Patients with high blood sugar variability much more likely to die than those with stable visit-to-visit readings

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New research presented at this year's Annual Meeting of the European Association for the Study of Diabetes (EASD) in Barcelona, Spain (16-20 Sept) shows that patients with the highest variability in their blood sugar control are more than twice as likely to die as those with the most stable blood sugar measurements. The study is by Professor Ewan Pearson, University of Dundee, UK and Dr. Sheyu Li, West China Hospital, Sichuan University, Chengdu, China, and University of Dundee, UK, and colleagues.

Measuring glycated haemoglobin (HbA1c) in a patient's blood has for many years been a standard method for measuring blood sugar control over previous weeks and months. Usually, there is focus on whether a patient's HbA1c level is at or below a treatment target for a patient. However, some patients have highly variable HbA1c, and others have stable HbA1c from visit to visit. It is unclear whether this variability in HbA1c is associated with altered prognosis of patients, independent of their average HbA1c from diagnosis. In this study, the authors aimed to investigate the association between visit-to-visit HbA1c variability and cardiovascular events and microvascular complications in patients with newly diagnosed type 2 diabetes.

The study retrospectively recruited patients from Tayside and Fife in the Scottish Care Information-Diabetes Collaboration (SCI-DC), who were observable from diagnosis and had at least five HbA1c measurements

before the outcomes. They used a measurement called the HbA1c variability score (HVS) calculated as the percentage of the number of changes in HbA1c more than 0.5% (5.5mmol/mol) among all HbA1c measurements in an individual.

Ten outcomes were studied including the combined outcome of major adverse cardiovascular events (known as MACE), all-cause mortality, cardiovascular death, coronary artery disease (CAD), ischemic stroke, heart failure, diabetic retinopathy (DR), diabetic peripheral neuropathy (DPN), diabetic foot ulcer (DFU) and the new onset of chronic kidney disease (CKD). Statistical models adjusting for baseline characteristics were used to assess the association of HVS with outcomes.

For each outcome, the patients were divided into 5 groups with the patients with the lowest variability (0-20%) as the reference. Compared with this group, patients with HVS of more than 60% (the 60-80% group and the 80-100% group) were associated with increased risks of all the outcomes studied. This means that the outcomes of patients are worse when more than 60% of their HbA1c measurements differ by 0.5% from the previous measure.

When looking specifically at the highest variation group (80-100%) versus the lowest (0-20%), the highest group was associated with a 2.4 times increased risk of all three outcomes of MACE, all-cause and cardiovascular mortality. There was also a 2.6 times increased risk of coronary artery disease, a doubling of risk of stroke, a tripled risk of heart failure, DPN, and CKD; a five-times increased risk of diabetic foot ulcer and seven times increased risk of DR. Adjustment for baseline characteristics confirmed the results.

The authors say: "Higher HbA1c variability is associated with increased risks of all-cause mortality, cardiovascular events and microvascular complication of diabetes independently of accumulated exposure of high

HbA1c."

The authors say HbA1c variability varies across individuals, explaining that: "A previous descriptive study we completed suggests higher HbA1c variability was associated with age, sex, body mass, social deprivation and treatment patterns and this difference may explain some of the increased risk in those with high variability in HbA1c. Frequent fluctuation of HbA1c can be driven by multiple clinical factors, including variation in diet and lifestyle, changing to different anti-diabetic drugs and/or withdrawing of anti-diabetic treatment, and general healthcare quality"

They explain further: "High variation of HbA1c is more common in patients with a higher average level of HbA1c. However, the association with adverse outcomes seen with high HbA1c variability remains even after adjusting for this baseline difference. Thus, a highly variable HbA1c should be considered as a major risk factor for adverse outcomes, even if the average HbA1c is not too high. At this stage, it is important to emphasize that we can't say that the adverse outcomes are definitively caused by the increased variability in HbA1c, and therefore we cannot yet be sure that reducing HbA1c variability will reduce that risk."

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