Epidemiological Characteristics of Lacunar Infarcts in a Population

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Background and Purpose: This study evaluated the characteristics and natural history of patients with lacunar (small, deep) cerebral infarcts in a defined population for comparison of these characteristics to those in patients with nonlacunar infarcts.

Methods: This is a population-based study in Rochester, Minnesota, from 1960 to 1984, that used the medical record-linkage system to identify and characterize patients with cerebral infarction.

Results: The age- and sex-adjusted average annual incidence rate of lacunar cerebral infarction was 13.4/100,000 persons, accounting for 12% of all first cerebral infarcts. Temporal trends in incidence rates, stroke recurrence rates, prevalence of diabetes mellitus, and causes of death (given survival for 30 days) for cases of lacunar infarction were not significantly different from those for cases of nonlacunar infarction. Hypertension was found in 81% of patients who had a lacunar infarct and in 70% of patients who had a nonlacunar infarct (p = 0.05). A potential cardiac source of embolism was found in 12% of patients who had a lacunar infarct and in 28% of patients who had a nonlacunar infarct (p = 0.002). Survival was significantly better after a lacunar infarct than after a nonlacunar infarct.

Conclusions: Small, deep cerebral infarcts had many of the epidemiological characteristics of other cerebral infarcts but there was a slightly higher frequency of hypertension, significantly lower frequency of a cardiac embolic source, and significantly better survival in patients with lacunar infarction than in those with nonlacunar infarction. (Stroke 1991;22:1236–1241)

The use of the term “lacunar infarct” has varied considerably in the literature, depending primarily on whether a clinical or pathological viewpoint was taken. Although Marie was the first to clearly define lacunar infarcts anatomically in 1901, Fisher and colleagues first described specific clinical “lacunar syndromes” with anatomic correlation: pure motor hemiplegia, pure sensory stroke, ataxic hemiparesis, and dysarthria–clumsy hand syndrome. In subsequent detailed pathologic examinations, Fisher found that some of these lesions were associated with specific abnormalities of the small arteries. On the basis of Fisher's observations, some have suggested that these small infarcts are a unique form of infarct and are the result of characteristic vascular lesions. Since Fisher's original work, there have been many descriptions of lacunar syndromes but only two population-based studies. This study evaluated some of the characteristics and natural history of this type of infarct in a well-defined population and compared these characteristics to those of nonlacunar infarcts.

Methods

The residents of Rochester, Minn., and the surrounding area receive their medical care from a limited number of providers: the Mayo Clinic and one smaller group practice. The diagnoses are coded and entered into a central index. Through the use of this medical records–linkage system, it was possible to retrieve the records of all 1,382 Rochester residents who had their first cerebral infarction between January 1, 1960, and December 31, 1984. Only those cases of first cerebral infarction were included in this analysis. All data were abstracted by one of two physicians or a trained nurse abstractor.

The Mayo Clinic health-care system has used a standard neurological examination sheet and scoring system for more than 60 years. On the basis of the history and evidence from the physical and neurological examination recorded in the medical and neuro-
logical record, patients were identified as having a lacunar infarct after presenting with one of the following clinical syndromes: pure motor hemiplegia; pure motor hemiplegia sparing the face; pure sensory stroke; pure sensory stroke sparing the face; ataxic hemiparesis; dysarthria–clumsy hand syndrome; or hemiballismus, hemiathetosis, or hemidystonia (see Appendix A for definitions). Because our judgment was based on the recorded information, the interpretation may or may not have been the same as that of the clinician who saw the patient. Patients presenting with loss of vision, altered consciousness, apraxia, or aphasia were not considered to have had lacunar infarcts. Because of long-standing teaching programs and frequent neurological consultation, persons with a stroke most often had a neurological examination by at least two examiners. We used the neurological signs at the time of maximal neurological deficit. Of the 1,382 persons in this study, 995 (72%) had a neurological examination recorded by a neurologist.

In the period from 1975 to 1984, 80% of these patients were seen by a neurologist.

Computed tomography (CT scan) of the head was available only for the last decade of this study. For the analysis of the 25 years from 1960 to 1984, only those patients who presented with one of the clinical lacunar syndromes listed above were included. For the period from 1975 to 1984, in addition to the clinical syndromes mentioned above, other stroke syndromes, such as sensorimotor stroke, were included if there was evidence of a lacunar infarct in a location on CT scan or at autopsy consistent with the symptoms. The size and location of deep infarcts were determined from the CT film directly or from the autopsy report. We defined lacunar infarction seen on CT scan as a sharply margined, hypodense, round, ovoid, or linear lesion without mass effect that measured <2 cm in its longest dimension and was located in the basal ganglia, internal capsule, deep hemispheric white matter, thalamus, or pons. In this analysis, patients with cortical infarct or deep hemorrage, who clinically demonstrated lacunar syndrome, were not considered to have a lacunar infarct.

Nonlacunar infarcts were defined as all first cerebral infarctions not meeting the definitions outlined for lacunar infarcts.

Trends in incidence rates were determined for 1960 to 1984 by using only the clinical criteria for lacunar infarct in order to avoid the bias created by the introduction of CT imaging. The age-specific and sex-specific incidence rates for the 25-year period and for each 5-year period were calculated by using the cumulative Rochester population for the time period. All rates were age-adjusted and sex-adjusted to the West North-Central (WNC) 1970 US white population.

To determine whether the difference in temporal trends in incidence rates for lacunar and nonlacunar infarcts was statistically significant, we used Poisson regression analysis on the crude incidence rates determined by combinations of sex, age, and calendar year of stroke. The natural logarithm of the crude rates was modeled as a linear combination of sex, age, and calendar year effect with the Generalized Linear Interactive Modeling (GLIM) software package.

Survival rates and stroke recurrence rates were determined from data for the period from 1975 to 1984 during which time lacunar infarcts were defined according to clinical and CT criteria. The probability of survival was determined by the Kaplan-Meier life-table method and comparison was made with expected survival for an age-matched and sex-matched WNC 1970 US white population. Cumulative probability of recurrent stroke, given survival, was also determined by the life-table method.

Major potential cardiac sources of emboli were determined for patients with lacunar and nonlacunar infarcts. The criteria for specific cardiac diagnoses are outlined in Appendix B. The presence of hypertension was determined by a diagnosis of hypertension prior to the stroke or by two blood pressure determinations prior to the stroke with diastolic blood pressure ≥95 mm Hg or a systolic blood pressure ≥160 mm Hg, or both. The diagnosis of diabetes mellitus was determined by criteria of the National Diabetes Data Group. Only those patients whose diagnosis of diabetes was made before stroke onset or within 1 month after the onset of the stroke were considered to have diabetes.

Results

Of the 1,382 cases of first cerebral infarction in the residents of Rochester from 1960 to 1984, 159 (12%) were diagnosed as lacunar infarction by clinical criteria, and 52% of these patients were women. The average age of patients was 70 years for those with lacunar infarction and 73 years for those with nonlacunar infarction (p=0.006).

The age-adjusted and sex-adjusted average annual incidence rate of lacunar infarction for the 25-year period 1960–1984 was 13/100,000 persons. The incidence rate of lacunar infarcts declined from 17/100,000 persons for 1960–1964 to 10/100,000 persons for 1975–1979 (p=0.01). The incidence rate increased to 12/100,000 persons during 1980–1984 but was not significantly different from that for 1975–1979 (Figure 1). The incidence rate of lacunar infarcts increased with age and was greater among men than women for each time period. The ratio of the age-adjusted incidence rate of nonlacunar to lacunar infarcts was not significantly different during the time of the study, and the ratio of men to women who had lacunar and nonlacunar infaracts did not change significantly over time (Figure 1).

Using Poisson regression analysis, we investigated the effects of age, sex, and calendar year on the natural logarithm of the incidence rate of stroke. The relative rate of decline in the incidence rate over time for lacunar infaracts was not significantly different from that for nonlacunar infarcts when age and sex were in the model (Table 1). The influence of age
and sex on the incidence rate was the same in lacunar and nonlacunar infarcts (Table 1).

For the period 1975–1984, patients were considered to have had lacunar infarcts if they had a CT lesion in a location consistent with the symptoms, whether or not they satisfied the specific clinical criteria in Appendix A. With these criteria, there were 78 cases of lacunar infarction (76% had CT scan, autopsy, or both), which represented 13% of all cerebral infarctions in this period. Based on these cases, the age-adjusted and sex-adjusted average annual incidence rate for lacunar infarction in this period was 14/100,000 persons. By clinical criteria only, there were 61 cases of lacunar infarction (9%) in this period.

For the remaining analyses lacunar infarcts were defined according to clinical and CT criteria because it was thought that these criteria were most likely to include cases of lacunar infarction and exclude cases of nonlacunar infarction.

During 1975–1984, all patients with the diagnosis of lacunar infarction survived 30 days. Survival and 95% confidence interval were 97% (84, 100) and 75% (64, 86) at 1 and 5 years, respectively, compared with an expected survival of 95% and 75%, respectively, from life tables for the WNC 1970 US white population. By contrast, the survival of patients who had nonlacunar infarcts was 86% (83, 89) at 30 days, 72% (68, 76) at 1 year (93% expected), and 45% (40, 49) at 5 years (68% expected). The relative survival (observed survival/expected survival) for patients with lacunar or nonlacunar infarcts is shown in Figure 2. Relative survival corrects for the difference in age of the two groups.

Relative survival at 5 years was 100% for lacunar infarcts and 66% for nonlacunar infarcts.

Among the 78 patients with lacunar infarcts (clinical and CT definition) during 1975–1984, the cumulative probability of a recurrent stroke, given survival, and 95% confidence interval was 4% (0.8) at 1 month and 10% (4, 17) at 12 months (Figure 3). The cumulative probability of recurrent stroke in the 516 patients with nonlacunar infarcts was 2% (1.3) and 8% (5, 11) for the same time periods, respectively (Figure 3), not significantly different from that of patients with lacunar infarcts. The actuarial rate of recurrence at 5 years among survivors was 26% (15, 37) for lacunar and 27% (22, 32) for nonlacunar infarcts.

Of the recurrent strokes in patients with lacunar infarcts, 18 (86%) were cerebral infarcts (17% were lacunar) and three (14%) were intracerebral hemorrhages. For patients with nonlacunar infarcts, 88 (94%) of the second strokes were cerebral infarcts and six (6%) were intracerebral hemorrhages.

During 1975–1984, there were 26 recorded deaths in patients with lacunar infarction, nine (35%) due to heart disease and three (12%) due to stroke. Of the 309 deaths in patients with nonlacunar infarction, 93 (30%) died of cardiac causes and 89 (29%) died of stroke. Seventy-two of the latter deaths occurred within the first 30 days.

During 1975–1984, by the clinical and ancillary criteria for a major potential cardiac source of embolus as defined in Appendix B, 12% of the patients with lacunar infarcts had an embolic source versus 28% of the patients with nonlacunar infarction ($p=0.0002$).

By the criteria for hypertension, during 1975–1984 81% of the 78 patients with lacunar infarcts had hypertension compared with 70% of those with nonlacunar infarcts ($p=0.05$). If those patients who had a cardiac source for emboli were excluded, the frequency of prior hypertension was 80% in those with lacunar infarcts and 70% in those with nonlacunar infarcts ($p=0.11$).

For the period 1975–1984, diabetes was found in 14% of patients who had lacunar infarcts and in 16%
of patients who had nonlacunar infarcts (a nonsignificant difference).

All but 7% of the cases in the period 1980–1984 had an investigation for the presence of a carotid bruit, using oculoplethysmography, Doppler study, or retinal artery pressure as an examination for a marker for severe carotid atherosclerosis. Of the patients with lacunar infarcts, 21% had abnormal findings in one or more of these studies compared with 27% in patients with nonlacunar infarcts (p=0.4).

The pathological specificity of our clinical definitions was evaluated by examining the 48 cases in which the CT scan of the head or the autopsy identified a lesion that correlated with one of the seven clinical presentations. Only three of these 48 cases had a pathological lesion other than a lacunar infarct. One case with a pure sensory stroke had a 1.0×1.0-cm thalamic hemorrhage. The second case, with a pure sensory stroke sparing the face, had a 1.5×1.5-cm hemorrhage in the right putamen, internal capsule, and deep white matter. The third case, with a pure motor hemiplegia, had a moderate-sized right frontal lobe infarct.

The most common syndrome identified was pure motor hemiplegia, which included those sparing the face. This syndrome was identified in 42 of the 78 patients (54%) with a lacunar infarct between 1975 and 1984. There were nine patients with pure sensory stroke (including those with facial sparing), seven with sensorimotor stroke, four with dysarthria-clumsy hand syndrome, three with ataxic hemiparesis, and two with hemiballismus.

Discussion

The use of the term “lacunar infarct” to describe small, deep infarcts and the hypothesis that lacunar infarcts are a unique form of infarct have generated controversy. We tried to assess the issue by comparing epidemiological characteristics of lacunar and nonlacunar infarcts.

In this study, we found that the trends in incidence rates, the effect of age and sex on incidence rates, the stroke recurrence rate, the prevalence of diabetes, the prevalence of severe carotid atherosclerosis, and the causes of death were not significantly different for patients with lacunar and with nonlacunar infarcts. However, the frequency of a major cardioembolic source of emboli was significantly less with lacunar than with nonlacunar infarcts (p=0.002), and the frequency of hypertension was higher in patients with lacunar infarcts, but the difference from those with nonlacunar infarcts was of borderline significance (p=0.05). In addition, patients with lacunar infarcts had much more favorable survival than did patients with nonlacunar infarcts, probably related to the small volume of infarction. These data indicate that patients with small, deep infarcts had the same types of covariables as those with infarcts of larger size or more superficial location except that cardiac source of embolism was a less frequent covariable of small, deep infarcts. These findings are quite similar to those reported for the Oxfordshire study. We believe that the term “lacunar infarct” is most appropriately used as a descriptor of size and location of an infarct rather than as a marker for a specific vascular pathological feature.

The proportion of all infarcts that met the clinical and CT criteria for lacunar infarct was lower than in other population-based studies that adequately characterized lacunar infarcts. Part of the difference is due to a broader definition of lacunar infarcts in the Oxfordshire and South Alabama studies. Bamford et al included patients with sensorimotor stroke and patients with pure motor hemiplegia and pure sensory stroke if two of the three anatomic locations (face, arm, and leg) were involved. Although pure motor hemiplegia and pure sensory stroke sparing the face were included in our study, sensorimotor stroke and faciobrachial weakness or sensory loss were included only if there was evidence of an appropriate lesion for the symptom on a CT scan of the head or at autopsy. The inclusion of these syndromes without radiographic or autopsy correlation would have resulted in misclassification of some nonlacunar infarcts as lacunar infarcts. Although our clinical definition of lacunar infarction was more restrictive than some, we believe it was more specific for small, deep infarcts.
The 1-year mortality rates of the Oxfordshire study16 (9.8%) and the South Alabama study15 (10%) are higher than the 3% reported in the present study for lacunar infarcts. The South Alabama study was not limited to first strokes, which would adversely affect the mortality rates. The broader definitions of lacunar infarction in both studies would have included some larger cerebral infarcts, which may have had an adverse effect on the mortality rate, but it is uncertain whether this is the only reason for the difference.

The survival of patients with nonlacunar infarcts was significantly less than that of patients with lacunar infarcts (p<0.0001). The difference may be related simply to the volume of the infarct. One might have expected to find more cardiac disease in those with nonlacunar infarcts, but given 30-day survival (after most acute deaths from stroke), cardiovascular causes accounted for about one third (35%) of all deaths in patients with lacunar infarcts, which is similar to the proportion of patients (34%) with nonlacunar infarcts and also to that of the general population.25 Relative survival (observed/expected survival) for patients with lacunar infarcts was 100% at 5 years and 89% at 10 years. Relative survival for lacunar infarction for the 25 years (1960-1984), using only clinical criteria, was 89% at 5 years and 75% at 10 years. These differences provide some evidence of the extent of possible misclassification by using clinical criteria only. It is also obvious that the favorable survival for small, deep infarcts makes it difficult to obtain timely pathologic examination of vascular lesions associated with the infarct.

The reported 1-year stroke recurrence rate after a lacunar infarct ranges from 5.6%26 to 11.8%.16 The stroke recurrence rate of 4% at 1 month, 11% at 1 year, and 27% at 5 years in patients with lacunar infarcts in this study was not significantly different from the recurrence rate for those with nonlacunar infarcts (Figure 3). By clinical criteria only for the whole 25 years, 1960-1984, the cumulative probability of stroke in 5 years was 32% for patients with lacunar infarcts.

Because some of the comparison between lacunar and nonlacunar infarcts in the present study is based on a clinical definition of lacunar infarct, we examined the specificity of our strictly defined clinical criteria with regard to pathological features (hemorrhage versus infarct) as well as location and size of the infarcts. Among the 48 cases in which a CT scan of the head or autopsy identified a lesion that correlated with one of the seven clinical presentations, only two had small, deep hemorrhages as a cause of the symptoms. Only one patient had an infarct in a location other than the deep cerebral hemisphere or basis pontis. In addition, six patients had a deep infarct in the cerebral hemisphere that was > 2 cm in diameter. Thus, our clinical definitions were quite specific for pathologic features and moderately specific for size of the infarct.

Although lacunar infarcts have been defined as small, deep infarcts, there has been considerable variation in the use of the term “small.” The lacunes first described by Fisher4 were 0.5-15 mm at autopsy, but they were subsequently characterized as being up to 2 cm2 or even as “giant” lacunes.27 Some authors have suggested that giant lacunes are often due to occlusion of the major trunk vessel from which the penetrating arteries arise rather than to primary occlusion of a penetrating artery.

The addition of CT scanning is believed to have increased the accuracy in the diagnosis of stroke,27 particularly the diagnosis of lacunar infarct.28-30 Comparison of the data obtained from clinical criteria alone to that including information from CT imaging for the period 1975-1984 shows that the proportion of cerebral infarcts that were diagnosed as lacunar infarcts increased from 9% to 13%. CT imaging is limited in its ability to detect small infarcts, particularly in the first day after stroke onset.26 For these reasons, the reported proportion of positive CT scans in patients with a clinical syndrome compatible with a small, deep infarct varies from 33% to 69%.15,30-32 and was 62% in the present study. Magnetic resonance imaging provides better resolution than CT, but the best resolution19,34 is obtained a few days after the infarct is clinically evident.

### Appendix A

**Definition of Lacunar Syndromes**

<table>
<thead>
<tr>
<th>Pure motor hemiplegia</th>
<th>Hemiparesis or hemiplegia involving the face, arm, and leg equally. The average grade of weakness did not differ among face, arm, and leg by more than 1 grade. Although mild sensory symptoms could be present, there was no sensory loss related to the infarct on examination.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure motor hemiplegia sparing the face</td>
<td>Same criteria as above but with normal facial strength.</td>
</tr>
<tr>
<td>Pure sensory stroke sparing the face</td>
<td>Sensory loss or disturbance involving the entire hemiface and hemibody. Motor weakness was not part of the stroke syndrome.</td>
</tr>
<tr>
<td>Ataxic hemiparesis</td>
<td>Hemiparesis with ipsilateral ataxia. Paresis more commonly crural.</td>
</tr>
<tr>
<td>Dysarthria-clumsy hand syndrome</td>
<td>Dysarthria with a clumsy hand. Facial weakness could be present.</td>
</tr>
<tr>
<td>Hemiballismus, hemiatheosis, or hemidystonia</td>
<td>Must have been of acute onset.</td>
</tr>
</tbody>
</table>

### Appendix B

**Major Potential Cardiac Source of Emboli**

Must have one or more of the following:

1. Congestive heart failure at stroke onset
2. Myocardial infarction ≤2 months before stroke onset
3. Atrial fibrillation or flutter at time of stroke
4. Mitral valve disease (stenosis, regurgitation, or mixed disease)
5. Artificial mitral valve
6. Artificial aortic valve
7. Stroke <48 hours after coronary bypass
8. Stroke <48 hours after operation for left ventricular aneurysm
9. Cardiomyopathy
10. Congenital heart disease (findings on physical examination) or related to recent operation for congenital heart disease
11. Clinical evidence of systemic emboli
12. Stroke related to cardiac catheterization
13. Stroke related to intracardiac pacemaker installation
14. Left ventricular aneurysm by echocardiogram or angiogram
15. Sinus node dysfunction (sick sinus syndrome) present at time of stroke
16. Intracardiac thrombus or valvular vegetations by echocardiogram or angiogram
17. Autopsy evidence of recent systemic arterial emboli
18. Autopsy evidence of rheumatic heart disease
19. Embolic occlusion of intracerebral vessel with little or no evidence of carotid disease at autopsy and possible cardiac source
20. Autopsy evidence of cardiac mural thrombus or aortic or mitral valve vegetations
21. Autopsy evidence of acute myocardial infarction (dated at the time of or before the cerebral infarction)

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References


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