Editorial Comment

Brachial-Ankle Pulse Wave Velocity and Microalbuminuria

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Patients with type-2 diabetes mellitus (DM), hypertension, metabolic syndrome, and chronic kidney disease (CKD) are at high risk for cardiovascular mortality and should be treated as early as possible in order to prevent the progression of systemic atherosclerosis. A huge increase in the number of patients at high risk has created an urgent need for the respective academic societies to publish guidelines and educate general practitioners. The insidious onset of these disorders makes it necessary to screen general populations for conventional risk factors and surrogate markers. Surrogate markers are also helpful to track the disease severity before and after the start of prevention therapy. Because atherosclerotic and atherothrombotic diseases progress slowly and attack suddenly, it will be important to establish a comprehensive set of surrogate markers to detect not only the active lesion state but also the hard endpoint. Currently, there are several structural and functional surrogate markers available; the former include carotid artery wall thickness and left ventricular mass, and the latter include blood pressure, endothelial dysfunction, arterial stiffness, and proteinuria (*1*, *2*).

Pulse wave velocity (PWV), a measure of arterial stiffness, has been related to established cardiovascular risk factors and clinical outcome (*2*, *3*). PWV measured at different sites may express different components of vascular physiology; for example, carotid-femoral PWV represents aortic elasticity and compliance, while femoral-ankle PWV mainly represents peripheral vascular resistance. The recently introduced brachial-ankle PWV (baPWV) measured with an automated device has been shown to correlate with catheter-measured aortic PWV with a correlation rate ($r=0.87$) equal to that of carotid-femoral PWV (*4*). Although the physiological significance of baPWV is rather complicated, it has been proposed that this measure be useful for assessing endothelial function (*5*). Because nitric oxide (NO) is involved in the maintenance of large artery compliance and plays a key role in arteriole dilatation, it is reasonable that increased baPWV would be implicated in endothelial dysfunction.

Microalbuminuria not only serves as an early marker of both diabetic and nondiabetic renal diseases but also predicts cardiovascular mortality in patients with DM and hypertension, and even in healthy subjects (*6–9*). Moreover, the Framingham Heart Study has recently shown that low-grade albuminuria, even when below the threshold for microalbuminuria, was associated with increased risk of cardiovascular mortality in non-hypertensive, non-diabetic individuals (*10*). These findings support the recommendation that microalbuminuria be included in general health checks and in the diagnostic criteria for metabolic syndrome. Importantly, urinary albumin is a sensitive and specific measure that can be easily applied in a clinical setting.

Although the underlying mechanisms for microalbuminuria remain unclear, podocytes and endothelial cells play pivotal roles as a glomerular barrier (*11*), and both are susceptible to degradation by reactive oxygen species (*12*). Accordingly, it has been hypothesized that microalbuminuria may be a highly sensitive indicator of generalized endothelial injury (*13*). Indeed, recent studies have demonstrated an association between microalbuminuria and endothelial damage (*14–16*).

Thus, baPWV and microalbuminuria are both useful mark-

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ers of systemic endothelial dysfunction. The association between them has been demonstrated in an elderly Japanese community (*17*). In this issue of *Hypertens Res*, Munakata *et al*. confirm the association in a large scale study of never-treated hypertensive patients (*18*). In a multicenter cohort study entitled the Japanese Trial on the Prognostic Implications of Pulse Wave Velocity (J-TOPP), microalbuminuria was found in 191 (26.6%) out of 718 patients with untreated hypertension. Moreover, there was a linear correlation between baPWV and the log [urinary albumin excretion]. Given the relatively low incidence of microalbuminuria, it may be appropriate to first evaluate baPWV in patients with never-treated hypertension.

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