Association of Magnetic Resonance Imaging Markers of Cerebrovascular Disease Burden and Cognition

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Background and Purpose—The present study sought to examine the association between the burden of cerebrovascular disease (CeVD) as assessed by multimodal magnetic resonance imaging and neurocognitive function.

Methods—Cognitively impaired patients and controls were tested on an extensive neuropsychological battery and underwent multimodal brain magnetic resonance imaging. CeVD markers determined from magnetic resonance imaging included the presence of multiple lacunes, multiple cerebral microbleeds, and moderate or severe white matter hyperintensities as markers for small-vessel disease and cortical stroke and intracranial stenosis as markers for large-vessel disease. A weighted CeVD burden score was constructed, and its association with global and domain-specific cognitive performance was investigated.

Results—A total of 305 cases and 94 controls were included in the analysis. A graded association of CeVD burden with neurocognitive function was found. Moreover, a clear threshold of CeVD burden was associated with severe impairment. White matter hyperintensities was associated with global neurocognitive deficits, whereas microbleeds were associated with domain-specific impairments.

Conclusions—The weighted CeVD burden score comprising markers of both small- and large-vessel diseases were associated with deficits in both global and domain-specific neurocognitive function. Additional studies are needed to validate the use of this CeVD burden score for the prediction of dementia. (Stroke. 2015;46:2808-2814. DOI: 10.1161/STROKEAHA.115.010700.)

Key Words: cerebrovascular disorders ■ cognition ■ magnetic resonance imaging ■ stroke

Magnetic resonance imaging (MRI) markers of cerebrovascular disease (CeVD) include those for small-vessel disease (SVD) and large-vessel disease (LVD). CeVD is recognized as a major contributor to cognitive impairment and dementia, especially in Asian populations.1-3 Although a growing body of evidence suggests that MRI markers of CeVD can predict cognitive decline, previous studies investigating CeVD and neurocognitive function have mainly focused on either the association between (1) ischemic stroke and cognition or (2) SVD and cognition.4-6 However, the concept of total CeVD burden, encompassing both SVD and LVD, has not been extensively examined in relation to cognitive status. Huijts et al7 using an unweighted summation of SVD markers reported that the co-occurrence of lacunes, white matter hyperintensities (WMH), microbleeds, and enlarged perivascular spaces was inversely correlated with cognitive impairment. Stakkenborg et al8 showed that mild cognitive impairment patients with coexisting severe WMH, more lacunes, and microbleeds at baseline had higher risk of converting to non-Alzheimer dementia at follow-up. Furthermore, vascular dementia (VaD) patients with co-occurring SVD and LVD showed significantly worse cognitive performance.9 These studies demonstrate that not all CeVD contributes equally to changes in cognition and the value of using a combined measure of CeVD burden to predict cognitive impairment. Moreover, a recent study using an unweighted SVD scale recommended that different cutoff points and weighting for MRI features should be investigated.10 Furthermore, it is important to consider whether each measure of CeVD, in any proposed scale, carries the same importance to patients11 and whether differential weighting of each MRI feature are needed to optimally predict outcomes of clinical importance, such as cognition. Therefore, we have explored whether a weighted assessment of total CeVD burden can improve understanding of the cognitive consequences of CeVD. Importantly, such a weighted total CeVD burden scale should be pragmatic and balance between practical use and the inherent complexity of disease, hence providing rapid and

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