

Ana M Gómez ^{1,2}, Oscar M Muñoz ^{1,2}, Alejandro Marin^{1,2}, Camila Fonseca ^{1,2}, Maira García³, Fabián León⁴, Martín Rondon¹.

¹Pontificia Universidad Javeriana, Bogotá, Colombia; ²Hospital Universitario San Ignacio, Bogotá, Colombia; ³ Universidad EAN, Bogotá, Colombia; ⁴ Universidad Manuela Beltrán, Bogotá, Colombia.

Introduction:

In the last decade multiple studies have shown the association between glucose variability (GV) and hypoglycemia. Recent publications constantly introduce new GV indexes, however there is still a lack of evidence supporting the use of one particular GV parameter, especially in clinical practice.

Objective:

The aim of this study was to evaluate the association of hypoglycemia with different GV indexes reported in recent literature in order to determine which one is better for routine use in clinical practice.

Research Design and Methods:

In this study, a cohort of diabetes mellitus type 2 patients (DMT2) in ambulatory care, were followed using continuous glucose monitoring sensor. Mean glucose (MG), standard deviation (SD), Coefficient of variation (CV), 1, 2 and 4 hour Continuous Overlapping Net Glycemic Action (CONGA 1, 2 and 4), Mean Amplitude of Glucose Excursions (MAGE), M Value, J Index, Interquartile Range (IQR) and both High and Low Blood Glucose Index (HBGI, LBGI) were estimated.

Hypoglycemia incidence was calculated defining hypoglycemic episodes as a interstitial glucose level < 54 mg/dl as detected by CGM for at least 20 minutes.

GV indexes were compared with Spearman rank correlation test. Area under the curve (AUC) were determined for different GV indexes as hypoglycemia predictors. Optimal cutoff thresholds were determined from receiver operating characteristic curve analyses.

Table 1. Baseline Characteristics of the Included Patients

VARIABLE	n=140
Gender, male % (n)	47.1% (66)
Age, years, mean (SD)	68.9 (11.2)
IMC Kg/mt2, mean (SD)	27.4 (4.2)
Duration of diabetes, years, mean (SD)	15.5 (9.7)
HbA1C (%) mean, (SD)	7.71 (1.44)
GFR mL/min/1.73m2, mean (SD)	64.3 (29.4)
On insulin treatment * % (n)	88.5 (124)
On sulfonylurea treatment % (n)	8.57 (12)
History of severe hypoglycemia % (n)	14.4 (20)

*On any regular/analog, basal and/or prandial insulin (including pump therapy) SD: standard deviation.

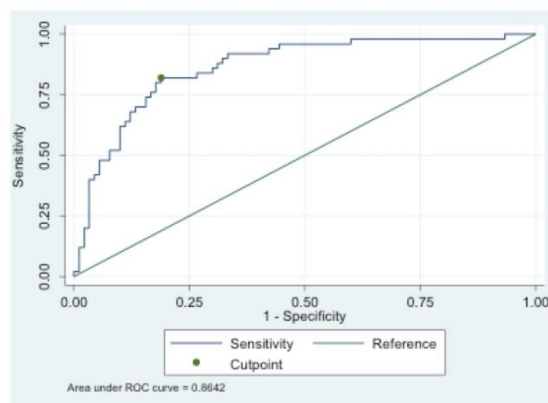
Results:

140 T2D patients were included (Table1). CGM data for 657 days from 140 type 2 diabetes patients (4,69 average days per patient) were analyzed.

Hypoglycemia was present in 54 patients, 144 events in 259 days of recording (1.03 events per patient/day). In the multivariate analysis both CV and MG proved a statistically significant association with hypoglycemia. OR for MG 0.98 (CI 0.965-0.997 p=0.022) and OR for CV 1.20 (CI 1.12-1.86 p=0.001).

A strong correlation was found between CV and other GV parameters including SD (r=0.84) CONGA 1,2 and 4 (r= 0.84), (r=0.89), (r=0.95) respectively, IQR (r=0.96), and MAGE (r=0.96). The AUC of GV indexes as hypoglycemia predictors were calculated. The CV had highest AUC (0.8642) (Figure 1)

Figure 1. Area under the curve for Coefficient of variation (CV) as predictor of hypoglycemia



Optimal cutoff thresholds for CV as predictor of hypoglycemia was 34. With 33.96 as the maximum value between patients without hypoglycemic episodes, and 34.06 as the minimum value between patients with those.

CONCLUSION:

This analysis shows that given the strong correlation of CV with other GV parameter, the significant association with hypoglycemia and considering the easy calculation, CV could be recommended as the preferred parameter of GV for use in clinical practice.

References

- Monnier L, Colette C, Wojtusciszyn A, Dejager S, Renard E, Molinari N, Owens DR, Toward Defining the Threshold Between Low and High Glucose Variability in Diabetes, Diabetes Care 2016 Dec 30. pii: dc161769. doi: 10.2337/dc16-1769. [Epub ahead of print]
- K. Khunti, S. Alsifri, R. Aronson, M. Cigrovski Berkovic, C. Enters-Weijnen, T. Forsén, G. Galstyan, P. Geelhoed-Duijvestijn, M. Goldfracht, H. Gydesen, R. Kapur, N. Lalic, B. Ludvik, E. Moberg, U. Pedersen-Bjergaard, A. Ramachandran on behalf of the HAT Investigator Group Rates and predictors of hypoglycaemia in 27 585 people from 24 countries with insulin-treated type 1 and type 2 diabetes: the global HAT study Diabetes Obes Metab 2016 Sep;18(9):907-15. doi: 10.1111/dom.12689. Epub 2016 Jun 20.
- Yoshifumi Saisho, Chihiro Tanaka, Kumiko Tanaka, Rachel Roberts, Takayuki Abe, Masami Tanaka, Shu Meguro, Junichiro Irie, Toshihide Kawai, Hiroshi Itoh Prim Care Diabetes. 2015 Aug; 9(4): 290–296. Published online 2014 Nov 16. doi: 10.1016/j.pcd.2014.10.001
- Monnier L, Wojtusciszyn A, Colette C, Owens D. The contribution of glucose variability to asymptomatic hypoglycemia in persons with type 2 diabetes. Diabetes Technol Ther. 2011;13:813–8.
- Kovatchev, Cobelli, Glucose Variability: Timing, Risk Analysis, and Relationship to Hypoglycemia in Diabetes, Diabetes Care 2016 Apr;39(4):502-10. doi: 10.2337/dc15-2035.