Ischemic Lacunar Stroke in Patients With and Without Potential Mechanism Other Than Small-Artery Disease

Ralf W. Baumgartner, MD; Claude Sidler, MD; Maria Mosso, MD; Dimitrios Georgiadis, MD

Background and Purpose—Autopsy studies found that lacunar strokes differ in the size of the underlying brain infarct and that small lacunes are usually caused by hypertensive small-artery disease (SAD) and larger ones by atheromatous or embolic perforator occlusion. These findings suggest that larger lacunar infarcts might cause more severe neurological deficits and a higher detection rate on brain imaging compared with lacunar strokes caused by SAD. This prospective observational study was performed to investigate whether (1) neurological outcome, (2) prevalence of stroke risk factors, (3) prevalence of clinically asymptomatic occlusive cerebral artery disease, and (4) detection rate of underlying lacunar infarcts at brain imaging differ in ischemic lacunar strokes with (non-SAD) and without potential etiologies other than SAD.

Methods—Consecutive patients with lacunar stroke (n=244), defined by both clinical findings and brain imaging, were studied. Neurological deficit was quantified at presentation with the use of the National Institutes of Health Stroke Scale (NIHSS) and after 3 months with the NIHSS and the modified Rankin Scale (mRS). Cerebral arteries were investigated by ultrasound.

Results—Compared with patients with SAD lacunar strokes (n=155; 64%), patients with non-SAD lacunar strokes (n=89; 36%) had (1) higher NIHSS scores at presentation and higher NIHSS and mRS scores after 3 months (P<0.05); a higher prevalence of (2) hypertension (P<0.05), (3) coronary artery disease (P<0.0001), (4) previous transient ischemic attacks (P<0.01), and (5) asymptomatic stenoses of intracranial cerebral (P<0.01 to P<0.0001) and extracranial carotid (30% to 50% narrowing; P<0.01) arteries; and (6) a higher detection rate of the underlying lesion at brain imaging (P<0.01).

Conclusions—Our data suggest that patients with non-SAD lacunar strokes have a worse clinical outcome and a higher prevalence of large cerebral and coronary artery disease than patients with SAD lacunar strokes. (Stroke. 2003;34:653-659.)

Key Words: lacunar infarction ■ stroke, ischemic

The earliest autopsy reports of lacunes as small foci of subcortical cerebral softening were published in the first half of the nineteenth century.1,2 In the next decades lacunes were correlated with clinical findings such as hemianesthesia3 and hemiplegia.4,5 In 1965, Fisher6 reported his clinicopathological observations and established the term lacunar infarct for small deep ischemic lesions forming irregular cavities 1 to 20 mm in diameter in the chronic stage. He found that lacunes resulted from occlusion of a single perforating artery and were associated with arterial hypertension in most cases.6 Fisher7–10 also reported that small lacunes were usually caused by hypertensive small-artery disease (SAD) and larger ones by atheromatous or embolic perforator occlusion. Subsequent clinical studies, including a community-based survey, generally failed to demonstrate significant differences in blood pressure or prevalence of hypertension between patients with lacunar strokes due to SAD or other causes.11–16 Moreover, the suggested relationship between cerebral atherosclerosis and lacunar stroke was not confirmed, and embolism was assumed to be a rare cause of lacunar stroke.14,15,17–22 Finally, it has not been investigated whether the larger size of lacunar infarcts that are potentially not caused by SAD is associated with more severe neurological deficits and a higher detection rate on brain imaging compared with lacunar strokes caused by SAD.

The aim of this prospective, observational study was to compare clinical outcome, prevalence of stroke risk factors and asymptomatic cerebral artery disease, and detection rate of underlying cerebral infarcts on brain imaging in patients with lacunar stroke due to SAD versus those with lacunar stroke of non-SAD etiology.

Subjects and Methods
The Zürich Ischemic Stroke Registry was established in August 1997 with the use of systematic computer coding of prospectively col-
lected data from all patients admitted with a first ischemic stroke (focal neurological deficit lasting ≥24 hours) to the Division of Neuroangiology of the Department of Neurology of the University Hospital of Zürich. Although this registry is not population based, we believe that it is of great value because this hospital has the only Stroke Unit and Department of Neurology in the entire county of Zürich, which has approximately 1’200’000 inhabitants. This report presents the analysis of all patients admitted with first lacunar strokes from August 1997 to December 2000.

Definition and Classification of Lacunar Strokes

Lacunar stroke due to SAD was defined according to the criteria of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification system.23 According to these criteria, a patient is required to have (1) one of the traditional clinical lacunar syndromes; (2) either normal CT/MRI or a relevant subcortical or brain stem lesion with a diameter <1.5 cm; and (3) no potential cardiac sources of embolism or stenosis ≥50% in an ipsilateral brain-supplying artery. Patients presenting with the following clinical syndromes were included in this study: pure motor hemiparesis, pure sensory hemisensory syndrome, sensorimotor syndrome, ataxic hemiparesis, and dysarthria–clumsy hand syndrome.6,24–26

Patients fulfilling the aforementioned clinical (criterion 1) and neuroradiological (criterion 2) criteria, in whom an atherothrombotic, cardioembolic, or other determined stroke etiology was found, were classified as suffering non-SAD lacunar strokes. Atherothrombotic non-SAD lacunar strokes characterize patients who presented with ischemic lacunar strokes and a >50% stenosis or occlusion of the supplying cerebral artery. Patients in whom aortic plaques with a diameter of ≥4 mm or mobile aortic thrombi located before the ostium of the left subclavian artery, but no signs of cardioembolic and other determined etiology of stroke, were diagnosed at transesophageal echocardiography (see below) were also assumed to have an atherothrombotic lacunar stroke.27 Cardioembolic non-SAD lacunar strokes characterize patients who presented with ischemic lacunar strokes and a potential cardiac source of embolism. Non-SAD lacunar strokes due to another determined etiology characterize patients with ischemic lacunar strokes due to arterial dissection, fibromuscular dysplasia, vasculitis, hematologic disorder, migraine, and other rare forms of stroke.

Neuroimaging Studies

All patients underwent either CT (n=140; 57% of cases) or MRI (n=56; 23% of cases), while both procedures were performed in 48 cases (20%). Native and contrast-enhanced cranial CT scans were obtained with a conventional CT scanner (GE). Contiguous axial slices were acquired with a 5-mm slice thickness. Conventional MRI was acquired with a 1.5-T system (GE) providing axial T1-, T2-, and proton density–weighted images and gadolinium-diethylenetriaminepenta-acetic acid–enhanced T1-weighted images with a slice thickness of 5 mm. We extended the aforementioned neuroradiological criteria to exclude lesions within the distribution consistent with border zone infarcts according to the criteria of Bladin and Chambers.28

Cardiological Evaluation

Twelve-lead ECG was performed in all cases, while 24-hour Holter monitoring (n=95; 39% of cases), transthoracic echocardiography (n=115; 47% of cases), and transesophageal echocardiography (n=92; 38% of cases) were performed at the discretion of the treating physician.

Evaluation of Brain-Supplying Vessels

Occlusive cerebral artery disease was assessed by ultrasound. Ultrasound studies were performed by experienced sonographers with color duplex scanners (Acuson XP 10 or Sequoia). For extracranial color duplex sonography (CDS) of the common, internal, and external carotid arteries and subclavian and vertebral arteries, 4- to 8-MHz linear probes were used. For extracranial insonation of the cervical internal carotid artery and transorbital and transcervical CDS studies, 2- to 3.5-MHz sector probes were used.

Extracranial CDS Studies

Carotid stenoses were quantified with the use of standard criteria established by a consensus meeting.29 Stenosis and occlusion of other extracranial cerebral arteries and the extracranial internal carotid artery were assessed by the criteria published by Von Büdingen and Von Reutern.30

Transorbital CDS Studies

Transorbital CDS studies assessed the ophthalmic arteries and the carotid siphon. Stenoses of the carotid siphon were diagnosed as described by Ley-Pozo et al.31

Transcranial CDS Studies

Transcranial CDS studies of the basal cerebral arteries were performed as reported previously.32,33 In brief, the terminal (C1) segment of the internal carotid artery; the middle, anterior, precommunicating posterior (P1), and postcommunicating posterior (P2) cerebral arteries; and the anterior communicating artery were sonicated through the circle of Willis according to previously published criteria.34–37 Patients with insufficient temporal or foraminal ultrasound windows were also investigated with the echo-contrast agent Levovist at concentrations of 400 mg/mL, as reported previously.38 This protocol was applied to all patients included in this study.

Exclusion Criteria

Patients who were treated with intravenous or intra-arterial fibrinolysis, who were included in a study evaluating glycoprotein IIb/IIIa receptor blockers or neuroprotective drugs, or who had suffered an iatrogenic stroke due to diagnostic or/and therapeutic interventions such as catheter angiography or cardiovascular surgery were not included in this study.

Stroke Risk Factors

The following stroke risk factors were differentiated: age; sex; current cigarette smoking, defined as cigarette smoking within the last 5 years, and former cigarette smoking, defined as abstention from cigarette smoking >5 years;39 hypertension, defined by preadmission history and medical records; diabetes mellitus, defined as venous plasma glucose concentration of ≥7.0 mmol/L after an overnight fast on at least 2 separate occasions and/or ≥11.1 mmol/L at 2 hours after the ingestion of 75 g of oral glucose and at 1 other occasion during the 2-hour test; hypercholesterolemia, defined as a total venous plasma cholesterol level >5.0 mmol/L; increased levels of LDL cholesterol (LDL cholesterol concentration >3.0 mmol/L), decreased levels of HDL cholesterol (HDL cholesterol concentration <1.0 mmol/L); ratio total/HDL cholesterol >5; hypertriglyceridemia (triglyceride concentration >1.6 mmol/L); a history of coronary and peripheral artery disease; a history of migraine with aura; and a history of amaurosis fugax (monocular blindness lasting <24 hours), retinal infarct (monocular blindness lasting ≥24 hours), or transient ischemic attack (TIA) (neurological deficit lasting ≥24 hours).

Evaluation of Neurological Deficit

Severity of the neurological deficit was assessed by the National Institutes of Health Stroke Scale (NIHSS)40 at presentation and by the NIHSS and the modified Rankin scale (mRS)41 after 3 months. The mRS score was used to classify strokes as nondisabling (score of 0 to 2) or disabling (score of 3 to 5). It was predefined that clinical outcome of patients who suffered a second stroke or died during follow-up would be excluded from analysis.
TABLE 1. Presenting Characteristics in 244 Patients With Lacunar Stroke

<table>
<thead>
<tr>
<th></th>
<th>Non-SAD, % (n)</th>
<th>SAD, % (n)</th>
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<tbody>
<tr>
<td></td>
<td>(n=89)</td>
<td>(n=155)</td>
</tr>
<tr>
<td>Age</td>
<td>65 (14)</td>
<td>64 (13)</td>
</tr>
<tr>
<td>Men</td>
<td>72 (64)</td>
<td>69 (107)</td>
</tr>
<tr>
<td>Smokers</td>
<td>52 (46)</td>
<td>52 (81)</td>
</tr>
<tr>
<td>Current/former</td>
<td>35/17 (31/15)</td>
<td>38/14 (59/22)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73 (64)*</td>
<td>57 (89)*</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>22 (20)</td>
<td>17 (27)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>76 (68)</td>
<td>76 (118)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>9 (8)</td>
<td>17 (26)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>70 (63)</td>
<td>76 (118)</td>
</tr>
<tr>
<td>Ratio total/HDL cholesterol &gt;5</td>
<td>33 (29)</td>
<td>37 (58)</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>51 (45)</td>
<td>43 (67)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>35 (31)***</td>
<td>9 (14)****</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>17 (15)</td>
<td>8 (13)</td>
</tr>
<tr>
<td>Amaurosis fugax and retinal infarct</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>25 (22)**</td>
<td>10 (16)**</td>
</tr>
</tbody>
</table>

HDL/LDL denotes high/low density lipoprotein; SAD, small artery disease.
P<0.05, **P<0.01, ****P<0.0001 that the difference between both groups is significant (Wilcoxon signed rank test).

Statistical Analysis

Statistical analysis was performed with the Systat software package. Differences between both groups of SAD were compared by non-parametric ANOVA (Wilcoxon signed rank test). Two-sided probability values of <0.05 were considered significant.

Results

Patients and Types of Lacunar Stroke

Two hundred forty-four patients with lacunar stroke (171 men, 73 women) with a mean age of 65±13 (range, 16 to 90) years were included in the study of 708 consecutive patients with a first ischemic stroke. Within the lacunar stroke cohort, 239 were white (98%), 2 black, 2 Asian, and 1 Hispanic. Non-SAD lacunar stroke was diagnosed in 89 (36%) and SAD lacunar stroke in 155 cases (64%). Complete follow-up was obtained in 238 of 244 patients (97.5%); 6 patients (2.5%) died during follow-up of cardiac disease (n=2), recurrent nonlacunar ischemic stroke (1 patient with non-SAD lacunar stroke), cancer (n=1), and unknown causes (n=2). No patient underwent autopsy. Neurological outcome of 9 other patients with recurrent nonfatal strokes occurring during follow-up was excluded (4 patients with non-SAD and 5 patients with SAD lacunar strokes). Thus, neurological outcome was analyzed for 229 of 244 patients (94%).

Comparison of Non-SAD With SAD Lacunar Strokes

Hypertension, coronary artery disease, and TIAs were the only presenting characteristics with a significantly higher prevalence in non-SAD compared with SAD lacunar strokes (Table 1). Neurological deficit at presentation and 3 months was more severe in non-SAD lacunar strokes (P<0.05), but the number of disabling and nondisabling strokes did not significantly differ between the 2 groups. No lacunar stroke was fatal, and mortality during follow-up was similarly low in both groups (Table 2).

Underlying non-SAD lacunes were significantly more often identified by cranial CT and MRI (P<0.01) and cranial CT alone (P<0.05). Time intervals between the onset of stroke symptoms and brain imaging were similar in both groups (Table 3).

TABLE 2. Severity of Neurological Deficit at Presentation and 3 Months, and Deaths During Follow-Up in 244 Patients With Lacunar Stroke

<table>
<thead>
<tr>
<th></th>
<th>Non-SAD, % (n)</th>
<th>SAD, % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=89)</td>
<td>(n=155)</td>
</tr>
<tr>
<td>Mean NIHSS ± SD (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td>4.2±2.8 (1–16)*</td>
<td>3.3±2.2 (0–11)*</td>
</tr>
<tr>
<td>3 months</td>
<td>1.5±1.7 (0–8)*</td>
<td>1.1±1.6 (0–8)*</td>
</tr>
<tr>
<td>Mean Rankin scale ± SD, 3 months</td>
<td>0.9±0.8 (0–4)*</td>
<td>0.7±0.8 (0–4)*</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nondisabling, % (n)</td>
<td>95 (79/83)</td>
<td>97 (143/146)</td>
</tr>
<tr>
<td>Disabling, % (n)</td>
<td>5 (4/83)</td>
<td>3 (4/146)</td>
</tr>
<tr>
<td>Lethal, n</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular, % (n)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Recurrent ischemic stroke, % (n)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Nonvascular, % (n)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Cause unclear, % (n)</td>
<td>1 (1)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

Nondisabling/disabling strokes denote strokes with a Rankin scale score of 0–2/3–5 points; NIHSS, National Institute of Health Stroke Scale; SAD, small artery disease.
P<0.05 that the difference between both groups is significant (Wilcoxon signed rank test).

Neurological outcome is reported for 229 of 244 patients, because during follow-up 6 patients died including 1 patient who suffered a recurrent ischemic stroke, and 9 patients had a recurrent nonfatal stroke.

Statistical analysis was performed with the Systat software package. Differences between both groups of SAD were compared by non-parametric ANOVA (Wilcoxon signed rank test). Two-sided probability values of <0.05 were considered significant.

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Underlying non-SAD lacunes were significantly more often identified by cranial CT and MRI (P<0.01) and cranial CT alone (P<0.05). Time intervals between the onset of stroke symptoms and brain imaging were similar in both groups (Table 3).

TABLE 3. Detection and Location of Symptomatic Lacunes by Brain Imaging in 244 Patients With Lacunar Stroke

<table>
<thead>
<tr>
<th></th>
<th>Non-SAD, % (n)</th>
<th>SAD, % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=89)</td>
<td>(n=155)</td>
</tr>
<tr>
<td>Location of symptomatic lacune detected</td>
<td>83 (74)**</td>
<td>67 (104)**</td>
</tr>
<tr>
<td>Internal capsule, basal ganglia, centrum semiovale</td>
<td>58 (52)†</td>
<td>51 (79)</td>
</tr>
<tr>
<td>Thalamus</td>
<td>13 (12)</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Brainstem</td>
<td>13 (12)†</td>
<td>8 (13)</td>
</tr>
<tr>
<td>Location of symptomatic lacune unclear</td>
<td>17 (15)**</td>
<td>33 (51)**</td>
</tr>
<tr>
<td>CT</td>
<td>19 (12/60)*</td>
<td>38 (46/123)*</td>
</tr>
<tr>
<td>MRI</td>
<td>6 (4/48)</td>
<td>24 (12/56)</td>
</tr>
<tr>
<td>Median latency (range) stroke onset to CT, days‡</td>
<td>1 (0–44)</td>
<td>1 (1–69)</td>
</tr>
<tr>
<td>MRI, days</td>
<td>6 (1–69)</td>
<td>5 (1–75)</td>
</tr>
</tbody>
</table>

CT denotes computed tomography; MRI, magnetic resonance imaging; SAD, small artery disease.
P<0.05, **P<0.01.
†Two patients had one the same side potentially symptomatic lacunar infarcts.
‡If 2 cranial CTs were done, the latency of the second study was used.
Patients with non-SAD lacunar strokes had a significantly higher prevalence of asymptomatic stenoses of the intracranial cerebral and extracranial carotid arteries (30% to 50% narrowing). Latencies between the onset of stroke symptoms and ultrasound studies were similar in both groups (Table 4).

Before stroke, aspirin (36% versus 17%; P<0.0001) and warfarin (6% versus 1%; P<0.05) were administered more often in patients with non-SAD lacunar strokes. Ticlopidine, clopidogrel, and dipyridamole were used with similar frequency in both groups. On discharge, SAD lacunar strokes were treated with aspirin (89% versus 61%; P<0.0001) and dipyridamole (31% versus 15%; P<0.05) significantly more often than non-SAD lacunar strokes; the opposite was true for prestroke treatment with aspirin was significantly more frequent in non-SAD than SAD lacunar strokes (P<0.05), whereas the prevalence of nondisabling and disabling strokes was similar in both groups. The weak statistical significance might result from the fact that the outcome of lacunar strokes is usually good42 and from the relatively low number of investigated patients. An additional cause might be that prestroke treatment with aspirin was significantly more frequent in patients of the non-SAD group.53

Underlying infarcts were detected significantly more frequently in patients with non-SAD lacunar strokes on brain imaging, despite the fact that time intervals between the onset of stroke symptoms and brain imaging were similar in both groups. Although we did not measure the volume of lacunes, the most likely cause of the higher detection rate of symptomatic non-SAD lacunes is their relatively larger lesional volume. This assumption is in agreement with the autopsy findings of Fisher,7–10 who reported that large lacunes were generally caused by non-SAD stroke mechanisms, whereas smaller ones were due to SAD. The greater lesional volume of non-SAD lacunes results from the occlusion of small arteries that range in size from 400 to 900 μm or atheromatous branch disease that blocks the perforators at their origin.9,10 Conversely, SAD is supposed to occlude vessels with a lumen that is usually <200 μm in diameter.7,8

Prevalence of hypertension was significantly higher in non-SAD than SAD lacunar strokes (P<0.05) in this series. This weak statistical significance is in accordance with the results of previous studies that failed to show a higher prevalence of hypertension in SAD lacunar compared with other types of ischemic stroke.11–16,18

Asymptomatic stenoses of intracranial cerebral arteries were significantly more frequent in non-SAD than SAD lacunar strokes. Furthermore, 6 asymptomatic stenoses of the intracranial cerebral arteries were associated with lacunar infarcts in the territory of the corresponding perforating arteries, suggesting a causal relationship. The prevalence of asymptomatic extracranial mild carotid artery stenoses as well as coronary artery disease was higher in patients with the origin of the symptomatic perforator, thus prohibiting the distinction between atherothrombotic lacunar stroke and atheromatous branch disease (group A). In an additional 26 cases, the stenosis was not located near the origin of the symptomatic perforator, suggesting arterio-arterial embolism as the most probable stroke etiology (group B). Finally, aortic atheroma was the sole potential embolic source in the remaining 9 patients. No significant differences in presenting characteristics and brain imaging or ultrasound findings were found when we compared patients from group A with those from group B.

**Discussion**

The main results of this study were that patients with non-SAD lacunar stroke had a significantly worse neurological outcome; a significantly higher prevalence of hypertension, history of TIAs, coronary artery disease, and asymptomatic cerebral artery stenoses; and a significantly higher detection rate of underlying lesions on brain imaging than patients with lacunar strokes due to other causes.

Neurological deficit at presentation and follow-up was more severe in non-SAD compared with SAD lacunar stroke (P<0.05), whereas the prevalence of nondisabling and disabling strokes was similar in both groups. The weak statistical significance might result from the fact that the outcome of lacunar strokes is usually good42 and from the relatively low number of investigated patients. An additional cause might be that prestroke treatment with aspirin was significantly more frequent in patients of the non-SAD group.53

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non-SAD than in patients with SAD lacunar strokes. These results suggest that patients with non-SAD lacunar stroke have occlusive atherosclerosis affecting at least the cerebral and coronary arteries.

Serial sections of all arteries supplying lacunar infarcts at autopsy are assumed to be the standard of reference for the detection of underlying SAD because in vivo assessment of these vessels is not possible at the present time. However, autopsy data proving a causal relationship between SAD and lacunar infarcts are scarce. Because of the low case fatality of lacunar strokes, the majority of autopsy studies were performed in the chronic stage, ie, between 3 months and 6.5 years after the onset of stroke symptoms, and only a few patients were examined within a delay of 10 days to 2 months. A correct interpretation of deep perforating arteries in the chronic stage at autopsy, however, is not straightforward because transient embolic occlusions are no longer visible, and it is difficult to distinguish whether structural changes of small arteries were the cause of the lacune or reactive to a transient perforator occlusion or the lacunar infarct. In this and other clinical studies it was assumed that the presence of a potential non-SAD cause indicated that this mechanism was responsible for the lacunar stroke. Conversely, ischemic lacunar strokes without potential non-SAD causes are generally assumed to result from SAD. Consequently, in vivo classification of lacunar strokes is limited by several methodological problems.

In the present investigation 36% of lacunar strokes had a non-SAD stroke mechanism, which is similar to the data from the Northern Manhattan Stroke Study (NOMASS). Detection of non-SAD etiologies depends on the extent of diagnostic workup. In contrast to NOMASS, all patients of this study had a complete ultrasonic assessment of the extracranial and intracranial cerebral arteries that included the use of echo-contrast agents in the presence of insufficient ultrasonic windows. Conversely, 24-hour Holter monitoring (41% versus 39%) and echocardiography (88% versus 47%) were performed more frequently in NOMASS than in the present study. Despite the different diagnostic evaluation, atherosclerosis was the most frequent stroke mechanism in non-SAD lacunes, followed by cardiac embolism and other determined etiologies in both studies.

Symptomatic intracranial occlusive cerebral artery disease consisting essentially of stenoses was found in 11% of our patients. The median time interval between the onset of stroke symptoms and ultrasound studies was 4 days. This suggests that some intracranial obstructions were caused by thromboembolism since catheter angiography studies performed within several days after the onset of anterior circulation strokes have detected emboli obstructing intracranial large arteries in 25% to 30% of patients. On the other hand, intracranial branch atheromatous disease leading to lacunar infarcts causes no or only mild luminal narrowing of the affected cerebral artery. Such atheromas are thus likely to be missed by transtemporal ultrasound, and the real prevalence of symptomatic intracranial atherosclerosis might have been higher in this study.

In conclusion, our data show that 36% of patients presenting with clinical and radiographic evidence of lacunar infarction have a potential non-SAD etiology. Some patients with lacunar infarction, especially those with a history of CAD or TIA, may require a more aggressive workup to find an etiology other than small-vessel disease.

References

Small Deep Brain Infarcts

What’s in a name—such as lacune or lacunar stroke? Small deep brain infarcts have attracted attention since Pierre Marie.1,2 These relatively small infarcts are now even more important since they are readily shown on brain images, and identification of their cause(s) should guide treatment. In the lacunar hypothesis, Fisher used the term lacune to imply an etiology related to intrinsic disease of the single perforating branch artery that supplied the infarct (either lipohyalinosis3,4 or atheromatous branch disease5-7). I prefer and urge others to reserve the designation lacune for those cases in which perforating artery disease is the posited mechanism of infarction. When the cause is uncertain or likely other than perforating artery disease, then a more general term—small deep infarct—is preferred.

The major differential cause of relatively small deep infarcts, other than single perforator disease, is occlusive disease of the intracranial artery from which the perforating artery originates. Occlusion or severe stenosis at the level of the perforating branches decreases flow in the perforators and leads to small deep infarcts, usually in the territory of multiple perforators, eg, lenticulostriate or thalamogeniculate arteries. The resulting infarcts are usually larger than single perforator artery disease (>15 mm). The authors limited small-artery disease (SAD) lacunes to those <15 mm. In this study, among the 244 patients, only 18 (7%) had such intracranial arterial occlusive disease. Intrinsic intracranial arterial disease is most common in blacks, individuals of Asian descent, and women, but these groups were underrepresented in this series (only 4 of 244 [2%] were blacks or Asians, and only 42% were women). Thus, this cause of deep infarcts is clearly less than would be found in populations with a higher proportion of blacks, Asians, and women.

In the other 71 patients, categorized as non-SAD by the authors, the guilt is only by association. These patients had potential cardiac, aortic, or proximal arterial lesions that could have been the source of embolism. The problem in assigning etiology is that many patients with lipohyalinosis and atheromatous branch disease also have atheromatous cardiac, aortic, and extracranial arterial occlusive disease. The mere presence of potential embolic cardioaortic and intra-arterial sources does not mean that they caused the small deep infarcts. Fisher,3,4 in his original autopsy studies of lacunar infarcts, emphasized the frequent co-occurrence of atheromatous disease elsewhere in the body and cerebrovascular system.

What do the results of this study mean for the practicing physician? Many patients have >1 condition.8,9 Secondary prevention should target all potential causes of stroke, not only the causative mechanism of the index event. At a minimum, patients with brain infarcts should have vascular studies that yield data about the intracranial arteries supplying the infarct: CT angiography, MR angiography, or transcranial Doppler sonography. Cardiac (and aortic) and extracranial arterial studies are also important. After all, stroke is a cerebrovascular disease, and identifying the vascular cause and the presence, location, and severity of cerebrovascular lesions is critical in guiding prognosis and both acute treatment and secondary prevention strategies. The vascular evaluation now can be done safely and quickly and at the same time as brain imaging. Most neuroradiologists and some neurologists still think that if they have...
obtained a brain image (CT or MRI) they have done it all. Identification of the vascular lesion in every stroke patient needs emphasis, as does choosing treatment depending on the vascular mechanism(s) found.

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Ischemic Lacunar Stroke in Patients With and Without Potential Mechanism Other Than Small-Artery Disease
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