Supplementary Table 1. Characteristics of the study participants

Female : Male	44 : 106	
Age (years old)	69.0 (64.0–72.0)	
Duration of diabetes (years)	14.0 (8.0–24.0)	
BMI (kg/m^2)	24.0 (22.3–26.0)	
HbA1c (%)	7.0 (6.6–7.6)	
GA (%)	18.3 (16.3–20.4)	
GA/HbA1c	2.6 (2.4–2.8)	
SBP (mmHg)	127.0 (116.0–137.0)	
DBP (mmHg)	75.0 (69.0–81.8)	
Non-HDL cholesterol (mg/dL)	122.0 (100.3–146.0)	
HDL cholesterol (mg/dL)	55.0 (46.3–66.0)	
eGFR (mL/min/1.73 m^2)	71.5 (59.0–82.0)	
UACR (mg/gCr)	15.1 (6.9–47.9)	
History of IHD (%)	13.3	
History of CVD (%)	10.7	
Current smoker (%)	21.3	
Dyslipidemia (%)	80.0	
Hypertension (%)	66.0	
MMSE	30.0 (29.0–30.0)	
Presence of severe DSWML (%)	32.7	
Presence of severe PWML (%)	15.3	
Presence of MTA (%)	13.3	
Z-scores in the target VOI	0.58 (0.43–0.83)	
Diabetes treatment		
Metformin (%)	47.3	
SU/glinides (%)	24.7	
Thiazolidines (%)	7.3	
DPP-4 inhibitors (%)	46.7	
SGLT2 inhibitors (%)	24.0	
α- glucosidase inhibitors (%)	10.7	
Insulin (%)	27.3	
GLP-1 receptor agonists (%)	14.0	
CGM metrics	All sensor data	day 3–day 12
Mean SG (mg/dL)	141.9 (125.1–165.8)	141.0 (124.2–165.7)

CV (%)	28.0 (24.6–31.7)	28.3 (24.5–31.5)
TIR (%)	77.9 (65.3–88.1)	77.0 (65.9–87.5)
$TAR^{>250}$ (%)	1.1 (0–6.7)	1.3 (0–6.7)
$TAR^{>180}$ (%)	18.1 (8.4–34.0)	17.8 (7.7–32.1)
$TBR^{<70}$ (%)	0.2 (0–2.1)	0.1 (0–2.3)
$TBR^{<54}$ (%)	0 (0–0)	0 (0–0.1)
GRI (%)	22.1 (12.6–40.9)	22.9 (12.7–43.8)
HyperCompo (%)	9.5 (4.2–20.2)	9.2 (4.0–18.3)
HypoCompo (%)	0.2 (0–1.8)	0.1 (0–1.9)
HBGI	3.8 (2.5–5.9)	3.7 (2.3–6.1)
LBGI	0.7 (0.3–1.6)	0.8 (0.3–1.9)

The results are the median values (interquartile range) or percentages.

Abbreviations: BMI, body mass index; CV, coefficient of variation; CVD, cerebrovascular disease; DBP, diastolic blood pressure; DSWML, deep subcortical white matter lesions; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GA, glycated albumin; GLP-1, glucagon-like peptide-1; GRI, glycemia risk index; HBGI, high blood glucose index; HDL, high-density lipoprotein; HyperCompo, hyperglycemia component of GRI; HypoCompo, hypoglycemia component of GRI; IHD, ischemic heart disease; LBGI, low blood glucose index; MMSE, mini-mental state examination; MTA, medial temporal lobe atrophy; PWML, periventricular white matter lesion; SBP, systolic blood pressure; SG, sensor glucose; SGLT2, sodium-glucose transporter 2; SU, sulfonylurea; TAR, time above range; TBR, time below range; TIR, time in range; VOI, volume of interest.

Supplementary Table 2. Differences in continuous glucose monitoring (CGM) metrics according to the presence or absence of severe cerebral white matter lesions and medial temporal atrophy

	Without severe WMLs (N = 101)	With severe WMLs (N = 49)	*P*	Without MTA (N = 130)	With MTA (N = 20)	*P*
CGM metrics (all data)						
Mean SG (mg/dL)	141.2 (126.6–159.8)	144.2 (123.2–192.4)	0.256	141.9 (124.5–165.6)	141.9 (133.6–165.9)	0.648
CV (%)	28.2 (24.4–31.2)	27.5 (24.7–32.5)	0.829	28.2 (24.6–31.7)	27.0 (24.5–31.2)	0.836
TIR of <50% (%)	8.9	26.5	0.006	14.6	15.0	1.000
$TAR^{>250}$ (%)	1.0 (0–4.0)	1.7 (0.1–10.9)	0.110	1.5 (0.1–5.5)	0.6 (0–9.2)	0.858
$TAR^{>250}$ of >10% (%)	8.9	28.6	0.003	13.8	25.0	0.195
$TAR^{>180}$ (%)	17.5 (8.5–29.7)	20.2 (8.1–54.3)	0.203	18.2 (8.1–34.0)	16.6 (8.4–32.0)	0.980
$TAR^{>180}$ of >50% (%)	8.9	26.5	0.006	14.6	15.0	1.000
$TBR^{<70}$ (%)	0.2 (0.0–1.9)	0 (0–2.5)	0.978	0.2 (0.0–2.3)	0.1 (0.0–1.4)	0.670
$TBR^{<70}$ of <4% (%)	11.9	20.4	0.255	15.4	10.0	0.739
$TBR^{<54}$ (%)	0 (0–0)	0 (0–0)	0.843	0 (0–0)	0 (0–0)	0.985
$TBR^{<54}$ of >1%	9.9	14.3	0.424	11.5	10.0	1.000
GRI (%)	20.9 (12.5–32.7)	35.2 (13.1–61.1)	0.013	21.9 (12.9–40.8)	24.1 (8.8–44.2)	0.941
HyperCompo (%)	9.3 (4.3–16.3)	13.4 (4.2–31.9)	0.169	9.7 (4.3–20.2)	8.6 (4.2–18.7)	0.936
HypoCompo (%)	0.2 (0–1.5)	0 (0–2.0)	0.978	0.2 (0–1.9)	0 (0–1.1)	0.657
HBGI	3.6 (2.5–5.0)	4.3 (2.4–9.5)	0.127	3.8 (2.5–5.8)	3.6 (2.2–6.3)	0.921
LBGI	0.8 (0.4–1.5)	0.6 (0.3–1.7)	0.765	0.8 (0.3–1.7)	0.5 (0.3–1.2)	0.280

CGM metrics (data from day 3 to day 12)						
Mean SG (mg/dL)	138.1 (124.9–159.3)	145.0 (122.6–190.7)	0.283	141.0 (123.4–166.2)	141.7 (130.4–162.5)	0.676
CV (%)	28.5 (24.5–31.4)	27.9 (24.5–31.9)	0.908	28.5 (24.6–31.5)	27.3 (24.3–32.6)	0.870
TIR (%)	78.6 (69.7–88.0)	71.3 (48.5–87.4)	0.052	77.6 (65.2–87.4)	72.9 (66.9–90.9)	0.776
TIR of <50% (%)	8.9	26.5	0.006	14.6	15.0	1.000
$TAR^{>250}$ (%)	1.3 (0–3.7)	1.3 (0–11.9)	0.192	1.3 (0–5.5)	0.6 (0–10.0)	0.931
$TAR^{>250}$ of >10% (%)	7.9	28.6	0.002	13.8	20.0	0.498
$TAR^{>180}$ (%)	17.1 (7.6–28.9)	20.4 (7.7–51.5)	0.241	18.3 (7.7–32.8)	17.1 (7.7–29.8)	0.892
$TAR^{>180}$ of >50% (%)	8.9	26.5	0.006	14.6	15.0	1.000
$TBR^{<70}$ (%)	0.1 (0–2.2)	0.1 (0–2.5)	0.892	0.1 (0–2.4)	0.1 (0–1.3)	0.755
$TBR^{<70}$ of <4% (%)	14.9	24.5	0.225	17.7	20.0	0.505
$TBR^{<54}$ (%)	0 (0–0.1)	0 (0–0.1)	0.940	0 (0–0.1)	0 (0–0)	0.747
$TBR^{<54}$ of >1%	11.9	16.3	0.621	13.8	10.0	0.480
GRI (%)	21.6 (12.5–33.3)	33.3 (13.9–56.9)	0.031	22.4 (13.0–43.8)	25.1 (11.6–44.7)	0.965
HyperCompo (%)	9.1 (4.1–16.1)	12.3 (3.9–29.8)	0.232	9.3 (4.1–18.3)	8.8 (3.9–18.6)	0.834
HypoCompo (%)	0.1 (0–1.8)	0.1 (0–2.1)	0.890	0.1 (0–2.0)	0.1 (0–1.0)	0.751
HBGI	3.5 (2.3–5.2)	4.0 (2.4–9.5)	0.181	3.8 (2.4–6.1)	3.5 (2.2–6.1)	0.989
LBGI	0.9 (0.4–1.9)	0.8 (0.2–2.0)	0.703	0.8 (0.3–1.9)	0.6 (0.3–1.5)	0.291

The results are the median values (interquartile range) or percentages. The Mann–Whitney U test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare categorical data.

Abbreviations: CV, coefficient of variation; GRI, glycemia risk index; HBGI, high blood glucose index; HyperCompo, hyperglycemia component; HypoCompo, hyperglycemia component; LBGI, low blood glucose index; MTA, medial temporal lobe atrophy; SG, sensor glucose; TAR, time

above range; TBR, time below range; TIR, time in range.

Supplementary Table 3. Association between the severity of cerebral white matter lesions and continuous glucose monitoring (CGM) derived glycemic control indices for 10 days

	Severe white matter lesions				
	OR (95% CI)	*P*		OR (95% CI)	*P*
Mean SG (day 3–day 12)			CV (day 3–day 12)		
Univariate	1.010 (0.999–1.020)	0.066	Univariate	1.018 (0.963–1.076)	0.525
Model 1	1.009 (0.998–1.019)	0.097	Model 1	1.019 (0.963–1.078)	0.507
Model 2	1.011 (1.000–1.022)	0.047	Model 2	1.012 (0.955–1.073)	0.684
Model 3	1.011 (1.000–1.022)	0.051	Model 3	1.008 (0.949–1.070)	0.807
TIR (day 3–day 12)			$TAR^{>250}$ (day 3–day 12)		
Univariate	0.977 (0.960–0.995)	0.011	Univariate	1.060 (1.017–1.105)	0.006
Model 1	0.978 (0.960–0.995)	0.013	Model 1	1.057 (1.013–1.102)	0.010
Model 2	0.974 (0.956–0.993)	0.007	Model 2	1.066 (1.021–1.113)	0.004
Model 3	0.974 (0.956–0.993)	0.006	Model 3	1.063 (1.018–1.110)	0.006
$TAR^{>180}$ (day 3–day 12)			$TBR^{<70}$ (day 3–day 12)		
Univariate	1.023 (1.008–1.038)	0.003	Univariate	1.030 (0.980–1.082)	0.244
Model 1	1.026 (1.011–1.042)	0.001	Model 1	1.036 (0.984–1.091)	0.173
Model 2	1.020 (1.002–1.038)	0.027	Model 2	1.031 (0.976–1.090)	0.275
Model 3	1.020 (1.002–1.038)	0.028	Model 3	1.032 (0.972–1.095)	0.298
$TBR^{<54}$ (day 3–day 12)			GRI (day 3–day 12)		
Univariate	1.109 (0.938–1.310)	0.226	Univariate	1.023 (1.008–1.038)	0.003
Model 1	1.128 (0.948–1.342)	0.176	Model 1	1.023 (1.008–1.039)	0.003

Model 2	1.117 (0.924–1.350)	0.253	Model 2	1.026 (1.010–1.043)	0.002
Model 3	1.112 (0.905–1.366)	0.312	Model 3	1.026 (1.009–1.043)	0.002
HyperCompo (day 3–day 12)			HypoCompo (day 3–day 12)		
Univariate	1.029 (1.005–1.053)	0.016	Univariate	1.035 (0.977–1.097)	0.238
Model 1	1.028 (1.004–1.052)	0.024	Model 1	1.043 (0.982–1.109)	0.169
Model 2	1.033 (1.008–1.059)	0.011	Model 2	1.038 (0.972–1.108)	0.269
Model 3	1.033 (1.007–1.059)	0.012	Model 3	1.038 (0.968–1.114)	0.294
HBGI (day 3–day 12)			LBGI (day 3–day 12)		
Univariate	1.122 (1.025–1.227)	0.012	Univariate	1.104 (0.948–1.286)	0.202
Model 1	1.118 (1.020–1.225)	0.017	Model 1	1.118 (0.939–1.330)	0.211
Model 2	1.137 (1.034–1.251)	0.008	Model 2	1.111 (0.932–1.325)	0.239
Model 3	1.135 (1.031–1.249)	0.010	Model 3	1.114 (0.934–1.329)	0.229

The results are the median values (interquartile range) or percentages. The Mann–Whitney U test was used to compare continuous variables, and the chi-square test or Fisher's exact test was used to compare categorical data.

Abbreviations: CI, confidence interval; CV, coefficient of variation; GRI, glycemia risk index; HBGI, high blood glucose index; HyperCompo, hyperglycemia component; HypoCompo, hyperglycemia component; LBGI, low blood glucose index; OR, odds ratio; SG, sensor glucose; TAR, time above range; TBR, time below range; TIR, time in range.

Supplementary Table 4. Relationship between medial temporal atrophy and glycemic control index

	Z-scores in the target VOI				
	β	*P*		*β*	*P*
Mean SG (day 3–day 12)			CV (day 3–day 12)		
Univariate	0.074	0.370	Univariate	-0.061	0.457
Model 1	0.042	0.594	Model 1	-0.062	0.428
Model 2	0.071	0.371	Model 2	-0.067	0.425
TIR (day 3–day 12)			$TAR^{>250}$ (day 3–day 12)		
Univariate	-0.032	0.694	Univariate	0.134	0.104
Model 1	-0.020	0.797	Model 1	0.093	0.240
Model 2	-0.053	0.510	Model 2	0.115	0.146
$TAR^{>180}$ (day 3–day 12)			$TBR^{<70}$ (day 3–day 12)		
Univariate	0.044	0.589	Univariate	-0.043	0.599
Model 1	0.023	0.767	Model 1	-0.013	0.870
Model 2	0.057	0.474	Model 2	-0.023	0.767
$TBR^{<54}$ (day 3–day 12)			GRI (day 3–day 12)		
Univariate	0.036	0.664	Univariate	0.034	0.684
Model 1	0.057	0.466	Model 1	0.030	0.699
Model 2	0.040	0.610	Model 2	0.058	0.466
HyperCompo (day 3–day 12)			HypoCompo (day 3–day 12)		
Univariate	0.076	0.358	Univariate	-0.038	0.644
Model 1	0.047	0.551	Model 1	-0.008	0.920
Model 2	0.078	0.325	Model 2	-0.019	0.810

HBGI (day 3–day 12)			LBGI (day 3–day 12)		
Univariate	0.069	0.400	Univariate	0.022	0.793
Model 1	0.043	0.586	Model 1	0.016	0.843
Model 2	0.069	0.378	Model 2	0.003	0.967

A simple linear regression analysis was performed with the Z-score in the volume of interest (VOI) as the objective variable and each glycemic control index as the explanatory variable. A multiple regression analysis was then performed on each glycemic control index plus age as explanatory variables in Model 1. Furthermore, in Model 2, a multiple regression analysis was performed by adding sex, body mass index, presence of hypertension and dyslipidemia, history of cerebrovascular disease, and smoking as explanatory variables to Model 1.

Abbreviations: β, standardized partial regression coefficient; CV, coefficient of variation; GRI, glycemia risk index; HBGI, high blood glucose index; HyperCompo, hyperglycemia component; HypoCompo, hypoglycemia component; LBGI, low blood glucose index; SG, sensor glucose; TAR, time above range; TBR, time below range; TIR, time in range.