Background and Purpose This study concerns the long-term prognosis of lacunar infarcts.

Methods We report the analysis of our hospital-based series of 178 patients consecutively admitted for a lacunar syndrome due to a lacunar infarct diagnosed with computed tomography and magnetic resonance imaging. Demographic data, medical history, vascular risk factors, and imaging data were recorded for each patient. The follow-up was 35±22 months.

Results The lacunar syndrome was pure motor hemiparesis in 69 patients (39%), ataxic hemiparesis in 45 patients (25.4%), pure sensory stroke in 15 patients (8.5%), sensorimotor stroke in 14 patients (7.9%), and miscellaneous syndromes described by Fisher. 

Using multivariate analysis, we studied the prognostic factors of disability were age more than 70 years (P<.01), diabetes (P<.01), history of stroke or transient ischemic attack (P<.01), and type of lacunar syndrome (P<.01). Imaging data, number of lacunes, and presence of leukoaraiosis were not predictors of outcome.

Conclusions Our study suggests that with a high survival rate, a low recurrence rate, and a relatively good functional recovery, lacunar infarcts have a relatively favorable prognosis.

Key Words • lacunar infarction • prognosis • survival • stroke
significant independent predictors of death or stroke recurrence were evaluated with Cox proportional-hazards regression. We performed a backward stepwise selection of variables. The assumption of proportional hazards for the final Cox model was verified graphically, and interactions were tested. In subgroups for which there were ≤15% (n=27), patients were not considered in the univariate and multivariate analyses for binary variables. We evaluated the effect of baseline characteristics on long-term functional ability with stepwise multivariate logistic regression analysis. For this study, we took into account only the patients followed for at least 1 year, for whom functional capacity could be considered stable. Thus, this multivariate analysis was performed in the 140 patients whose lacunar infarct occurred between 1985 and 1989. The population was separated into two groups, patients having a normal Barthel Index (Barthel=100; group 1) and patients having a residual disability (Barthel <100; group 2). We considered values of P≤0.05 in bidirectional testing as indicating statistical significance. For the survival analysis, univariate comparisons, and logistic regression, we used SPSS/PC+14. The receiver operating characteristics (ROC) curve was drawn for the model obtained with multivariate logistic regression analysis.

Results

General Data

Between June 1985 and December 1991, 178 patients participated in the study. We obtained the follow-up data for a period averaging 35±22 months (ranging from 23 days—date of an early death—up to 81 months) in 172 of the 178 patients (96.6%). One hundred twelve patients (63%) were examined in hospital outpatient clinics. For 33 patients (18.5%), data were obtained from the general practitioners. Thirty patients had died. Six patients (3%) dropped out of follow-up, and we obtained vital information by administrative inquiry for all except one patient, who was a foreigner and for whom we have no data. Therefore, we could determine a vital status for 177 (99.5%) patients. The characteristics of the population are reported in Table 1.

Mortality

Thirty patients died: 10 from cardiovascular diseases, 9 from cancer, 3 from various other causes, and 8 from undetermined causes. The mean age of these 30 patients was 73±12 years. After the qualifying lacunar infarct the survival rate decreased steadily to reach 90±2.5% at 2 years and 80±4% at 4 years (Fig 1). Univariate predictors of death were diabetes mellitus (P=.048), cardiomegaly (P=.046), and age over 70 years at the onset of the stroke (P=.025). The other baseline data, sex, type of lacunar syndromes, number of lacunes, or presence of leukoaraiosis, were not significant univariate predictors of death (Table 2). In the multivariate stepwise Cox regression analysis, the baseline variables predicting death were diabetes, age over 70 years, and cigarette smoking, with an interaction between age and cigarette smoking. It is likely that cardiomegaly was not taken into account in the multivariate analysis because there was comorbidity with diabetes mellitus (cardiomegaly was significantly more frequent in patients with diabetes than without: P=.0186). On the other hand, the survival curve of cigarette-smoking patients did not differ significantly from that of nonsmokers (P=.17). However, the age of the smokers (63±11 years) was lower than that of nonsmokers (68±13 years; P=.0112). It is likely, therefore, that cigarette smoking was a predictor of death when adjusted for age (Table 3). Imaging variables were not taken into account in the multivariate model.

Recurrent Stroke

During follow-up, 16 of the 172 patients had at least one recurrent stroke (3 had two recurrent strokes); 13 patients had a CT scan or an MRI after this recurrence. There were four lacunar infarcts, five cortical infarcts, one recurrent stroke (3 had two recurrent strokes); 13 infarcts, five cortical infarcts, two transient ischemic attacks, and two intracerebral

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients</th>
<th>Frequency % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>111</td>
<td>62.7 (55.5-70.0)</td>
</tr>
<tr>
<td>Female</td>
<td>66</td>
<td>37.3 (30.0-44.5)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>134</td>
<td>75.7 (69.3-82.0)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>114</td>
<td>64.4 (57.2-71.5)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>81</td>
<td>45.8 (43.5-48.1)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>40</td>
<td>22.6 (16.4-28.8)</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>65</td>
<td>36.9 (29.7-47.0)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>11</td>
<td>6.2 (2.7-9.7)</td>
</tr>
<tr>
<td>Lower limb claudication</td>
<td>26</td>
<td>14.8 (9.5-20.1)</td>
</tr>
<tr>
<td>Left valvular diseases</td>
<td>23</td>
<td>13.0 (8.0-18.0)</td>
</tr>
<tr>
<td>History of ischemic heart disease</td>
<td>28</td>
<td>15.8 (10.4-21.2)</td>
</tr>
<tr>
<td>History of stroke or TIA</td>
<td>47</td>
<td>26.6 (20.0-33.1)</td>
</tr>
</tbody>
</table>

TABLE 1. Baseline Characteristics of the 177 Patients

CI indicates confidence interval; TIA, transient ischemic attack.
TABLE 2. Markers of Death or Recurrent Stroke: Bivariate Comparisons (Log-Rank Test)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Deaths (P) (n=30)</th>
<th>Recurrences (P) (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70 y</td>
<td>.025</td>
<td>.851</td>
</tr>
<tr>
<td>Diabetes</td>
<td>.048</td>
<td>.826</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>.046</td>
<td>.394</td>
</tr>
<tr>
<td>Sex</td>
<td>.450</td>
<td>.348</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>.170</td>
<td>.102</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>.498</td>
<td>.338</td>
</tr>
<tr>
<td>Hypertension</td>
<td>.452</td>
<td>.220</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>.173</td>
<td>.576</td>
</tr>
<tr>
<td>History of stroke</td>
<td>.228</td>
<td>.528</td>
</tr>
<tr>
<td>Type of lacunar syndrome</td>
<td>.847</td>
<td>...</td>
</tr>
<tr>
<td>Number of lacunes ≥2</td>
<td>.300</td>
<td>.070</td>
</tr>
<tr>
<td>Leukoaraiosis</td>
<td>1.000</td>
<td>.500</td>
</tr>
</tbody>
</table>

hemoaraiosis. In 2 patients, CT scans showed no new abnormal image; however, the clinical features suggested large-artery infarction. The second recurrent stroke was a cortical infarct in 1 patient, an intracerebral hemorrhage in 1 patient, and unknown cause in 1 patient. The survival rate without recurrence decreased steadily over the 6 years after the lacunar infarct. It was 94±2% at 2 years and 85±3.5% at 4 years (Fig 2). Bivariate and multivariate analyses of the clinical and imaging baseline data did not show any predictor of recurrent stroke (Table 2).

Functional Recovery

The proportion of patients with a Barthel Index equal to 100 at 1 year or more was 74%. In their daily lives, 8% of the patients needed minor help (80< Barthel Index ≤95) and 18% needed considerable help (Barthel Index ≤80). Multivariate logistic regression analysis showed that the main independent predictors of disability were age (P=.0086), diabetes (P=.0106), history of stroke or transient ischemic attack (P=.0403), and type of lacunar syndrome (pure motor hemiparesis, P=.0013; sensorimotor stroke, P=.0150) (Table 4). Imaging data had no influence in bivariate and multivariate analyses. The ROC curve is shown in Fig 3.

Discussion

In our study, the survival rate decreased progressively over the 6 years after lacunar infarct by 5% per year.
In our study, cardiovascular diseases explained one third of the deaths occurring during the follow-up period. Among these, only one death was directly due to a recurrent stroke and another to a complication after a recurrent stroke. Gandolfo et al reported a higher proportion of deaths (73.4%) due to cardiovascular diseases during the 7-year follow-up period. Among these, seven were due to fatal strokes. Among 26 recorded deaths in patients with lacunar infarction, Sacco et al reported 9 deaths (35%) due to heart disease and 3 deaths (12%) due to recurrent stroke. In our study, cancer, which was the second cause of death (30%), appeared to be higher than in other studies (13% for Gandolfo et al). Nevertheless, the high proportion of deaths of undetermined cause may be at the origin of some discrepancies between the series.

Concerning prediction of death, the differences between the methods used in the studies may be at the origin of differences in the results. In particular, some studies were population based and others were hospital based. The clinical inclusion and exclusion criteria were different (inclusion after the first-ever strokes or after recurrence, inclusion of miscellaneous syndromes, inclusion of partial syndromes, inclusion of lacunar transient ischemic attack). Moreover, the inclusion of patients without CT scan or MRI in some series may have caused diagnostic uncertainty. Predictors of death have rarely been studied in lacunar infarcts. Moreover, the low number of these events necessitates great care when commenting on the results. Gandolfo et al reported an excess of mortality in patients with pseudobulbar palsy, poor functional recovery, badly controlled hypertension, and age over 65 years. We only studied characteristics present at the onset of the qualifying lacunar infarct. We found a significant difference in survival in cigarette smokers, in patients with diabetes mellitus, and in patients over 70 years of age. Our results are close to those of Brainin et al (risk ratio for death, 2.43 for age and 2.27 for diabetes). The other characteristics, history of stroke, type of lacunar syndrome, sex, and arterial risk factors, were not predictors of death in the study of Brainin et al, nor were they in our series.

In our study, the short-term recurrent rate was similar to those reported in other studies, whereas the midterm recurrent rate appeared to be lower (6.5% at 2 years in our study, 12% in the study of Gandolfo et al, and 11% in the study of Giroud et al). The long-term recurrent rate was 15% at 4 years in our study, 26% at 5 years in the study of Sacco et al, and 34% at 7 years in the study of Gandolfo et al.

The recurrent type of stroke was not reported in most of the studies, especially in population-based studies. Recurrent lacunar infarcts accounted for about one quarter of the recurrences (4 of 21 for Sacco, 7 of 24 for Gandolfo, of 16 in our series). Moreover, the rate of ischemia versus hemorrhage was very close to the usual 80% rate reported in stroke. However, in one series, the recurrences were mainly lacunar infarcts (6 of 7), suggesting recurrences of the identical pathophysiology of the qualifying stroke. Therefore, the discrepancy between the results of these studies is not a major contribution to the controversy concerning the hypothesis of a single mechanism being at the origin of lacunar infarcts that could be indirectly approached by recurrent stroke subtype analysis.

In our series, no baseline variable predicted recurrences. Treatment of the risk factors, regular use of antiaggregants, and the small number of events may contribute to this negative result.

Favorable functional prognosis has been reported after a lacunar infarct. However, this finding has not been confirmed in other studies. In the OCSP, the proportion of independent patients was 66.3% after 1 year and 64% in Dijon after 2 years. In our study, it was 74% after 1 year. The functional prognosis depends on the type of lacunar syndrome, age, and history of stroke or transient ischemic attack. In the study of Gandolfo et al, as in ours, patients with motor deficit (sensorimotor strokes, pure motor hemiparesis) had the worst functional prognosis, whereas patients with ataxic hemiparesis and other lacunar syndromes recovered almost completely. Diabetic patients needed more help in their daily lives.

Boiten et al recently reported that patients with one or more asymptomatic lacunes had a higher frequency of hypertension and leukoaraiosis than patients with one symptomatic lacune. They suggested that the vasculopathies may be different, the former group having leukoaraiosis. In our results, we found an association between hypertension and leukoaraiosis ($\chi^2=11.6; P=0.001$) and between multiple lacunes and leukoaraiosis ($\chi^2=2.7; P=0.034$). However, the association between hypertension and the number of lacunes $\geq 2$ did not reach statistical significance ($\chi^2=4.45; P=0.034$). They did not report the effects of their hypothesis on prognosis. Miyao et al reported that leukoaraiosis was a predictor of higher mortality, stroke recurrence, and disability. Our results did not support their findings.

Conclusions

The long-term prognosis of lacunar infarcts is favorable. They have a higher survival rate, a lower recurrence rate, and a relatively good functional prognosis compared with the other subgroups of strokes. Some predictive factors could be isolated (cigarette smoking, age, and diabetes for death; type of lacunar syndrome, age, history of stroke or transient ischemic attack, and diabetes for disability). It appears that a hospital-based study, ensuring high diagnostic precision and facilitating
the obtention of data, is helpful in the study of the prognosis of one stroke subgroup. It highlights the possibility that both population-based and hospital-based studies have complementary uses.

Appendix

Hypertension was defined as a previous history of known hypertension with antihypertensive therapy or three or more blood pressure recordings ≥160 mm Hg for systolic and/or ≥95 mm Hg for diastolic pressure (WHO criteria) before or after the first week after the stroke. 

Diabetes mellitus was defined as a known and treated diabetes, a fasting serum glucose concentration ≥1.4 g/L, or a serum glucose concentration ≥2 g/L, 2 hours after the ingestion of 75 g of glucose.

Dyslipidemia was defined as a known and treated dyslipidemia or a total fasting cholesterol level ≥2.4 g/L in men (≥2.2 g/L in women) and/or a triglyceride level ≥1.4 g/L in men (≥1.2 g/L in women).

Cigarette smoking was defined as a total consumption of ≥20 cigarette packs per year.

History of ischemic heart disease included previous myocardial infarction and/or angina pectoris.

Arrythmia included previous myocardial infarction and/or angina pectoris.

Cardiomegaly is defined as a cardiothoracic index ≥0.5 on chest radiography.

Cardiac valve diseases included left valve diseases, prosthetic aortic or mitral valve, and aortic and/or mitral valve stenosis.

Lower limb claudication is defined as either lower limb claudication or as being due to atheromatous lower limb arterial disease.

References

Long-term prognosis of symptomatic lacunar infarcts. A hospital-based study.
I Clavier, M Hommel, G Besson, B Noëlle and J E Perret

doi: 10.1161/01.STR.25.10.2005

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1994 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/25/10/2005

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/