COMMENT ON ECHOUFFO-TCHEUGUI ET AL.

Visit-to-Visit Glycemic Variability and Risks of Cardiovascular Events and All-Cause Mortality: The ALLHAT Study. Diabetes Care 2019;42:486–493

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The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) study group (1) reported that, based on a post hoc analysis, visit-to-visit variability of fasting blood glucose (FBG) is positively associated with all-cause mortality but not with cardiovascular events in subjects without diabetes, while the association is not statistically significant in those with diabetes. Glycemic variability was assessed from FBG values at baseline, 24 months, and 48 months in persons without cardiovascular disease prior to a follow-up period of up to several years. Metrics of glycemic variability were derived including SD, coefficient of variation (CV), variability independent of the mean (VIM), and average successive variability (ASV). Comparisons of participants in the highest versus lowest quartiles of the VIM showed that the hazard ratios (HR) (95% CI) for all-cause mortality were 2.50 (1.46–4.46) and 1.08 (0.56–2.11) in subjects without and with diabetes, respectively. The authors give particular emphasis to VIM, which was designed to be independent of the mean glucose value; however, similar results (in the Supplementary Data) were observed using the CV for glucose: HR for all-cause mortality was 3.09 (1.58–6.06) in people without diabetes vs. 0.77 (0.31–1.88) in those with diabetes. Unfortunately, these interesting data were only provided in the Supplementary Tables.

To gain insight into the apparent discrepancies between the findings observed in the current study and the well-recognized role of sustained hyperglycemia as risk factor for macrovascular complications in diabetes (2,3), it would have been best to analyze first the potential associations of mean FBG concentrations ("ambient hyperglycemia") with the rates of incident deaths and cardiovascular events and then check whether an interaction exists between the mean of FBG and the various indices of glycemic variability during the disease-free 48-month period. The present analysis is unable to provide an answer to whether the variability of overall glucose exposure is a risk factor or a simple marker of adverse clinical outcomes, and the authors of this interesting article appear to have failed to fully capture all the potentialities provided by this long-term study. In addition, the authors have overestimated the value of the VIM as a marker of glucose variability, which does not appear to exhibit any better superiority when compared with the CV for glucose (4,5) and therefore can rarely be used in routine clinical practice.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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The authors of the cited article did not respond.