

Glycemic patterns assessed by continuous glucose monitoring in people with type 2 diabetes treated with insulin glargine 100 U/mL in primary care: the GPDetect Study.

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Running title: Glycemic patterns by CGM in basal insulin T2D

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** A list of the study group members appears in the Supplementary Appendix.

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Supplementary Material

Bellido et al. “Glycemic patterns assessed by continuous glucose monitoring in people with type 2 diabetes treated with insulin glargine 100 U/mL in primary care: the GPDetect Study”.

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Supplementary Table S1

Supplementary Table S1: Concomitant medication (N=136).

Concomitant medication* category	n (%)**
Cardiovascular system	128 (94.1)
Alimentary tract metabolism	91 (66.9)
Nervous system	86 (63.2)
Blood and blood forming organs	80 (58.8)
Respiratory system	26 (19.1)
Genitourinary system and sex hormones	24 (17.6)
Muscle-skeletal system	22 (16.2)
Sensory Organs	14 (10.3)
Systemic hormonal preparations***	12 (8.8)
Anti-infectives for systemic use	6 (4.4)
Antineoplastic and immunomodulating agents	6 (4.4)
Dermatological agents	4 (2.9)

Concomitant medication was coded according to the current version of the Anatomical Therapeutic Chemical (ATC) classification.

* Refers to the 2-month period prior to signing of the informed consent

** Multiple response table, so the sum of percentages may exceed 100%.

*** Excludes sex hormones and insulins

ATC= Anatomical Therapeutic Chemical.

Supplementary Table S2

Supplementary Table S2: Analysis according to the use of SGLT2i (N=136).

	SGLT2i as non-insulin treatment		
	No	Yes	<i>p</i> value
N (%)	60 (44.1)	76 (55.9)	-
Variable			
Age	71.0 (10.4)	68.7 (8.2)	0.15 ^a
Sex, <i>n</i> (%)			
Male	35 (58.3)	50 (65.8)	0.37 ^b
Female	25 (41.7)	26 (34.2)	
Ethnicity, <i>n</i> (%)			
Caucasian	60 (100.0)	75 (98.7)	>0.99 ^c
Other	0 (0.0)	1 (1.3)	
	<i>Clinical</i>		
T2DM family history, <i>n</i> (%)			
Yes	27 (50.0)	26 (36.6)	0.13 ^b
No	27 (50.0)	45 (63.4)	
Relevant disease and/or surgery, <i>n</i> (%**)			
Yes	10 (16.7)	16 (21.1)	0.52 ^b
No	50 (83.3)	60 (78.9)	
Active smoker, <i>n</i> (%)			
Yes	52 (86.7)	63 (86.3)	0.95 ^b
No	8 (13.3)	10 (13.7)	
Hypertension, <i>n</i> (%)			
Yes	13 (21.7)	17 (22.7)	0.89 ^b
No	47 (78.3)	58 (77.3)	
Dyslipidemia, <i>n</i> (%)			
Yes	16 (26.7)	16 (21.3)	0.47 ^b
No	44 (73.3)	59 (78.7)	
T2DM evolution time, years	18.4 (7.1)	16.8 (6.3)	0.36 ^d
Age T2DM diagnosis, years	- (11.2)	51.7 (10.2)	0.94 ^d
Complications associated with diabetes, <i>n</i> (%)			
Nephropathy	13 (21.7)	15 (19.7)	0.78 ^b
Neuropathy	5 (8.3)	7 (9.2)	0.86 ^b
Retinopathy	14 (23.3)	19 (25.0)	0.82 ^b
Cerebrovascular disease	4 (6.7)	6 (7.9)	>0.99 ^c
Ischemia	4 (6.7)	9 (11.8)	0.31 ^b
Coronary artery disease	8 (13.3)	15 (19.7)	0.32 ^b
Arrhythmia	3 (5.0)	6 (7.9)	0.73 ^c
Ketoacidosis	1 (1.7)	0 (0.0)	0.44 ^c
Other	1 (1.7)	3 (3.9)	0.63 ^c
HbA1c levels, %	7.7 (0.5)	7.6 (0.5)	0.28 ^d
FPG, mg/dL	131.5 (34.2)	130.4 (32.3)	0.82 ^d
SMBG, mg/dL			

	SGLT2i as non-insulin treatment		
	No	Yes	<i>p</i> value
1st SMBG measure	118.8 (19.1)	115.7 (17.1)	0.45 ^d
2nd SMBG measure	116.8 (15.7)	118.6 (16.9)	0.73 ^d
3rd SMBG measure	118.1 (18.5)	119.8 (16.5)	0.70 ^d
Mean blood glucose*	117.9 (13.4)	118.0 (13.5)	0.95 ^d
<i>Anthropometric</i>			
Weight, Kg	77.3 (13.4)	80.7 (13.0)	0.14 ^a
Height, m	1.6 (0.1)	1.7 (0.1)	0.40 ^a
BMI†	28.8 (4.6)	29.5 (3.8)	0.36 ^a
Waist circumference, cm	101.5 (11.3)	102.0 (11.9)	0.84 ^a
SBP, mmHg	138.8 (17.9)	136.9 (16.3)	0.53 ^a
DBP, mmHg	76.9 (9.3)	79.4 (9.8)	0.13 ^a
HR, bpm	76.5 (11.6)	78.5 (11.8)	0.34 ^a
<i>Laboratory</i>			
Creatinine, mg/dL	0.9 (0.3)	1.0 (0.3)	0.80 ^a
eGFR, mL/min/1.73 m²	75.1 (18.6)	75.5 (19.2)	0.91 ^a
Uric acid, mg/dL	5.5 (1.6)	5.2 (1.7)	0.41 ^a
Total cholesterol, mg/dL	159.5 (35.3)	159.6 (40.6)	0.98 ^a
LDL cholesterol, mg/dL	82.3 (24.6)	81.5 (35.0)	0.89 ^a
HDL cholesterol, mg/dL	44.8 (10.8)	47.2 (16.9)	0.36 ^a
Triglycerides, mg/dL	162.6 (87.8)	162.4 (67.8)	0.99 ^a
AST/GOT, UI/L	19.8 (9.3)	33.2 (49.3)	0.07 ^a
ALT/GPT, UI/L	24.3 (16.5)	30.1 (45.4)	0.44 ^a
C-peptide, mg/dL	1.3 (1.4)	1.3 (0.9)	0.92 ^a
<i>T2DM treatment</i>			
Insulin glargine-100 U/mL	30.1 (11.0)	30.9 (13.0)	0.98 ^d
Daily Dose			
Daily dose, IU/ [weight (Kg)]	0.40 (0.16)	0.39 (0.16)	0.61 ^d
Daily dose, IU/ [weight (Kg)] ‡	0.40 (0.16)	0.39 (0.16)	0.58 ^d
Non-insulin treatments, n (%)			
Use of non-insulin treatments			
No	4 (6.7)	0 (0.0)	0.036^c
Yes	56 (93.3)	76 (100.0)	
<i>Biguanides</i>	45 (75.0)	61 (80.3)	0.46 ^b
<i>SGLT2i</i>	5 (8.3)	1 (1.3)	0.09 ^c
<i>DPP-4 inhibitor</i>	4 (6.7)	9 (11.8)	0.31 ^c
<i>GLP-1 agonist</i>	2 (3.3)	0 (0.0)	0.19 ^c
<i>Glinides</i>	1 (1.7)	0 (0.0)	0.44 ^c
<i>Sulfonylureas</i>	8 (13.3)	23 (30.3)	0.019^b
<i>Thiazolidinediones</i>	30 (50.0)	24 (31.6)	0.029^b
<i>History of hypoglycemia§</i>			
Event incidence, n (%)			
Level 1	7 (11.7)	6 (7.9)	0.56 ^c
Level 2	3 (5.0)	0 (0.0)	0.08 ^c
Level 3	1 (1.7)	0 (0.0)	0.44 ^c
Hypoglycemic events			
Level 1	1.6 (3.1)	1.2 (4.2)	0.377
Level 2	0.4 (1.0)	0.0 (0.0)	0.352
Level 3	0.1 (0.3)	0.0 (0.0)	0.765

	SGLT2i as non-insulin treatment		
	No	Yes	<i>p</i> value
<i>Questionnaires</i>			
EsHFS total score	60.0 (21.6)	53.0 (21.4)	0.043^d
MMSE total score	28.3 (3.1)	28.4 (3.2)	0.56 ^d
<i>Primary endpoint</i>			
Percent of patients with TBR (glucose <70 mg/dL), <i>n</i> (%)			
≤ 4%	50 (83.3)	63 (82.9)	0.95 ^b
> 4%	10 (16.7)	13 (17.1)	
<i>Secondary endpoints</i>			
<i>Glycemic control during CGM</i>			
Number of 24-hours days CGM data were collected	13.5 (1.1)	13.1 (1.4)	0.21 ^d
Percentage of time CGM is active	100.0 (0.0)	100.0 (0.1)	0.92 ^d
Average glucose, <i>mg/dL</i>	163.7 (38.3)	148.0 (26.7)	0.013^d
CV	29.5 (6.8)	28.1 (5.4)	0.11 ^d
<i>Patients with a CV ≤36%, n (%)</i>	53 (88.3)	72 (94.7)	0.21 ^c
<i>Patients with a CV >36%, n (%)</i>	7 (11.7)	4 (5.3)	
GMI [§] , %	7.2 (0.9)	6.8 (0.6)	0.013^d
TIR (glucose 70-180 mg/dL)			
Patients with TIR ≥ 70%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	25 (41.7)	51 (67.1)	0.003^b
<i>Daytime (06:00-23:59)</i>	23 (38.3)	49 (64.5)	0.002^b
<i>Nighttime (00:00-05:59)</i>	31 (51.7)	57 (75.0)	0.005^b
Mean minutes/day in TIR			
<i>Full day (24 hours)</i>	893.9 (316.5)	1068.4 (242.5)	0.001^d
<i>Daytime (06:00-23:59)</i>	866.8 (331.2)	1042.8 (258.5)	0.001^d
<i>Nighttime (00:00-05:59)</i>	975.4 (324.1)	1144.1 (242.0)	0.001^d
TBR			
Patients with TBR (glucose 54-69 mg/dL)			
≤ 4%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	50 (83.3)	63 (82.9)	0.945 ^b
<i>Daytime (06:00-23:59)</i>	53 (88.3)	66 (86.8)	0.79 ^b
<i>Nighttime (00:00-05:59)</i>	47 (78.3)	57 (75.0)	0.65 ^b
Mean minutes/day in TBR (glucose 54-69 mg/dL)			
<i>Full day (24 hours)</i>	35.7 (83.9)	26.4 (43.0)	0.56 ^d
<i>Daytime (06:00-23:59)</i>	30.0 (75.1)	21.2 (34.0)	0.63 ^d
<i>Nighttime (00:00-05:59)</i>	52.6 (118.6)	42.2 (77.9)	0.92 ^d
Patients with TBR (glucose <54 mg/dL) ≤1%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	53 (88.3)	71 (93.4)	0.30 ^b
<i>Daytime (06:00-23:59)</i>	54 (90.0)	75 (98.7)	0.044^c
<i>Nighttime (00:00-05:59)</i>	51 (85.0)	64 (84.2)	0.90 ^b
Mean minutes/day in TBR (glucose < 54 mg/dL)			
<i>Full day (24 hours)</i>	6.4 (18.6)	3.4 (11.6)	0.63 ^d
<i>Daytime (06:00-23:59)</i>	5.0 (15.5)	1.9 (7.2)	0.77 ^d

	SGLT2i as non-insulin treatment		
	No	Yes	p value
<i>Nighttime (00:00-05:59)</i>	10.4 (31.2)	7.8 (26.5)	0.84 ^d
TAR			
Patients with TAR			
(glucose 181-250 mg/dL)			
≤ 25%, n (%)			
<i>Full day (24 hours)</i>	25 (41.7)	48 (63.2)	0.013^b
<i>Daytime (06:00-23:59)</i>	21 (35.0)	42 (55.3)	0.019^b
<i>Nighttime (00:00-05:59)</i>	35 (58.3)	56 (73.7)	0.06 ^b
Mean minutes/day in TAR			
(glucose 181-250 mg/dL)			
<i>Full day (24 hours)</i>	359.4 (185.6)	286.7 (186.4)	0.021^d
<i>Daytime (06:00-23:59)</i>	380.5 (190.3)	311.4 (191.2)	0.026^d
<i>Nighttime (00:00-05:59)</i>	295.7 (221.4)	213.3 (212.8)	0.028^d
Patients with TAR			
(glucose >250 mg/dL) ≤5%, n (%)			
<i>Full day (24 hours)</i>	34 (56.7)	63 (82.9)	0.001^b
<i>Daytime (06:00-23:59)</i>	32 (53.3)	61 (80.3)	0.001^b
<i>Nighttime (00:00-05:59)</i>	40 (66.7)	67 (88.2)	0.002^b
Mean minutes/day in TAR			
(glucose >250 mg/dL)			
<i>Full day (24 hours)</i>	144.7 (213.0)	55.1 (105.2)	0.004^d
<i>Daytime (06:00-23:59)</i>	157.6 (213.4)	62.7 (124.0)	0.005^d
<i>Nighttime (00:00-05:59)</i>	105.9 (239.1)	32.6 (68.5)	0.033^d

Data for variables are presented as mean (SD), unless otherwise indicated.

* Mean blood glucose profile based on three capillary blood glucose measurements (mg/dL).

† BMI= weight/(height)².

‡ With mean imputation for weight.

§ Hypoglycemia data is shown for level 1 (glucose 54-69 mg/dL), level 2 (glucose <54 mg/dL) and level 3, which is a serious event characterized by an altered mental and/or physical state requiring assistance²⁹.

¥ GMI= 3.31 + 0.02392 x (glucose value reading in mg/dL)

^a T-test; ^b Chi-Square; ^c Fisher's exact test; ^d Mann-Whitney.

ALT= Alanine Aminotransferase; AST= Aspartate Aminotransferase; CGM= Continuous Glucose Monitoring; CV= Coefficient of Variation; DBP= Diastolic blood pressure; DPP-4= Dipeptidyl peptidase-4; eGFR= estimated Glomerular Filtration Rate; EsHFS= Hypoglycemia Fear Survey in Spanish; FPG= Fast Plasma Glucose; GLP-1= Glucagon-like peptide-1; GMI= Glucose Management Index; GOT= serum Glutamic Oxaloacetic Transaminase; GPT= serum Glutamic Pyruvic Transaminase; HbA1c= glycated hemoglobin; HDL= High-density Lipoprotein; HR= Heart rate; LDL= Low-density Lipoprotein; MMSE= Mini-Mental Cognitive Examination; SBP= Systolic blood pressure; SD= Standard Deviation; SGLT2i= Sodium-glucose cotransporter-2 inhibitor; SMBG= Self Measured Plasma Glucose; T2DM= Type 2 Diabetes mellitus; TAR= Time above Range; TBR= Time Below Range; TIR= Time in Range; IU= International Units.

Supplementary Table S3

Supplementary Table S3: Analysis according to the timing of basal insulin administration (N=127*).

	Schedule of insulin administration		
	Morning	Evening	<i>p</i> value
N (%)	47 (37.0)	80 (63.0)	-
<u>Variable</u>			
Age	70.4 (9.7)	69.4 (9.2)	0.55 ^a
Sex, <i>n</i> (%)			
Male	32 (68.1)	46 (57.5)	0.24 ^b
Female	15 (31.9)	34 (42.5)	
Ethnicity, <i>n</i> (%**)			
Caucasian	47 (100.0)	79 (98.8)	>0.99 ^c
Other	0 (0.0)	1 (1.3)	
<i>Clinical</i>			
T2DM family history, <i>n</i> (%**)			
Yes	20 (47.6)	49 (66.2)	0.05^b
No	22 (52.4)	25 (33.8)	
Relevant disease and/or surgery, <i>n</i> (%**)			
Yes	35 (74.5)	67 (83.8)	0.20 ^b
No	12 (25.5)	13 (16.3)	
Active smoker, <i>n</i> (%**)			
Yes	7 (15.6)	9 (11.4)	0.51 ^b
No	38 (84.4)	70 (88.6)	
Hypertension, <i>n</i> (%**)			
Yes	37 (80.4)	60 (75.0)	0.48 ^b
No	9 (19.6)	20 (25.0)	
Dyslipidemia, <i>n</i> (%**)			
Yes	37 (80.4)	57 (71.3)	0.25 ^b
No	9 (19.6)	23 (28.8)	
T2DM evolution time, years	17.1 (6.9)	18.1 (6.7)	0.29 ^d
Age T2DM diagnosis, years	53.1 (9.7)	52.0 (11.1)	0.27 ^a
Complications associated with diabetes, <i>n</i> (%**)			
Retinopathy	9 (19.1)	24 (30.0)	0.18 ^b
Nephropathy	8 (17.0)	18 (22.5)	0.46 ^b
Coronary artery disease	8 (17.0)	13 (16.3)	0.91 ^b
Ischemia	5 (10.6)	8 (10.0)	>0.99 ^c
Neuropathy	3 (6.4)	8 (10.0)	0.74 ^c
Cerebrovascular disease	3 (6.4)	6 (7.5)	>0.99 ^c
Arrhythmia	3 (6.4)	5 (6.3)	>0.99 ^c
Ketoacidosis	0 (0.0)	1 (1.3)	>0.99 ^c
Other	1 (2.1)	3 (3.8)	>0.99 ^c
HbA1c levels, %	7.5 (0.4)	7.7 (0.5)	0.002^d
FPG, mg/dL	128.1 (33.7)	135.3 (33.1)	0.20 ^d
SMBG, mg/dL			
1st SMBG measure	118.4 (18.6)	116.9 (17.9)	0.77 ^d
2nd SMBG measure	115.8 (14.0)	119.4 (18.0)	0.30 ^d

	Schedule of insulin administration		
	Morning	Evening	<i>p</i> value
3rd SMBG measure	119.5 (17.1)	118.2 (18.1)	0.79 ^d
Mean blood glucose***	117.9 (12.8)	118.2 (14.2)	0.81 ^d
<i>Anthropometric</i>			
Weight, Kg	77.0 (12.4)	79.7 (13.4)	0.26 ^a
Height, m	1.6 (0.1)	1.6 (0.1)	0.93 ^a
BMI†	28.4 (3.5)	29.5 (4.5)	0.17 ^a
Waist circumference, cm	98.9 (12.9)	102.9 (10.2)	0.11 ^a
SBP, mmHg	134.7 (13.4)	140.0 (18.9)	0.07 ^a
DBP, mmHg	76.6 (8.8)	79.0 (9.8)	0.18 ^a
HR, bpm	76.2 (11.7)	77.8 (11.6)	0.48 ^a
<i>Laboratory</i>			
Creatinine, mg/dL	0.9 (0.2)	1.0 (0.3)	0.17 ^a
eGFR, mL/min/1.73 m²	78.1 (15.3)	73.3 (20.8)	0.15 ^a
Uric acid, mg/dL	5.1 (1.4)	5.4 (1.7)	0.39 ^a
Total cholesterol, mg/dL	158.8 (35.3)	158.9 (39.5)	0.98 ^a
LDL cholesterol, mg/dL	83.9 (31.1)	81.4 (30.1)	0.68 ^a
HDL cholesterol, mg/dL	45.3 (10.8)	46.9 (16.6)	0.58 ^a
Triglycerides, mg/dL	165.0 (71.7)	154.8 (74.1)	0.47 ^a
AST/GOT, UI/L	32.9 (52.8)	24.5 (32.8)	0.40 ^a
ALT/GPT, UI/L	32.5 (58.0)	24.4 (18.5)	0.32 ^a
C-peptide, mg/dL	1.5 (1.4)	1.3 (1.0)	0.73 ^a
<i>T2DM treatment</i>			
Insulin glargine-100 U/mL	29.9 (11.4)	29.2 (10.7)	0.85 ^d
Daily Dose			
Daily dose, U/ [weight (Kg)]	0.40 (0.16)	0.37 (0.13)	0.29 ^a
Daily dose, U/ [weight (Kg)] ‡	0.39 (0.16)	0.37 (0.13)	0.33 ^a
Non-insulin treatments, n (%**)			
Use of non-insulin treatments			
No	1 (2.1)	3 (3.8)	>0.99 ^c
Yes	46 (97.9)	77 (96.3)	
<i>Biguanides</i>	38 (80.9)	60 (75.0)	0.45 ^b
<i>SGLT2i</i>	28 (59.6)	43 (53.8)	0.52 ^c
<i>DPP-4 inhibitor</i>	18 (38.3)	32 (40.0)	0.85 ^c
<i>GLP-1 agonist</i>	10 (21.3)	20 (25.0)	0.63 ^b
<i>Glinides</i>	2 (4.3)	8 (10.0)	0.32 ^c
<i>Sulfonylureas</i>	1 (2.1)	5 (6.3)	0.41 ^c
<i>Thiazolidinediones</i>	0 (0.0)	1 (1.3)	>0.99 ^c
<i>History of hypoglycemia§</i>			
Event incidence, n (%**)			
Level 1	3 (6.4)	8 (10.0)	0.74 ^c
Level 2	0 (0.0)	0 (0.0)	>0.99 ^c
Level 3	0 (0.0)	0 (0.0)	>0.99 ^c
Hypoglycemic events			
Level 1	2.00 (5.72)	0.54 (0.93)	0.88 ^d
Level 2	0.00 (0.0)	0.14 (0.64)	0.84 ^d
Level 3	0.00 (0.0)	0.05 (0.21)	0.84 ^d
<i>Questionnaires</i>			

	Schedule of insulin administration		
	Morning	Evening	<i>p</i> value
EsHFS total score	57.7 (22.8)	56.0 (21.4)	0.66 ^d
MMSE total score	28.5 (3.1)	28.2 (3.3)	0.97 ^d
<i>Primary endpoint</i>			
Percent of patients with TBR (glucose <70 mg/dL), <i>n</i> (%)			
≤ 4%	41 (87.2)	66 (82.5)	0.48 ^b
> 4%	6 (12.8)	14 (17.5)	
<i>Secondary endpoints</i>			
<i>Glycemic control during CGM</i>			
Number of 24-hours days CGM data were collected	13.3 (1.1)	13.3 (1.3)	0.62 ^d
Percentage of time CGM is active	100.0 (0.2)	100.0 (0.1)	0.63 ^d
Average glucose, mg/dL	154.5 (32.6)	155.6 (34.7)	0.76 ^d
CV	28.4 (5.7)	28.8 (6.5)	0.86 ^d
<i>Patients with a CV ≤36%, n (%)</i>	43 (91.5)	73 (91.3)	>0.99 ^c
<i>Patients with a CV >36%, n (%)</i>	4 (8.5)	7 (8.8)	
GMI [‡] , %	7.0 (0.8)	7.0 (0.8)	0.76 ^d
TIR (glucose 70-180 mg/dL)			
Patients with TIR ≥ 70%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	24 (51.1	47 (58.8)	0.40 ^b
	)		
<i>Daytime (06:00-23:59)</i>	22 (46.8)	45 (56.3)	0.30 ^b
<i>Nighttime (00:00-05:59)</i>	33 (70.2)	49 (61.3)	0.31 ^b
Mean minutes/day in TIR			
<i>Full day (24 hours)</i>	996.7 (277.1)	986.5 (306.2)	0.93 ^d
<i>Daytime (06:00-23:59)</i>	963.2 (300.3)	964.5 (317.1)	0.86 ^d
<i>Nighttime (00:00-05:59)</i>	1095.6 (271.3)	1052.5 (309.3)	0.52 ^d
TBR			
Patients with TBR (glucose 54-69 mg/dL)			
≤ 4%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	41 (87.2)	66 (82.5)	0.48 ^b
<i>Daytime (06:00-23:59)</i>	41 (87.2)	72 (90.0)	0.64 ^b
<i>Nighttime (00:00-05:59)</i>	38 (80.9)	61 (76.3)	0.55 ^b
Mean minutes/day in TBR (glucose 54-69 mg/dL)			
<i>Full day (24 hours)</i>	29.9 (85.5)	30.6 (51.3)	0.47 ^d
<i>Daytime (06:00-23:59)</i>	26.4 (75.9)	23.9 (43.3)	0.59 ^d
<i>Nighttime (00:00-05:59)</i>	40.4 (117.6)	50.5 (88.7)	0.15 ^d
Patients with TBR (glucose <54 mg/dL) ≤ 1%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	43 (91.5)	74 (92.5)	>0.99 ^c
<i>Daytime (06:00-23:59)</i>	45 (95.7)	75 (93.8)	>0.99 ^c
<i>Nighttime (00:00-05:59)</i>	39 (83.0)	69 (86.3)	0.62 ^b
Mean minutes/day in TBR (glucose < 54 mg/dL)			
<i>Full day (24 hours)</i>	3.9 (8.2)	5.3 (18.5)	0.18 ^d

	Schedule of insulin administration		
	Morning	Evening	<i>p</i> value
<i>Daytime (06:00-23:59)</i>	2.5 (6.1)	3.9 (14.4)	0.18 ^d
<i>Nighttime (00:00-05:59)</i>	8.0 (19.0)	9.6 (34.0)	0.72 ^d
TAR			
Patients with TAR (glucose 181-250 mg/dL) ≤ 25%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	23 (48.9)	45 (56.3)	0.42 ^b
<i>Daytime (06:00-23:59)</i>	20 (42.6)	38 (47.5)	0.59 ^b
<i>Nighttime (00:00-05:59)</i>	32 (68.1)	53 (66.3)	0.83 ^b
Mean minutes/day in TAR (glucose 181-250 mg/dL)			
<i>Full day (24 hours)</i>	320.9 (193.7)	314.2 (187.2)	0.77 ^d
<i>Daytime (06:00-23:59)</i>	346.5 (207.0)	335.9 (186.8)	0.78 ^d
<i>Nighttime (00:00-05:59)</i>	245.5 (212.6)	248.8 (222.5)	0.94 ^d
Patients with TAR (glucose >250 mg/dL) ≤5%, <i>n</i> (%)			
<i>Full day (24 hours)</i>	36 (76.6)	54 (67.5)	0.28 ^b
<i>Daytime (06:00-23:59)</i>	34 (72.3)	53 (66.3)	0.48 ^b
<i>Nighttime (00:00-05:59)</i>	38 (80.9)	61 (76.3)	0.55 ^b
Mean minutes/day in TAR (glucose >250 mg/dL)			
<i>Full day (24 hours)</i>	88.6 (145.8)	103.6 (186.4)	0.93 ^d
<i>Daytime (06:00-23:59)</i>	101.5 (168.6)	111.9 (187.5)	0.97 ^d
<i>Nighttime (00:00-05:59)</i>	50.4 (105.1)	78.7 (205.7)	0.45 ^d

Data for variables are presented as mean (SD), unless otherwise indicated.

* The following patients were excluded from the analysis: (i) those receiving insulin twice daily (morning/evening) (N=4), (ii) those without a defined administration pattern (N=4), and (iii) one patient administering insulin at noon (N=1).

** Percentages were calculated based on the total number of patients following a morning (N=47) or evening (N=80) insulin administration schedule.

*** Mean blood glucose profile based on three capillary blood glucose measurements (mg/dL).

† BMI= weight/(height)².

‡ With mean imputation for weight.

§ Hypoglycemia data is shown for level 1 (glucose 54-69 mg/dL), level 2 (glucose <54 mg/dL) and level 3, which is a serious event characterized by an altered mental and/or physical state requiring assistance ²⁹.

¥ GMI= 3.31 + 0.02392 x (glucose value reading in mg/dL)

^a T-test; ^b Chi-Square; ^c Fisher's exact test; ^d Mann-Whitney.

ALT= Alanine Aminotransferase; AST= Aspartate Aminotransferase; CGM= Continuous Glucose Monitoring; CV= Coefficient of Variation; DBP= Diastolic blood pressure; DPP-4= Dipeptidyl peptidase-4; eGFR= estimated Glomerular Filtration Rate; EsHFS= Hypoglycemia Fear Survey in Spanish; FPG= Fast Plasma Glucose; GLP-1= Glucagon-like peptide-1; GMI= Glucose Management Index; GOT= serum Glutamic Oxaloacetic Transaminase; GPT= serum Glutamic Pyruvic Transaminase; HbA1c= glycated hemoglobin; HDL= High-density Lipoprotein; HR= Heart rate; LDL= Low-density Lipoprotein; MMSE= Mini-Mental Cognitive Examination; SBP= Systolic blood pressure; SD= Standard Deviation; SGLT2i= Sodium-glucose cotransporter-2 inhibitor; SMBG= Self Measured Plasma Glucose; T2DM= Type 2 Diabetes mellitus; TAR= Time above Range; TBR= Time Below Range; TIR= Time in Range; U= Units.

Supplementary Table S4

Supplementary Table S4: CGM monitoring technical issues (N=136).

	n (%)
Has the patient reported any technical issues related to the CGM* device?	
No	110 (80.9)
ND	1 (0.7)
Yes	25 (18.4)
<i>Accidental sensor removal</i>	16 (64.0) †
<i>Sensor activation error</i>	1 (4.0) †
<i>Sensor reading error</i>	8 (32.0) †

* FreeStyle Libre® Pro iQ® (Abbott Laboratories).

† Percentage calculated for a total of N=25 patients who reported technical issues.

CGM= Continuous Glucose Monitoring.