Retinal microvasculature in acute lacunar stroke: a cross-sectional study

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Summary

Background Lacunar stroke accounts for a quarter of cases of acute ischaemic stroke; however, its underlying pathophysiology remains unclear. Our aim was to establish whether there is an association between changes in the retinal microvasculature and lacunar stroke that might provide clues to the pathology of cerebral small vessel disease.

Methods In this cross-sectional study, we recruited patients who presented with acute stroke at three centres in two countries (Sydney and Melbourne, Australia, and Singapore). Each patient had standardised clinical assessments, retinal photography, and CT or MRI of the brain. Changes in the retinal microvasculature were assessed from retinal photographs by graders who were masked to the patients' clinical details. Lacunar stroke was diagnosed according to a modified version of the TOAST criteria (Treatment of Acute Stroke Trial) or the OCSP criteria (Oxfordshire Community Stroke Project) and by MRI findings.

Findings We recruited 1321 patients aged 19 to 94 years with acute ischaemic stroke; 410 (31%) had lacunar stroke. Patients with acute lacunar stroke were no more likely to have hypertension (p=0·12), diabetes (p=0·51), or hypercholesterolaemia (p=0·91) than were patients with other types of ischaemic stroke. However, patients with lacunar stroke were more likely to have retinal microvessel signs, particularly when stroke subtype was confirmed using diffusion-weighted MRI, than were patients with other stroke subtypes. After adjustment for age, sex, study site, smoking history, hypertension, and diabetes, the patients with lacunar stroke were more likely than those with other stroke subtypes to have microvessel signs, and when stroke subtype was confirmed by diffusion-weighted MRI the odds ratios were: 3·55 (95% CI 1·77–7·12) for focal arteriolar narrowing; 1·96 (1·19–3·24) for arteriovenous nipping; 2·32 (1·42–3·79) for enhanced light reflex of the arteriolar wall; 1·33 (0·74–2·41) for generalised retinal arteriolar narrowing; 1·45 (0·84–2·51) for small retinal arteriole:venule ratio; and 1·35 (0·80–2·26) for retinal venular widening.

Interpretation Our findings suggest that acute lacunar stroke is a manifestation of non-atherothrombotic occlusive small vessel disease, which might have implications for the prevention and treatment of this stroke subtype.

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Introduction Lacunar stroke is a disease of the small (40–200 μm) penetrating arteries in the brain. Although lacunar stroke accounts for a quarter of all acute ischaemic strokes,1 its underlying pathology is largely unknown. Previous pathological studies have proposed three main causes of lacunar stroke: lipohyalinosis (a destructive wall lesion containing mural foam cells, and fibrinoid necrosis in some acute lesions); hyaline arteriosclerosis (a concentric thickening of the hyaline wall seen commonly in old age); and microatheroma (atheromatous plaques that usually affect the proximal part or the origin of the perforating artery).2 Breakdown of the blood–brain barrier with subsequent damage to the walls of the small vessels and perivascular oedema, rather than thrombosis, was recently proposed as a potential mechanism of lacunar stroke,3 although other, more unusual, mechanisms are also possible (eg, embolic occlusion of the perforating arteries, haematological disorders, and infection).4 However, whether lacunar stroke results from thrombotic disease and whether it differs pathologically from other subtypes of acute ischaemic stroke remain controversial questions.5

Improved understanding of the underlying pathophysiology of lacunar stroke has wide-ranging implications for the prevention and management of acute stroke.6 Research on lacunar stroke has, however, been hindered by several factors: lacunar stroke has a low case-fatality rate, which restricts the number of pathological specimens available from patients with acute stroke; pathological studies are laborious and require large numbers of serial sections, which is not feasible in routine pathology; and the brain imaging techniques for examining the small cerebral arteries and arterioles that are affected in lacunar stroke do not produce images of high-enough resolution.

The retinal vasculature can be used as a model to study the relation between cerebral microvascular disease and lacunar stroke. Retinal and cerebral small vessels have...