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Evaluating Ischemic Stroke Subtypes: Does the Retinal Microvasculature Hold Clues to What Lies Beneath?

To the Editor:

We read with great interest the article entitled 'Retinopathy in ischemic stroke subtypes'¹ appearing in *Stroke*, and would like to congratulate the authors for this novel effort. Doubal et al hypothesized that there would be higher rates of retinopathy in patients with acute lacunar infarcts but failed to demonstrate any significant correlation. We have reason to suggest that it may be due to the *basis* of their hypothesis. Doubal et al essentially believe that retinopathy and lacunar infarcts are both, by large, manifestations of disordered small vessel endothelium and an increased permeability in the blood-retinal or blood-brain barrier.

Our knowledge concerning lacunes is largely derived from Fisher's landmark autopsy studies in which he reported 2 main causes of small vessel obstruction: small, multiple lacunes usually caused by lipohyalinosis and larger, single ones by atheromatous or embolic perforator occlusion. Much research, and an even greater debate, was generated after Boiten et al² proposed the existence of 2 lacunar infarct entities which could be clinically distinguished from each other. Ensuing studies highlighted various associations between proposed subtypes of lacunar infarcts suggesting that patients with larger lacunar strokes (associated with hypertension, dementia, leucoariosis and age) have a worse clinical outcome than the small lacunar strokes (associated with hypercholesterolemia, diabetes and myocardial infarction).³ Because the 2 subtypes have different risk factor profiles, their respective patho-physiological processes are also likely to differ. One of the reasons for no strong association being demonstrated by Doubal et al could be that not all lacunes have the same pathological cause, supporting the lacunar infarct subtype theory. Had Doubal et al grouped smaller lacunar infarcts (<1.5 cm) separate from the larger ones (1.5 to 2.0 cm), as proposed by Caplan,⁴ we believe that it could have produced some valuable associations, and thus shed some light on the pathophysiology of lacunar infarcts.

Doubal et al have correctly pointed out the similarities in the retinal and small cerebral vessels. Pathological changes in the retinal arteries have been found to parallel those in the small cerebral arteries, which incidentally, are also one of the proposed causes of lacunar infarcts. These changes are independent of hypertension.⁵ The retinal vascular system can be more readily

visualized using noninvasive means. They are also a cheaper and quicker method of evaluating systemic small vessel disease. This has significant implications in developing countries where diagnosis, prognosis and treatment rely more heavily on clinical methods rather than advanced neuro-imaging and intervention.

Recently, Lindley et al⁶ have published the protocol of the clinical trial, MultiCentre Retinal Stroke Study (MCRS, on which Doubal et al too serve as collaborators) which aims to establish the higher association of retinal microvasculature signs with lacunar infarcts. We propose that lacunes be subtyped and then its association with retinopathy investigated. This would not only reveal if retinopathy is significant with any particular pathogenesis of stroke but could also help in furthering the theory that lacunes are basically distinct pathological entities under the same umbrella term. In any case, the results of the trial promise to shed some valuable light onto the association between retinal microvascular changes and ischemic stroke.

Disclosures

None.

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