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Editorial

Structural Abnormality or Vascular Dysfunction? A Road to Ruin

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Changes in vascular function and structure of vessels are evaluated by flow-mediated vasodilation (FMD) and intima-media thickness (IMT), respectively, which are surrogate markers for atherosclerosis[1-3]. Increased IMT of the carotid artery and impaired brachial FMD are indeed prevalent in patients with a high risk of cardiovascular diseases, such as those with diabetes, dyslipidemia, and hypertension, and serve as independent predictors of future cardiovascular events in those subjects[1-3]. However, decreased brachial FMD is not necessarily correlated with increased IMT of the carotid artery, suggesting that these two markers reflect distinct and independent processes of atherosclerosis[4, 5]. In other respects, stages of atherosclerosis may differ among different vasculatures.

In this issue, Iwamoto *et al.*[6] examined IMT, FMD, and nitroglycerine-induced vasodilation (NID), another marker of vascular function that detects endothelium-independent smooth muscle function at the same popliteal artery of patients with Buerger disease ($N=20$) and atherosclerotic peripheral artery disease (PAD) ($N=30$); they compared the values with those of age- and sex-matched controls. The authors showed that (1) IMT was significantly increased, whereas FMD and NID were impaired in atherosclerotic PAD patients compared with control subjects and (2) although IMT was larger in patients with Buerger disease than in control subjects, there was no significant difference in FMD or NID between the two groups. These findings demonstrate that even in the same leg artery, structural abnormalities and vascular dysfunction are not necessarily correlated in patients with some types of PAD, such as Buerger disease. In addition, preservation of endothelial and smooth muscle function evaluated by FMD and NID, respectively, may partly explain the low risk of cardiovascular events and death in Buerger disease patients compared with atherosclerotic PAD patients[7, 8].

The present findings also underscore the need to evaluate both morphological and functional abnormalities of arteries for predicting cardiovascular morbidity and mortality. However, their observations could raise novel questions; which clinical and biochemical factors are involved in the disassociation between structural and functional derangements of vasculatures, that are two different aspects of atherosclerosis? Do prognostic values of IMT and FMD depend on patient background? We previously found that some patients developed carotid atherosclerosis without vascular inflammation, as detected by fluorodeoxyglucose-positron emission tomography, whereas others had vascular inflammation without structural abnormalities of the carotid artery[9]. The observations suggest that the severity of vascular inflammation within atherosclerotic plaques is a possible candidate to separate structural abnormalities of popliteal artery from vascular dysfunction. Therefore, it would be interesting to compare high-sensitivity C-reactive protein (hs-CRP) levels in Buerger disease patients with those in atherosclerotic PAD patients and examine the correlation of hs-CRP, the best-characterized biomarker for systemic low-grade inflammation, with IMT, FMD, and NID. Although the findings of Iwamoto et al. are interesting, further experimental and clinical studies are required to clarify the mechanism why popliteal vascular function is preserved in Buerger disease patients with structural atherosclerosis, which could shed light on risk stratification and appropriate treatment for atherosclerotic cardiovascular disease in humans.

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