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## *Association of glycaemic variability assessed by continuous glucose monitoring with subclinical diabetic polyneuropathy in type 2 diabetes patients*

*Aims:* The relationship between peripheral nerve function and glucose variability is unclear. The study investigated the association of glucose variability with sub-clinical diabetic polyneuropathy (DPN) in a large sample of individuals with type 2 diabetes.
*Methods:* In 509 well selected participants with type 2 diabetes, free of symptoms and signs of DPN, glycaemic variability parameters, including the mean amplitude of glycaemic excursions (MAGE), glucose standard deviation ($SD_{gluc}$) and glucose coefficient of variation ($CV_{gluc}$) were derived from 3-day continuous glucose monitoring (CGM). All participants underwent nerve conduction studies (NCS), and the composite Z-scores for nerve conduction parameters were calculated.
*Results:* Multivariate logistic regression analyses showed that $SD_{gluc}$ and HbA1c were independently associated with abnormal NCS with similar odds ratio [odds ratios 1.198 (95% CI 1.027-1.397) for $SD_{gluc}$ and 1.182 (1.061–1.316) for HbA1c]. The composite Z-scores of nerve conduction velocity and of amplitude decreased while the composite Z-score of distal latency increased with increasing tertiles of $SD_{gluc}$ (all P trend <0.05). After adjusting for age, sex, body mass index, diabetes duration and HbA1c, $SD_{gluc}$ was still independently associated with nerve conduction velocity (P=0.021).
*Conclusions:* The $SD_{gluc}$ is a significant independent contributor to subclinical DPN, in addition to conventional risk factors including diabetes duration and HbA1c.

**Comments.** This study brings forward two interesting elements for discussion - clinical and research.
From the ***clinical*** perspective, with more widespread use of glucose sensor, there has been a paradigm shift of glucocentric focus from HbA1c to time in range (TIR) and glucose variability. Better achievement of TIR has been shown to have many benefits, including reduced hypoglycaemic episodes, length of hospital stay, better quality of life and compares with short-term HbA1c changes. However, this as other studies support the beneficial effects of short-term glucose change on neural assessments despite the short duration of observation.
From the ***research*** perspective, DPN is often described as a "longer-term" microangiopathy developing over months to years. This study contradicts such belief and indicates that changes in neural pathophysiology can occur with short term changes in glucose flux. In this study, NCS was used but it would be worth researching if methods of small fibre function like $LDI_{FLARE}$ or structure like corneal confocal microscopy would reflect similar changes when used with glycaemic measures like CGM in addition to HbA1c. There are however studies which show reversal association of TIR with autonomic neuropathy assessments independent of HbA1c.

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**Reference.** Pan J, Yan X, Li F, Zhang Y, Jiang L, Wang C. Association of glycaemic variability assessed by continuous glucose monitoring with subclinical diabetic polyneuropathy in type 2 diabetes patients. J Diabetes Investig. 2022 Feb;13(2):328-335. doi: 10.1111/jdi.13652. Epub 2021 Sep 17.
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