Effects of Patient-Driven Lifestyle Modification Using Intermittently Scanned Continuous Glucose Monitoring in Patients With Type 2 Diabetes: Results From the Randomized Open-label PDF Study

Hun Jee Choe,[1,2] Eun-Jung Rhee,[3] Jong Chul Won,[4] Kyong Soo Park,[1,2] Won-Young Lee,[3] and Young Min Cho[1,2]

Diabetes Care 2022;45:2224–2230 | https://doi.org/10.2337/dc22-0764

OBJECTIVE

To investigate the effects of patient-driven lifestyle modification using intermittently scanned continuous glucose monitoring (isCGM) in patients with type 2 diabetes (T2D).

RESEARCH DESIGN AND METHODS

We conducted a 12-week, open-label, randomized controlled trial. A total of 126 participants were 1:1 randomized to either the intervention group (structured education + isCGM) or the control group (standard care with blood glucose monitoring). The Self-Evaluation Of Unhealthy foods by Looking at postprandial glucose (SEOUL) algorithm was developed and applied to aid structured education in guiding patients to follow healthy eating behavior depending on the postprandial glycemic response. The primary end point was the change in HbA_{1c} level from baseline.

RESULTS

Implementation of the SEOUL algorithm with isCGM was associated with greater improvement in HbA_{1c} than with standard care (risk-adjusted difference −0.50%, 95% CI −0.74 to −0.26, $P < 0.001$). Participants in the intervention group had a greater reduction in fasting blood glucose and body weight (−16.5 mg/dL, 95% CI −30.0 to −3.0, $P = 0.017$; −1.5 kg, 95% CI −2.7 to −0.3, $P = 0.013$, respectively). The score sum for the Korean version of the revised Summary of Diabetes Self-Care Activities Questionnaire increased in both groups but to a greater extent in the intervention group (mean difference 4.8, 95% CI 1.7–8.0, $P = 0.003$). No severe hyperglycemia or hypoglycemia was reported in either group of patients.

CONCLUSIONS

Patient-driven lifestyle modification primarily focused on eating behavior using isCGM effectively lowered HbA_{1c} levels in patients with T2D.

Type 2 diabetes (T2D) is a chronic debilitating disease requiring continuous medical care. The cornerstone of diabetes care is self-management, which encompasses

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
[2]Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[3]Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea
[4]Division of Endocrinology and Metabolism, Department of Internal Medicine, Sanggye Paik Hospital, Inje University, Seoul, Republic of Korea

Corresponding author: Young Min Cho, ymchomd@snu.ac.kr

Received 19 April 2022 and accepted 10 July 2022

Clinical trial reg. no. NCT04932928, clinicaltrials.gov

This article contains supplementary material online at https://doi.org/10.2337/figshare.20382915.

H.J.C., E.-J.R., and J.C.W. contributed equally to this study as first authors.

This article is featured in a podcast available at diabetesjournals.org/journals/pages/diabetes-core-update-podcasts.

lifestyle modification and self-monitoring of blood glucose levels (1). Medical nutrition therapy should be individualized. However, there is no one-size-fits-all eating pattern for individuals with diabetes (2), which adds complexity to patient education and implementation of medical nutrition therapy in daily life (3).

In a study by Zeevi et al. (4), high interpersonal variability in postmeal glucose even with the same meal was observed in an 800 person cohort when assessed with continuous glucose monitoring (CGM). A machine learning tool integrating extensive information from dietary habits to the gut microbiota was validated to guide personally tailored dietary interventions. This data-driven approach is highly desirable but challenging to use in real-world clinical settings (5). Postprandial glycemic response was more predictable when a personalized approach was applied with consideration of a variety of characteristics of the individuals than when only total calories or carbohydrate counting was applied (5). Therefore, we hypothesized that more personalized lifestyle modifications would result in better glycemic outcomes in patients with T2D.

Although many patients with T2D adhere to the current recommendation of blood glucose monitoring (BGM) in the morning, it is often not feasible to perform BGM to monitor postprandial glucose at every meal or at night. In addition, frequent glucose monitoring with autolancet can be painful. However, with the advent of CGM, it is possible to monitor glucose patterns every few minutes without repeatedly pricking fingers (6). Moreover, CGM has empowered patients and health care providers to appraise glycemic patterns comprehensively and incorporate individual glycemic responses to diet and physical activity (7).

CGM studies conducted in patients with T2D showed that intensive insulin regimens resulted in mixed outcomes regarding improvements in HbA_{1c} (8–10). In the Randomised Controlled Study to Evaluate the Impact of Novel Glucose Sensing Technology on HbA_{1c} in Type 2 Diabetes (REPLACE), T2D patients who were on an intensive insulin regimen did not show differences in HbA_{1c} at 6 months with intermittently scanned CGM (isCGM) compared with control subjects with BGM, although hypoglycemia was reduced in the group with isCGM (8). In the Multiple Daily Injections and Continuous Glucose Monitoring in Diabetes (DIAMOND) study, a higher proportion of patients with T2D who received multiple daily insulin injections had improved glycemic control with reduction in HbA_{1c} when real-time CGM (rtCGM) was used compared with patients who received usual care for 24 weeks (9). In another study, by Vigersky et al. (10), patients with T2D not on prandial insulin who used rtCGM intermittently for 12 weeks had improved HbA_{1c} levels at 12 weeks, and this improvement was sustained during the 40 week follow-up without rtCGM, compared with the BGM group. The MOBILE Study Group recently affirmed the benefits of rtCGM for basal insulin in patients with T2D (11,12). However, data on whether isCGM is equally advantageous for patients with T2D who do not use prandial insulin are scarce.

In this study, we used isCGM to motivate lifestyle modification primarily focused on eating behavior according to the Self-Evaluation Of Unhealthy foods by Looking at postprandial glucose (SEOUL) algorithm and investigated the effects of these patient-driven lifestyle modifications on glycemic control in patients with T2D not on an intensive insulin regimen.

RESEARCH DESIGN AND METHODS

Study Design and Participants

The Patient-Driven lifestyle modification using FreeStyle Libre in patients with T2D (PDF) study was a 12 week open-label, randomized controlled trial comparing the effect of education to support patient behavior modification and self-management with the use of isCGM (intervention group) and conventional diabetes care (control group). This study was performed in the endocrinology division of three university hospitals in Seoul, Korea. Participants were ages 19–80 years with a diagnosis of T2D. Additional inclusion criteria were HbA1c levels between 7.0% (53 mmol/mol) and 10.0% (86 mmol/mol) without any change in antidiabetes medication in the previous 3 months. Participants taking antidiabetes medication, including oral agents and basal insulin, but not prandial insulin, were eligible for screening. A complete list of the inclusion and exclusion criteria is available in Supplementary Material.

Screening (visit 1 [V1]) was performed during routine outpatient visits by clinical staff without use of any advertisements. The subsequent study procedures were primarily performed by the research nurses of each site. Participants eligible for screening were assigned randomly to the intervention group or control group. Randomization was conducted by an independent research nurse not involved in the study using permuted block randomization of 1:1 stratified by the study site. Participants in both groups were provided general education for diabetes care using educational materials created by the PDF study team and movie clips provided by the Korean Diabetes Association (13). The research nurses collected self-reported data regarding diabetes self-care assessed with use of the Korean version of the revised Summary of Diabetes Self-Care Activities Questionnaire (SDSCA-K).

Participants in the intervention group started isCGM (FreeStyle Libre; Abbott Diabetes Care, Witney, U.K.) and were advised to pursue use of the SEOUL algorithm based on CGM measures (Fig. 1). The SEOUL algorithm provides simple dietary advice in a 2 × 2 table that can be applied to enhance food consumption behavior based on individual postprandial glycemic responses. Elements in the row of the matrix denote healthfulness as perceived by the participants, and the elements in the column indicate the actual postprandial glucose response of each meal. Briefly, a participant may continue eating a healthy meal with a tolerable glycemic response after consuming the food and avoid an unhealthy meal that provokes postprandial hyperglycemia; if hyperglycemia is detected after consuming a meal that is generally considered to be healthy, reducing the amount of food is recommended; the amount of unhealthy food should also be reduced even if it does not generate hyperglycemia upon ingestion. Participants in the intervention group were trained to use the isCGM system and SEOUL algorithm with official instructional videos and a movie clip created by the PDF team. Each participant received the PDF CGM diary to review daily glycemic response based on the SEOUL algorithm. Any device issues requiring troubleshooting could be discussed with the research nurses during the study period. Participants in the control group were not provided with the isCGM or SEOUL algorithm

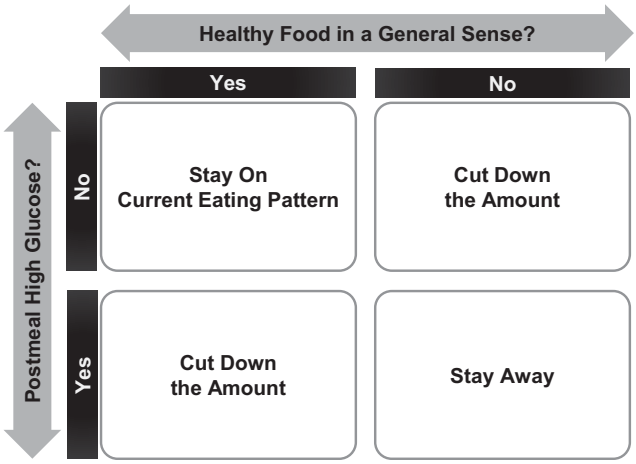

Figure 1—The SEOUL algorithm. Participants are encouraged to continue eating a healthy meal with tolerable glycemic response after consuming the food and should avoid an unhealthy meal that provokes postprandial hyperglycemia. If hyperglycemia is detected after consuming a meal that is generally considered to be healthy, reducing the amount of food is recommended; the amount of unhealthy food should also be reduced even if it does not generate hyperglycemia on ingestion. Decisions on lifestyle modification will be made on an individual basis according to the SEOUL algorithm.

but were given glucometers (FreeStyle Optimum Neo; Abbott Diabetes Care), lancets, glucose test strips sufficient for BGM twice daily, and a logbook created by the PDF team to record the BGM results. Both groups attended a visit 2 (V2) at week 12.

This study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was reviewed and approved separately from each of the three recruitment hospitals (approval no. H-2011-062-1171). Written informed consent was obtained from all participants prior to any activity related to the study procedure. This study was registered at ClinicalTrials.gov (clinical trial reg. no. NCT04932928).

Study Outcomes

The primary outcome was the change in HbA_{1c} levels at 12 weeks after adjustment for baseline values and recruitment sites. The key secondary outcomes were changes in fasting glucose, body weight, and waist circumference at 12 weeks. Other secondary outcomes included changes in systolic blood pressure (SBP), diastolic blood pressure, total cholesterol, serum triglyceride, HDL cholesterol, LDL cholesterol, and the score sum for the SDSCA-K. All outcome measures were adjusted for baseline values and recruitment sites.

We divided the participants into subgroups according to HbA_{1c} levels of $<$6.5% (48 mmol/mol), $<$7.0% (53 mmol/mol), $<$7.5% (58 mmol/mol), $<$8.0% (64 mmol/mol), $<$8.5% (69 mmol/mol), $<$9.0% (75 mmol/mol), $<$9.5% (80 mmol/mol), and $<$10.0% (86 mmol/mol) based on the V1 and V2 values for exploratory analysis. The proportion of participants in each subgroup was compared according to study groups. For the subgroup of participants whose HbA_{1c} was $<$7.0% (53 mmol/mol) at V2 or those who had an HbA_{1c} reduction of $\geq$0.5% during the study period, additional subgroup analyses were performed according to the baseline characteristics of age, sex, BMI, duration of diabetes, use of insulin, and HbA_{1c} at V1. Adjustment of the insulin dosage from V1 to V2 was additionally evaluated in insulin users.

For participants in the intervention group, CGM outcome metrics, including time in the target range (TIR) of 70–180 mg/dL, time above the target range ($>$180 and $>$250 mg/dL), time below the target range (TBR) ($<$70 and $<$54 mg/dL), and coefficient of variation (CV), were additionally assessed in the exploratory analysis.

Statistical Analysis

The sample size was calculated to have at least 80% power, assuming a group difference of 0.35%, SD of 0.8, and two-sided α-level of 0.05 (8,14,15). Considering a 10% dropout rate, 63 participants per group were required to detect a significant difference in the mean HbA_{1c} level at 12 weeks. Of the 126 participants, 46, 40, and 40 were recruited from the Seoul National University Hospital, Inje University Sanggye Paik Hospital, and Sungkyunkwan University Kangbuk Samsung Hospital, respectively.

Continuous variables are expressed as mean ± SD, and categorical variables are presented as numbers and percentages. Differences in means and proportions were tested with Student *t* test or ANOVA for continuous variables and the χ^2 test for categorical variables to describe characteristics in both groups. End points were analyzed with the linear model approach, ANCOVA with V2 measures as outcomes, recruitment site as random effects, and V1 measures as covariates. For variables that did not follow a normal distribution, the rank transformation approach of ANCOVA was applied.

Subgroup analyses were performed according to the baseline characteristics of age, sex, BMI, duration of diabetes, use of insulin, and HbA_{1c} at V1, and the interaction between covariates was also assessed. A linear relationship between the scan frequency, CGM active time, baseline values, and improvement in HbA_{1c}, TIR, and CV was evaluated in the intervention group with bivariate correlation analysis, and Pearson correlation coefficient was reported. The primary analysis was based on the modified intention-to-treat analysis, with planned sensitivity analyses performed using per-protocol analysis. All analyses were performed with IBM SPSS Statistics (version 27.0; IBM Corp., Armonk, NY) and R, version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) (https://www.R-project.org). A two-sided *P* value of $<$0.05 was considered statistically significant.

RESULTS

Between 23 March and 3 November 2021, 135 adults with T2D were screened. Of the 126 participants who proceeded to randomization, 63 were assigned to the intervention and control groups (Fig. 2). The follow-up was completed on 9 February 2022. The 12-week primary study outcome visit was completed by 58 (92.1%) patients in the intervention group and 62 (98.4%) in the control group and included in the modified intention-to-treat analysis.

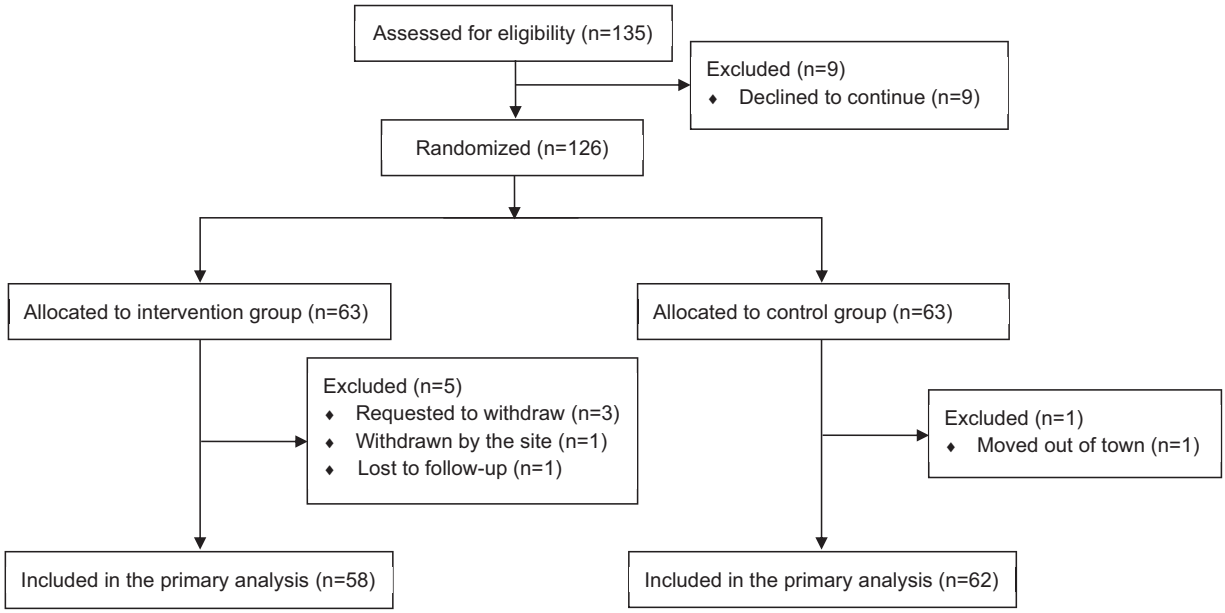

Figure 2—Consort diagram.

Mean ± SD age of the total study participants was 58.0 ± 11.9 years, and 48 (40.0%) were women (Supplementary Table 1). Mean HbA_{1c} was 7.9 ± 0.7%, duration of T2D was 13.3 ± 7.8 years, and 27.5% of the participants were receiving basal insulin therapy. These baseline characteristics, family history of diabetes, and use of glucose-lowering medications did not differ between the intervention and control groups at baseline (Supplementary Table 1 and Supplementary Table 2).

Over the 12 weeks of follow-up, mean ± SD HbA_{1c} level significantly improved in the intervention group compared with the control group (7.3 ± 0.6 vs. 7.8 ± 0.9% for intervention and control group at V2, respectively; 3 month adjusted difference −0.50%, 95% CI −0.74 to −0.26, $P < 0.001$) (Table 1 and Fig. 3*A*). Statistical significance remained significant after further adjustment for baseline BMI in the exploratory analysis (Supplementary Table 3). The proportion of participants achieving HbA_{1c} <7.0% (53 mmol/mol) at V2 was considerably higher in the intervention group than in the control group (Fig. 3*B* and *C* and Supplementary Table 4). In the exploratory subgroup analyses, no statistically significant interaction was found for the achievement of HbA_{1c} <7.0% (53 mmol/mol) at V2 or reduction of ≥0.5% from baseline HbA_{1c} according to age, sex, obesity, duration of diabetes, use of insulin, or baseline HbA_{1c} (Supplementary Fig. 1 and Supplementary Fig. 2). The fasting glucose level was also lower at V2 in the intervention group than in the control group (136 ± 35 vs. 154 ± 43 mg/dL; 3 month adjusted difference −16.5 [−30.0 to 3.0], $P = 0.017$) (Table 1).

Diabetes self-care assessed with the SDSCA-K improved overall over the study period (Supplementary Table 5). In particular, the scores for items on diet, exercise, and foot care were higher in the intervention group at V2 than V1 (Supplementary Fig. 3).

Other key secondary outcomes included changes in metabolic measures, such as body weight, waist circumference, blood pressure, and cholesterol levels. Body weight decreased to a greater extent in the intervention group, but there was no statistical difference in waist circumference between the groups over the 12 weeks with adjustment for both baseline values and recruitment site (Table 1). Lipid profiles did not differ between the groups and did not significantly improve compared with baseline values when assessed for all participants (Supplementary Table 5). SBP was unexpectedly higher in the intervention group, both at baseline and follow-up.

Various CGM metrics were evaluated in the intervention group. Mean ± SD TIR in the CGM device was 70.4 ± 14.6% in weeks 1 and 2 and did not change significantly in the inserted CGM in weeks 11 and 12 ($P = 0.562$) (Supplementary Table 6 and Supplementary Fig. 4). Mean glucose, time above the target range, and TBR were similar throughout the study period (Supplementary Table 6 and Supplementary Fig. 5). However, CV slightly decreased at the end of 12 weeks in comparison with the first CGM device (33.8 ± 7.2% vs. 32.4 ± 6.3%, $P = 0.032$). When further assessment was made to decipher participants with better glycemic outcomes in the intervention group, we discovered that participants with a higher percentage of CGM active time and higher scan frequency were intimately associated with a decrease in CV during the study period (Supplementary Fig. 6). The number of active scans, but not the percentage of CGM active time, was associated with a greater HbA_{1c} reduction. The use of basal insulin was not associated with changes in HbA_{1c}, but more remarkable improvement in TIR was observed in insulin users, by reducing the TBR (Supplementary Fig. 7). When assessed for insulin users in the total cohort, improvement in glycemic control was not attributable to an increase in total insulin dosage (41.8 ± 15.6 vs. 40.1 ± 15.9 units/day insulin dosage at V1 and V2, respectively, $P = 0.665$) (Supplementary Table 7). In the per-protocol analysis, 10 patients with CGM active time of <80% and two patients with incomplete V2 outcome variables were additionally excluded (Supplementary Fig. 8). Participants included in the per-protocol

Table 1—Study outcomes according to treatment groups

	V1			V2			Risk-adjusted difference	
	Intervention	Control	*P*	Intervention	Control	*P*	(95% CI)	*P**
N	58	62		58	62			
Primary outcome								
HbA_{1c} (%)	7.9 ± 0.6	7.9 ± 0.7	0.808	7.3 ± 0.6	7.8 ± 0.9	<0.001	−0.50 (−0.74 to −0.26)	<0.001
Secondary outcome								
Fasting glucose (mg/dL)	142 ± 27	147 ± 36	0.420	136 ± 35	154 ± 43	0.013	−16.5 (−30.0 to −3.0)	0.017
Body weight (kg)	70.5 ± 11.7	72.7 ± 12.5	0.331	69.1 ± 11.3	72.8 ± 12.8	0.105	−1.5 (−2.7 to −0.3)	0.013
Waist circumference (cm)	87.7 ± 8.1	91.8 ± 10.2	0.018	87.4 ± 8.8	92.1 ± 10.6	0.010	−0.6 (−1.7 to 0.5)	0.262
SBP (mmHg)	133 ± 16	126 ± 16	0.022	134 ± 14	124 ± 21	0.003	7.7 (1.3–14.1)	0.019
DBP (mmHg)	79 ± 10	77 ± 10	0.153	78 ± 9	79 ± 9	0.530	−2.3 (−5.0 to 0.4)	0.100
Total cholesterol (mg/dL)	138 ± 29	140 ± 25	0.707	136 ± 34	140 ± 28	0.565	−1.5 (−9.1 to 6.0)	0.690
Triglyceride (mg/dL)	131 ± 68	153 ± 73	0.094	149 ± 197	141 ± 72	0.761	33.9 (13.6 to 79.4)	0.164
HDL-C (mg/dL)	48 ± 13	48 ± 17	0.965	47 ± 12	48 ± 15	0.627	−1.3 (−4.5 to 1.9)	0.415
LDL-C (mg/dL)	74 ± 22	75 ± 20	0.852	70 ± 25	74 ± 25	0.487	−2.4 (−8.3 to 3.6)	0.432
SDSCA-K total score	26.6 ± 13.6	25.1 ± 12.8	0.533	44.4 ± 9.2	39.2 ± 10.1	0.005	4.8 (1.7 to 8.0)	0.003

*These *P* values represent the comparison of the V2 intervention vs. V2 control using ANCOVA with adjustment for respective baseline values and hospital of recruitment. DBP, diastolic blood pressure; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol.

analysis exhibited a good adherence to the PDF diary fill-up—as high as 86.6%. Similar results were obtained in the per-protocol analysis (Supplementary Figs. 8 and 9 and Supplementary Tables 8 and 9).

There was one occurrence of hyperglycemia related to binge alcohol consumption in the intervention group that required withdrawal from the study. In the intervention group, hyperglycemia (>250 mg/dL) was detected in 56 patients on review of the transmitted CGM data (Supplementary Table 10). Hypoglycemia of <70 mg/dL and 54 mg/dL was detected in 56 and 45 participants, respectively, but duration of TBR was 0.62 h (2.6%) and 0.09 h (0.4%) per day and there was no severe hypoglycemic event that accompanied loss of consciousness or necessitated assistance from another person. Direct comparison of adverse glycemic events between the control and intervention groups was not possible due to the discrete nature of BGM and less frequent glucose data in the control group during the follow-up.

CONCLUSIONS

PDF is the first multicenter, randomized controlled trial comparing the effect of isCGM adopting the SEOUL algorithm with standard care in patients with T2D who have not attained optimal glycemic control. While there is no doubt that CGM has brought us one step closer to precision medicine, obstacles arise from the burden of overloading information for physicians. Furthermore, by the time a patient arrives at the outpatient clinic, many cumulative CGM metrics will be outdated. Thus, we postulated that by applying the SEOUL algorithm, which enables patients to personalize nutrition therapy based on individual postprandial glycemic response, we would be able to shift the paradigm from physician driven to a data-based, patient-driven lifestyle modification that would allow the patients to achieve better glycemic control. In this study, the use of isCGM with the SEOUL algorithm led to improvement in HbA_{1c} in patients who were not on an intensive insulin regimen significantly greater than that in the control group over 12 weeks. Self-management of diabetes, assessed with the SDSCA-K scores, which is vital in achieving better glycemic outcomes, also increased to a greater extent in the intervention group than in the control group. In the secondary outcomes, a decrease in fasting blood glucose and more significant body weight reduction were observed in the intervention group than in the control group.

Among the participants in the intervention group, the superior glycemic outcome of −0.5% HbA_{1c} difference compared with that in the control group was closely associated with scanning frequency and the percentage of active CGM time. This is in line with a previous study with analysis of the effects of isCGM, the results of which suggested that a higher scanning frequency was strongly associated with improved glycemic parameters, including reduction of HbA_{1c} and time spent in a state of hypoglycemia (16). Higher baseline HbA_{1c} was linked to a greater reduction at 3 months, but no other baseline measures, including fasting blood glucose, body weight, waist circumference, and LDL cholesterol, or the use of basal insulin was associated with improved HbA_{1c}, TIR, and CV over the study period.

Divergent outcomes have been reported in CGM studies involving participants on intensive insulin regimen (8,17,18). In REPLACE, involving patients with T2D (8), and the IMPACT trial conducted in patients with type 1 diabetes (17), the time <70 mg/dL was >1 h and 3 h per day at baseline, respectively, partly due to the complexity of prandial insulin regimen and severity of insulin deficiency. In these groups of patients at high risk of hypoglycemia, the use of isCGM reduced the time in hypoglycemic range, but HbA_{1c} was essentially unchanged compared with baseline values. In the DIAMOND study on patients with T2D where hypoglycemic events were infrequent at baseline in spite of multiple daily injections (the time <70 mg/dL only 11 min per day), use of rtCGM reduced HbA_{1c} levels as well (9). In this regard, research outcomes may differ according to the study characteristics such as devices (rtCGM or isCGM), types of diabetes (type 1 or type 2), use of prandial insulin, and susceptibility to hypoglycemia. In our PDF study, the participants were patients with T2D who were not on prandial insulin. Hence, these

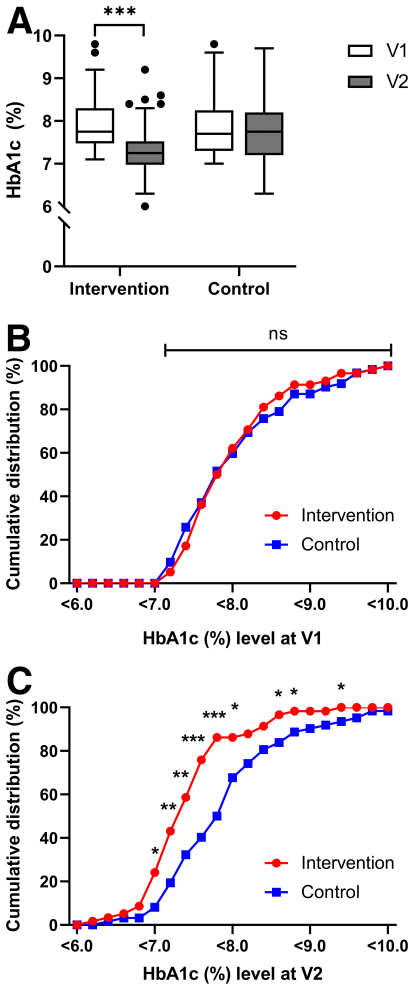

Figure 3—Glycemic outcome according to treatment groups. *A*: Box plot of HbA_{1c} (%) in the intervention and control groups at V1 and V2. HbA_{1c} levels were significantly decreased in the intervention group at 12 weeks. *B*: Cumulative distribution of HbA_{1c} (%) levels at V1. *C*: Cumulative distribution of HbA_{1c} (%) levels at V2. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. ns, not significant.

patients were less prone to hypoglycemia, which might have led to improvement in HbA_{1c} with the proper use of isCGM.

In the intervention group, weight loss and improved SDSCA-K scores were noteworthy findings in addition to a reduction in HbA_{1c}, implying refinement in lifestyle management, which is the mainstay of diabetes management. The mean BMI of this cohort was >25 kg/m^2, which falls within the range of obesity according to Asian criteria (19). Modest weight loss was associated with improved glycemic control without increasing the insulin dose or the number of antidiabetes medications. The combination of adhering to a tailored healthy meal plan, engaging in exercise regularly, and subsequently inspecting inside the shoes are all parts of recommended patient-centered care to achieve optimal diabetes care (1). SDSCA-K scores improved in both groups but particularly increased in aspects of not only adhering to a diabetes meal plan but also engaging in physical activities and foot inspection in the intervention group. Taken together, scanning CGM conveniently before and after exercise and experiencing fewer glycemic excursions from exercise may have served as positive feedback in the intervention group. CGM scanning with respect to exercise was not mandated in this study but may nevertheless have guided comprehensive diabetes self-care, including enhancing physical activities with reduced fear of hypoglycemia.

Behavior modification improved immediately upon insertion of the CGM sensor and receipt of education based on the SEOUL algorithm in the intervention group, with demonstration of an optimal glucose profile throughout the study period. It can be speculated from the consistent ambulatory glucose profile from the first to the last inserted CGM that maintaining healthy behavior over the study period yielded enduring benefits that consequently led to improved HbA_{1c} levels at V2. Similar findings were also noted in our previous mDiabetes study where we evaluated the efficacy of a smartphone-based, patient-centered diabetes care system for T2D (20, 21).

This study has some limitations. First, baseline BMI was slightly higher in the control group. However, the results were consistent after adjustment for BMI as a covariate, in addition to the recruitment site and the respective baseline values for primary and secondary outcomes. In addition, despite having a lower BMI at baseline, the participants in the intervention group managed to achieve significant weight loss compared with the control group. Second, although the participants in the control group exhibited good adherence to BGM, it was not feasible to compare the frequency of hyperglycemic and hypoglycemic events during the study period with different numbers of measured glucose data points for both groups. Third, we did not collect information on socioeconomic status or the education level of the study population, which could affect the efficacy of the current intervention. Fourth, the SDSCA-K measure is based on self-reported scores, which is subjective rather than objective. However, SDSCA-K has previously been validated in Koreans (22), demonstrating adequate reliability. Finally, the study duration was relatively short. Therefore, further studies are warranted to examine the long-term sustained benefits of the SEOUL algorithm incorporating isCGM.

In conclusion, we demonstrated that the patient-centered approach of isCGM with the SEOUL algorithm, focused mainly on eating behavior, was highly effective in reducing HbA_{1c} and facilitating behavior change to improve general diabetes care in patients with T2D who are not on prandial insulin.

Acknowledgments. The authors acknowledge the clinical research coordinators Jung Min Cho, Inyoung Baek, Kyunghee Kim (all three from the Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea), Jung Mi Kim (Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea), and Hae Lan Won (Division of Endocrinology and Metabolism, Department of Internal Medicine, Sanggye Paik Hospital, Inje University, Seoul, Republic of Korea), for their assistance with data management. The authors also thank all of the individuals who participated in the PDF study.

Funding. Daewoong Pharmaceuticals Co., Ltd., provided the CGM devices.

Daewoong Pharmaceuticals Co., Ltd., had no approval authority for the manuscript before submission and no right to veto publication.

Duality of Interest. Y.M.C. received grant funding from Daewoong Pharmaceuticals Co., Ltd., to conduct the study. Y.M.C. received research grants from Daewoong Pharmaceuticals Co., Ltd., and Sanofi and consultation fees from Hanmi Pharmaceutical and LG Chem. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. H.J.C., E.-J.R., J.C.W., and Y.M.C. designed the study protocols. E.-J.R., J.C.W., K.S.P., W.-Y.L., and Y.M.C. collected data. E.-J.R., J.C.W., and Y.M.C. served as the site investigators responsible for conducting the protocol at each site. H.J.C. conducted the statistical analyses and wrote the first draft of the manuscript, and all other authors worked collaboratively to review and prepare the final manuscript. H.J.C. and Y.M.C. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. Parts of this study were included in an oral presentation at the 35th Spring Congress of the Korean Diabetes Association, Gyeongju, Korea, 12–14 May 2022.

References

1. American Diabetes Association Professional Practice Committee. 5. Facilitating behavior change and well-being to improve health outcomes: *Standards of Medical Care in Diabetes—2022*. Diabetes Care 2022;45(Suppl. 1):S60–S82
2. Franz MJ, MacLeod J, Evert A, et al. Academy of Nutrition and Dietetics Nutrition Practice Guideline for Type 1 and Type 2 Diabetes in Adults: systematic review of evidence for medical nutrition therapy effectiveness and recommendations for integration into the nutrition care process. J Acad Nutr Diet 2017;117:1659–1679
3. Evert AB, Boucher JL, Cypress M, et al.; American Diabetes Association. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 2013;36:3821–3842
4. Zeevi D, Korem T, Zmora N, et al. Personalized nutrition by prediction of glycemic responses. Cell 2015;163:1079–1094
5. Mendes-Soares H, Raveh-Sadka T, Azulay S, et al. Assessment of a personalized approach to predicting postprandial glycemic responses to food among individuals without diabetes. JAMA Netw Open 2019;2:e188102
6. Edelman SV, Argento NB, Pettus J, Hirsch IB. Clinical implications of real-time and intermittently scanned continuous glucose monitoring. Diabetes Care 2018;41:2265–2274
7. Perez-Guzman MC, Shang T, Zhang JY, Jornsay D, Klonoff DC. Continuous glucose monitoring in the hospital. Endocrinol Metab (Seoul) 2021;36:240–255
8. Haak T, Hanaire H, Ajjan R, Hermanns N, Riveline JP, Rayman G. Flash glucose-sensing technology as a replacement for blood glucose monitoring for the management of insulin-treated type 2 diabetes: a multicenter, open-label randomized controlled trial. Diabetes Ther 2017;8:55–73
9. Beck RW, Riddlesworth TD, Ruedy K, et al.; DIAMOND Study Group. Continuous glucose monitoring versus usual care in patients with type 2 diabetes receiving multiple daily insulin injections: a randomized trial. Ann Intern Med 2017;167:365–374
10. Vigersky RA, Fonda SJ, Chellappa M, Walker MS, Ehrhardt NM. Short- and long-term effects of real-time continuous glucose monitoring in patients with type 2 diabetes. Diabetes Care 2012;35:32–38
11. Martens T, Beck RW, Bailey R, et al.; MOBILE Study Group. Effect of continuous glucose monitoring on glycemic control in patients with type 2 diabetes treated with basal insulin: a randomized clinical trial. JAMA 2021;325:2262–2272
12. Aleppo G, Beck RW, Bailey R, et al.; MOBILE Study Group; Type 2 Diabetes Basal Insulin Users: The Mobile Study (MOBILE) Study Group. The effect of discontinuing continuous glucose monitoring in adults with type 2 diabetes treated with basal insulin. Diabetes Care 2021;44:2729–2737
13. Korean Diabetes Association. Diabetes education, 2022. Accessed 3 November 2021. Available from https://www.diabetes.or.kr
14. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group; Tamborlane WV, Beck RW, Bode BW, et al. Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 2008;359:1464–1476
15. Ehrhardt NM, Chellappa M, Walker MS, Fonda SJ, Vigersky RA. The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. J Diabetes Sci Technol 2011;5:668–675
16. Dunn TC, Xu Y, Hayter G, Ajjan RA. Real-world flash glucose monitoring patterns and associations between self-monitoring frequency and glycaemic measures: a European analysis of over 60 million glucose tests. Diabetes Res Clin Pract 2018;137:37–46
17. Bolinder J, Antuna R, Geelhoed-Duijvestijn P, Kröger J, Weitgasser R. Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. Lancet 2016;388:2254–2263
18. Castellana M, Parisi C, Di Molfetta S, et al. Efficacy and safety of flash glucose monitoring in patients with type 1 and type 2 diabetes: a systematic review and meta-analysis. BMJ Open Diabetes Res Care 2020;8:e001092
19. World Health Organization Regional Office for the Western Pacific International Association for the Study of Obesity and the International Obesity Task Force. The Asia-Pacific Perspective: Redefining Obesity and Its Treatment. 2002
20. Kim EK, Kwak SH, Baek S, et al. Feasibility of a patient-centered, smartphone-based, diabetes care system: a pilot study. Diabetes Metab J 2016;40:192–201
21. Kim EK, Kwak SH, Jung HS, et al. The effect of a smartphone-based, patient-centered diabetes care system in patients with type 2 diabetes: a randomized, controlled trial for 24 weeks. Diabetes Care 2019;42:3–9
22. Chang S, Song M. The validity and reliability of a Korean version of the Summary of Diabetes Self-Care Activities Questionnaire for older patients with type 2 diabetes. J Korean Acad Adult Nurs 2009;21:235–244