Could Plaque Composition-Related Endothelial Dysfunction Predict Poor Prognosis in Coronary Vasospastic Angina?

We read with interest the report by Ishii et al. (1) of their retrospective study in which patients with clinical suspicion of coronary vasospastic angina (CVA) underwent coronary angiography using a preset acetylcholine (ACh) protocol. Patients with positive results on ACh provocation testing were divided into 2 groups on the basis of the comorbidity of significant coronary stenosis, defined as ≥75% stenosis by angiography. The type of coronary spasm with stenosis was classified on the basis of the positional relation of ACh-provoked coronary spasm to significant stenosis. The investigators concluded that spasm at the site of significant stenosis was an independent predictor of major adverse cardiovascular events (MACEs) in patients with CVA.

ACh testing through cardiac catheterization has been used mainly for the assessment of endothelial function. Endothelial dysfunction is an early marker of atherosclerosis, contributing to its genesis and progression. Endothelial dysfunction plays a key role in precipitating myocardial ischemia and is a known independent predictor of major adverse cardiovascular events (MACEs) (2).

The use of intracoronary imaging techniques has dramatically improved understanding of the pathophysiology and relationship between endothelial dysfunction and atherosclerosis. Serial volumetric evaluations by intravascular ultrasound have found accelerated progression of atherosclerosis in coronary segments with endothelial dysfunction. Coronary segments with endothelial dysfunction may represent areas with abnormal vascular repair, rapid plaque progression, and propensity to rupture (3). Moreover, in a near-infrared spectroscopic study, endothelial dysfunction was related to coronary artery segments with higher quantities of lipid-rich plaques; these plaques with vulnerable characteristics are the cause of acute coronary syndromes (4). Finally, an intravascular ultrasound-virtual histology study found that coronary segments with endothelial dysfunction had larger necrotic core plaques and microcalcification. The size of necrotic core plaques was the principal determinant of coronary endothelial dysfunction (5).

For these reasons, we have some concerns about the proposed relationship between CVA with spasm at the site of significant stenosis and a higher rate of MACEs. In our opinion, the higher rate of MACEs can be explained by endothelial dysfunction and vulnerable plaque rupture rather than by CVA and spasm at the site of stenosis. The absence of intracoronary imaging is an important limitation, because the characteristics of the plaque are not known, so it cannot be excluded that the higher rate of MACEs is related to endothelial dysfunction and plaque rupture.

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REPLY: Could Plaque Composition-Related Endothelial Dysfunction Predict Poor Prognosis in Coronary Vasospastic Angina?

We thank Dr. Ortega-Paz and colleagues for their interest in and comments on our study (1). They indicate that the lack of information on the morphological features of coronary plaque by intracoronary imaging (e.g., optical coherence tomography, grayscale and intravascular ultrasound-virtual histology) is an important limitation of our retrospective study. We agree with their comment and that endothelial dysfunction contributes to the pathogenesis of atherosclerosis, and vulnerable plaque rupture plays an important role in the manifestation of acute coronary syndromes, and we agree that intracoronary imaging should be performed to evaluate the