

Glycemic Variability Measures in a Group of Subjects with Type 1 Diabetes and Repeated Severe and Non-Severe Hypoglycemia

Verónica Perea, M.D., Antonio Amor, M.D., Marga Giménez, M.D., Jesús Blanco, M.D., and Ignacio Conget, M.D., Ph.D.

There is some evidence that not only hemoglobin A1c (HbA1c) but also short-term variations in blood glucose could represent an independent risk factor for hypoglycemia.¹ Normative ranges for measures of glycemic variability (GV) in normal subjects and in continuous glucose monitoring (CGM) data sets obtained from subjects with type 1 diabetes mellitus (T1DM) have been published.² We sought to describe GV in T1DM patients with repeated episodes of severe hypoglycemia and non-severe hypoglycemia (SH/NSH).

Thirty-six T1DM subjects underwent CGM for up to 72 h. Twenty-five of 36 were considered the hypoglycemic group [(H-group), presenting repeated SH/NSH], while the remaining 11 were evaluated as the control group (C-group). General characteristics, biochemical measurements, the number of hypoglycemic episodes, and the awareness of hypoglycemia (Clarke Sign Test) were evaluated. Glycemic variability was calculated using EasyGV[®] (by N. R. Hill, University of Oxford, Oxford, UK; available at www.easygv.co.uk) for the following: standard deviation (SD), M-value (mg glucose per kg body weight per min), mean amplitude of glucose excursions (MAGE), average daily risk ratio, lability index, J-Index, low blood glucose index (LBGI), high blood glucose index, continuous overlapping net glycemic action, mean of daily differences, glycemic risk assessment diabetes equation (GRADE), and mean absolute glucose. No differences were found in the entire set of clinical data or in HbA1c (H-group: age 34.5 ± 7.8 years, T1DM duration 16.0 ± 6.3 years, HbA1c 6.6 ± 1.0 %). Scores for the Clarke Sign Test differed for both groups, with higher values in the H-group. The H-group showed higher percentages of values and areas under the curve (AUC) <70 mg/dl with respect to the C-group (11.3 ± 8.4 vs $5.3 \pm 5.3\%$ <70 mg/dl; $p < .05$ and 2.5 ± 1.8 vs 0.8 ± 1.0 mg/dl AUC <70 mg/dl; $p < .005$ for the H-group and the C-group, respectively). The H-group presented significantly higher scores than the T1DM C-group in LBGI (9.3 ± 5.0 vs 4.3 ± 2.4), GRADE (8.0 ± 3.4 vs 4.8 ± 3.5), GRADE-hypoglycemia (GRADE-hypo) (22.8 ± 22.0 vs 9.2 ± 8.9), and M-value (17.7 ± 6.5 vs 10.3 ± 6.0).

Using CGM glucose profiles, we have shown that only the variability measures representing increased glycemic risk related to hypoglycemia and the quality of glycemic control differ significantly in T1DM subjects who are prone to repeated episodes of hypoglycemia. Almost all measurements (EasyGV software) from our entire group of subjects

Author Affiliation: Diabetes Unit, Endocrinology and Nutrition Department IDIBAPS (Institut d'Investigacions Biomèdiques August Pi i Sunyer), CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Hospital Clínic i Universitari, Barcelona, Spain

Abbreviation: (AUC) area under the curve, (CGM) continuous glucose monitoring, (C-group) control group, (GRADE) glycemic risk assessment diabetes equation, (GRADE-hypo) glycemic risk assessment diabetes equation-hypoglycemia, (GV) glycemic variability, (HbA1c) hemoglobin A1c, (H-group) hypoglycemic group, (LBGI) low blood glucose index, (MAGE) mean amplitude of glucose excursions, (M-value) mg glucose per kg body weight per min, (SD) standard deviation, (SH/NSH) severe hypoglycemia and non-severe hypoglycemia, (T1DM) type 1 diabetes mellitus

Keywords: continuous glucose monitoring, glucose variability, hypoglycemia, type 1 diabetes mellitus

Corresponding Author: Ignacio Conget, M.D., Ph.D, Diabetes Unit, Endocrinology and Nutrition Department, Villarroel 170, 08036 Barcelona, Spain; email address iconget@clinic.ub.es

with T1DM were above the mean + 2 SD normative values that are described in a nondiabetic population. We could not find differences in the majority of measures, except for four (LBGI, GRADE, GRADE-hypo, and M-value), in our group of patients with repeated hypoglycemic episodes in comparison with the control group of T1DM patients without significant hypoglycemia and with good metabolic control. We found differences only in those glucose measures that mainly focused on increased glycemic risk coming from hypoglycemic episodes (LBGI and GRADE-hypo) and those mostly representing quality of glycemic control (GRADE and M-value). The only exception for a glucose measure specifically related to variability was MAGE, which was close to significantly higher in the group of patients with repeated hypoglycemia. As it has been claimed using self-monitoring blood glucose information,³ our data suggest that measures of glucose variability and quality of glucose control derived from CGM data could be used as instruments to estimate the risk of hypoglycemia and could help to prevent it.

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