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Glycemic control and variability in association with body mass index and body composition over 18 months in youth with type 1 diabetes

Leah M. Lipsky^{a,*}, Benjamin Gee^a, Aiyi Liu^b, and Tonja R. Nansel^a

^aHealth Behavior Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, North Bethesda, MD, United States

^bBiostatistics and Bioinformatics Branch, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, North Bethesda, MD, United States

Abstract

Aims: The impact of adiposity on glycemic control in type 1 diabetes patients has important implications for preventing complications. This study examined associations of glycemic outcomes with body mass index (BMI, kg/m²) and body composition in youth with type 1 diabetes.

Methods: This is a secondary analysis of an 18-month randomized controlled dietary intervention trial ($N = 136$, baseline age = 12.3 ± 2.5 y, HbA1c = $8.1 \pm 1.0\%$ (65 ± 11 mmol/mol)). Measured height and weight every 3 months were abstracted from medical records. Body composition was assessed by dual energy X-ray absorptiometry (DXA) at baseline, 12 and 18 months. Glycated hemoglobin (HbA1c) and glycemic variability assessed by masked 3-day continuous blood glucose monitoring (CGM) were obtained every 3 months. 1,5-Anhydroglucitol (1,5-AG) was assessed every 6 months. Adjusted random effects models for repeated measures estimated associations of time-varying BMI and body composition with time-varying glycemic outcomes.

Results: There was no treatment effect on glycemic outcomes. HbA1c was not associated with BMI or body composition indicators. 1,5-AG was inversely associated with BMI and adiposity indicators (%fat, trunk fat mass and trunk %fat), adjusting for developmental covariates. Adiposity indicators were positively associated with %glucose >180 mg/dL and >126 mg/dL when adjusting for developmental covariates, and %glucose >126 mg/dL when additionally adjusting for diabetes-related covariates. Fewer consistent relationships were observed for 3-day mean glucose and

*Corresponding author. lipskylm@mail.nih.gov (L.M. Lipsky).

Author contributions

L.L. conceived the paper, designed and conducted the analysis, interpreted the data and wrote the manuscript. T.R.N. designed and led the main research study, interpreted the data and reviewed and edited the manuscript. B.G. contributed to data analysis and interpretation, drafting of the manuscript, and critically reviewing and editing the manuscript. A.L. contributed to study design, statistical analysis, interpretation of the data, and critical review of the manuscript. All authors approved the final version.

Conflicts of interest

None.

%glucose <70.2 mg/dL. BMI and body composition variables were not associated with standard deviation of glycemic values or mean amplitude of glycemic excursions.

Conclusions: The role of greater BMI and adiposity in diabetes management in youth with type 1 diabetes may relate specifically to increased hyperglycemic excursions.

Keywords

Body mass index; Body composition; Diabetes mellitus, type 1; Adolescent; Hemoglobin A glycosylated; 1,5-Anhydroglucitol

1. Introduction

The overall impact of body weight and adiposity on glycemic control in patients with type 1 diabetes is unclear. Despite the macro- and micro-vascular benefits of glycemic control achieved through intensive insulin treatment in patients with type 1 diabetes [1], numerous studies have shown increased risk of weight gain [2,3], which in turn may have adverse cardiovascular effects [4,5]. Increased adiposity in this population has been associated with increased insulin resistance [6–8], which may adversely impact glycemic control [9]. Reported associations of glycated hemoglobin (HbA1c) with body mass index (BMI, kg/m²) are inconsistent with regards to direction, magnitude and significance [10–13]. While findings from a recent prospective study of U.S. youth suggest that modest weight gain is associated with concomitant improvement in glycemic control [14], other studies have reported both positive [10,15] and null associations [12,16]. Differences in study design, analytic methods, and advancements in treatment regimen likely contribute to discrepancies in the findings.

Research on the association of glycemic control with body weight in type 1 diabetes patients has relied almost exclusively on BMI as a measure of adiposity. While BMI is strongly correlated with body fat, it is an indirect measure, and does not reflect body fat distribution [17], which may be differentially associated with glycemic control. Similarly, while HbA1c is the clinical benchmark for assessing chronic glycemic control, the measure does not reflect short-term glucose excursions shown to predict diabetes complications [18]. Complementary measures of overall glycemic control include 1,5-anhydroglucitol (1,5-AG), which is sensitive to recent glucose excursions in moderately well-controlled type 1 diabetes [19–22], and continuous glucose monitoring, which can be used to assess glycemic variability. To our knowledge, the associations of BMI and body composition with 1,5-AG and glycemic variability have not been evaluated. Examination of these relationships may reveal important mechanistic linkages between weight status, glycemic control, and diabetes complications.

The purpose of this study is to estimate the longitudinal associations of BMI and body composition with multiple indicators of glycemic control and variability in youth with type 1 diabetes participating in a randomized controlled dietary intervention trial.

2. Methods

2.1. Design, setting and recruitment

This is a secondary analysis of data from a randomized controlled trial of an intervention conducted from Aug 2010 to May 2013 at an outpatient, free-standing, multidisciplinary tertiary diabetes center in the northeast United States. Details regarding recruitment and randomization are described in detail elsewhere [23]. Eligibility criteria included age 8.0–16.9 years, diagnosis of type 1 diabetes ≥ 1 year, daily insulin dose ≥ 0.5 units per kilogram, most recent HbA1c $\geq 6.5\%$ (48 mmol/mol) and $\leq 10.0\%$ (86 mmol/mol), with either an insulin regimen of ≥ 3 injections daily or insulin pump, at least one clinic visit in the past year, and ability to communicate in English. Exclusion criteria included daily use of premixed insulin, transition to insulin pump therapy in the last three months, real-time continuous glucose monitoring use in the last three months, participation in another intervention study in the last six months, and presence of gastrointestinal disease such as celiac disease, multiple food allergies, use of medications that interfere significantly with glucose metabolism, or significant mental illness.

Families were enrolled in the study for 18 months, and attended study visits in the clinic. Those in the intervention condition received six “core” sessions during the first seven months of the study period and three “booster” sessions during the next five months. Session content was designed to increase intake of whole plant foods (fruit, vegetables, whole grains, legumes, nuts and seeds); sessions focused on healthful eating but did not address weight management. Participants in the control condition received equal frequency of contacts with research staff. Further details regarding the intervention and control conditions have been previously reported [23]. At enrollment, all youth provided assent, and parents provided written informed consent; youth turning 18 years of age during the trial additionally provided written informed consent. Study procedures were approved by the institutional review boards of the participating institutions. Of 622 eligible families invited to participate, 148 (24%) enrolled in the study, 139 (22%) completed baseline assessments, and 136 were randomized to intervention or control group after excluding 1 sibling each from 3 sibling pairs. The primary reason for declining to participate was lack of time.

2.2. Measures

2.2.1. Body mass index (BMI) and body composition—Measured height and weight at clinic visits at baseline and at 3 months, 6 months, 9 months, 12 months and 18 months were abstracted from the medical records and used to calculate BMI (kg/m^2). Body composition was assessed by dual energy X-ray absorptiometry (DXA; Hologic Inc.) at baseline, 12 and 18 months. Body composition variables for these analyses included total fat mass (g), total lean mass (g), percent of total fat mass (%fat), trunk fat mass (g), trunk lean mass (g) and percent of trunk fat mass (trunk %fat).

2.2.2. Glycemic control—Glycated hemoglobin (HbA1c) was assessed at baseline and at 3 months, 6 months, 9 months, 12 months and 18 months during routine clinical care and processed on-site using a laboratory assay standardized to the Diabetes Control and Complications Trial (reference range, 4–6%, [20–42 mmol/mol]). Initial HbA1c assays were

performed with the Tosoh (Tosoh Medics, South San Francisco, CA, USA); subsequent assays were performed by the Roche Cobas Integra (Indianapolis, IN), and Tosoh values were standardized to the Roche assay. Samples were kept at room temperature for 20–30 min following collection, then centrifuged for 15 min at ~3000 RPM at temperature of 4 °C, aliquoted and frozen at –80 °C for later assay. 1,5-Anhydroglucitol (1,5-AG) was measured using enzymatic (glucokinase) assay (GlycoMark®, New York, NY, USA) at baseline and every 6 months.

Three-day masked continuous glucose monitoring (CGM) was implemented at baseline and at 3, 6, 9, 12, and 18 months using the Medtronic iPro™ Continuous Glucose Monitor. A diabetes nurse educator inserted the monitor subcutaneously and performed calibration according to standard operating guidelines. Participants were directed to conduct blood glucose checks four times per day before meals or at bedtime. The device was returned to the clinic and data downloaded for analysis at the end of the monitoring period. CGM data were summarized using the online version of the GlyCulator [24] to calculate measures of glycemic control and variability over 3 days including mean glucose, standard deviation, percent of glucose values (%glucose) >180 mg/dL (10 mmol/L), % glucose >126 mg/dL (7 mmol/L) and %glucose <70.2 mg/dL (4 mmol/L); mean amplitude of glycemic excursions (MAGE), which reflects major glucose swings, was also calculated as the arithmetic mean of differences between consecutive peaks and nadirs of more than 1 standard deviation. Data from participants at any time point where CGM record time was less than 24 h were not included.

2.2.3. Diabetes characteristics and Tanner stage—Insulin regimen, frequency of self-monitoring of blood glucose at each visit, and baseline diabetes duration calculated from the date of diagnosis were obtained from the medical records. Tanner criteria were obtained from the medical records using last observation carried forward for missing visit-specific data.

2.3. Analysis

Baseline characteristics were summarized using means and standard deviations for continuous variables and frequencies for categorical variables. Independent t-test and Pearson's χ^2 was used to evaluate baseline differences by treatment assignment.

Separate random effects models for repeated measurements were used to evaluate associations of time-varying glycemic outcomes with time-varying BMI and body composition variables. Three models were tested: Model 1 included only a covariate for time (days since baseline visit) and treatment assignment, Model 2 additionally adjusted for developmental characteristics (baseline age, sex, time-varying height, time-varying Tanner stage), and Model 3 additionally adjusted for diabetes-related variables (baseline diabetes duration, time-varying insulin regimen and time-varying frequency of self-monitoring of blood glucose). All analyses were performed using Stata version 14 (College Station, TX). Models use maximum likelihood estimation, using all available data for subjects with non-missing independent and dependent variables for a given visit in order to reduce bias relative to listwise deletion or complete case analysis [25].

3. Results

There were no treatment group differences in baseline sex, age or disease-related characteristics (Table 1). Total fat mass and %fat were higher at baseline in control versus intervention participants, while %glucose <70.2 mg/dL (3.9 mmol/L) was higher at baseline in the intervention group as compared with the control group.

Coefficient estimates from the random effects models indicate that time-varying HbA1c was not associated with BMI or body composition (Table 2). An inverse association of HbA1c with BMI in the two adjusted models did not reach statistical significance ($p = 0.06$). In contrast, 1,5-AG was inversely associated with BMI, %fat, trunk fat mass and trunk % fat in the base model and the model adjusted for developmental covariates, but only the association with %fat was statistically significant in the model additionally adjusted for diabetes-related covariates. Statistically significant inverse associations of 1,5-AG with total lean mass and trunk lean mass were observed only in the base model, and 1,5-AG was not significantly associated with total fat mass in any model.

Associations of CGM-assessed glycemic outcomes with BMI and body composition differed by model specification (Table 3). Total fat mass, %fat and trunk %fat were positively associated with %glucose >180 mg/dL (10 mmol/L) in models adjusted for developmental covariates, but associations were not statistically significant after additionally adjusting for diabetes-related covariates. Similarly, total fat mass and % fat were positively associated with 3-day mean blood glucose after adjusting for development covariates only. In contrast, total fat mass, %fat, trunk fat mass and trunk %fat were positively associated with %glucose >126 mg/dL (7 mmol/L) in both adjusted models. BMI and body composition variables were not associated with hypoglycemic excursions other than an inverse association with total fat mass in both adjusted models. Standard deviation and MAGE were not statistically significantly associated with BMI or body composition variables. There was no treatment effect on any of the glycemic outcomes (not shown).

4. Discussion

In this sample of youth with type 1 diabetes followed prospectively for 18 months, time-varying BMI and body composition were not associated with glycemic control as indicated by HbA1c, but were associated to varying degrees with 3-day mean blood glucose and hyperglycemic excursions as indicated by 1,5-AG and %glucose values above 126 mg/dL (7 mmol/L) and 180 mg/dL (10 mmol/L). On the other hand, BMI and body composition were not statistically significantly associated with the standard deviation of 3-day blood glucose values or hypoglycemic excursions (%glucose <70.2 mg/dL (3.9 mmol/L)) other than an inverse association of hypoglycemic excursions with total fat mass. Taken together, these findings suggest that the importance of increased BMI and adiposity in type 1 diabetes management in youth may relate specifically to the occurrence of hyperglycemia.

Previous studies of the association of glycemic control with BMI have been conducted primarily in the context of initiating intensive insulin therapy (IIT), and show a general association of IIT and improved glycemic control with weight gain [2,3,26,27]. Fewer

studies have examined the association of glycemic control with BMI in patients undergoing intensive regimens. One cross-sectional study of older Scottish adolescents and young adults, of whom 74% underwent IIT, demonstrated a correlation of higher BMI with lower HbA1c in men only [28]. We are aware of only one previous study examining the association of glycemic control with BMI in a repeated measures design, which showed an overall inverse association in longitudinal models, but no cross-sectional association at baseline [29]. In contrast, the inverse association of time-varying HbA1c with time-varying BMI in the current study did not reach statistical significance. Similarly, the current study did not replicate the bivariate association of poor metabolic control with greater percent body fat as estimated from skinfold measurements in 48 adolescent females with type 1 diabetes in Finland [16], or as indicated by greater abdominal fat:leg fat as assessed by DXA in a small sample ($n = 18$) of older adolescent females in Sweden [30]. Discrepancies in the findings may be attributable to differences in samples (e.g. source population and recruitment rate), body composition assessments and analytic approaches across studies.

The association of 1,5-AG or glycemic outcomes assessed by continuous glucose monitoring with BMI and body composition has not been examined in type 1 diabetes patients. Such measures of short-term fluctuations in blood glucose are increasingly recognized as important supplementary indicators, together with long-term average glycemic control, of risk of diabetes complications [31]. In the current study, 1,5-AG was inversely associated with BMI, %fat, trunk fat mass and trunk %fat, although associations with trunk fat mass and trunk %fat did not reach statistical significance in the model adjusted for both developmental and diabetes-related covariates ($p = 0.09$). These findings suggest that more frequent short-term fluctuations in glycemic control, particularly hyperglycemia, are associated with higher BMI and adiposity. Evidence from CGM-assessed glycemic variability corroborates this interpretation given the positive associations of %glucose >180 mg/dL (10 mmol/L) with total fat, % fat and trunk %fat in the models adjusted for developmental covariates, and of %glucose >126 mg/dL (7 mmol/L) with total fat, %fat, trunk fat and trunk %fat in both adjusted models. In addition, the observed findings extend previous research by demonstrating differences in associations of glycemic outcomes with BMI versus DXA-measured indicators of body composition, suggesting that less optimal glycemic outcomes related to increased BMI may be attributable specifically to increased adiposity rather than overall mass.

Interpretation of the findings should take into account the relative strengths and limitations of the study design. Strengths include the prospective follow-up and repeated measures of the variables of interest and the use of objective measures of height and weight for calculating BMI and DXA for assessing body composition. On the other hand, although these data were collected in the context of a behavioral nutrition intervention trial, these findings are presented as secondary data analyses and, therefore, represent observational associations, which limit inferences regarding causality. Additionally, the racial/ethnic homogeneity of the sample and the 24% recruitment rate limits generalizability of these findings, although we do not anticipate that the physiologic mechanisms underlying the associations of interest would differ substantially with a more representative sample. Eligibility criteria required that participants' glycemic control fall within a pre-specified

range, which may have limited our ability to detect associations that would have been observable with a wider range of glycemic control.

5. Conclusions

Results from this study of youth with type 1 diabetes indicate significant associations of 1,5-AG, 3-day mean blood glucose and %glucose >126 mg/dL (7 mmol/L) and >180 mg/dL (10 mmol/L) with indicators of adiposity. In contrast, evidence does not support a consistent association of adiposity with long-term average glycemic control (HbA1c), overall glycemic variability (standard deviation and MAGE) or hypoglycemic excursions (percent glucose values <70.2 mg/dL (4 mmol/L)). These findings suggest that the role of BMI and adiposity in disease management in this population may specifically relate to hyperglycemia. The identification of specific factors contributing to these hyperglycemic excursions in patients with greater BMI and adiposity is an important area for future research.

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Abbreviations:

HbA1c	glycated hemoglobin
BMI	body mass index
1,5-AG	1,5-anhydroglucitol
DXA	dual energy X-ray absorptiometry
CGM	continuous glucose monitoring
MAGE	mean amplitude of glycemic excursions
IIT	intensive insulin therapy

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Table 1-

Baseline sample characteristics (N= 136)

	Overall n = 136	Treatment n = 66	Control n = 70	P
Age	12.8 ± 2.6	12.6 ± 2.7	13.0 ± 2.5	0.27
Sex (n, % female)	70 (51)	31 (47)	39 (56)	0.31
Tanner stage (min = 1, max = 5)	2.5 ± 1.4	2.4 ± 1.4	2.6 ± 1.5	0.38
Diabetes duration (y)	6.0 ± 3.1	5.6 ± 2.5	6.3 ± 3.6	0.15
Insulin regimen (n, % pump)	94 (69)	46 (70)	48 (69)	0.89
Insulin dose (U/kg/day)	0.9 ± 0.3	0.9 ± 0.2	0.9 ± 0.3	0.16
Self-monitoring of blood glucose (times/day)	5.7 ± 2.4	5.8 ± 2.4	5.6 ± 2.5	0.60
Body composition				
BMI (kg/m ²)	21.3 ± 4.2	21.0 ± 4.1	21.6 ± 4.3	0.37
Weight status ¹				
Underweight	1 (.7)	1 (1.5)	0(0)	0.30
Normal weight	91 (66.9)	42 (63.6)	49 (53.9)	
Overweight	28 (20.6)	17 (25.8)	11 (15.7)	
Obese	16 (11.8)	6 (9.1)	10 (14.3)	
BMI z-score	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.63
Total fat mass (kg) ²	15.7 ± 8.9	13.7 ± 6.5	17.4 ± 10.3	0.02
Total lean mass (kg)	38.3 ± 12.4	39.0 ± 14.0	37.6 ± 10.9	0.54
Percent fat (%)	27.5 ± 7.9	25.9 ± 7.4	29.0 ± 8.2	0.03
Trunk fat mass (kg)	5.9 ± 3.8	5.2 ± 3.1	6.5 ± 4.2	0.08
Trunk lean mass (kg)	17.7 ± 6.1	17.9 ± 6.8	17.6 ± 5.3	0.82
Trunk percent fat (%)	23.7 ± 8.7	22.2 ± 7.8	25.1 ± 9.4	0.06
Glycemic control and variability				
HbA1c (%; mmol/mol)	8.1 ± 1.0, 65 ± 11	8.1 ± 1.1, 65 ± 12	8.1 ± 1.1, 65 ± 11	0.95
1,5-AG (µg/ml)	3.3 ± 2.0	3.5 ± 2.0	3.1 ± 1.9	0.29
Mean 3-day blood glucose (mg/dL)	180.2 ± 36.5	177.7 ± 38.6	182.5 ± 34.6	0.47
Standard deviation (mg/dL)	73.8 ± 16.3	74.2 ± 15.4	73.4 ± 17.1	0.80
MAGE (mg/dL)	216.7 ± 43.6	217.4 ± 42.0	216.0 ± 45.2	0.86
% Glucose > 180 mg/dL	43.7 ± 18.2	42.6 ± 18.7	44.7 ± 17.8	0.52

	Overall <i>n</i> = 136	Treatment <i>n</i> = 66	Control <i>n</i> = 70	<i>P</i>
%Glucose <70.2 mg/dL	5.8 ± 6.4	7.1 ± 7.5	4.5 ± 5.0	0.02

BMI, body mass index; HbA 1c, glycated hemoglobin; 1,5-AG, 1,5-anhydroglucitol; MAGE, mean amplitude of glycemic excursions; %glucose, percent glucose values from 3-day masked continuous glucose monitoring.

Values are mean ± SD or n (%).

¹Defined using Centers for Disease Control and Prevention sex- and age-adjusted percentiles, underweight: BMI percentile <5, normal weight: 5 ≤BMI percentile <85, overweight: 85 ≤BMI percentile <95, obese: BMI percentile ≥95.

²Baseline dual energy X-ray absorptiometry data missing for 13 subjects (9 treatment, 4 control); baseline masked continuous glucose monitoring data missing for 15 subjects (7 treatment, 8 control).

Table 2-

Coefficient estimates from random effects models¹ examining associations of glyated hemoglobin (HbA1c) and 1,5-anhydroglucitol (1,5-AG) with body mass index (BMI) and body composition.

	HbA1c (%)			1,5-AG (µg/ml)		
	β	se	P	B	se	P
BMI (kg/m ²)						
Model 1	-0.009	0.02	0.55	-0.11	0.03	<0.001
Model 2	-0.03	0.02	0.06	-0.07	0.03	0.04
Model 3	-0.03	0.02	0.06	-0.06	0.03	0.07
Total fat(kg)						
Model 1	0.007	0.005	0.23	-0.02	0.01	0.11
Model 2	0.005	0.006	0.40	-0.01	0.01	0.34
Model 3	0.004	0.006	0.53	-0.008	0.01	0.42
Total lean (kg)						
Model 1	0.004	0.007	0.53	-0.03	0.01	0.01
Model 2	-0.02	0.01	0.10	-0.006	0.03	0.82
Model 3	-0.02	0.01	0.21	-0.01	0.02	0.70
Percent fat						
Model 1	0.01	0.009	0.24	-0.02	0.02	0.04
Model 2	0.02	0.01	0.12	-0.04	0.02	0.02
Model 3	0.01	0.01	0.29	-0.03	0.02	0.047
Trunk fat (kg)						
Model 1	0.03	0.02	0.10	-0.11	0.03	0.001
Model 2	0.02	0.02	0.32	-0.07	0.04	0.047
Model 3	0.01	0.02	0.47	-0.06	0.04	0.09
Trunk lean (kg)						
Model 1	0.01	0.01	0.32	-0.07	0.02	0.008
Model 2	-0.03	0.03	0.36	-0.02	0.05	0.69
Model 3	-0.01	0.03	0.60	-0.03	0.05	0.53
Trunk percent fat						
Model 1	0.007	0.008	0.38	-0.03	0.01	0.03
Model 2	0.01	0.009	0.33	-0.03	0.02	0.04
Model 3	0.005	0.009	0.59	-0.03	0.02	0.09

¹Model 1 covariates include time (weeks) and treatment assignment; Model 2 additionally adjusts for baseline child age, sex, height, and Tanner stage; Model 3 additionally adjusts for baseline diabetes duration, insulin regimen and time-varying frequency of blood glucose monitoring.

Table 3-

Coefficient estimates from random effects models predicting 3-day continuous glucose monitoring outcomes.¹

Mean (mg/dL)			Standard deviation (mg/dL)			MAGE (mg/dL)			%Glucose values > 180 mg/dL			%Glucose values > 126 mg/dL			%Glucose values < 70.2 mg/dL		
β	se	p	β	se	p	β	se	p	β	se	p	β	se	p	β	se	p
BMI (kg/m ²)																	
Model 1	-0.58	0.54	0.29	-0.16	0.24	0.52	-0.44	0.65	0.49	-0.17	0.26	0.53	-0.14	0.21	0.50	0.13	0.10
Model 2	-0.09	0.60	0.88	-0.06	0.28	0.84	-0.11	0.75	0.89	0.05	0.30	0.88	0.11	0.24	0.64	0.02	0.85
Model 3	-0.33	0.58	0.57	-0.23	0.27	0.40	-0.49	0.73	0.50	-0.07	0.29	0.82	0.11	0.24	0.66	-0.003	0.97
Total fat (kg)																	
Model 1	0.27	0.23	0.24	-0.10	0.10	0.32	-0.31	0.28	0.26	0.16	0.12	0.17	0.19	0.10	0.04	-0.05	0.18
Model 2	0.48	0.24	0.04	-0.03	0.11	0.79	-0.10	0.30	0.73	0.24	0.12	0.047	0.29	0.10	0.004	-0.08	0.03
Model 3	0.38	0.24	0.11	-0.09	0.11	0.42	-0.23	0.30	0.43	0.20	0.12	0.11	0.28	0.10	0.006	-0.09	0.03
Total lean (kg)																	
Model 1	-0.27	0.22	0.23	-0.15	0.09	0.12	-0.40	0.25	0.11	-0.11	0.11	0.35	-0.06	0.09	0.49	0.02	0.56
Model 2	-0.49	0.50	0.32	-0.11	0.22	0.62	-0.19	0.60	0.76	-0.19	0.26	0.45	-0.08	0.21	0.68	0.07	0.32
Model 3	-0.38	0.48	0.43	-0.07	0.22	0.74	-0.08	0.59	0.89	-0.15	0.25	0.55	-0.06	0.20	0.78	0.07	0.38
Percent fat																	
Model 1	0.40	0.33	0.22	0.03	0.14	0.84	0.04	0.38	0.93	0.27	0.16	0.11	0.22	0.13	0.10	-0.02	0.70
Model 2	0.71	0.34	0.04	0.06	0.16	0.70	0.15	0.43	0.74	0.41	0.18	0.02	0.39	0.14	0.006	-0.08	0.15
Model 3	0.47	0.35	0.18	-0.07	0.16	0.64	-0.15	0.44	0.72	0.29	0.18	0.10	0.36	0.15	0.01	-0.08	0.14
Trunk fat (kg)																	
Model 1	0.55	0.67	0.41	-0.25	0.29	0.38	-0.81	0.77	0.29	0.43	0.34	0.20	0.42	0.27	0.12	-0.07	0.46
Model 2	1.29	0.74	0.08	-0.12	0.34	0.73	-0.40	0.91	0.66	0.74	0.38	0.05	0.80	0.30	0.007	-0.20	0.07
Model 3	0.90	0.73	0.22	-0.33	0.33	0.32	-0.86	0.90	0.34	0.55	0.38	0.15	0.75	0.30	0.01	-0.21	0.06
Trunk lean (kg)																	
Model 1	-0.47	0.46	0.30	-0.33	0.19	0.09	-0.91	0.52	0.08	-0.17	0.23	0.47	-0.09	0.19	0.64	0.04	0.57
Model 2	-0.30	1.02	0.77	-0.28	0.46	0.54	-0.54	1.24	0.67	-0.04	0.53	0.94	0.15	0.42	0.72	0.09	0.58
Model 3	-0.19	0.98	0.85	-0.24	0.45	0.59	-0.43	1.22	0.73	0.004	0.51	0.99	0.18	0.42	0.67	0.08	0.61
Trunk percent fat																	
Model 1	0.33	0.30	0.27	-0.02	0.13	0.87	-0.14	0.35	0.70	0.23	0.15	0.12	0.20	0.12	0.11	-0.02	0.61
Model 2	0.59	0.32	0.07	-0.01	0.15	0.95	-0.08	0.40	0.84	0.35	0.17	0.04	0.35	0.13	0.008	-0.08	0.11

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<u>Mean (mg/dL)</u>			<u>Standard deviation (mg/dL)</u>			<u>MAGE (mg/dL)</u>			<u>%Glucose values > 180 mg/dL</u>			<u>%Glucose values > 126 mg/dL</u>			<u>%Glucose values < 70.2 mg/dL</u>			
β	se	p	β	se	P	β	se	P	β	se	P	β	se	P	β	se	P	
Model 3	0.39	0.32	0.22	-0.12	0.15	0.42	-0.32	0.40	0.42	0.25	0.17	0.13	0.33	0.14	0.02	-0.08	0.05	0.10

MAGE, mean amplitude of glycemic excursions.

Model 1 covariates include time (weeks) and treatment assignment; Model 2 additionally adjusts for baseline age, sex, and time-varying height and Tanner stage; Model 3 additionally adjusts for baseline diabetes duration, insulin regimen and time-varying frequency of blood glucose monitoring.