Could Glucose Management After Acute Myocardial Infarction Cure Myocardial Damage?

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At one time, patients with acute myocardial infarction (AMI) would have had as poor a prognosis as fatal arrhythmia, cardiac rupture or left ventricular dysfunction. In modern countries, mortality after AMI has been greatly decreased by developments in coronary revascularization, antiarrhythmic agents and the treatment of hypertension and congestive heart failure using angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, aldosterone receptor antagonists or β-blockers. However, myocardial damage often proceeds and not a few patients suffer from severe heart failure after MI.

Diabetes mellitus (DM) is becoming a burden on society because of its endemic increase and high cardiovascular morbidity and mortality. The decline in insulin’s action comprises insulin resistance and/or insulin secretion insufficiency, which leads to various degrees of hyper- or hypoglycemia. In patients with advanced DM, various prospective randomized trials such as ACCORD (the Action to Control Cardiovascular Risk in Diabetes), ADVANCE (the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) and VADT (the Veterans Affairs Diabetes Trial) trials have been conducted to investigate the effects of intensive glycemic control on macrovascular disease, but have failed to show benefit. It has long been recognized that postprandial hyperglycemia is also an accelerating factor in coronary atherosclerosis, but unfortunately a reduction in coronary stenosis by treatment with voglibose or nateglinide of patients with borderline DM or postprandial hyperglycemia has not been achieved. We often see cases of patients with AMI who have elevated glucose levels regardless of their diabetic status. And acute hyperglycemia on admission after AMI is associated with predischarge left ventricular ejection fraction and short-term poor prognosis. Recently, the widespread use of continuous glucose monitoring has clarified the existence of various grades of glucose fluctuation depending on disease status (Figure 1). Several studies indicate that glucose fluctuation has an important role in atherogenesis. Glucose fluctuation augments monocyte adhesion on endothelial cells in rats, and accelerates atherogenesis in apolipoprotein E-deficient mice. In humans also, glucose fluctuation is associated with vascular endothelial dysfunction in type 2 DM.

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In this issue of the Journal, Teraguchi et al report that glucose fluctuation negatively correlates with the degree of cardiac functional recovery (myocardial salvage index) after AMI. They also imply that proinflammatory monocytes (CD14+CD16−) or oxidative marker (urinary 8-isoprostane) were also proportionally decreased in accordance with cardiac functional recovery whereas the area under the curve (AUC) of GLP-1 reflected cardiac functional recovery. Inflammation has a fundamental role in left ventricular remodeling after AMI, as it is well known that an increased peripheral white blood cell count is associated with the prognosis of AMI. However, there is no effective approach to ameliorating the proinflammatory setting after AMI. Treatment with DPP-4 inhibitors or GLP-1 analog might be expected as a strategy to improve cardiac function after AMI (Figure 2). However, 2 recent randomized controlled trials of DPP-4 inhibitors for cardiovascular outcomes in patients with type 2 DM have been reported as results that were not expected. One found no beneficial effects on cardiovascular outcome despite favorable glucose control, though the rate of hospitalization for heart failure was increased. And the other, which enrolled patients with type 2 DM at 15–90 days after acute coronary syndrome, found neither beneficial nor harmful effects on the cardiovascular endpoints. Further careful examination is necessary to recognize the degree of glucose control necessary to prevent adverse cardiovascular outcomes.

References