Editorial Comment

Cerebral White Matter Lesions and Microbleeds: Tiny but Meaningful Indicators of Hypertensive Damage

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The development of MRI has enabled small subclinical cerebral abnormalities to be detected. Among these various abnormalities, patchy or confluent cerebral white matter lesions (WMLs), referred to as leukoaraiosis (from the Greek leuko = white and araiosis = rarefied) (*1*), are seen as hyperintensities on T_2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences. WMLs are common in the general elderly population (*2*), as Ohmine *et al*. (*3*) report in this issue of *Hypertension Research*. Stenosis or occlusion of small cerebral vessels with sudden or chronic ischemia can lead to incomplete white matter infarction and is considered to play a central role in the pathogenesis of WMLs (*4*). Alternative mechanisms include alterations of blood-brain barrier permeability either during chronic hypertension or in relation to impaired venous return within the deep white matter (*5*). Major trials have reported that the presence of WMLs is an independent predictor of stroke (*6–8*). Although several studies including a recent multicenter, multinational Leukoaraiosis and Disability (LADIS) study (*9*) showed a strong association between WMLs and general cognitive dysfunction, the contribution of WMLs to vascular dementia is still controversial (*4*).

In addition to age, hypertension is one of the most important risk factors for WMLs (*10*). Increased office blood pressure (BP) levels (*11–13*), as well as ambulatory BP levels (*14–16*), are associated with severe WMLs. Successful antihypertensive treatment ameliorates (*11–13*) and a nondipping circadian pattern enhances the severity of WMLs (*16*). WMLs are associated with both large-artery atherosclerosis and small-artery endothelial dysfunction (*10*). In addition, WMLs have been found to be related to new clinical entities, including the metabolic syndrome (*17*) and chronic kidney disease (*18*). Thus, WMLs are good predictors of subtle, as well as advanced, systemic vascular organ damage.

The study by Ohmine *et al*. (*3*) is unique in that it sought to identify a "predictor" of this "MRI-detectable predictor." The results revealed that an increase in arterial stiffness, which is easily and non-invasively evaluated by the brachial-ankle pulse wave velocity (ba-PWV), is associated with the presence of WMLs. Furthermore, the authors categorized WMLs into two distinct types, periventricular hyperintensities (PVH) and deep WMLs; after adjustment for traditional risk factors, they found that elevated ba-PWV was independently related to PVH, but not deep WMLs. The authors suggest that this difference between the two types may be explained by the fact that, in the early phase of atherosclerosis, ba-PWV mainly reflects functional change (sclerosis) rather than morphological change (atherosis) of the vascular wall, and the functional damage can affect PVH more than deep WMLs. However, one cannot yet conclusively state that the two types of WMLs have a different association with ba-PWV, mainly because the study of Ohmine *et al*. (*3*) had such a small number of patients, particularly patients having advanced WMLs. I anticipate that the authors will do further studies to determine the detailed contribution of ba-PWV to the two types of WMLs, since their studies based on brain MRIs of an elderly population in a rural community (Sefuri, Japan) have already identified several clinical characteristics of WMLs and silent

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brain infarction (*19–22*).

Cerebral microbleeds may be another important indicator of arteriosclerosis; they are tiny, subclinical lesions that are detectable only by gradient-echo T_2*-weighted MRI (*23*, *24*). Although the clinical significance of cerebral microbleeds has not been established, several studies suggest that they are associated with hypertension and vascular organ damage. An interesting study on microbleeds has been previously published in this journal (*25*). Both WMLs and microbleeds are related to small-artery cerebrovascular lesions, which are common in the Asian population. Many issues related to these tiny cerebral abnormalities will need to be elucidated by hypertension researchers.

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