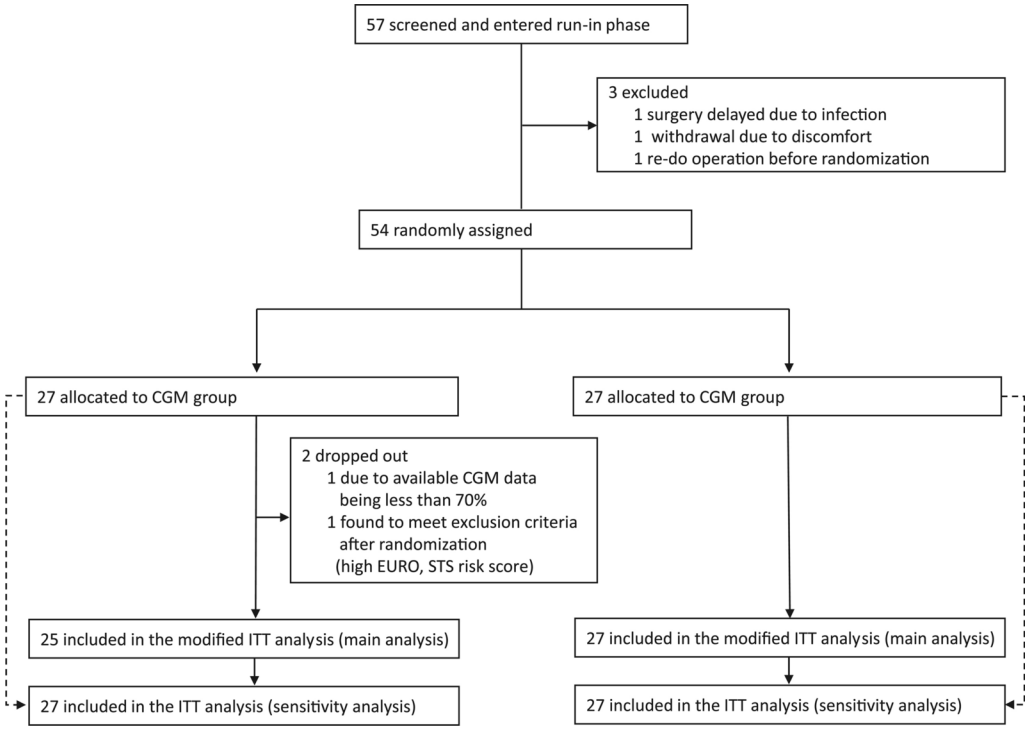


Fig. 1 Flow diagram of study participant selection. Abbreviations: CGM, Continuous Glucose Monitoring; EURO, European System for Cardiac Operative Risk Evaluation; ITT, intention-to-treat; POC, Point-of-Care; STS, Society of Thoracic Surgeons

Table 1 Baseline characteristics of total participants

	Total (n = 52)	POC (n = 25)	CGM (n = 27)	P value
Age, year	63.8 ± 10.8	64.3 ± 10.3	63.4 ± 11.5	0.765
Male, n	27 (51.9)	11 (44.0)	16 (59.3)	0.411
Body mass index, kg/m^2	25.5 ± 3.4	25.5 ± 3.3	25.5 ± 3.6	0.970
Weight, kg	65.8 ± 11.0	64.7 ± 10.6	66.8 ± 11.5	0.514
Hypertension, n	43 (82.7)	21 (84.0)	22 (81.5)	> 0.999
Diabetes or prediabetes				> 0.999
Diabetes, n	31 (59.6)	15 (60.0)	16 (59.3)	
Prediabetes, n	21 (40.4)	10 (40.0)	11 (40.7)	
Dyslipidemia, n	47 (90.4)	22 (88.0)	25 (92.6)	0.928
Atrial fibrillation, n	18 (34.6)	7 (28.0)	11 (40.7)	0.501
Hemodialysis, n	2 (3.8)	1 (4.0)	1 (3.7)	> 0.999
Systolic blood pressure, mmHg	127.9 ± 19.0	130.1 ± 17.6	125.9 ± 20.2	0.431
Diastolic blood pressure, mmHg	71.0 ± 11.9	72.2 ± 11.5	69.9 ± 12.3	0.495
HbA1c, %	6.3 ± 1.3	6.4 ± 1.7	6.1 ± 0.7	0.435
HbA1c, mmol/mol	45.1 ± 13.9	46.7 ± 18.3	43.6 ± 8.1	0.435
Serum creatinine, mg/dL	1.0 ± 1.1	1.1 ± 1.3	1.0 ± 0.9	0.750
Estimated GFR, mL/min/1.73 m^2	82.9 ± 26.4	80.4 ± 25.8	85.1 ± 27.3	0.526
CRP, mg/dL	2.9 ± 11.2	3.6 ± 15.4	2.2 ± 5.3	0.653
C peptide (fasting), ng/mL	2.6 ± 1.9	2.5 ± 1.8	2.6 ± 1.9	0.870
C peptide (2 h prandial), ng/mL	11.0 ± 6.5	11.1 ± 6.7	11.0 ± 6.5	0.937
EURO score	1.8 ± 1.3	1.6 ± 1.2	2.0 ± 1.3	0.202
STS score	2.6 ± 1.8	2.5 ± 1.8	2.7 ± 1.8	0.655
Anti-diabetic medications				
Metformin, n	14 (26.9)	8 (32.0)	6 (22.2)	0.630
Sulfonylurea, n	7 (13.5)	4 (16.0)	3 (11.1)	0.913
DPP4 inhibitor, n	9 (17.3)	3 (12.0)	6 (22.2)	0.544
SGLT2 inhibitor, n	8 (15.4)	5 (20.0)	3 (11.1)	0.615
TZD, n	3 (5.8)	2 (8.0)	1 (3.7)	0.945
Alpha glucosidase inhibitor, n	1 (1.9)	0 (0.0)	1 (3.7)	> 0.999
Insulin, n	4 (7.7)	0 (0.0)	4 (14.8)	0.138
GLP-1 receptor agonist, n	0 (0.0)	0 (0.0)	0 (0.0)	> 0.999
ICU stay during the study period, days (%)	3.3 ± 2.1 (47.0 ± 30.6)	3.0 ± 1.8 (42.3 ± 25.9)	3.6 ± 2.4 (51.3 ± 34.4)	0.292
Postoperative day of MDI transition				0.043
POD 1, n	26 (50.0)	12 (48.0)	14 (51.9)	
POD 2–3, n	21 (40.4)	13 (52.0)	8 (29.6)	
POD ≥ 4, n	5 (9.6)	0 (0.0)	5 (18.5)	

Data are presented as mean (standard deviation) or n (%)

Abbreviations: CGM, continuous glucose monitoring; CRP, C-reactive protein; DPP4, dipeptidyl peptidase-4; EURO, European System for Cardiac Operative Risk Evaluation; GFR, glomerular filtration rate; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; ICU, intensive care unit; MDI, multiple daily injection; POC, point-of-care; POD, post-operative day; SGLT2, sodium-glucose cotransporter-2; STS, Society of Thoracic Surgeons; TZD, thiazolidinedione

file 1: Table S6, Figures S1, S4, and S5). In prediabetes patients, glycemic outcomes were comparable between groups, with the CGM group showing improvement in TITRs only on several specific days (Fig. 2, Additional file 1: Table S7, Figures S1, S6, and S7).

During IV insulin periods, TIR 70–180 mg/dL showed initial improvement (64.6 ± 33.3% vs 85.0 ± 13.7%; adj. diff. 23.6% [95% CI 1.1 to 46.0]) but lost significance after FDR adjustment (Additional file 1: Table S8 and Figure S3B). In MDI periods, the CGM group showed improvements in TITR 100–140 mg/dL (37.5 ± 18.9% vs 48.4 ± 16.7%; adj. diff. 11.1% [95% CI 2.8 to 19.3], $P = 0.029$) and TITR 70–140 mg/dL (42.1 ± 22.7% vs 5.8.1 ± 18.1%; adj. diff. 16.3% [95% CI 6.3 to 26.3], P = 0.010) (Additional file 1: Table S9 and Figure S3C).

Surgical outcomes

Postoperative AF incidence was lower in the CGM group (55.6% vs. 18.8%; adjusted odds ratio 0.04 [95% CI 0.00 to 0.46], FDR-adjusted $P = 0.04999$) (Table 2). Other complications, including pneumonia, wound infection, CRRT, symptomatic CVA, and 30-day mortality, showed no differences. ICU and hospital stays were comparable between groups. Surgical outcomes in the diabetes subgroup showed no significant differences (Additional file 1: Table S10). In prediabetes patients, the CGM group showed lower CRP level increases (adj. diff. – 9.3 mg/dL [95% CI – 16.3 to – 2.2], FDR-adjusted $P = 0.040$) (Additional file 1: Table S11). There were no unintended adverse effects in each group regarding to the intervention. As sensitivity analyses, ITT analyses showed similar results presented in Additional file 1: Table S5.

Insulin requirements

Post-prandial positive correction insulin doses (0.000 ± 0.000 vs. 0.009 ± 0.011 U/kg/day; FDR-adjusted $P < 0.001$) and frequency (0.0 ± 0.0 vs. 0.3 ± 0.3 times/day, FDR-adjusted $P < 0.001$) were higher in the CGM group. Pre-prandial corrections, total correction doses, and total daily insulin requirements were comparable between groups (Additional file 1: Table S12). Initial differences in total correction frequency (1.1 ± 1.0 vs. 1.3 ± 1.1 times/day; adj. diff. 0.4 [95% CI 0.1 to 0.8]) lost significance after FDR adjustment. Insulin requirements for diabetes and prediabetes subgroups are presented in Additional file 1: Tables S13 and S14.

Discussion

In this randomized controlled trial of cardiac surgery patients with diabetes or prediabetes, RT-CGM with a CGM-specialized protocol showed improvements in several secondary glycemic metrics, despite no significant difference in the primary outcome of TIR 100–180 mg/dL. The CGM group achieved higher TIR 70–180 mg/

Table 2 CGM and surgical outcomes of total participants

	Baseline		Study period				
	POC	CGM	POC	CGM	Adjusted difference or odds ratio (95% CI)	Adjusted p value	FDR adjusted p value
CGM outcomes							
TIR 100–180 mg/dL, %	67.9 ± 25.3	64.0 ± 20.3	71.6 ± 17.8	74.7 ± 12.0	3.5 (– 3.4 to 10.3)	0.313	0.376
TIR 70–180 mg/dL, %	72.4 ± 26.3	68.8 ± 23.6	75.8 ± 18.9	83.8 ± 10.6	8.8 (1.9 to 15.6)	0.013	0.026
TITR 100–140 mg/dL, %	32.4 ± 24.0	25.3 ± 20.8	36.3 ± 19.0	46.3 ± 15.4	11.4 (3.5 to 19.4)	0.006	0.018
TITR 70–140 mg/dL, %	37.0 ± 28.3	30.0 ± 26.8	40.5 ± 22.5	55.3 ± 15.3	16.8 (7.5 to 26.0)	< 0.001	0.003
TAR > 180 mg/dL, %	27.0 ± 26.7	30.9 ± 23.6	24.2 ± 18.9	16.0 ± 10.5	– 8.9 (– 15.8 to– 2.1)	0.012	0.026
TAR > 250 mg/dL, %	7.6 ± 20.1	3.9 ± 8.0	3.8 ± 7.1	1.8 ± 2.7	– 2.2 (– 4.6 to 0.2)	0.067	0.101
TBR < 70 mg/dL, %	0.58 ± 2.25	0.38 ± 1.55	0.03 ± 0.11	0.18 ± 0.39	0.15 (– 0.02 to 0.32)	0.082	0.109
TBR < 54 mg/dL, %	0.29 ± 1.39	0.22 ± 0.78	0.01 ± 0.04	0.00 ± 0.02	– 0.01 (– 0.03 to 0.01)	0.385	0.420
Mean glucose, mg/dL	163.4 ± 43.0	163.3 ± 27.6	157.3 ± 23.3	142.5 ± 13.0	– 16.3 (– 24.4 to– 8.1)	< 0.001	0.001
SD, mg/dL	30.8 ± 13.1	32.9 ± 11.4	35.3 ± 13.8	36.2 ± 10.6	0.8 (– 4.0 to 5.6)	0.733	0.733
CV, %	19.3 ± 7.8	20.3 ± 6.3	22.0 ± 6.2	25.0 ± 5.9	3.3 (0.6 to 5.9)	0.017	0.029
Surgical outcomes							
Atrial fibrillation, n (%)	7 (28.0)	11 (40.7)	10 (55.6)	3 (18.8)	0.04 (0.00 to 0.46)	0.010	0.050
Pneumonia, n (%)	0 (0.0)	0 (0.0)	2 (8.0)	2 (7.4)	0.16 (0.01 to 5.23)	0.306	0.765
Wound infection, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	NA[†]	NA	NA
CRRT, n (%)	1 (4.0)	1 (3.7)	0 (0.0)	0 (0.0)	NA[†]	NA	NA
Symptomatic CVA, n (%)	2 (8.0)	2 (7.4)	0 (0.0)	0 (0.0)	NA[†]	NA	NA
CRP change, mg/dL*	3.6 ± 15.4	2.2 ± 5.3	15.2 ± 18.4	14.9 ± 7.1	– 1.5 (– 9.5 to 6.5)	0.704	0.880
Length of hospital stay, days	NA	NA	17.6 ± 7.9	18.9 ± 8.3	– 0.2 (– 4.6 to 4.3)	0.937	0.937
Length of ICU stay, days	NA	NA	3.9 ± 5.7	5.1 ± 5.8	– 0.6 (– 3.0 to 1.8)	0.618	0.880
Mortality within 30 days, n (%)	NA	NA	0 (0.0)	0 (0.0)	NA	NA	NA

Data are presented as mean (standard deviation) or n (%). Diabetes and prediabetes status, baseline A1c, baseline TIR 70–180 mg/dL, postoperative day of multiple daily injection transition were adjusted were adjusted for in the analyses. When analyzing surgical outcomes, participants who had already experienced the outcomes at baseline were excluded

* CRP values are reported as follows: for baseline, the actual baseline CRP value is given; for the study period, the change from the baseline value is reported

† The variables are presented as adjusted odds ratio otherwise are presented as adjusted difference

Abbreviations: CGM, continuous glucose monitoring; CI confidence interval; CRP, C-reactive protein; CRRT, continuous renal replacement therapy; CV, coefficient of variation; CVA, cerebrovascular accident; FDR, false discovery rate; ICU, intensive care unit; NA, not applicable; POC, point-of-care; SD, standard deviation; TAR, time above range; TBR, time below range; TIR, time in range; TITR, time in tight range

dL (75.8% vs. 83.8%, FDR-adjusted $P = 0.026$) and TITR for both 100–140 mg/dL (36.3% vs. 46.3%, FDR-adjusted $P = 0.018$) and 70–140 mg/dL (40.5% vs. 55.3%, FDR-adjusted $P = 0.003$). Both groups maintained minimal hypoglycemia (TBR < 70 mg/dL: 0.03% vs. 0.18%, FDR-adjusted $P = 0.109$). Notably, AF incidence was lower in the CGM group (55.6% vs. 18.8%, FDR-adjusted $P = 0.04999$). These findings suggest potential benefits of CGM use in the post-operative setting, though further research is needed to confirm these observations.

Previous inpatient CGM studies have primarily focused on accuracy [19–21]. Moreover, there have been no intervention studies using CGM in cardiac surgery patients for perioperative use, where glucose control is critical for outcomes. Of the four existing RCTs using RT-CGM in hospitalized patients, none specifically targeted cardiac surgery patients or perioperative settings, and most were conducted in non-ICU settings [22–25]. These studies showed varying results: Fortmann et al. found no significant difference in TIR 70–180 mg/dL but improved TIR 70–250 mg/dL (64.0% vs. 72.9%, P = 0.0404) [22]; Singh et al. improved TBR < 70 mg/dL (1.88% vs. 0.40%, P = 0.002) but not TIR [23]; and neither Klarskov et al. nor Spanakis et al. found significant differences in TIR 70–180 mg/dL [24, 25]. Given that glucose control immediately after surgery is critical for cardiac patients, our study addresses an important gap.

Our inability to demonstrate significance in the primary outcome (TIR 100–180 mg/dL) may reflect our choice of target range, which was based on pre-CGM inpatient guidelines [31]. At the time of study design, there was no consensus on inpatient CGM targets. While our choice of primary outcome may have influenced the statistical findings, it is worth noting that other inpatient studies have used TIR 70–180 mg/dL as their primary outcome [24, 25], which may be better suited for capturing the full range of glycemic control in the inpatient setting. Although TIR 70–180 mg/dL was a secondary

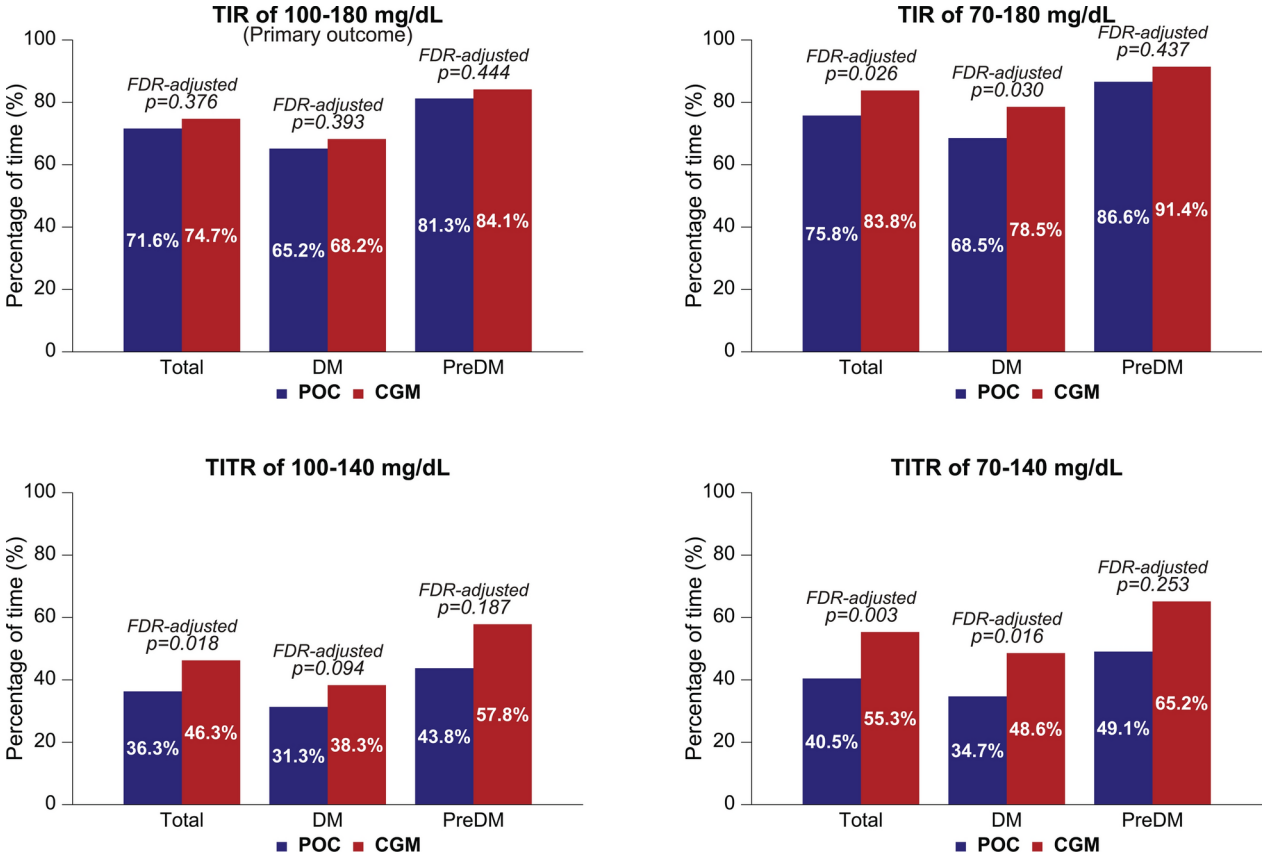


Fig. 2 Proportion of time in ranges and time in tight ranges. P values are for FDR-adjusted analyses, where diabetes and prediabetes status, baseline A1c, baseline TIR 70–180 mg/dL, and postoperative day of multiple daily injection transition were adjusted for. Abbreviations: CGM, continuous glucose monitoring; DM, diabetes; FDR, false discovery rate; POC, point-of-care; PreDM, prediabetes; TIR, time in range; TITR, time in tight range

outcome in our study, the observed difference with multiplicity correction between groups suggests potential benefits. The marked improvement in TIR 70–180 mg/dL, TITRs, and extremely low hypoglycemia rate likely stemmed from our CGM-specialized titration protocol.

Previous studies used well-designed standardized protocols. Fortmann et al. adjusted basal insulin based on fasting glucose and early morning hypoglycemia, with correction insulin for high pre-meal or bedtime glucose [22]. Singh et al. applied basal dose adjustment based on fasting glucose [23], while Spanakis et al. employed a systematic approach, adjusting basal insulin based on fasting and pre-dinner glucose, with correction insulin for high pre-meal and bedtime glucose [25]. However, these protocols relied on single-point glucose measurements, which was no different from POC, and did not utilize CGM's benefits. Our study aimed to utilize CGM's advantages over POC, including graphical information, trend arrows, and ease of frequent glucose checks (Additional file 2). While total daily insulin doses remained similar between groups, additional post-prandial corrections may have contributed to improved glycemic outcomes.

Traditional approaches suggest higher glucose targets for cardiac surgery patients due to hypoglycemia risks [35, 36]; studies showed 120–180 mg/dL was preferable to 90–120 mg/dL [37], 110–140 mg/dL was better than 80–110 mg/dL [38], and 141–180 mg/dL was superior to 100–140 mg/dL [17]. However, for non-diabetic patients, there have been evidences that lower targets (100–140 mg/dL and 80–110 mg/dL) are associated with lower post-cardiac operative complications [17, 39]. Therefore, current American Diabetes Association guideline recommend 141–180 mg/dL, with 110–140 mg/dL for patients at low risk of hypoglycemia [13]. However, those studies did not utilize CGM. Our study demonstrated that RT-CGM's alarm function and trend arrows enabled safe achievement of broader, lower targets (100–180 mg/dL) while maintaining minimal hypoglycemia and high TIR/TITR.

The lower postoperative AF incidence in the CGM group, though a secondary finding, warrants attention. Postoperative AF negatively affects both short-term outcomes and long-term survival [40, 41]. Previous research showed reduced AF with better glycemic control in cardiac surgery patients (16.6% vs. 42% for targets

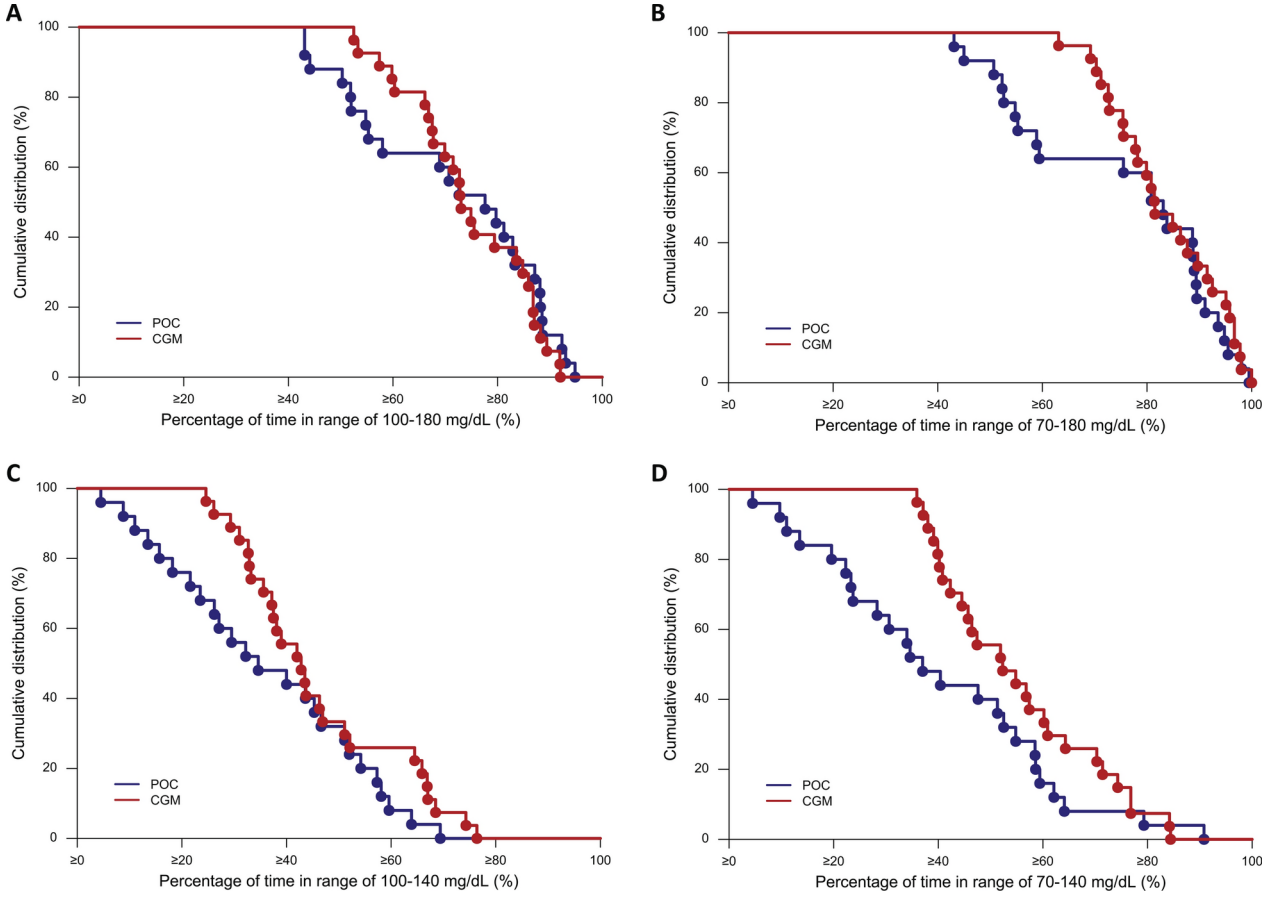


Fig. 3 Cumulative distributions of time in ranges and time in tight ranges among total population. Abbreviations: CGM, continuous glucose monitoring; IV, intravenous; MDI, multiple daily insulin injection; POC, point-of-care

125–200 mg/dL vs < 250 mg/dL) [10]. Hyperglycemia can induce arrhythmia through Ca2 + /calmodulin-dependent kinase II alterations [42]. While some studies suggest links between hypoglycemia and AF [43, 44], recent evidence from a long-term study in type 1 diabetes indicates hyperglycemia, rather than hypoglycemia, may be more strongly associated with arrhythmia risk [45]. However, larger studies are needed to confirm these relationships, as our study wasn't powered for this outcome.

Our study's strengths include being the first RCT of CGM in cardiac surgery patients during immediate postoperative care, which is crucial for these patients, spanning both ICU and general ward settings. Furthermore, we presented results for a broader range of indications, including not only diabetes but also prediabetes patients. We demonstrated the feasibility of a CGM-specialized insulin titration protocol for hospitalized patients that achieved its safety objectives.

Several limitations should be noted. First, the lack of significant primary outcome difference may reflect our choice of outcome measure, though we performed multiplicity correction for secondary outcomes. Second, our single-center design and relatively small sample size, although based on proper calculations, limit generalizability. Particularly for subgroup analyses, since these weren't included in original power calculations, results should be interpreted as exploratory. Third, the open-label nature potentially introduced bias, despite following predetermined protocols. Fourth, additional healthcare provider (HCP) workload was required due to postprandial correction insulin injections and alarms for the CGM group. While this may have been compensated by reduced POC workload, satisfaction surveys for HCPs should be included in future studies. Fifth, while CGM accuracy in inpatient settings remains a concern, we used a well-studied system (Dexcom G6) [19–21] with calibration protocols for significant POC differences. Sixth, since OGTTs were performed while some patients were on diuretics and beta-blockers, which can affect glucose levels, there is a possibility that diabetes or prediabetes might have been misclassified. Seventh, since there was no study comparing TIR between CGM vs. POC among prediabetes patients at the time of study design, we calculated the sample size based on studies of diabetes patients. Lastly, this study enrolled relatively well-controlled diabetes patients and prediabetes patients with

relatively low TDD. However, considering the higher tendency of TDD and more frequent correction insulin in the CGM group even in this low TDD setting, it may be more effective in higher insulin-requiring participants, which may need further study.

Conclusions

In conclusion, while our study didn't achieve its primary outcome, it provides important insights into RT-CGM use with specialized protocols for cardiac surgery patients with diabetes and prediabetes. The significant improvements in secondary outcomes, including TIR 70–180 mg/dL and TITRs without increased hypoglycemia risk, along with the observed lower incidence of postoperative AF, suggest this approach warrants further evaluation in larger trials. Our findings indicate that CGM may enable safer achievement of tighter glycemic targets in this high-risk population.

Abbreviations

AF	Atrial fibrillation
CI	Confidence interval
CGM	Continuous glucose monitoring
CRP	C-reactive protein
CRRT	Continuous renal replacement therapy
CV	Coefficient of variation
CVA	Cerebrovascular accident
CVD	Cardiovascular disease
DPP4	Dipeptidyl peptidase-4
EURO	European system for cardiac operative risk evaluation
FDR	False discovery rate
GFR	Glomerular filtration rate
GLP-1	Glucagon-like peptide-1
HCP	Healthcare provider
ICU	Intensive care unit
IRB	Institutional review board
ITT	Intention-to-treat
MDI	Multiple daily injection
NA	Not applicable
OGTT	Oral glucose tolerance test
POC	Point-of-care
POD	Post-operative day
RCT	Randomized controlled trial
RT-CGM	Real-time continuous glucose monitoring
SD	Standard deviation
SGLT2	Sodium-glucose cotransporter-2
STS	Society of thoracic surgeons
T2D	Type 2 diabetes
TAR	Time above range
TBR	Time below range
TIR	Time in range
TITR	Time in tight range
TZD	Thiazolidinedione

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12933-025-02747-z.

Additional file 1.

Additional file 2.

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Author contributions

S.J.M. was involved in the literature review and synthesis, project conception, protocol development, statistical analysis, critical discussion, and drafting of the first manuscript. M.S.K. and E.S.C. were involved in patient enrollment, project conception, protocol development, data acquisition, critical discussion, and revising the manuscript. H.E.L., Y.W.L., and S.J.L. were involved in data acquisition, device management, and conducting the protocol. C.Y.P. was involved in the project conception, critical discussion, and revising the manuscript. S.J.M. 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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This research was conducted as an investigator-led study. Although Dexcom contributed to the study by providing the CGM devices, their input was limited to technical support. The company reviewed the study protocol for funding purposes but had no role in protocol development or study execution. All aspects of data management, monitoring, and analysis were independently conducted by the coordinating center at Kangbuk Samsung Hospital in Seoul, Korea.

Availability of data and materials

Requests for access to the study data will be considered by the investigators and may be shared at their discretion following review of the research proposal. The titration protocol is available in Additional file 2.

Declarations

Ethics approval and consent to participate

The study was conducted following approval from the Institutional Review Board of Kangbuk Samsung Hospital (KBSMC 2022-07-006). Written informed consent was obtained from all study participants before enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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