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 read with interest the results of the Innovation to Reduce Cardiovascular Complications of Diabetes at the Intersection (ARTEMIS) study (1). The authors conclude that cardiac events in patients with coronary artery disease and prediabetes (revascularized or medically treated) were similar to those in patients with normal glucose tolerance.

The study includes a rather low-risk population with prediabetes. About 46% of patients had stable angina (patients who have very low event rates), and the rest had remote acute coronary syndrome (ACS). Recruitment 3–6 months after the coronary angiography with or without revascularization excluded the highest-risk ACS patients who are expected to have events early. Without the baseline Global Registry of Acute Coronary Events (GRACE) or Thrombolysis in Myocardial Infarction (TIMI) scores, we are unaware of the risk tertiles of these patients. Even though about 55% and 24% of the patients with prediabetes underwent percutaneous coronary intervention and coronary artery bypass grafting, respectively, SYNTAX scores in these groups were extremely low, suggesting that these patients had very simple low-risk coronary anatomy. It is also perplexing to see patients with such low-risk anatomy undergoing coronary artery bypass grafting. Mean baseline left ventricular ejection fraction of 65% suggests that very few patients had left ventricular systolic dysfunction. The use of a primary end point of cardiac death or resuscitated cardiac arrest, events that often occur early if not during the index admission, is rather unconventional. Thus, the patients included are a self-selected group who have survived these initial events.

Prediabetes has been shown to independently predict post-ACS prognosis (2,3). In a study of exclusively ACS patients (2), prediabetes, adjusted for several covariates including the GRACE score, independently predicted prognosis. Major adverse cardiac events (MACE) were higher in patients with prediabetes compared with patients with normal glucose tolerance even when comparing matched groups. MACE-free survival was lower in ACS patients (3). MACE, in ACS patients, increased with increasing quartiles of 2-h postload glucose at levels well below the conventional threshold for diagnosis of diabetes, suggesting that prediabetes glucose levels affect prognosis (4). The fact that 2-h postload glucose, but not fasting plasma glucose, improved the predictive performance of models containing GRACE score suggests that prediabetes affects prognosis (4).

Thus, the conclusion that prognosis in all patients with coronary artery disease with prediabetes does not differ from patients with normal glycemic status is an unqualified generalization. This may be true in patients that are inherently low risk as included in this study, but not in an ACS cohort. It would be reasonable to make a clear distinction between these two populations with vastly diverse pathologies when considering the effect of plasma glucose on prognosis. In the absence of that, we are not only likely to miss the opportunity of diagnosing prediabetes but also to fail to appropriately prognosticate and therefore advise the ACS survivors. Rydén et al. (5) highlighted this in an editorial last year.

The authors' assertion that "prediabetes does not increase the risks for cardiac death and major cardiac morbidities in the current treatment era" (1) should be appended with considerable qualification. It should be emphasized that these results may apply only to patients with prognostic risk near to that of the general population.

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

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