RESPONSE TO COMMENT ON KIVINIEMI ET AL.

Prediabetes and Risk for Cardiac Death Among Patients With Coronary Artery Disease: The ARTEMIS Study. Diabetes Care 2019;42:1319–1325

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We appreciate the comments by Chattopadhyay and John (1) on our recent study on prognostic significance of prediabetes in patients with stable coronary artery disease (CAD) (2). They raise concerns about a self-selected low-risk population, which they claim compromises the generalization of the results. The aim of the Innovation to Reduce Cardiovascular Complications of Diabetes at the Intersection (ARTEMIS) study was to assess prognostic significance of prediabetes among CAD patients in stable-phase CAD. Approximately half had history of myocardial infarction (MI). Authors Chattopadhyay and John are correct that patients with severe cardiac condition were excluded (2) and some may have even died before enrollment. In this case, it would be interesting to know whether treatment of prediabetes could improve prognosis among patients at highest risk for cardiac death in short-term follow-up.

Chattopadhyay and John were interested to find out the Global Registry of Acute Coronary Events (GRACE) score of the patients of the ARTEMIS study. The median GRACE score (1st to 3rd quartile) at enrollment was 89 (77–101) and 87 (73–97) for patients with prediabetes and normal glycemic status (NG), respectively ($P = 0.001$), representing somewhat intermediate risk on average. Notably, a higher GRACE score in the patients with prediabetes did not convert into worse prognosis. Also, SYNTAX scores, presented in our original study (2), were measured after revascularization. Before revascularization, median SYNTAX scores were 9 (4–19) and 10 (5–18) for patients with prediabetes and NG, respectively ($P = $ not significant). These results may help Chattopadhyay and John to reevaluate the CAD status of the ARTEMIS patients before revascularization.

We performed subanalyses in patients with history of MI as well as with Canadian Cardiovascular Society (CCS) classification for angina pectoris ≥ 2. Notably, among patients with history of MI or CCS class ≥ 2, patients with prediabetes did not have increased risk for cardiac death or major adverse cardiac events. In patients with CCS class ≥ 2, mortality risk appeared to be higher in those with prediabetes compared with the NG group, but the risk did not remain significant after adjustment for GRACE score. The results were similar when using 2-h postload glucose as continuous risk marker. These subanalyses are limited by the number of end points. Nevertheless, the results indicate that in CAD patients with prior MI or residual angina pectoris symptoms and, thus, presumably higher risk, prediabetes may not increase risk for cardiac death or events. We do acknowledge that the CAD patients at highest risk were still not involved in these analyses and there may be a threshold for severity of CAD after which prognostic significance of prediabetes may turn out to be significant as in prior studies among acute coronary syndrome patients in short-term follow-up (3). It is also noteworthy that prediabetes was associated with higher incidence of new type 2 diabetes (2) as observed also in the EUROASPIRE IV (EUROpean Action on Secondary and Primary prevention through Intervention to Reduce Events) (4), which resulted in worse prognosis. In conclusion, we strongly feel that it is necessary to tackle development of type 2 diabetes even if it seems that prediabetes itself does not worsen cardiac prognosis among patients with stable CAD.

References
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