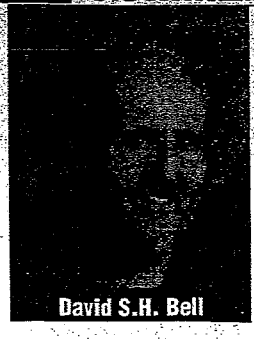
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# Postprandial dysmetabolism may explain increased cardiac events

by David S. H. Bell, MD, FACE
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Traditional risk factors cannot totally account for the increased cardiac events in patients with type 2 diabetes or patients who are glucose intolerant.

Postprandial elevation of glucose, free fatty acids and triglycerides cause inflammation, oxidative stress, endothelial dysfunction, vasoconstriction, hypercoagulation, hypofibrinolysis and atherosclerosis. Therefore, postprandial dysmetabolism is a pro-inflammatory and oxidative state that may explain the increased number of cardiac events that would be predicted by traditional cardiac risk factors, especially in patients who are glucose intolerant.

Results of several epidemiologic studies have shown that high postprandial serum glucose levels measured after an oral glucose challenge were predictive for cardiovascular events.

## Studies reviewed

In the Honolulu Heart Study, the prevalence of CHD was doubled in patients with a one-hour postprandial between 157 mg/dL and 180 mg/dL, compared with patients with a level <144 mg/ dL. Association Detection Project in Industry. The Fungata Diabetes Study results showed a 2.2-fold increase in cardiovascular mortality in nonglucose-tolerant patients, and utilizing a two-hour serum glucose level, the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study results showed a 1.37-fold significant increase in cardiovascular mortality in those with glucose intolerance without a significant association with fasting glucose.

Postprandial hypertriglyceridemia has been associated with increased intima-medial thickening in the carotid arteries and progression of coronary atherosclerosis over a five-year period.

In the Physicians Health Study, elevation of postprandial triglyceride levels was associated with an increased incidence of MI so that for each 100 mg/dL increase in postprandial triglyceride, there was a 40% increase in MI. The Nurse's Health Study results showed that nonfasting triglyceride levels – independent of traditional risk factors, levels of other lipids and markers of insulin resistance – were associated with incident cardiovascular events, whereas there was no independent association with fasting triglyceride levglucose intolerance. Compared with placebo, the use of acarbose in the Study To Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial was associated not only with a 25% decrease in the development of diabetes but also with reduced progression of carotid intima-medial thickness by half and a 49% reduction in cardiovascular events. These surprising findings resulted in a retrospective meta-analysis of seven long-term randomized studies of patients with type 2 diabetes utilizing acarbose. Compared with placebo, those who used acarbose were free of cardiac events for a longer period of time, had a 64% relative reduction in MI and had a 33% reduction in cardiac events. These outcomes were independent of the effects of other cardioprotective drugs.

The alpha glucosidase inhibitor miglitol has been shown to reduce cardiac events compared with glyburide, and another alpha glucosidase inhibitor, voglibose, decreased the progression of carotid intima-medial thickness.

Use of rapid-acting insulins (aspart, lispro and glulisine) lower both postprandial hyperglycemia and oxidative stress and improve endothelial function when compared with regular insu-

The rate of sudden death doubled with a postprandial glucose >151 mg/dL, and a twofold increase in CAD-related mortality was also shown with a two-hour glucose >96 mg/dL.

The Islington Diabetes Survey results showed that a two-hour glucose >120 mg/dL was associated with an almost doubling of major coronary events, and the Bedford Study results showed that protection from developing CAD was lost with a two-hour glucose value >140 mg/dL. Results of a recent angiographic study showed that in glucose-tolerant women with diabetes who had CAD, the higher the two-hour glucose level >87 mg/dL, the greater the progression of CAD over three years.

The Oslo Study results showed an association of stroke with nonfasting glucose levels, and the Hoorn Study results showed that the two-hour glucose level was an independent predictor for peripheral vascular disease. Cardiac mortality was increased in both black and white men with high one-hour glucose levels in the Chicago Heart els. Similar results were reported from a large prospective Danish study of men and women. After an MI, progression of coronary atherosclerosis as documented by angiography over a five-year period is proportional to postprandial levels of triglyceride-rich chylomicron remnants.

In the Multiple Risk Factor Intervention Study, the risk factor-adjusted risk for fatal and nonfatal coronary events was 1.46 for nonfasting hypertriglyceridemia. The additive effects of postprandial hyperlipidemia and hyperglycemia were shown in a study where normoglycemic hyperinsulinemic relatives of patients with type 2 diabetes had endothelial dysfunction that was proportional to the level of postprandial triglyceride. When postprandial hyperglycemia subsequently developed, the endothelial function worsened due to increased oxidative stress and inflammation caused by postprandial hyperglycemia.

The effects of improving postprandial dysmetabolism have been shown with the use of the alpha glucosidase inhibitor acarbose in patients with lin. Metformin has little effect on postprandial glucose, whereas physiological sulfonylureas (such as glimepiride) and the meglitanides have been shown to not only decrease post-prandial glucose but also carotid intima-medial thickness and fibrinolysis. TZDs lower post-prandial glucose, free fatty acids and triglycerides. The effect of TZDs on triglycerides is mediated through decreasing intestinal overproduction of lipoproteins which is a feature of the metabolic syndrome.

Postprandial dysmetabolism may be the missing link that could explain the increased cardiac events that occur with minimal traditional cardiac risk factors in both patients with diabetes and patients who are glucose intolerant. In addition, even in patients who are glucose tolerant, higher glycemic and lipemic excursions within the normal range could play a role in progression of CVD and cardiovascular events. **CT**

**For more information:**

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