Editorial

What Is a Lacune?

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See related article, pages 3083–3085.

The terms “lacune”, “lacunar infarct” and “lacunar stroke” are often used interchangeably, but they are not the same thing. Lacunes are 3 to 15 mm cerebrospinal fluid (CSF)-filled cavities in the basal ganglia or white matter, frequently observed coincidentally on imaging in older people, often not clearly associated with discrete neurological symptoms. “Lacunar stroke” describes a clinical stroke syndrome with the typical symptoms and signs referable to a small subcortical or basal ganglia lesion.1,2 “Lacunar infarct” should refer to a filled cavities in the basal ganglia or white matter, frequently observed coincidentally on imaging in older people, often not clearly associated with discrete neurological symptoms. “Lacunar stroke” describes a clinical stroke syndrome with the typical symptoms and signs referable to a small subcortical or brain stem lesion.1,2 “Lacunar infarct” should refer to a clinical stroke syndrome of lacunar type where the underlying lesion is an infarct on brain-imaging. On CT or MR T2-weighted and fluid-attenuated inversion recovery (FLAIR) imaging, an acute lacunar infarct can look just like a white matter lesion (WML), difficult to distinguish from an asymptomatic WML without diffusion-imaging to show a hyperintense signal (reduced on ADC), or a prior scan for comparison, especially in patients with WMLs. Some clinically evident acute lacunar infarcts may evolve with time into lacunes. These points are well-established.

Less well-established is how many clinically evident lacunar infarcts ever cavitate to become “lacunes”. It seems generally assumed that all lacunes start life as an infarct, even if the patient did not notice anything, and therefore share the same risk factors, etiology, prognosis, pathogenesis, etc., as clinically evident lacunar infarcts.3–5 However, suppose only a proportion of lacunar stroke lesions, perhaps as few as a third, ever cavitate, with the majority that fail to cavitate retaining the appearance of a WML.6 Counting lacunes could result in spurious risk factor and etiologic associations for lacunar stroke. We should not assume that the pathogenesis of clinically evident lacunar stroke is the same as for clinically silent lacunes. Equally, similarity in appearance between WMLs and clinically evident acute lacunar infarct could imply similar causation. However, surely the fact that one has caused symptoms (lacunar stroke/infarct) and the other not (WML/lacune) is important in itself and should lead to their careful distinction in any research at least until we know more.

The Leukoaraiosis and Disability Study (LADIS) was designed to investigate the association between radiological signs of small-vessel disease, mainly WML, and the subsequent development of disability,7 not lacunar stroke. Because lacunes and WMLs are signs of cerebral small-vessel disease and are increasingly recognized to be associated with cognitive impairment and future stroke risk, this is important work. In this issue of Stroke, the present analysis by Guow et al suggests that new lacunes in subcortical white matter develop in existing WML and were also accompanied by development of new WML, whereas basal ganglia new lacunes occurred in radiologically normal tissue without new WML. Subcortical lacunes were associated with hypertension and stroke, basal ganglia lacunes with atrial fibrillation. This was interpreted as evidence for different etiologies of lacunes in different brain regions, i.e., that basal ganglia lacunes might be more likely to arise from embolic lenticulostriate artery occlusion, whereas subcortical lacunes could arise from progressive hypoxia/ischemia secondary to stenosed deep perforating arterioles. Several factors should be considered in interpreting this work.5

Who were the subjects? Six hundred and thirty-nine subjects aged 65 to 84 years with WML of any degree on MR (half had moderate or severe WML7 at baseline), with no or only mild disability in activities of daily living, were recruited.7 After 3 years, 358 had repeat MR. The remaining 44% dropped out for various reasons,7 leaving younger, less disabled, less cognitively impaired, less risk factor–affected subjects in the study, thus restricting generalization.7

How did the subjects change? Sixty-two patients (19%) developed 106 new lacunes (CSF containing “holes”) over 3 years: 58 in subcortical white matter, 35 in basal ganglia and 13 infratentorial. These new lacunes were not clinically evident acute lacunar strokes because LADIS did not collect details of clinical stroke recurrences so was unable to link new “holes” to specific symptoms.

What about methodology? The ascertainment of new lacunes was performed by a rater with the baseline and follow-up scans side-by-side. The scans were not coregistered; therefore, we rely on the rater’s anatomic skills to determine whether a lacune was indeed new or had been present previously but appeared different because of differences in head-positioning, a particular problem with small lesions. Thus, prior beliefs about relationships between WMLs and lacunes could have influenced scan-rating. Multivariate-modeling requires a minimum of 10 outcomes per variable: 58 subcortical lacunes allows for 5 variables and 35 basal ganglia for 3 (LADIS tested 6). WMLs are more common in subcortical white matter than in basal ganglia, possibly because there simply is more subcortical white matter. Therefore, an apparent association with WMLs in subcortical white matter but not basal ganglia could simply reflect the lower likelihood of WMLs being present in basal ganglia, not that the etiology was different.5

It seems important to make several points. The term “lacunar infarct” should be reserved for lesions that were
clearly associated with a clinical lacunar syndrome, and clearly shown to be ischemic and not hemorrhagic by use of appropriate imaging in the acute phase. The term “lacune” should be used for CSF-containing subcortical “holes” found on imaging that are either clinically silent or have no clear association with symptoms. Asymptomatic lacunar “holes” should not be assumed to be infarcts until we know more about what causes them—although “infarct” may be a convenient term for a lesion which resembles the late stage of clinically definite infarct, it implies a pathogenesis for which there is insufficient direct evidence. Rather, we should describe what we see radiologically and not infer etiology. The LADIS investigators propose that lacunes and WMLs result from perforator vessel stenoses, compromised perfusion and progressive ischemia. However, other processes could result in similar appearances. The brain has a limited set of responses to widely differing insults: very different etiologies can produce the same appearances on imaging. After all, cerebromalacea looks the same (CSF-containing area of tissue loss) whether arising from a cortical arterial occlusion, a venous occlusion, or a bang on the head. We cannot assume that the etiology of clinically evident lacunar infarcts and lacunes is similar and extrapolate from one to the other; for example, to assume that because lacunes are associated with increasing dementia, clinically evident lacunar stroke must also be—this might be, but counting lacunes would not be the way to establish this link. Whether or not lacunar lesions cavitate may depend more on the patient’s response to an insult than on factors related to the insult itself (a “per patient” rather than “per lacune” analysis in the present study could address this). Determining cerebral small-vessel disease etiology would benefit from standardization of terminology and avoidance of assumptions about causation.

Disclosures

None.

References


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