This may prompt unnecessary anxiety in a patient population already at risk for a recessive disorder.

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STAGING AND NATURAL HISTORY OF CEREBROVASCULAR PATHOLOGY IN DEMENTIA

Vladimir Hachinski, London, Canada: This recently published study makes a laudable attempt at quantification of the cerebrovascular burden as well as one that tries to conform to the recommended standards of doing so.[1,2]

The major limitation is that the vascular burden is not correlated with cognition. This is particularly relevant when considering those who do not have dementia. Schneider et al.[3] have shown that isolated vascular lesions, amyloid plaques, and Lewy bodies are relatively common in elderly individuals. However, it is the combination that multiplies the likelihood that many will develop dementia.

This study could be complemented by trying to correlate whatever cognitive data are available in the brain banks of the 2 centers with the vascular burden and also with the presence or absence of the *APOE4* allele, correlating not only the likelihood of amyloid deposition, but also with the development of atherosclerotic vascular disease.

Another possible approach is to take the vascular index developed by the authors and apply it as a hypothesis to existing clinical pathologic studies that have clinical, imaging, and pathologic data.

This study is welcome, given the increased recognition of the vascular component of cognitive impairment in the elderly, which at the moment is the only component that is both treatable and preventable.[4]

Author Response: Raj N. Kalaria, Newcastle upon Tyne, UK; Vincent Deramecourt, Lille, France: We welcome Dr. Hachinski's views on these longstanding issues, which have dogged the cerebrovascular disease field. Currently, when it seems we should quantify all we examine, how should we relate brain vascular pathology to cognitive dysfunction?

Our first goal was to establish a conceptual model that vascular pathology can be "measured" in all types of dementias.[1] This step would advance the field by reconsidering previous strategies[5] and guidelines[2] yet still refining the oft-quoted work of Tomlinson et al.[6] We have not only shown which lesions are relevant including microinfarction but hopefully provided a clear means to achieve quantification without major modifications in ongoing protocols in various centers.

We recognize the limitations of our study. It is expected that the proof of this concept will eventually be revealed from correlative analyses of large cohorts with brain autopsy collections such as the Honolulu Asia Aging Study USA, Cognitive Function in Ageing Study UK, Europe Brain Net II, and Brains for Dementia UK.

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Author disclosures are available upon request (journal@neurology.org).

Staging and Natural History of Cerebrovascular Pathology in Dementia

Vladimir Hachinski, Raj N. Kalaria and Vincent Deramecourt

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