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Effects of intermittently scanned continuous glucose monitoring on body weight and glycemic variability in individuals with overweight and impaired glucose tolerance or mild diabetes: A pilot randomized controlled trial

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ABSTRACT

Objective: To investigate the effect of visualizing blood glucose variability by intermittently scanned continuous glucose monitoring (isCGM) on weight reduction in overweight individuals with impaired glucose tolerance (IGT) or mild type 2 diabetes mellitus (T2DM).
Materials and methods: Forty overweight (BMI, ≥25 kg/m2) individuals with IGT or T2DM (drug naïve; HbA1c, ≤7.0 %) were included in this 24-week randomized controlled trial. Participants were randomly assigned to the control group (diet and exercise therapy) or the isCGM group (diet and exercise therapy plus isCGM). The primary endpoint was the change in body weight during the 24-week intervention period.
Results: One participant in the isCGM group withdrew consent. We therefore analyzed 19 individuals in the isCGM group and 20 in the control group. Baseline BMI was significantly higher in the isCGM group (35.2 ± 5.7 kg/m^2) compared to the control group (31.6 ± 6.8 kg/m^2). Weight change in the isCGM and control groups (–1.8 and –2.2 kg) did not differ. However, the change in coefficient of variation (–0.9 and 2.9 %) of sensor glucose differed significantly between the two groups. isCGM scan frequency was positively correlated with time above range (TAR) during the first month, positively correlated with the change in protein intake, and negatively correlated with that in TAR.
Conclusion: While isCGM use in overweight individuals with IGT or mild T2DM did not reduce body weight, it might have influence dietary behavior. The negative correlation between scan frequency and TAR, and the positive correlation between scan frequency and protein intake suggest that self-awareness of glucose fluctuations contributed to behavioral change.

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1. Introduction

Obesity is strongly associated with the development of type 2 diabetes mellitus (T2DM) [1], the risk of which is substantially higher in obese than in nonobese individuals [2,3]. Lifestyle interventions that promote weight reduction in obese individuals are effective in preventing or ameliorating T2DM [4,5]. In the treatment of obesity, behavioral therapy plays a key role in maintaining the effectiveness of diet and exercise therapy [6,7]. The importance of self-monitoring in behavioral therapy is emphasized in several guidelines [8–10], with such self-monitoring being recommended as a component of standard obesity treatment. Recent studies have highlighted the benefit of self-monitoring of diet and exercise with the use of mobile tools [11,12]. The development of new and effective self-monitoring approaches would be expected to further contribute to the treatment of obesity and to the prevention and management of T2DM.

Substantial advances in the development of devices for monitoring of blood glucose levels have been achieved in recent years. One such device, the intermittently scanned continuous glucose monitoring (isCGM) system, allows individuals to self-monitor their blood glucose variability. Individuals with T2DM who frequently administer insulin injections have been shown to undergo behavioral changes as a result of the visualization of blood glucose variability with isCGM [13]. In addition, in individuals with T2DM managed with basal insulin, isCGM has been linked to changes in eating behavior and improvement in glycemic indices [14].

On the other hand, there have been no studies examining the effects of CGM devices in overweight individuals with IGT or T2DM not treated with antidiabetes medication. Furthermore, there are no studies that have used the effectiveness of CGM devices in weight loss as the main outcome.

To explore further the potential benefit of isCGM in terms of triggering behavioral change, we have now evaluated its effect on body weight in overweight individuals with impaired glucose tolerance (IGT) or with T2DM not treated with diabetes medications.

2. Materials and methods

2.1. Study design

This multicenter, randomized, open-label study was conducted at four Japanese centers. This study was conducted from January 2018 to January 2023. The trial consisted of a screening period of no more than 4 weeks before study entry and an intervention or control period (24 weeks) (Fig. S1). The trial randomized participants and assigned them to the intervention and control groups in a 1:1 ratio.

2.2. Study participants

This study was conducted in an outpatient setting. The study participants were required to fulfill all inclusion criteria and not to meet any of the exclusion criteria. All individuals provided written informed consent before participation in the study. Screening tests were performed on participants after obtaining consent. Inclusion criteria were (1) an age of 20 years or older at the time of consent acquisition, (2) overweight status with a body mass index (BMI) of at least 25 kg/m^2 and either a diagnosis of IGT based on a 75-g oral glucose tolerance test (OGTT) (blood glucose values of 140 mg/dL or higher but less than 200 mg/dL at 2 hours after glucose loading, with fasting blood glucose values of less than 126 mg/dL) [15] or a diagnosis of T2DM with a hemoglobin A1c (HbA1c) level of 7.0 % or less without the taking of oral hypoglycemic medication, and (3) receipt of outpatient care only. Exclusion criteria were (1) participation in other clinical studies, (2) severe skin disease on the upper arm, (3) use of other implantable medical devices such as a pacemaker, (4) inappropriateness for other reasons as judged by a study investigator, and (5) overweight status with a BMI of $\geq$ 25 and $<$ 30 kg/m^2 and with a diagnosis of IGT by a 75-g OGTT, but without dyslipidemia or hyperuricemia. Regarding exclusion criterion (5), in Japan, insurance does not cover nutritional guidance for individuals with these characteristics. To ensure consistency, we excluded these individuals since the study assumed participants would receive insurance-covered nutritional guidance. The study included 40 participants recruited from four medical institutions: Kobe University Hospital, Akashi Medical Center, Shinko Memorial Hospital, and Yokota Medical Clinic. The criteria for discontinuation of participation in the study included (1) a request from a participant to withdraw from the study or withdrawal of consent, (2) continuation in the study made difficult by illness or other reasons, (3) discontinuation of the entire study, (4) an HbA1c level of $\geq$ 8.5 %, (5) administration of oral hypoglycemic agents deemed clinically necessary, and (6) discontinuation deemed necessary by a physician for other reasons.

The study was conducted in an outpatient setting. Data downloaded from the FreeStyle Libre sensor (Abbott Diabetes Care, Alameda, CA, USA) used in the isCGM group and the FreeStyle Libre Pro sensor (Abbott Diabetes Care, Alameda, CA, USA) used in the control group were collected at the data center. All other data were collected at each study site.

2.3. Interventions

After enrollment in the study, participants were randomized to ensure an equal distribution of IGT and T2DM patients between the control and isCGM groups.

2.3.1. Control group

Participants in the control group received dietary guidance from a dietitian according to the “Guidelines for the Management of Obesity Disease 2016” [16], with target energy intake of 25 kcal per kg of body weight. They were also instructed to perform at least 30 minutes of exercise per day, or at least 150 minutes per week, following the same guidelines.

2.3.2. isCGM group

Participants in the isCGM group received the same dietary and exercise therapy as the control group. They wore the FreeStyle Libre sensor for the 24-week study period. At the beginning of the study, participants were instructed on how to insert the sensor, scan the FreeStyle Libre sensor, and scan at least every 8 hours to avoid data loss. The device was used as a self-monitoring tool, and no feedback on the FreeStyle Libre data was provided by physicians or registered dietitians during visits. No recommendations on scan frequency or behavior changes based on the data were given.

2.3.3. Data Collection

In the control group, the FreeStyle Libre Pro sensor was worn for 2 weeks from visit 1 and again from visit 4 (Fig. S1). For both groups, data collection occurred at weeks 4, 12, 20, and 24 after study entry.

2.4. Outcome

The primary endpoint was the change in body weight during the 24-week intervention period. Secondary endpoints included the amelioration of glucose intolerance assessed using a 75 g OGTT, changes in HbA1c levels, blood pressure, serum levels of lipids, uric acid, and liver enzymes, as well as dietary and protein intake. Additionally, CGM indices such as time above range (TAR; >180 mg/dL [>10.0 mmol/L]), time in range (TIR; 70–180 mg/dL [3.9–10.0 mmol/L]), time below range (TBR; <70 mg/dL [<3.9 mmol/L]), mean sensor glucose (SG) level, the coefficient of variation (CV) and standard deviation (SD) of SG levels, and the number of scans were also evaluated as secondary endpoints.

Participants recorded their dietary intake for 3 days before each visit,

including photographs of their meals. A dietitian reviewed this information to assess the types and amounts of foods consumed. When nutritional content was not available, the dietitian used the "Food Exchange Lists for Diabetes" [17] to calculate caloric and protein intake.

2.5. Sample size

The primary endpoint of the study was weight reduction achieved using isCGM. In the absence of comparable studies, we based our sample size estimation on a study examining lifestyle intervention on weight reduction [5], which reported a 3.5 kg intergroup difference with a 5.1 kg SD. Anticipating a smaller effect size for our study, we set an expected difference of 2.3 kg and an SD of 2.5 kg. Using a two-sided *t*-test with a significance level of 5 % and a power of 0.8, a sample size of 20 participants per group was required, calculated using IBM SPSS version 29.0 (Armonk, NY: IBM Corp).

2.6. Randomization

Participants' eligibility was verified by the study office. Randomization was performed using the envelope method with stratification to ensure that participants with type 2 diabetes mellitus (T2DM) and participants with IGT were equally distributed in a 1:1 ratio between the control and isCGM groups.

2.7. Blinding

Due to the nature of the intervention, we did not perform blinding.

2.8. Statistical analysis

For assessment of the primary outcome, the difference in body weight between visit 1 and visit 5 was calculated for each participant in the isCGM and control groups, and the mean value for each group was then calculated. Secondary endpoints were evaluated in the same manner. The correlation between the number of scans and each endpoint in the isCGM group was also evaluated. Differences between groups for data following a normal or nonnormal distribution were assessed with Student's *t* test or the Mann-Whitney *U* test, respectively. Data are presented as means ± SD unless indicated otherwise. Correlations for each parameter were determined with Pearson's correlation coefficient. A P value of < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS version 29.0. As a post-hoc analysis, an analysis of covariance (ANCOVA) was conducted to adjust for the significant baseline BMI difference and assess the impact on weight reduction outcomes. Specifically, the analysis examined whether the difference in weight change between the isCGM group and the control group remained significant after adjusting for baseline BMI. Additionally, post-hoc analyses were performed to compare weight changes in the isCGM and control groups within the IGT and T2DM subgroups.

3. Results

The CONSORT flow diagram of the study is shown in Fig. 1. Forty participants were randomized to the two study groups, 20 to the isCGM group and 20 to the control group. Participants were enrolled between June 11, 2018 and September 9, 2020, with observation completed on February 24, 2021. One participant in the isCGM group withdrew consent after the study began because of a refusal to continue wearing the isCGM device. All other thirty-nine participants completed the study, and all of them were analyzed, with the retention rate was 97.5 %. No adverse events were reported during the study period in either group.

The baseline characteristics of the study participants including clinical laboratory data, CGM results, and nutritional intake are presented in Table 1. At baseline, BMI was 35.2 ± 5.7 kg/m^2 in the isCGM group and 31.6 ± 6.8 kg/m^2 in the control group, with this difference being statistically significant ($P < 0.05$). The 39 participants who completed the study did so with no missing data for the primary endpoint of change in body weight or missing clinical laboratory or CGM data, and they were therefore subjected to the corresponding analyses. On the other hand, two participants in the isCGM group and five participants in the control group were excluded from the analysis of protein intake because they were unable to collect such data, with only the remaining 32 participants being included in the analysis of protein intake.

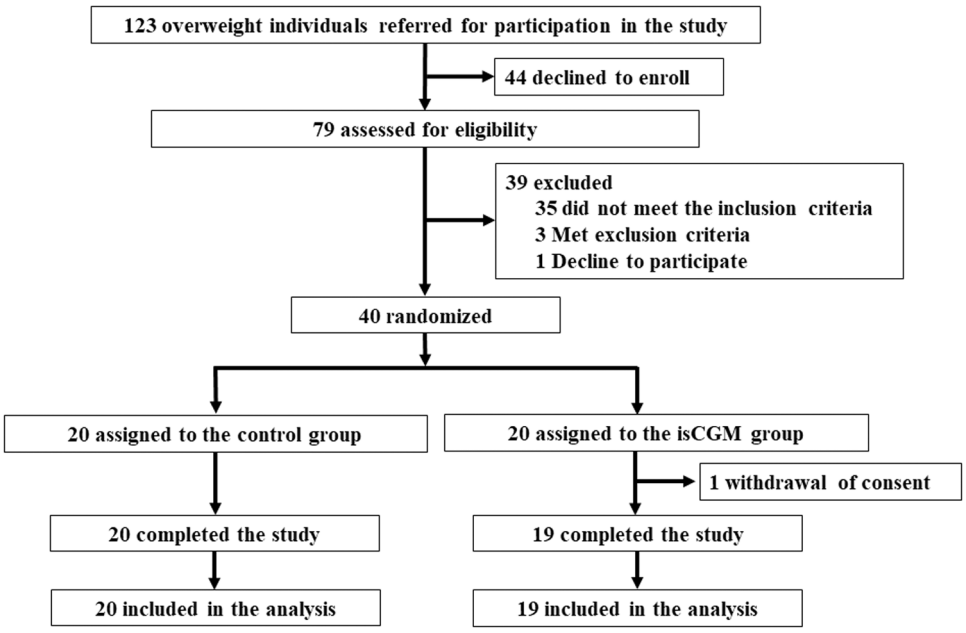

Fig. 1. Flow of the study participants. Forty participants were randomized after screening. In the intermittently scanned continuous glucose monitoring (isCGM) group, one participant withdrew consent after study onset. All other participants completed the study. BMI, body mass index; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus; HbA_{1c}, hemoglobin A_{1c}.

Table 1
Baseline characteristics of the two study groups.

Characteristic	isCGM group ($n = 19$)	Control group ($n = 20$)	P value
Age (years)	53.8 ± 11.5	54.3 ± 14.0	0.93
Sex (male/female)	6/13	8/12	
BMI (kg/m^2)	35.2 ± 5.7	31.6 ± 6.8	< 0.05
Body weight (kg)	93.7 ± 20.0	86.6 ± 22.5	0.14
Condition (T2DM/IGT)	6/13	6/14	
75-g OGTT fasting plasma glucose (mg/dL)	104.5 ± 19.9	109.6 ± 14.74	0.28
75-g OGTT 2-h plasma glucose (mg/dL)	182.1 ± 30.8	193.6 ± 50.4	0.73
SBP (mmHg)	131.0 ± 13.1	136.8 ± 18.3	0.27
DBP (mmHg)	81.8 ± 12.3	80.1 ± 10.3	0.33
Heart rate (beats/min)	76.0 ± 11.8	73.4 ± 11.1	0.13
HbA_{1c} (%)	6.2 ± 0.3	6.2 ± 0.3	0.13
Triglyceride (mg/dL)	148.7 ± 84.4	154.1 ± 122.4	0.72
LDL-C (mg/dL)	116.7 ± 30.0	115.1 ± 18.0	0.93
HDL-C (mg/dL)	55.9 ± 12.8	55.7 ± 17.0	0.93
Uric acid (mg/dL)	6.2 ± 1.3	5.9 ± 1.5	0.56
AST (U/L)	30.9 ± 18.2	33.9 ± 24.6	0.80
ALT (U/L)	46.7 ± 27.7	44.0 ± 31.3	0.70
γ-GTP (U/L)	46.5 ± 1.3	41.4 ± 27.9	0.44
eGFR (mL min^{-1} 1.73 m^{-2})	78.6 ± 21.3	74.5 ± 15.3	0.49
HOMA-R	4.4 ± 2.0	4.8 ± 2.9	0.96
HOMA-β	189.4 ± 145.5	148.4 ± 90.3	0.48
Insulinogenic index	1.1 ± 0.9	0.7 ± 0.5	0.09
Composite index	2.2 ± 1.0	2.5 ± 1.5	0.56
Calorie intake (kcal/day)	1608.6 ± 472.8	1732.4 ± 465.0	0.76
Protein intake (g/day)[a]	61.4 ± 18.2	64.1 ± 15.5	0.62
Average SG (mg/dL)	103.9 ± 14.5	101.6 ± 13.6	0.57
TAR (%)	2.4 ± 4.7	1.7 ± 4.2	0.41
TIR (%)	90.0 ± 8.5	91.2 ± 7.3	0.63
TBR (%)	7.6 ± 8.1	7.2 ± 7.5	0.89
CV of SG (%)	24.2 ± 5.5	22.3 ± 4.4	0.29
SD of SG (mg/dL)	25.4 ± 7.7	23.0 ± 6.9	0.40
MAGE (mg/dL)	62.1 ± 17.0	58.9 ± 21.8	0.38

With the exception of sex and clinical condition, data are means ± SD. The P values for comparisons between the two groups were determined with the Mann-Whitney U test. The OGTT was performed at the screening visit, and the CGM data are for the first month and first 2 weeks of the study in the isCGM and control groups, respectively.
[a]n values are only 17 and 15 for the isCGM and control groups, respectively.
isCGM, intermittently scanned continuous glucose monitoring; BMI, body mass index; T2DM, type 2 diabetes mellitus; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA_{1c}, hemoglobin A_{1c}; LDL-C, low density lipoprotein–cholesterol; HDL-C, high density lipoprotein–cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ–glutamyl transpeptidase; eGFR, estimated glomerular filtration rate; HOMA-R, homeostasis model assessment of insulin resistance; HOMA-β, homeostatic model assessment of beta-cell function; SG, sensor glucose; TAR, time above range; TIR, time in range; TBR, time below range; CV, coefficient of variation; SD, standard deviation; MAGE, mean amplitude of glycemic excursions.

The primary endpoint of weight change at 24 weeks was –1.78 kg in the isCGM group and –2.20 kg in the control group and did not differ significantly between the two groups ($P = 0.54$) (Fig. 2). Post-hoc ANCOVA indicated the group effect was not significant [F(1, 37) = 0.058, p = 0.81]. In the IGT group, weight change in the isCGM group (n = 13) was −1.2 ± 4.2 kg, compared to −2.7 ± 3.1 kg in the control group (n = 14) (p = 0.24). In the T2DM group, weight change in the isCGM group (n = 6) was −3.0 ± 5.7 kg, compared to −1.2 ± 2.6 kg in the control group (n = 6) (p = 0.82). The primary endpoint of weight change was not significantly different between the isCGM group and the control group in both the IGT and T2DM subgroups.

Changes in each parameter between before and after intervention are shown in Table 2. With regard to secondary endpoints, no significant differences were apparent in blood test data, caloric intake, or protein intake between the two groups. On the other hand, analysis of CGM data showed that the CV and SD of SG levels, both of which are measures of glycemic variability, decreased in the isCGM group but increased in the control group, with these differences between the two groups being statistically significant ($P < 0.05$). No significant differences in other CGM indices were detected between the two groups.

In the isCGM group, the scan frequency throughout the trial period was 7.1 ± 4.8/day. There was no significant correlation between the isCGM scan frequency and weight reduction at 24 weeks ($r = 0.02$, $P = 0.95$). Furthermore, no significant correlation was apparent between the isCGM scan frequency and either baseline body weight ($r = –0.04$, $P = 0.88$) or baseline HbA_{1c} level ($r = 0.44$, $P = 0.06$) (Table 3). On the other hand, the scan frequency was positively correlated with the 120-min blood glucose level in the 75-g OGTT performed at screening ($r = 0.59$, $P < 0.01$), TAR in the first month of the study ($r = 0.79$, $P < 0.001$), and the mean SG level in the first month of the study ($r = 0.61$, $P < 0.01$) (Table 3). The number of isCGM scans was also negatively correlated with the change in TAR ($r = –0.54$, $P < 0.05$) and positively correlated with the change in protein intake ($r = 0.52$, $P < 0.05$) between the first and last months of the study (Fig. S2); it was not correlated with the change in caloric intake ($r = 0.30$, $P = 0.22$) (Table 3).

4. Discussion

We here investigated the effect of visualizing glucose fluctuations with isCGM on weight reduction in overweight individuals with IGT or T2DM who were not taking antidiabetic medications. To the best of our knowledge, such a trial has never been reported before. The extent of weight reduction, the primary outcome of the study, was similar in the isCGM and control groups. In addition, no differences were observed between the two groups in terms of obesity-related biochemical parameters, OGTT-related parameters, or CGM-related parameters such as time ranges and average SG value. However, the use of isCGM was associated with a significant reduction in glucose variability, a prespecified secondary outcome. Of note, we did not provide any specific guidance on the importance of glucose fluctuations or how to respond to them, but participants autonomously changed their behavior in response to recognizing them. Given that blood glucose variability affects various physiological and pathological processes in blood vessels and is consequently associated with the development of cardiovascular disease [18–21], the visualization of glucose fluctuations by isCGM may contribute to the prevention of such disease in overweight individuals with IGT or mild T2DM, even if not accompanied by weight reduction.

The study participants did not use antidiabetic drugs, suggesting that the reduction in glucose variability in the isCGM group was due to changes in eating behavior. The ingestion of high amounts of carbohydrate typically results in postprandial hyperglycemia, thereby contributing to increased fluctuations in blood glucose levels. Several studies have shown that the frequency of isCGM scans correlates with improvements in blood glucose management in individuals with diabetes [22–24]. In our study, there was a significant correlation between scan frequency and change in protein intake, suggesting that awareness of glucose variability through frequent scanning led to changes in eating behavior. Although we did not collect data on carbohydrate intake, the observed increase in protein intake in the isCGM group may imply a decrease in carbohydrate intake, given that increased scan frequency did not correlate with increased total caloric intake. Scan frequency also correlated with the 120-min blood glucose level in the 75-g OGTT conducted at screening as well as with TAR and the mean SG level in the first month of the study, indicating that individuals with higher glucose levels at the start of the study tended to perform more frequent scans.

The use of isCGM in conjunction with a smartphone-based application that collects isCGM data as well as lifestyle habit information was recently shown to lower carbohydrate intake in individuals at risk of T2DM [25]. This finding supports the notion that isCGM can facilitate changes in eating behavior, even in individuals not treated with antidiabetes medication. Moreover, this recent study found that body

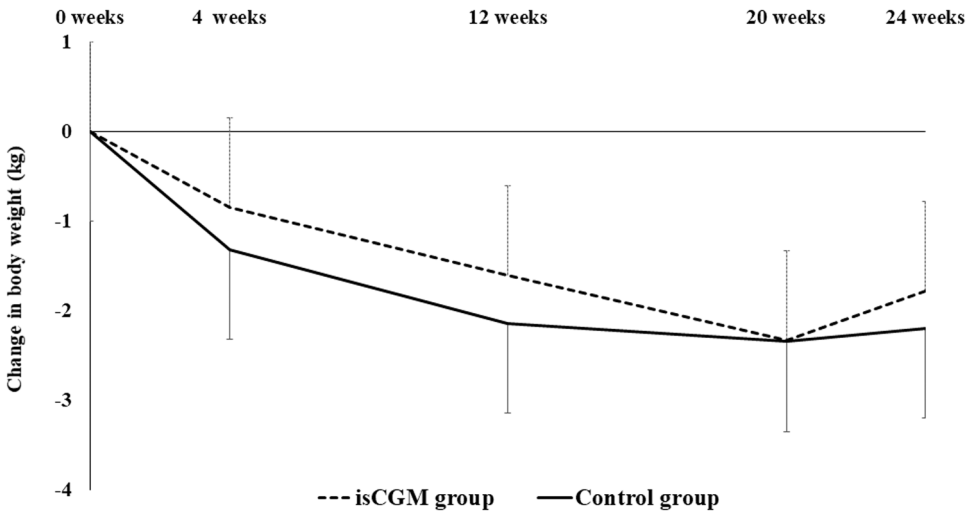

Fig. 2. Change in body weight at each visit relative to baseline for the intermittently scanned continuous glucose monitoring (isCGM) and control groups. Data are means ± standard deviation. No significant difference in weight change was apparent between the two groups at any visit (tested by the Mann-Whitney U test).

Table 2
Changes in parameters between before and after intervention.

Parameter	isCGM group ($n = 19$)	Control group ($n = 20$)	*P* value
Weight change (kg)	−1.8 ± 4.7	−2.2 ± 3.0	0.54
Weight change rate (%)	−1.7 ± 4.4	−2.9 ± 4.1	0.37
Excess weight loss (%)	5.4 ± 11.8	18.2 ± 37.8	0.21
Calorie intake change (kcal/day)	17.4 ± 469.8	266.6 ± 537.9	0.89
Protein intake change (g/day)[a]	6.0 ± 22.2	3.7 ± 23.8	0.69
HbA_{1c} change (%)	−0.11 ± 0.25	−0.25 ± 0.33	0.13
Triglyceride change (mg/dL)	−24.5 ± 69.2	−7.2 ± 67.6	0.63
LDL-C change (mg/dL)	4.4 ± 20.0	2.4 ± 18.5	0.98
HDL-C change (mg/dL)	1.2 ± 6.5	4.0 ± 5.1	0.07
Uric acid change (mg/dL)	−0.2 ± 1.0	−0.5 ± 0.7	0.23
AST change (U/L)	−4.3 ± 15.1	−8.0 ± 19.8	0.84
ALT change (U/L)	−10.0 ± 19.6	−12.3 ± 22.5	0.70
γ-GTP change (U/L)	−6.8 ± 18.5	−6.9 ± 12.3	0.75
eGFR change (mL min^{-1} 1.73 m^{-2})	2.8 ± 6.6	1.2 ± 5.9	0.48
HOMA-R change	0.3 ± 1.9	0.1 ± 3.9	0.33
HOMA-β change	−4.5 ± 62.6	11.1 ± 57.3	0.91
Insulinogenic index change	0.2 ± 0.6	0.1 ± 0.6	0.59
Composite index change	0.0 ± 0.9	0.6 ± 2.0	0.50
CV of SG change (%)	−0.9 ± 3.3	2.9 ± 5.0	< 0.05
SD of SG change (mg/dL)	−2.1 ± 4.0	1.4 ± 5.3	< 0.05
MAGE change (mg/dL)	−3.6 ± 16.5	−1.8 ± 14.4	0.35
Average SG change (mg/dL)	−4.3 ± 15.7	−6.0 ± 14.7	0.76
TAR change (%)	−0.5 ± 4.0	0.2 ± 1.5	0.66
TIR change (%)	−3.5 ± 11.9	−8.3 ± 14.8	0.45
TBR change (%)	4.0 ± 13.4	8.2 ± 15.2	0.69

Data are means ± SD. The *P* values for comparisons between the two groups were determined with the Mann-Whitney *U* test. The CGM data are for changes between the first and last months of the study for the isCGM group and between the 2-week periods at the start of the study and beginning 1 month before the end of the study in the control group.
[a]*n* values are only 17 and 15 for the isCGM and control groups, respectively.
Abbreviations as in Table 1.

Table 3
Correlation analysis for the number of scans and each parameter in the isCGM group.

Parameter	Pearson's correlation coefficient	*P* value
BMI	0.00	0.99
Body weight	−0.04	0.88
HbA_{1c}	0.44	0.06
75-g OGTT fasting plasma glucose	0.26	0.29
75-g OGTT 1-h plasma glucose	0.30	0.21
75-g OGTT 2-h plasma glucose	0.59	< 0.01
HOMA-R	0.04	0.89
HOMA-β	−0.26	0.28
Insulinogenic index	−0.03	0.90
Composite index	0.06	0.81
Calorie intake	0.34	0.16
Protein intake	0.24	0.33
CV of SG	0.05	0.84
SD of SG	0.36	0.13
MAGE	0.45	0.06
Average SG	0.61	< 0.01
TAR	0.79	< 0.001
TIR	−0.12	0.63
TBR	−0.34	0.16
Weight change	0.02	0.95
HbA_{1c} change	0.14	0.56
HOMA-R change	0.50	0.03
HOMA-β change	0.38	0.11
Insulinogenic index change	−0.08	0.78
Composite index change	−0.24	0.33
Calorie intake change	0.30	0.22
Protein intake change	0.52	0.03
Average SG change	−0.16	0.52
TAR change	−0.54	0.02
TIR change	−0.12	0.63
TBR change	−0.03	0.91

Abbreviations as in Table 1.

weight reduction was significantly greater in the intervention group than in the control group, suggesting that not only the recognition of glucose variability through isCGM, but also the feedback provided by the application, may have contributed to this positive outcome. Whereas our findings indicate that recognition of glucose fluctuations autonomously leads to behavioral changes, feedback based on this information might be important for achieving a greater benefit. In this context, interventions involving remotely programmed lifestyle changes or algorithms for modifying eating behavior on the basis of CGM data are effective for weight reduction in individuals with T2DM [26].

Our study has several limitations. First, the baseline BMI was slightly higher in the intervention group than in the control group. Given the relatively small sample size, we considered it inappropriate to set multiple stratification factors. Since the intervention focused on visualizing glycemic fluctuations, we performed randomization based on the presence of IGT or T2DM rather than BMI. A post-hoc analysis using ANCOVA indicated that the baseline BMI difference did not significantly impact the weight reduction outcomes. Second, we did not collect data on the educational level or socioeconomic status of the study population.

Educational level might have influenced the effective use of the isCGM device and the effectiveness of the intervention. Third, we did not collect data for diabetes-related health disorders, such as fatty liver or chronic kidney disease, which affect insulin resistance and glucose metabolism. Fourth, the study period. A total of 24 weeks, was relatively short. In many intervention studies targeting weight reduction, weight regain is a common issue [27]. In our study, the intervention group achieved peak weight reduction at 20 weeks, with a slight weight regain apparent at 24 weeks. It was not possible to assess whether there might have been further weight regain after the intervention concluded. Further studies are necessary to determine the long-term, sustainable benefits of isCGM use in overweight individuals with IGT or T2DM who are not taking diabetes drugs. Fifth, this study population included both IGT and mild T2DM. Post-hoc analysis revealed no significant differences in weight change between the isCGM and control groups in either subgroup. Further larger studies are needed to determine whether differences in IGT and T2DM affect the effect of isCGM on weight reduction.

In conclusion, while the use of isCGM in individuals with IGT or mild T2DM did not reduce body weight, this treatment was associated with a reduction in glycemic fluctuation likely through dietary behavioral changes, even in the absence of specific feedback from the CGM data. The use of real-time CGM has recently increased in the clinical setting, and evidence suggests that such devices result in better outcomes with regard to both blood glucose management and behavioral changes compared with isCGM. It will be of interest to investigate whether real-time CGM might lead to more effective behavioral changes in the management of overweight individuals with IGT or T2DM not treated with antidiabetes medication.

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Ethical statement

The study was conducted from January 2018 to January 2023. It was approved by the Kobe University Clinical Research Review Board (accreditation number: CRB5180009), registered with the Japan Registry of Clinical Trials (jRCTs052180079, registered on 27 February 2019), and performed in accordance with the principles of the Declaration of Helsinki and with the CONSORT guidelines.

CRediT authorship contribution statement

Takeda Akihiko: Resources, Investigation. **Yokota Kazuki:** Resources, Investigation. **Nakamura Tomoaki:** Resources, Investigation. **Nishikage Seiji:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Sakaguchi Kazuhiko:** Resources, Investigation. **Nakagawa Yasushi:** Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ogawa Wataru:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition, Conceptualization. **Hirota Yushi:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Yoshimura Kai:** Methodology. **Ueda Mariko:** Methodology. **Yamamoto Akane:** Resources, Methodology, Investigation. **Takayoshi Tomofumi:** Resources, Methodology, Investigation. **Matsuoka Atsuko:** Resources, Methodology, Investigation. **Takahashi Michiko:** Resources, Investigation.

Declaration of Competing Interest

Y.H. has received lecture fees from Eli Lilly Japan K.K., Sanofi Aventis, Abbott Japan, Terumo Co., and Sumitomo Pharma Co. Ltd.; research funding from Sumitomo Pharma Co. Ltd., Medtronic Japan Co. Ltd., and Kyowa Kirin Co. Ltd.; and a donation from Abbott Japan. K.S. has received lecture fees from Eli Lilly Japan K.K., Sanofi Aventis, Novo Nordisk Pharma Ltd., Sumitomo Pharma Co. Ltd.; research funding from Sumitomo Pharma Co. Ltd. W.O. has received lecture fees from Sumitomo Pharma Co. Ltd., Nippon Boehringer Ingelheim Co. Ltd., Abbott Japan, and Novo Nordisk Pharma Ltd.; research grants from Noster Inc., Nippon Boehringer Ingelheim Co. Ltd., Eli Lilly Japan K.K., Abbott Diabetes Care UK Ltd., Sumitomo Pharma Co. Ltd., and Teijin Pharma Ltd.; and donations from Kowa Co. Ltd., Novo Nordisk Pharma Ltd., Sumitomo Pharma Co. Ltd., Takeda Pharmaceutical Co. Ltd., and Teijin Pharma Ltd. All remaining authors declare that they have no conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.orcp.2025.01.008.

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