

Determinants of hemoglobin A1c level in patients with type 2 diabetes after in-hospital diabetes education: A study based on continuous glucose monitoring

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Keywords

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ABSTRACT

Aims/Introduction: We investigated the relationship between blood glucose profile at hospital discharge, evaluated by continuous glucose monitoring (CGM), and hemoglobin A1c (HbA1c) level at 12 weeks after discharge in patients with type 2 diabetes who received inpatient diabetes education.

Materials and Methods: This was a retrospective study. The participants were 54 patients with type 2 diabetes who did not change their medication after discharge. The mean blood glucose (MBG), standard deviation, coefficient of variation, mean postprandial glucose excursion, maximum blood glucose, minimum blood glucose, percentage of time with blood glucose at ≥ 180 mg/dL (time at ≥ 180), percentage of time with blood glucose at ≥ 140 mg/dL, and percentage of time with blood glucose at < 70 mg/dL were measured at admission and discharge using CGM. The primary end-point was the relationship between CGM parameters and HbA1c level at 12 weeks after discharge.

Results: The HbA1c level at 12 weeks after discharge correlated with MBG level ($r = 0.30$, $P = 0.029$). Multivariate analysis showed that MBG level and disease duration were predictors of 12-week HbA1c level. Multivariate logistic regression analysis was carried out considering goal achievement as a HbA1c level $< 7.0\%$ 12 weeks after discharge. Disease duration and time at ≥ 180 were associated with goal achievement.

Conclusions: The present results suggested that blood glucose profile at discharge using CGM seems useful to predict HbA1c level after discharge in patients with type 2 diabetes who received inpatient diabetes education. Early treatment to improve MBG level, as well as postprandial hyperglycemia, is important to achieve strict glycemic control.

INTRODUCTION

Hemoglobin A1c (HbA1c) is used as an index of chronic hyperglycemia in the diagnosis and treatment of diabetes mellitus^{1,2}. Many epidemiological studies have shown that HbA1c is associated with the risk of diabetic vasculopathy^{3,4}. HbA1c is the most important index of glycemic control, and has been used to set the goal of appropriate treatment for each patient⁵.

Generally speaking, the aim of the majority of inpatient diabetes education programs is to improve lifestyle habits and enhance treatment within a short period of time^{6,7}. Through

such programs, patients learn the benefits of diet and exercise, and receive information about acute and chronic complications of diabetes and preventive measures⁸. The primary goal of such programs is to achieve good long-term glycemic control; and HbA1c level after discharge is one of the most important indexes used to evaluate the effect of such programs.

The HbA1c value reflects the net mean blood glucose level over the preceding 1 or 2 months, and does not reflect immediate changes in the blood glucose profile after treatment. In clinical practice, self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) are often used to assess circadian variation in blood glucose and changes in blood

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glucose after treatment. Among the parameters measured by SMBG and CGM, the mean blood glucose level is reported to be strongly correlated with HbA1c^{9,10}. To our knowledge, however, there is little or no information on the relationship between blood glucose profile at discharge and HbA1c level after discharge.

The aim of the present study was to determine the relationship between blood glucose profile at discharge and HbA1c levels at 12 weeks after discharge in patients who did not change their medications after discharge. For this purpose, we evaluated blood glucose profile at admission and discharge as measured with CGM in patients with type 2 diabetes who received inpatient diabetes education.

MATERIALS AND METHODS

Participants

This was a retrospective study. Participants were selected from patients with type 2 diabetes admitted to the Hospital of the University of Occupational and Environmental Health and Wakamatsu Hospital of the University of Occupational and Environmental Health, Kitakyushu-shi, Japan, between April 2011 and July 2015. Each of the selected patients had undergone assessment for blood glucose profile with a continuous glucose monitoring system (CGMS[®] System Gold[™] or iPro2; Medtronic MinMed Inc., Northridge, California, USA) within 4 days of admission (for at least 2 days) and within 4 days before discharge (for at least 2 days), and did not change their medications and insulin dose until 12 weeks after discharge. The following other inclusion criteria were applied in the present study: (i) age >20 years; (ii) blood glucose level at admission of <300 mg/dL; (iii) no diabetic ketosis or non-ketotic hyperosmolar coma, and (iv) absence of cardiac arrhythmias. Patients with aspartate aminotransferase ≥ 100 IU/L or alanine aminotransferase ≥ 100 IU/L, patients with serum creatinine level ≥ 2.0 mg/dL or estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m², infectious diseases, acute coronary syndrome, anemia and/or using erythropoiesis stimulating agents were also excluded from the study. The study protocol was approved by the ethics committees of the University of Occupational and Environmental Health and the participating medical centers. Informed consent was obtained from all participants.

The baseline definition of diabetic microangiopathy was as follows. Diabetic nephropathy is graded¹¹ according to the urinary albumin excretion rate. The urinary albumin excretion rate is presented as the albumin-to-creatinine ratio (mg/g creatinine). In the present study, diabetic nephropathy was defined as albumin-to-creatinine ratio ≥ 30 mg/g creatinine. Diabetic retinopathy was defined as simple retinopathy or more severe conditions judged according to the results of fundoscopic examinations carried out by expert ophthalmologists. Diabetic neuropathy was diagnosed by the presence of two or more components among clinical symptoms (bilateral spontaneous pain, hypoaesthesia or paresthesia of the legs), absence of ankle

tendon reflexes and decreased vibration sensations using a C128 tuning fork.

Continuous glucose monitoring system

The mean blood glucose (MBG) level, standard deviation (SD), mean postprandial glucose excursion (MPPGE), maximum (Max), minimum (Min), percentage of time with blood glucose at ≥ 180 mg/dL, percentage of time with blood glucose at ≥ 140 mg/dL and percentage of time with blood glucose at <70 mg/dL were measured from the data recorded through CGM using the SMBG device. To assess postprandial glucose excursions from the CGM data, MPPGE was calculated as the arithmetic mean of the differences between the postprandial peak glucose values and the corresponding preprandial glucose values for meals. Previous studies showed that interstitial glucose concentrations measured by CGM correlate with venous blood glucose levels¹². CGM measurements represent glucose concentrations in the interstitial fluid, but since the introduction of the SMBG technique, the measured value is considered to represent blood glucose level. Analysis was limited to the data obtained from the intermediate 48 h of recording to avoid bias as a result of insertion and removal of CGM or insufficient stability of the monitoring system. All patients received optimal meals (25 kcal/kg of ideal bodyweight; 60% carbohydrate, 15–20% protein and 20–25% fat) during CGM.

Laboratory procedures

HbA1c levels (%) were measured with a high-performance liquid chromatography method using Tosoh HLC-723 G8 (Tosoh Co., Kyoto, Japan). HbA1c level was estimated according to the National Glycohemoglobin Standardization Program by adding 0.4% to the HbA1c level expressed as conventional Japanese standard substance value (Japan Diabetes Society values)¹³. HbA1c levels were measured at admission, and 4 and 12 weeks after discharge. In the present study, the HbA1c level at 12 weeks after discharge was used as the index for the effects on glycemic control after discharge.

Interventions during hospitalization

A 2-week hospitalization educational program was provided for the patients, which included lectures using brochures, slides, and videos from physicians, pharmacists and nurses; at least one personalized nutrition education session provided by managerial dieticians; interventions other than lectures, such as explanations about the use of self-monitoring blood glucose devices, as well as target glucose level and hypoglycemia; and education and confirmation of techniques for self-injection of insulin and glucagon-like peptide 1 preparation for patients requiring such self-injection.

Statistical analysis

Data are expressed as mean \pm SD. Data distribution was determined using the Shapiro–Wilk test. Comparisons between CGM data at admission and discharge were carried out using

the paired *t*-test for normally distributed data and the Wilcoxon signed-rank test for data with skewed distribution. Correlation analyses between HbA1c and CGM data were carried out using Pearson's correlation analysis for normally distributed variables and Spearman's correlation analysis for variables with skewed distribution.

Multivariate analysis using a forward selection method was carried out with the HbA1c level at 12 weeks after discharge as the dependent variable, and age, sex, body mass index, disease duration, eGFR, pharmacotherapy, MBG, SD, CV, MPPGE, Max, Min, percentage of time with blood glucose at ≥ 180 mg/dL, percentage of time ≥ 140 mg/dL and percentage of time < 70 mg/dL as the independent variables. Univariate and multivariate logistic regression analyses were carried out considering patients with HbA1c $< 7.0\%$ at 12 weeks after discharge as the goal-achieving group and all others as the non-goal-achieving group. Data were expressed as odds ratios and 95% confidence intervals (CIs). In the multivariate logistic regression analysis using a forward selection method, the independent variables were chosen from factors that had a *P*-value of < 0.25 in the univariate logistic regression analysis after excluding the factors with multicollinearity by Spearman's correlation analysis. All statistical analyses were carried out using Spss version 22.0 (SPSS Inc., Chicago, Illinois, USA). Statistical significance was set at *P* < 0.05 .

RESULTS

Baseline characteristics

Table 1 summarizes the clinical characteristics of the participating patient. They included 54 patients (26 men and 28 women) with a mean age of 59.9 ± 13.2 years (range 30–81 years), mean disease duration of 5.9 ± 6.7 years (range 0–31 years) and mean HbA1c level of $8.9 \pm 1.8\%$ (range 6.6–15.5%).

Pharmacotherapy and CGM parameters at admission and discharge

Table 1 shows the pharmacotherapy at discharge. After admission, all patients received diet therapy and changed their medications. The number of patients receiving each drug changed from 15 to 4 patients for sulfonylurea, from 3 to 8 for pioglitazone, from 13 to 23 for metformin, from 5 to 9 for α -glucosidase inhibitor, from 23 to 32 for dipeptidyl peptidase-4 inhibitor, from 8 to 4 for insulin, from 1 to 11 for sodium-glucose co-transporter 2 inhibitor, and from 1 to 9 for glucose-like peptide 1 receptor agonists.

A significant reduction was observed in MBG (from 168.2 mg/dL at admission to 130.3 mg/dL at discharge), SD (from 35.6 to 25.1 mg/dL), CV (from 21.2 to 18.8 mg/dL), MPPGE (from 74.9 to 58.8 mg/dL), Max (from 251.4 to 196.3 mg/dL) and Min (from 109.9 to 90.4 mg/dL). The percentage of time with blood glucose at ≥ 180 mg/dL was significantly decreased from 31.3 to 8.3%, and the percentage of time with blood glucose at ≥ 140 mg/dL was significantly decreased from 63.6 to 29.1%, whereas the percentage of time with blood

Table 1 | Clinical characteristics of study participants with type 2 diabetes

Variables	
Age (years)	59.9 ± 13.2
Sex (male/female)	26/28
Body mass index (kg/m ²)	27.9 ± 5.5
Duration of diabetes (years)	5.9 ± 6.7
Diabetes complications	
Neuropathy, <i>n</i> (%)	23 (42.6)
Retinopathy, <i>n</i> (%)	12 (22.2)
Nephropathy, <i>n</i> (%)	16 (29.6)
Fasting glucose (mg/dL)	153.9 ± 39.7
HbA1c (%)	8.9 ± 1.8
eGFR (mL/min/1.73 m ²)	88.4 ± 42.1
Diabetes therapy at discharge	
Diet only, <i>n</i> (%)	0 (0)
Oral agents only, <i>n</i> (%)	42 (77.8)
GLP-1 RA only, <i>n</i> (%)	1 (1.9)
Insulin only, <i>n</i> (%)	0 (0)
Oral agents + GLP-1 RA, <i>n</i> (%)	7 (13.0)
Oral agents + insulin, <i>n</i> (%)	3 (5.6)
GLP-1 RA + insulin, <i>n</i> (%)	1 (1.9)

Data are mean \pm SD or *n* (%); *n* = 54. eGFR, estimated glomerular filtration rate; GLP-1 RA, glucose-like peptide 1 receptor agonist; HbA1c, hemoglobin A1c.

glucose at < 70 mg/dL did not show a significant change (from 0.4 to 0.2%; Table 2).

Relationship between HbA1c level at 12 weeks after discharge and CGM parameters at discharge

The mean HbA1c level was 8.9% at admission, 7.4% at 4 weeks after discharge and 6.6% at 12 weeks after discharge, showing a significant improvement (*P* < 0.001). The relationship between HbA1c level at 12 weeks after discharge and CGM parameters at discharge is shown in Table S1. The HbA1c level at 12 weeks after discharge correlated with MBG (*r* = 0.30, *P* = 0.029), but not with SD, CV, Max, MPPGE, Min, percentage of time with blood glucose at ≥ 180 mg/dL, percentage of time with blood glucose at ≥ 140 mg/dL or percentage of time with blood glucose at < 70 mg/dL.

Multivariate analysis was carried out with the level of HbA1c at 12 weeks after discharge as the dependent variable, and age, sex, body mass index, disease duration, eGFR, pharmacotherapy, MBG, SD, CV, MPPGE, Max, Min, percentage of time with blood glucose at ≥ 180 mg/dL, percentage of time with blood glucose at ≥ 140 mg/dL and percentage of time with blood glucose at < 70 mg/dL as the independent variables. The analysis identified MBG and disease duration as the two independent and significant determinants of HbA1c levels at 12 weeks after discharge (Table 3).

The HbA1c level at 12 weeks after discharge was $< 8\%$ in 98.1% (53 patients), $< 7\%$ in 75.9% (41 patients) and $< 6\%$ in

Table 2 | Continuous glucose monitoring parameters at admission and discharge

CGM parameters	At admission	At discharge	Change of CGM parameters	* <i>P</i> -value
MBG (mg/dL) [†]	168.2 ± 43.5	130.3 ± 19.9	-37.8 ± 34.3	<0.001
SD (mg/dL) [†]	35.6 ± 14.7	25.1 ± 11.9	-10.5 ± 13.2	<0.001
CV (%)	21.2 ± 6.9	18.8 ± 7.1	-2.4 ± 8.1	0.018
MPPGE (mg/dL) [†]	74.9 ± 28.8	58.8 ± 29.3	-16.3 ± 33.6	0.001
Max (mg/dL) [†]	251.4 ± 56.7	196.3 ± 48.3	-55.1 ± 49.2	<0.001
Min (mg/dL) [†]	109.9 ± 35.8	90.4 ± 16.2	-19.5 ± 33.8	<0.001
Time at ≥180 mg/dL (%) [†]	31.3 ± 28.4	8.3 ± 12.7	-23.0 ± 23.6	<0.001
Time at ≥140 mg/dL (%) [†]	63.6 ± 28.1	29.1 ± 22.8	-34.5 ± 28.2	<0.001
Time at <70 mg/dL (%) [†]	0.4 ± 1.9	0.2 ± 0.8	-0.3 ± 2.1	0.463

Data are mean ± SD or *n* (%). [†]Measured by the continuous glucose monitoring system. There were no significant differences among each baseline values. *P*-values are for differences between baseline and discharge. CGM, continuous glucose monitoring; CV, coefficient of variation; Max, maximum; MBG, mean blood glucose; Min, minimum; MPPGE, mean postprandial glucose excursions; SD, standard deviation.

Table 3 | Linear multivariate analyses with hemoglobin A1c after 12 weeks as the dependent variable at discharge

Variable	Unstandardized coefficients		Standardized coefficients β	<i>t</i> value	<i>P</i> -value
	B	SE			
Intercept	4.957	0.458		10.824	<0.001
MBG	0.010	0.003	0.329	2.961	0.005
Duration of diabetes	0.052	0.003	0.571	5.138	<0.001
Adjusted multiple <i>R</i> ²	0.358				

Multivariate stepwise regression analysis with hemoglobin A1c after 12 weeks as the dependent variable, and age, sex, duration of the disease, estimated glomerular filtration rate, pharmacotherapy, hemoglobin A1c at baseline and mean blood glucose (MBG) as the independent variables. MBG was measured by the continuous glucose monitoring system. SE, standard error.

18.5% (10 patients). Univariate and multivariate logistic regression analyses were carried out considering the patients with HbA1c <7.0% at 12 weeks after discharge as the goal-achieving group (41 patients), and those with HbA1c ≥7.0% as the non-goal-achieving group (13 patients; Table 4). The analysis identified that disease duration and percentage of time with blood glucose at ≥180 mg/dL were significantly associated with goal achievement. The odds of achieving an HbA1c of <7.0% was 0.83-fold the value with each 1-point increase in disease duration (95% CI: 0.72–0.93), and 0.91-fold the value with each 1-point increase in the percentage of time with blood glucose at ≥180 mg/dL (95% CI: 0.84–0.97).

Relationship between change in HbA1c level at 12 weeks after discharge and change in CGM parameters during hospitalization

Finally, we analyzed the relationship between changes in CGM parameters during hospitalization (between admission and discharge) and changes in HbA1c level at 12 weeks after discharge. The change in HbA1c level correlated with changes in MBG ($r = 0.582$, $P < 0.001$), SD ($r = 0.448$, $P = 0.001$), Max ($r = 0.586$, $P < 0.001$), Min ($r = 0.411$, $P = 0.002$), percentage of time with blood glucose at ≥180 mg/dL ($r = 0.630$,

$P < 0.001$) and percentage of time with blood glucose at ≥140 mg/dL ($r = 0.396$, $P = 0.003$), but not with changes in MPPGE or percentage of time with blood glucose at <70 mg/dL (Table S2). Multivariate analysis was carried out with the change in HbA1c until 12 weeks after discharge as the dependent variable, and with age, sex, disease duration, eGFR, pharmacotherapy, ΔMBG, ΔMin, Δpercent of time ≥180 mg/dL, Δpercent of time ≥140 mg/dL and Δpercent of time <70 mg/dL as independent variables, which showed that ΔMBG is a factor that affects change in HbA1c until 12 weeks after discharge (adjusted multiple $R^2 = 0.508$, standardization coefficient $\beta = 0.036$, $t = 7.461$, $P < 0.001$).

DISCUSSION

Based on the data obtained using CGM, the present study showed that: (i) the HbA1c level after discharge was associated with disease duration and the mean blood glucose level at discharge; and (ii) the achievement of HbA1c <7.0% after discharge was dependent on disease duration and percentage of postprandial hyperglycemia at discharge. The aim of diabetes education during hospitalization for patients with type 2 diabetes is to improve lifestyle habits and enhance treatment in a short period of time^{6,7,14}. Only a few studies have so far

Table 4 | Clinical markers of glycemia variables at discharge and recording of hemoglobin A1c after 12 weeks of <7% analyzed by univariate and multiple logistic regression analyses

	Univariate logistic regression			Multiple logistic regression		
	Wald χ^2	<i>P</i>	OR (95% CI)	Wald χ^2	<i>P</i>	OR (95% CI)
Sex (male/female)	0.4	0.425	1.68 (0.48–6.38)			
Duration of diabetes	6.8	<0.001	0.87 (0.77–0.96)	8.4	0.004	0.83 (0.72–0.93)
HbA1c at baseline	3.0	0.086	0.73 (0.49–1.03)			
eGFR	0.1	0.730	1.00 (0.99–1.02)			
MBG	3.4	0.059	0.97 (0.94–1.00)			
SD	6.3	0.012	0.93 (0.87–0.98)			
CV	4.9	0.026	0.90 (0.81–0.98)			
MPPGE	1.7	0.195	0.99 (0.96–1.01)			
Max	2.8	0.095	0.99 (0.98–1.00)			
Min	2.1	0.147	1.03 (0.99–1.08)			
Time at ≥ 180	6.0	0.014	0.94 (0.88–0.98)	7.4	0.007	0.91 (0.84–0.97)
Time at ≥ 140	3.8	0.058	0.97 (0.94–1.00)			
Time at <70	1.4	0.24	0.63 (0.23–1.39)			

Only factors with $P < 0.25$ on univariate logistic regressions (duration and hemoglobin A1c [HbA1c] at baseline, MBG, mean blood glucose; SD, standard deviation; CV, coefficient of variation; MPPGE, mean of postprandial glucose excursion; Max, maximum; Min, minimum; time at blood glucose ≥ 180 mg/dL, time at blood glucose ≥ 140 mg/dL and time at blood glucose <70 mg/dL) were included in this multiple factor logistic regression. MBG, SD, MPPGE, Max, Min, time at blood glucose ≥ 180 mg/dL, time at blood glucose ≥ 140 mg/dL and time at blood glucose <70 mg/dL were measured by the continuous glucose monitoring system.

examined the time-course of changes in HbA1c level after discharge. Sonoda *et al.*¹⁵ reported that fasting and urine C-peptide immunoreactivity are significant predictors of HbA1c level after discharge. In clinical practice, a clear understanding of the relationship between diurnal blood glucose and HbA1c is important for setting the appropriate target level of HbA1c for each patient in order to prevent vascular complications. To our knowledge, this is the first study that examined the association between blood glucose parameters evaluated in detail using CGM at discharge and HbA1c after discharge.

Several previous studies have investigated the relationship between mean blood glucose and HbA1c levels in patients with diabetes mellitus. Koenig *et al.*¹⁶ reported the association between MBG and HbA1c in five patients with diabetes mellitus. Subsequently, the association between MBG and HbA1c was reported in patients with both type 1 and type 2 diabetes through blood glucose measurement using SMBG testing^{17,18} and CGM^{9,10,19,20}. However, no studies have examined the association between blood glucose profile and future HbA1c levels. The results of the present study showed that the MBG level measured using CGM correlated with HbA1c 12 weeks after the measurement, and the change in mean blood glucose during admission was associated with the change in HbA1c after discharge, suggesting that improvement in MBG level until the time of discharge is essential for improvement of HbA1c.

Monnier *et al.*²¹ investigated the relationship between postprandial and fasting blood glucose levels and HbA1c in 290 patients with type 2 diabetes. They reported that the contribution of fasting blood glucose and postprandial blood glucose to

HbA1c were equal when HbA1c was $\geq 7.3\%$, whereas the contribution of postprandial blood glucose was greater than that of the fasting blood glucose in patients with HbA1c of <7.3%. Similarly, Woerle *et al.*²² studied 164 patients with type 2 diabetes and reported that improvement in postprandial blood glucose, as well as fasting blood glucose, was essential to achieve HbA1c <7%²². In the present study, blood glucose fluctuation and time spent at blood glucose ≥ 140 mg/dL; that is, factors related to postprandial hyperglycemia, significantly influenced the achievement of HbA1c <7.0% after inpatient diabetes education. We consider that improvement in blood glucose fluctuation and postprandial hyperglycemia, as well as fasting blood glucose, is necessary in order to achieve good glycemic control (HbA1c <7.0%).

With regard to the prevention of diabetic vasculopathy, the importance of early intervention has been acknowledged⁴. It has been reported that early and strict blood glucose control can, at least in part, prevent microvascular and macrovascular complications²³. The results of the present study showed that the shorter the duration of diabetes mellitus, the greater was the improvement in HbA1c after inpatient diabetes education. We consider that inpatient diabetes education for patients in the early phase of diabetes is useful to achieve strict glycemic control, as well as to prevent vascular complications.

The present study had several limitations. First, the treatment goal differed from patient to patient. According to the Japanese guideline, a treatment goal should be determined taking into consideration the age of the patient, disease duration, organ disorder, risk of hypoglycemia and support systems¹¹. The

treatment goal for each patient in the present study was determined by the attending physicians. Second, this was a retrospective study carried out in two hospitals. The patients were limited to those who did not change medications after discharge. Third, the interindividual variability in the educational effect was not included in the analysis. Given that educational outcomes are affected by socioeconomic status²⁴, there might have been a difference in the educational effect among the patients.

The present study showed that HbA1c level after discharge was associated with disease duration and MBG level at discharge. Furthermore, the study identified disease duration and postprandial hyperglycemia at discharge as significant factors that influenced the achievement of HbA1c <7.0%. Based on the data obtained using CGM, the present study showed that blood glucose profile at discharge might be useful in predicting HbA1c level after discharge for patients who received diabetes education during hospitalization. We consider that early treatment to improve blood glucose fluctuation and prevent postprandial hyperglycemia, in addition to lower mean blood glucose, is essential for achieving strict glycemic control.

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DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Saudek CD, Derr RL, Kalyani RR. Assessing glycemia in diabetes using self-monitoring blood glucose and hemoglobin A1c. *JAMA* 2006; 295: 1688–1697.
2. American Diabetes Association. Standards of medical care in diabetes–2007. *Diabetes Care* 2007; 30(Suppl. 1): S4–S41.
3. The DCCT Research Group. The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes* 1995; 44: 968–983.
4. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352: 837–853.
5. Inzucchi SE, Bergenstal RM, Buse JB, *et al.* Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2012; 35: 1364–1379.
6. Wei NJ, Grant RW, Nathan DM, *et al.* Effect of hospital admission on glycemic control 1 year after discharge. *Endocr Pract* 2012; 18: 456–463.
7. Koproski J, Pretto Z, Poretsky L. Effects of an intervention by a diabetes team in hospitalized patients with diabetes. *Diabetes Care* 1997; 20: 1553–1555.
8. Healy SJ, Black D, Harris C, *et al.* Inpatient diabetes education is associated with less frequent hospital readmission among patients with poor glycemic control. *Diabetes Care* 2013; 36: 2960–2967.
9. Nathan DM, Turgeon H, Regan S. Relationship between glycosylated haemoglobin levels and mean glucose levels over time. *Diabetologia* 2007; 50: 2239–2244.
10. Nathan DM, Kuenen J, Borg R, *et al.* Translating the A1C assay into estimated average glucose values. *Diabetes Care* 2008; 31: 1473–1478.
11. Treatment Guide for Diabetes 2014–2015: Edited by the Japan Diabetes Society, Tokyo: Bunkodo, 2015.
12. Boyne MS, Silver DM, Kaplan J, *et al.* Timing of changes in interstitial and venous blood glucose measured with a continuous subcutaneous glucose sensor. *Diabetes* 2003; 52: 2790–2794.
13. Committee of the Japan Diabetes Society on the Diagnostic Criteria of Diabetes Mellitus. Report of the committee on the classification and diagnostic criteria of diabetes mellitus. *J Diabetes Investig* 2010; 1: 212–228.
14. Wexler DJ, Beauharnais CC, Regan S, *et al.* Impact of inpatient diabetes management, education, and improved discharge transition on glycemic control 12 months after discharge. *Diabetes Res Clin Pract* 2012; 98: 249–256.
15. Sonoda R, Tanaka K, Kikuchi T, *et al.* C-peptide level in fasting plasma and pooled urine predicts HbA1c after hospitalization in patients with type 2 diabetes mellitus. *PLoS One* 2016; 11: e0147303.
16. Koenig RJ, Peterson CM, Jones RL, *et al.* Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus. *N Engl J Med* 1976; 295: 417–420.
17. Rohlfing CL, Wiedmeyer HM, Little RR, *et al.* Defining the relationship between plasma glucose and HbA(1c): analysis of glucose profiles and HbA(1c) in the Diabetes Control and Complications Trial. *Diabetes Care* 2002; 25: 275–278.
18. Murata GH, Hoffman RM, Duckworth WC, *et al.* Contributions of weekly mean blood glucose values to hemoglobin A1c in insulin-treated type 2 diabetes: the Diabetes Outcomes in Veterans Study (DOVES). *Am J Med Sci* 2004; 327: 319–323.
19. Wilson DM, Kollman ; Diabetes Research in Children Network (DirecNet) Study Group. Relationship of A1C to glucose concentrations in children with type 1 diabetes: assessments by high-frequency glucose determinations by sensors. *Diabetes Care* 2008; 31: 381–385.
20. Borg R, Kuenen JC, Carstensen B, *et al.* Associations between features of glucose exposure and A1C: the A1C-Derived Average Glucose (ADAG) study. *Diabetes* 2010; 59: 1585–1590.
21. Monnier L, Lapinski H, Colette C. Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations

- with increasing levels of HbA(1c). *Diabetes Care* 2003; 26: 881–885.
22. Woerle HJ, Neumann C, Zschau S, *et al.* Impact of fasting and postprandial glycemia on overall glycemic control in type 2 diabetes Importance of postprandial glycemia to achieve target HbA1c levels. *Diabetes Res Clin Pract* 2007; 77: 280–285.
 23. Holman RR, Paul SK, Bethel MA, *et al.* 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008; 359: 1577–1589.
 24. Ayyagari P, Grossman D, Sloan F. Education and health: evidence on adults with diabetes. *Int J Health Care Finance Econ* 2011; 11: 35–54.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1 | Correlation coefficients between HbA1c after 12 weeks and CGM parameters at discharge.

Table S2 | Correlation coefficients between change in HbA1c level at 12 weeks after discharge and change in CGM parameters during hospitalization.