Prognostic Factors in First-Ever Stroke in the Carotid Artery Territory Seen Within 6 Hours After Onset

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Background and Purpose: We sought to detect prognostic factors related to functional outcome during the first 6 hours after a first-ever stroke in the carotid artery territory.

Methods: All patients with these characteristics seen during a 3-year period were included. Outcome was evaluated according to a modified Rankin scale. The following variables were examined at univariate analysis: sex, age, severity of deficit at entry and at day 7, level of consciousness at entry, time after symptom onset, history of smoking, history of hypertension, diabetes, myocardial infarction, atrial fibrillation, rheumatic heart disease, dilated cardiomyopathy, all potential cardioembolic sources, presence of a consistent lesion on computed tomography at entry and at days 5–9, and the size of such lesion.

Results: All entry criteria were met by 172 patients. Age >70 years, a Canadian Neurological Scale score <6.5 at entry and at day 7, atrial fibrillation, presence of a potential cardioembolic source, and a “large” lesion (involving more than half the cerebral lobe) on computed tomography at days 5–9 were associated with a significantly worse outcome both at 30 days and at 6 months. After multivariate analysis, a Canadian Scale score <6.5 at entry ($p<0.0001$) and atrial fibrillation ($p=0.005$) were associated with a significant handicap or death at 30 days, whereas only a Canadian Scale score $<6.5$ ($p<0.0001$) was associated with a worse prognosis at 6 months. An association of age $>70$ years with a worse outcome at 6 months was of borderline significance ($p=0.054$).

Conclusions: Some prognostic indicators are available during the first few hours after onset of a carotid ischemic stroke and may be useful in the stratification of patients in clinical trials. Severity of deficit is the most important indicator, whereas the presence of atrial fibrillation worsens the prognostic outlook with respect to early handicap but not mortality. (Stroke 1993;24:532–535)

Key Words • carotid arteries • prognosis • stroke onset

Experimental and clinical research on ischemic stroke has highlighted the importance of the first few hours after onset of ischemia, which may represent a “therapeutic window” for effective treatment.1–4 From this perspective, it is important to know the natural history of early-observed strokes and the prognostic factors related to their outcome; this may be of use in the planning of clinical trials based on very early intervention. Unfortunately, despite the number of investigations of stroke prognosis,5–11 few data are available on patients seen during the first few hours after the presentation of symptoms.12

We report here the results of a study on prognostic variables related to 30-day and 6-month functional outcome, evaluated in 172 patients seen within the first 6 hours after onset of a first-ever carotid territory infarction.

Subjects and Methods

We evaluated all patients consecutively admitted to our Stroke Unit during the period January 1, 1988 to December 31, 1990, who fulfilled the following criteria: 1) a first-ever ischemic stroke; 2) location in the carotid artery territory; 3) arrival at hospital within 6 hours after onset of symptoms; and 4) nonlacunar stroke. Lacunar strokes were defined as pure motor hemiparesis, pure sensory stroke, sensorimotor stroke, and ataxic hemiparesis associated with an infarct $\leq 1.5$ cm in size in the territory of the lenticulostriate arteries, or associated with no lesion, on computed tomographic (CT) scan performed 5–9 days after the stroke.13 Patients with lacunar stroke were excluded because many authors believe that such strokes have a better prognosis than other stroke types13,14 and they may be due to lesions in the vertebrobasilar artery territory not visualized by CT scan.15,16 Patients with symptoms that resolved after admission but within 24 hours after onset (i.e., transient ischemic attacks) were also retrospectively excluded.
On admission, all patients underwent neurological examination, which was scored according to the Canadian Neurological Scale, routine blood tests, electrocardiogram, Doppler study of neck vessels, and brain CT scan. Neurological examination was repeated daily until day 7 and then weekly.

Thirty-day and 6-month functional outcomes were evaluated according to a modified Rankin scale, in which death is scored 6; grade 2 on this scale represents the inability to perform everyday chores without assistance; grade 3 represents moderate need for help in everyday chores. Grades 1 and 2 were considered a good outcome; grades 3–6 were considered a poor outcome.

The following variables were assessed in all patients: sex, age (categorized as <70 versus ≥70 years), time from symptom onset to observation (dichotomized as > or ≤120 minutes), history of smoking, history of hypertension (treated or >160 mm Hg systolic or >90 mm Hg diastolic on repeated measurements in the year before stroke), diabetes, atrial fibrillation (chronic or paroxysmal), previous myocardial infarction, rheumatic heart disease, dilated cardiomyopathy, level of consciousness at admission (dichotomized as normal/drowsy versus stuporous/comatose), the Canadian Scale score at entry and at day 7 (dichotomized as <6.5 versus ≥6.5), the presence of a focal hypodensity consistent with an ischemic lesion on nonenhanced CT scan at entry and at days 5–9 from stroke onset, and the size of such lesion (categorized as absent, involving less than or equal to half the cerebral lobe, or more than half the cerebral lobe). The presence of a focal hypodensity consistent with an ischemic lesion on nonenhanced CT scan at entry or at days 5–9 from stroke onset, and the size of such lesion was dichotomized as normal/drowsy versus stuporous/comatose, the Canadian Scale score <6.5 at entry and at day 7 (dichotomized as <6.5 versus ≥6.5), the presence of a focal hypodensity consistent with an ischemic lesion on nonenhanced CT scan at entry or at days 5–9 from stroke onset, and the size of such lesion (categorized as absent, involving less than or equal to half the cerebral lobe, or more than half the cerebral lobe).

Univariate analysis was performed for each variable by comparing the number of functionally independent (Rankin grade ≤2) versus dependent or dead patients (Rankin grade >2) at 30 days and at 6 months by means of the χ² test with Yates’ correction. The significant variables at univariate analysis were subjected to multivariate analysis with a backward logistic regression procedure to find those with an independent effect on outcome.

### Results

All entry criteria were met by 172 patients, who represented 18.1% of all admissions to our Stroke Unit for ischemic stroke/transient ischemic attacks during the 3-year period. The group was composed of 79 men (45.9%) and 93 women (54.1%), with a mean±SD age of 73.4±11.6 years (range, 21–95 years). Time from symptom onset to observation was 136.6±82.8 minutes, with time ≤120 minutes in 97 patients (56.4%). Level of consciousness was normal/drowsy in 156 patients (90.7%) and stuporous/comatose in 16 (9.3%). Thirty-day and 6-month functional outcomes are shown in Table 1; risk factors for cerebrovascular disease are shown in Table 2.

A consistent ischemic lesion or indirect signs of lesion were present on entry CT scan in 32.4% of patients and in 84.1% of those who had the examination repeated at days 5–9. Lesion size at entry was less than or equal to half the lobe in 19.4% and greater than half the lobe in 13.0% of patients. At days 5–9 lesion size was less than or equal to half the lobe in 37.2% and greater than half the lobe in 46.9% of patients.

At univariate analysis, both 30-day and 6-month outcomes were significantly worse in patients aged ≥70 years, with a Canadian Scale score <6.5 at entry and at 7 days, with atrial fibrillation, with a potential cardioembolic source, and with a lesion greater than half the lobe on the second CT scan (Table 3). All other variables were not related to outcome.

Because atrial fibrillation is also included in the variable potential cardioembolic sources, multivariate analysis was performed twice, first including atrial fibril-

### Table 3. Results of Univariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>30 Days</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; or ≥70 years</td>
<td>0.0117</td>
<td>0.0005</td>
</tr>
<tr>
<td>Sex</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Level of consciousness</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Time from stroke ≤ or &gt;120 minutes</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Canadian Scale score &lt; or ≥6.5 at day 0</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Canadian Scale score &lt; or ≥6.5 at day 7</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Rheumatic heart disease</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>&lt;0.0001</td>
<td>0.005</td>
</tr>
<tr>
<td>Potential cardioembolic sources</td>
<td>0.0006</td>
<td>0.0139</td>
</tr>
<tr>
<td>Lesion on CT at day 0</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>“Large” lesion on CT at days 5–9</td>
<td>&lt;0.0001</td>
<td>0.002</td>
</tr>
</tbody>
</table>

See text for definition of variables. CT, computed tomography.
lating and excluding potential cardioembolic sources, and then excluding atrial fibrillation and including potential cardioembolic sources.

After multivariate analysis, a Canadian Scale score at entry $<6.5$ ($p=0.0001$) and atrial fibrillation ($p=0.005$) appeared to be independent prognostic indexes for a poor 30-day outcome, whereas only a Canadian Scale score $<6.5$ was significantly associated with a poor outcome at 6 months ($p<0.0001$) (Table 4). Age $\geq$70 years showed only a borderline significant association with poor 6-month outcome ($p=0.054$; odds ratio, 2.20; 95% confidence interval, 0.99–4.9).

In an attempt to define whether atrial fibrillation was associated with handicap or mortality, we subdivided patients into the categories of absent/mild handicap (i.e., Rankin grades 1 or 2), severe handicap (grades 3–5), or death (grade 6) at 30 days. Patients with atrial fibrillation were then compared with nonfibrillating patients with respect to 1) death versus all other outcomes and 2) absent/mild versus severe handicap, excluding deaths, by means of the $\chi^2$ test. With this approach, a severe handicap appeared to be significantly more frequent among patients with atrial fibrillation ($p<0.02$; odds ratio, 2.19; 95% confidence interval, 0.60–7.50), whereas mortality was not different in the two groups.

With the same approach, age $\geq$70 years was significantly associated with both a worse handicap ($p=0.016$; odds ratio, 2.756; 95% confidence interval, 1.188–6.446) and a higher mortality ($p=0.0003$; odds ratio, 4.928; 95% confidence interval, 1.943–13.075) at 6 months.

**Discussion**

Our study suggests that few predictors of short- and long-term outcome are of value during the first few hours of a carotid ischemic stroke. The most powerful predictors appear to be of the clinical type, whereas instrumental investigations are perhaps more useful in assessing mechanisms of infarction (i.e., embolic, atherosclerotic, hemodynamic). This finding is in accordance with studies that have evaluated prognostic factors at longer intervals after stroke onset and with the data of Fieschi et al, who assessed patients within 5 hours after onset of ischemia. The availability of an early predictor of outcome at 6 months appears to be particularly desirable, because functional level is not likely to change much after this date.

Level of consciousness at entry did not show clear associations with outcome, in contrast with other studies that have assessed this variable at longer intervals after symptom onset. This discrepancy is probably due to the fact that very few patients (9.3%) were stuporous or comatose in our study, since disturbances of consciousness in carotid artery strokes require edema, herniation, or very large lesions that develop over a period longer than that of our time window.

In accordance with other observations, early CT scan did not appear to be of use for prognostic purposes. The earlier the CT scan is performed after stroke, the less likely it will be to detect ischemic lesions, even when clinical deficit is very severe.

The relation between outcome and delayed CT lesion size has been reported previously. The disappearance of this association at multivariate analysis probably depends on the strict relation between lesion size at this time and severity of initial deficit, as shown by Brott et al.

The relation of atrial fibrillation to 30-day handicap may have more than one explanation. Some authors have found that patients with this arrhythmia have a significant reduction in basal cerebral blood flow. At the same time, collateral circulation in the brain may be less developed in patients with a cardiac embolism than in those who suffer a stroke as the result of an underlying chronic arterial disease such as atherosclerosis. These two factors may concur in slowing recovery of functions after ischemia associated with atrial fibrillation.

Despite the importance attributed to age in other studies, this factor appeared to be only marginally significant for 6-month prognosis once severity of deficit at entry was taken into account. This confirms that severity of deficit at entry is in general the crucial clinical parameter to consider for prognostic purposes.

The availability of outcome predictors such as those found in this study may prove especially useful in the planning of clinical trials based on treatments that require early admission of patients, such as thrombolysis.

**References**

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*Stroke*. 1993;24:532-535
doi: 10.1161/01.STR.24.4.532

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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/24/4/532

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