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Effect of Daily Glucose Fluctuation on Coronary Plaque Vulnerability in Patients Pre-Treated With Lipid-Lowering Therapy

A Prospective Observational Study

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CME Objective for This Article: At the completion of this article, the learner should be able to: 1) define the mean amplitude of glycemic excursion (MAGE); and 2) discuss the association between glycemic control and plaque vulnerability.

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ABSTRACT

OBJECTIVES This study sought to investigate the effect of daily glucose fluctuation on coronary plaque properties in patients with coronary artery disease (CAD) pre-treated with lipid-lowering therapy.

BACKGROUND There is growing evidence that glucose fluctuation, as a residual risk apart from dyslipidemia, is an important factor contributing to the development of CAD.

METHODS This prospective study enrolled 70 consecutive CAD patients who were referred for percutaneous coronary intervention and whose low-density lipoprotein cholesterol level was <120 mg/dl under statin treatment or <100 mg/dl without statins. Daily glucose fluctuation was analyzed by measuring the mean amplitude of glycemic excursion (MAGE). The plaque properties in the culprit and nonculprit lesions were assessed by virtual histology intravascular ultrasound, and the volume percentage of necrotic core within the plaque (%NC) and the presence of thin-cap fibroatheroma were evaluated.

RESULTS In total, 165 lesions were evaluated in 70 patients (40 diabetic and 30 nondiabetic patients). %NC was well correlated with MAGE ($r = 0.490$, $p < 0.001$). A linear mixed effect model showed that MAGE had the strongest effect on %NC (coefficient $\beta = 0.080 \pm 0.020$ [standard error], $p < 0.001$). The generalized linear mixed effect model revealed that MAGE was the only independent predictor of the presence of thin-cap fibroatheroma (odds ratio: 1.037; 95% confidence interval: 1.010 to 1.065; $p = 0.007$).

CONCLUSIONS Daily glucose fluctuation may have an effect on coronary plaque vulnerability in patients with CAD pre-treated with lipid-lowering therapy. Further investigations should address the rationale for the early detection and control of glucose fluctuation in the era of universal statin use for CAD patients. (J Am Coll Cardiol Intv 2015;8:800–11)

Solid evidence has accumulated to show that intervention against dyslipidemia can prevent coronary artery disease (CAD), and statin administration is now widely used for both primary and secondary prevention of CAD. However, the reduction of risk of CAD by statins has been reported to be only 30% (1), and the target level of plasma low-density lipoprotein (LDL) cholesterol is still controversial (2). Thus, there has been a focus on further managing the residual risk apart from dyslipidemia. Meanwhile, the number of patients with diabetes mellitus (DM) has been greatly increasing worldwide, and the clinical effect of abnormal glucose metabolism has been recognized in the management of CAD.

There is increasing evidence that the post-prandial blood glucose state is an important contributing factor to the development of atherosclerosis (3,4). The STOP-NIDDM (Study to Prevent Non-Insulin-Dependent Diabetes Mellitus) trial revealed that a poor post-prandial state accelerates atherosclerosis, whereas improving it prevents atherosclerosis progression. It has long been recognized that glucose levels measured by a 2-h post-oral glucose tolerance test (OGTT) are strongly associated with mortality and cardiovascular disease (5,6). The DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study reported that high blood glucose concentrations 2 h after OGTT were associated with an increased risk of death that was independent of fasting blood glucose (5). However, whether glucose fluctuation may affect the coronary plaque properties in CAD patients pre-treated with lipid-lowering therapy remains largely unknown.

Virtual histology (VH) intravascular ultrasound (IVUS), which uses amplitude and frequency analysis