Proceedings of the Nutrition Society (2022), **81 (OCE1)**, E8 doi:10.1017/S0029665122000088

Winter Conference 2021, 7–8 December 2021, Obesity and the brain

Measures of optimal glucose "time in range" and variability using continuous glucose monitors in 4,805 healthy non-diabetic individuals is discriminatory of cardiovascular health risk

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Measurement of glucose time in range (TIR) and glycemic variability (GV) are informative measures of glycemic control, now possible with the evolution of continuous glucose monitoring (CGM). In diabetic cohorts, studies demonstrate measures of GV and TIR (American Diabetes Association (ADA) targets; 70–140 mg/dL) are superior to HbA1c in the discrimination of future disease development[(1)]. However, the prevalence of unfavorable TIR and GV and their relationship with disease risk in healthy populations is unknown, questioning the utility of CGMs in healthy individuals.

Aims: To; 1) describe GV and TIR distribution in a non-diabetic population; 2) establish normative ranges for TIR specific to healthy populations and 3) explore the relationship between GV and TIR with health outcomes.

The PREDICT studies examining personalised responses to food, include PREDICT 1 (n = 1,002, UK), PREDICT 2 (n = 987, US) and PREDICT 3 (n = 4,500, US) cohorts. Demographic information, habitual diet, free-living diet data, cardiometabolic blood biomarkers and postprandial responses to standardized test meals in clinic and in free-living settings were collected. Abbott Freestyle Libre-Pro CGMs were worn by participants for 10–14 days, and free living (2–4 days) CGM data was selected for analysis. After exclusions, 4,805 participants (78% females, mean age 46 ± 12y) were included (PREDICT 1 n = 868, PREDICT 2 n = 843, PREDICT 3 n = 3,094). GV was measured by coefficient of variation (%) and TIR was calculated using; 1) ADA cut-offs (TIR_{ADA}; 70–140 mg/dL) and 2) optimised cut-offs ($TIR_{optimised}$; 70–100 mg/dL). To explore sensitivity of both TIR targets and the stratification of health outcomes based on variation in TIR and GV, the top and bottom quintiles of measures were selected for comparisons.

Mean fasting glucose was 91 ± 10 mg/dl, HbA1c was 5.3 ± 0.4%, GV was 15.6 ± 4.3%, $TIR_{optimised}$ was 70.4 ± 17% and TIR_{ADA} was 91 ± 13% (n = 4,805). When applying different TIR target ranges in PREDICT 1 (n = 868) there were no significant differences in HbA1c and ASCVD risk between the top and bottom quintiles using the TIR_{ADA}. However, when using $TIR_{optimised}$, HbA1c and ASCVD was significantly higher in the top versus bottom quintiles ($p = 0.0002$ and 0.0005 respectively). In our healthy population (n = 4,805), those with a greater $TIR_{optimised}$ and lower GV had (mean difference); lower HbA1c (GV by 14%, TIR by 23%), higher fasting glucose (GV by 0.26 mmol/L, TIR by 0.33 mmol/L) and were of a younger age (GV and TIR by 3 yrs), $p < 0.0001$ for all.

In the most comprehensive study of its kind, we demonstrate that optimised TIR targets (70–100 mg/dL) using CGM is discriminatory of ASCVD risk despite normal fasting HbA1c. Exploration of key determinants of GV and TIR and their complex interplay with diet will advance our use of CGMs in healthy individuals.

Reference

1. Vigersky RA & McMahon C (2019) *Diab Technol Ther* **21**, 1–5.