Mechanisms in Lacunar Infarction

Deborah R. Horowitz, MD; Stanley Tuhrim, MD; Jesse M. Weinberger, MD; and Steven H. Rudolph, MD

Background and Purpose: Lacunes are thought to occur in patients with hypertension or diabetes mellitus as a result of small-vessel disease. This study evaluated the importance of other stroke mechanisms in a population of patients with lacunar infarction.

Methods: We evaluated 108 consecutive patients with a lacune in the lenticulostriate distribution for other stroke risk factors such as carotid and cardiac disease.

Results: Hypertension was present in 68% of the patients and diabetes mellitus in 37%; both occurred in 28% and neither occurred in 23%. Noninvasive carotid studies identified atherosclerotic plaque as a possible embolic source in 23%. By previously established criteria, 18% were at high risk for cardioembolism. Of those with hypertension or diabetes mellitus, 36% were at risk for a carotid or cardiac embolus. Of those without hypertension or diabetes mellitus, 32% had a possible carotid or cardiac etiology.

Conclusions: The high incidence of carotid and cardiac disease in those with and without hypertension or diabetes mellitus suggests the importance of other stroke mechanisms in this population. Patients with lacunar infarction should therefore be evaluated for other causes of stroke that may be treatable. (Stroke 1992;23:325–327)

KEY WORDS • embolism • lacunar infarction

Lacunes are small, deep infarcts that occur in the subcortical regions of the brain, including the deep white matter, basal ganglia, internal capsule, thalamus, and brain stem.1-3 The various syndromes resulting from lacunar infarctions have been well described by Fisher.4 Small-vessel lipohyalinosis or microatheroma formation are the usual underlying pathologic lesions. Hypertension and, possibly, diabetes mellitus are the most frequent risk factors associated with the development of lipohyalinosis and subsequent lacunar infarction.1,2,4,5 These risk factors are not present in all cases, and pathologic investigation has not always confirmed the presence of small-vessel disease.6 In addition, hypertension has not always been found to be more common in patients who develop lacunes when compared with those who develop cortical infarctions in the carotid distribution.7 Other etiologies of lacunar infarctions, including middle cerebral artery atherosclerotic disease,8-10 embolism or hemodynamic compromise from a carotid lesion,11-18 or embolism from a cardiac source13,15,17,19 have been postulated. The occurrence of multiple possible etiologies in many patients with lacunar infarction further obscures the determination of a precise cause. We studied 108 consecutive patients with the diagnosis of lacunar infarction to determine the prevalence and clinical significance of the various factors.

Subjects and Methods

All patients admitted over a 2-year period with a final diagnosis of lacunar infarction in the lenticulostriate distribution were selected from the Mount Sinai Stroke Data Bank. The data bank is a computerized registry that contains all information collected on each patient by a member of the stroke service. This information includes demographics, medical and neurologic history, physical examination, laboratory results, and events of hospital course.

The patient population included 54 women (median age 66.5 years) and 54 men (median age 71 years). Diagnosis of lacunar infarction was based on clinical impression and computed tomographic (CT) scan result. These patients typically had a lacunar syndrome, defined as pure motor, sensory, or sensorimotor stroke; ataxic hemiparesis; dysarthria–clumsy hand syndrome; and milder variations of these syndromes, such as faciobrachial weakness. The CT scan was either normal or showed a focal deep infarction.

Patients entered into the data bank routinely undergo evaluation of medical history; general physical and neurologic examinations; and laboratory tests, including blood work, electrocardiography, and chest x-ray. Echocardiography was performed when patient history, electrocardiogram, or clinical examination suggested the possibility of a cardioembolic source or when no other etiology of stroke was found. Hypertension was considered to be present if there was a history of hypertension or if blood pressure was consistently >160/90 mm Hg and required treatment after the acute stroke period (7 days after stroke onset). Diabetes mellitus was present if there was a past history or if fasting blood glucose remained >155 mg/dl and required treatment after the acute stroke period.

Carotid testing was done with a noninvasive test battery consisting of Doppler carotid flow studies, real-time duplex B-mode ultrasonography of the carotid
bifurcation, oculary pneumoplethysmography, and supraorbital directional Doppler analysis. A hemodynamically significant lesion was identified when there was a >5.0-kHz frequency shift on spectral analysis, supraorbital directional Doppler measured flow reversal or oculary pneumoplethysmography pressure was <65% of the brachial artery pressure, or there was >10-mm Hg difference between the two sides. A potential embolic carotid source of stroke was defined as the presence of a hemodynamically significant lesion or an ipsilateral heterogeneous plaque on real-time B-mode ultrasonography or a 4.0–5.0-kHz frequency shift on spectral analysis measured with a 4.0-MHz duplex Doppler probe.

Midway through the study, we were able to perform transcranial Doppler examinations. Using the method described by Aaslid et al., we evaluated patients with a standard pulsed 2-MHz transcranial Doppler. Middle cerebral artery (MCA) velocities >100 cm/sec were considered to be consistent with MCA stenosis, whereas diminished MCA velocity associated with increased velocity in the anterior cerebral artery indicated MCA occlusive disease.21,22

Patients were considered to have a possible cardiac source of embolus if they met any of the criteria for high cardioembolic risk as defined by Kittner et al.23 These criteria include history of valvular surgery, atrial fibrillation, atrial flutter or sick sinus syndrome with or without valvular heart disease, echocardiographic evidence of a ventricular aneurysm, mural thrombus, cardiomyopathy, and left ventricular hypokinesis or akinetic region.

**Results**

Hypertension or diabetes mellitus was present in 77% of patients, with hypertension occurring in 68% and diabetes mellitus in 37%. Both diabetes mellitus and hypertension occurred in 28%. Hypertension occurred in the absence of other risk factors in 25%, and diabetes mellitus or an embolic source each occurred as the only risk factor in 8%.

Carotid Doppler ultrasonography performed on 98 of the patients identified atherosclerotic plaque as a possible embolic source in 23% of patients. Eight of these lesions were also considered to be hemodynamically significant. A history of a transient ischemic attack occurring on the same side as the lacunar infarction was obtained in 12% (12 of 98) of patients with a lacune who underwent carotid Doppler and in 27% (6 of 22) of those patients with either an embolic or hemodynamic carotid lesion (χ² = 4.3, p < 0.05).

Of the 44 patients evaluated with transcranial Doppler, two had MCA stenosis on the side of the infarction and three had ipsilateral MCA occlusive disease. One patient with an MCA occlusion was at high risk for carotid embolism and may have suffered an embolism to the MCA. Another patient with a MCA occlusion had evidence of thrombocytosis (platelet count of 727,000). The other three patients had hypertension but no other stroke risk factors.

Based on the cardioembolic risk criteria listed above, 18% of patients were in the high-risk group for a cardiac embolic source. Atrial fibrillation was present in 13 patients, three had severe hypocontractility of the left ventricle, two had aortic valve replacements, and one had sick sinus syndrome.

Of the patients who had either hypertension or diabetes mellitus, 36% also had significant ipsilateral carotid pathology or were at high risk for cardiac embolism. In 23% of the patients, there was no evidence of hypertension or diabetes mellitus. Of these, 32% had a possible carotid or cardiac etiology.

There were no risk factors identified in 13 of the patients, while three had other less-common etiologies such as thrombocytosis or cocaine abuse.

**Discussion**

Lacunes are traditionally thought to be due to lipo-hyalinosis or microatheroma formation that occurs secondary to hypertension or diabetes mellitus. Hypertension occurred in 68% of patients. This is within the 47–75% range reported in other series.12–14,17–23,25 Diabetes mellitus was present in 37% of patients, a rate similar to that reported by Ghika et al.14

Approximately one third of patients with hypertension or diabetes mellitus also had a possible carotid or cardiac etiology. Similarly, one third of the patients without these traditional risk factors had a carotid or cardiac etiology. In a study of small, deep infarcts diagnosed with CT scan, Pullicino et al.13 also found a possible cardiac or carotid embolic source in 33% of patients.

An ipsilateral potential carotid embolic source was identified in 23% of patients. The incidence of a contralateral carotid lesion was much lower and occurred as the only evidence of carotid disease in two patients. In eight patients, significant bilateral carotid disease was present. Ghika et al.14 reported that 28% of patients with lacunes had ipsilateral carotid artery stenosis of >75%. Others have also found evidence of ipsilateral carotid stenosis or occlusion in patients with lacunar infarction.12,13,17,18 We found that, in addition to carotid stenosis, a heterogeneous carotid plaque may also be a potential embolic source associated with lacunar infarction because this lesion was seen in 14% of our patients undergoing carotid Doppler.

Transient ischemic attacks are reported to precede lacunar infarcts in 20% of cases.24 Our patients with lacunar infarction and ipsilateral carotid disease had a higher incidence of transient ischemic attacks than did the patients without carotid disease, a finding which suggests that lacunes preceded by transient ischemic attacks may be more likely due to carotid disease.

A potential cardiac embolic source was found in 18% of patients. Although they used different criteria to define cardioembolic source, Ghika et al.14 found 17% of their patients to be at risk. Others have also suggested that embolism from a cardiac source could result in a lacunar infarct.

There were 10 patients with large or “giant” lacunes (>1.5 cm). Hypertension occurred in six of these patients, and diabetes mellitus with hypertension occurred in only one patient. There were three patients with atrial fibrillation and one with an aortic valve replacement. None of these patients had evidence of ipsilateral carotid artery disease. Santamaria et al.13 found a cardiac source of emboli in eight patients with deep infarcts of the basal ganglia and internal capsule who had no
other risk factors for small-vessel disease. Although deep, these infarcts were larger, involved the territory of more than one lenticulostriate artery, and produced deficits of higher cortical functions in some patients. Others have also suggested that larger subcortical infarcts may result from a carotid or cardiac embolism. A cardiac source of embolism was more common in our patients with larger lacunes, but the numbers are too small to draw any conclusions. Further investigation is needed to determine whether other stroke mechanisms might result in larger infarctions in the same vascular distribution as small lacunes.

Middle cerebral artery stenosis or occlusion can be associated with infarction of the basal ganglia and internal capsule. An abnormal ipsilateral MCA flow velocity was found by transcranial Doppler in five patients. Although transcranial Doppler was performed on only a limited number of patients, these results suggest that MCA disease as diagnosed by transcranial Doppler is rarely associated with lacunar infarction.

Although lacunes are traditionally thought to be due to microatheroma or lipohyalinosis that occur in the presence of hypertension or diabetes mellitus, carotid or cardiac disease was present in approximately one third of patients with the traditional risk factors for lacunar infarction. Hypertension or diabetes mellitus was not present in patients with larger lacunes, but the numbers are too small to draw any conclusions. Further investigation is needed to determine whether other stroke mechanisms might result in larger infarctions in the same vascular distribution as small lacunes.

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References

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