Tissue Characterization of Coronary Plaques as a Key to Reno-Cardiac Syndrome

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It is generally accepted that mortality from cardiovascular disease (CVD) is significantly higher in patients with chronic kidney disease (CKD) than in the general population.^{1,2} It has been considered that vascular calcification and arterial stiffness are major contributors to this elevated mortality,³ but a clinical study shed new light on the relationship between CVD and CKD.⁴ A high concentration of indoxyl sulfate (IS), a protein-bound uremic toxin that results from the metabolism of dietary tryptophan, was found to be a predictor of increased CVD risk, independent of potentially confounding coronary risk factors.⁴ Studies demonstrating relationships between a high IS level and poor prognosis in patients with dilated cardiomyopathy,⁵ and between the IS level and glomerular filtration rate,⁶ followed the previous study. Animal studies showed that IS causes inflammation,⁷ endothelial dysfunction,^{8,9} and vascular smooth muscle cell proliferation.¹⁰ However, clinical studies of the mechanism by which a high IS level promotes CVD have been scarce, owing to the fact there are few methods of evaluating the tissue components of coronary plaques.

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Integrated backscatter intravascular ultrasound (IB-IVUS) was developed for the tissue characterization of coronary plaques to help elucidate the mechanism of progression of coronary atherosclerosis (Figure).¹¹ The reliability and usefulness of IB-IVUS have been demonstrated in many studies.^{12–14} It was recently reported that the axial resolution of IB-IVUS is $69 \pm 6 \mu\text{m}$. As there was good agreement between fibrous cap thickness measured by IB-IVUS and that by optical coherent tomography, IB-IVUS can be used to identify plaques with a high prevalence of thin cap fibroatheroma (TCFA).¹⁴ IB-IVUS-identified TCFA, defined as “lipid core abutting the lumen”, was found to correlate with periprocedural myocardial infarction after elective percutaneous coronary intervention, both on univariate analysis and after adjusting for potential confounders.¹⁴

In this issue of the Journal, Yamazaki et al¹⁵ report that the IS level was associated with the relative lipid volume as

Figure. Detection of lipid distribution by integrated backscatter intravascular ultrasound (IB-IVUS). (A) Representative image of coronary plaque indicating each tissue component constructed by IB-IVUS. (B) Representative image of coronary plaque showing lipid core. (C) Representative image of coronary plaque indicating lipid distribution constructed by IB-IVUS throughout an entire coronary artery.

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measured by IB-IVUS, independent of potentially confounding coronary risk factors such as glomerular filtration rate and low-density lipoprotein cholesterol. By contrast, they found that other uremic toxins, such as asymmetric dimethylarginine and p-cresol, were not associated with relative lipid volume in plaques. Furthermore, although asymmetric dimethylarginine did not correlate with oxidative stress, IS correlated with both oxidative stress and endothelial dysfunction. Yamazaki et al concluded that only serum IS was associated with lipid-rich coronary plaques on IB-IVUS in patients with CVD, and that IS might therefore be a useful new biomarker for detecting and monitoring lipid-rich coronary plaques.¹⁵

The cardiorenal syndrome is a disorder of the heart and kidneys in which acute or chronic dysfunction of one organ may induce acute or chronic dysfunction of the other.¹⁶ This general definition has been expanded to include 5 subtypes reflecting the primacy of organ dysfunction and the sequence of the syndrome, as proposed by Rencó et al.¹⁶ The type in which chronic abnormalities of heart function lead to kidney injury or dysfunction (type II) can justifiably be termed “cardiorenal syndrome”. In contrast, enhancement of cardiovascular dysfunction initiated by kidney disease (type IV) can be termed “reno-cardiac syndrome”.¹⁷

Is the difference between “cardiorenal syndrome” and “reno-cardiac syndrome” merely a semantic issue?¹⁷ Yamazaki et al also focus on this important question. We cardiologists should collaborate with nephrologists to manage patients with “cardiorenal syndrome” and “reno-cardiac syndrome” to improve their prognosis. Just as a B-type natriuretic peptide became a prominent indicator of heart failure, the IS level may become a promising indicator of cardiovascular dysfunction initiated by kidney disease.

Disclosures

I have no financial or other relations that could lead to a conflict of interest.

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