Prognosis After Transient Ischemic Attack and Ischemic Stroke in Young Adults

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Background and Purpose

We undertook this study to describe the risk of stroke recurrence and functional and occupational status in the long-term follow-up of young adults with ischemic strokes and to identify possible predictors for stroke recurrence, disability, and working status.

Methods

A cohort of 215 patients aged ≤45 years with ischemic cerebral events (43 transient ischemic attacks, 135 minor strokes, 37 major strokes), evaluated at our institution from May 1985 through March 1992, was followed for a mean of 43.1 months (SD, 39.7 months; range, 1 to 228 months).

Information on death and recurrent cerebral vascular events, functional disability (Rankin Scale), retirement, and working status was obtained from direct observation, mail questionnaire, and telephone interviews.

Results

Four patients (2%) with major strokes died acutely. Information on stroke recurrence and disability was available for 184 (87%) of the survivors and on retirement and working status for 140 (67%) of the patients. Two patients died from cancer. Seven transient ischemic attacks and eight strokes (two hemorrhagic) occurred during follow-up. Patients with strokes of unknown cause experienced no recurrent strokes, contrasting with two deaths and eight strokes in those whose stroke cause was identified (difference between proportions: 8%; 95% confidence interval, 3 to 13). Eighty-eight patients had a complete recovery, and only 21 were disabled (Rankin grades 4 or 5). Logistic regression analysis identified the severity of the initial stroke (Rankin grade >3) as the only significant predictor of disability (odds ratio, 10.7; 95% confidence interval, 0.8 to 3.4).

Conclusions

Ischemic stroke in young adults has a low acute mortality and few recurrences, more so if the cause is not identified. The majority of patients return to an active professional life. Severity of the initial stroke is the major predictor of independence. The relation between disability and return to work or retirement is less clear. (Stroke. 1994;25:1611-1616.)

Key Words • cerebral ischemia • prognosis • young adults

Subjects and Methods

Subjects

For all consecutive ischemic stroke patients aged less than 46 years and admitted to the Department of Neurology of St Maria Hospital or referred to its outpatient stroke clinic from May 1985 through March 1992, demographic and clinical data and results of ancillary procedures were registered on a standard form and stored on a database. Etiologic investigation was pursued following the usual guidelines.19,20 Brain imaging was obtained by computed tomography (CT) or magnetic resonance imaging (MRI). Duplex/transcranial Doppler sonography and/or angiography were used to investigate extracranial and intracranial vessel disease, while transthoracic and more recently transesophageal echocardiograms were performed to rule out a cardiac source of emboli. When these investigations were negative, immunologic, hematologic (including proteins C and S, antithrombin III, lupus anticoagulant, and anticardiolipin antibodies), syphilis, and other serologies or appropriate tests to identify rare causes of stroke were carried out.

Functional disability was graded following the modified Rankin Scale21 at both (1) discharge from acute hospitalization or at the first outpatient visit and (2) the last follow-up. Strokes were classified as minor if the Rankin grade was ≤3 and as major if Rankin grade was >3.

Follow-up

For patients that were regularly followed at our outpatient clinic, follow-up data was obtained from direct observation and chart review. During 1993 a mail questionnaire and telephone interviews were used to obtain information from the remaining patients. We specifically collected the following data: (1) number and dates of any of the following events: death, stroke, transient ischemic attack (TIA), and myocardial infarction (all patients who reported new vascular events were reexamined, and CT was repeated, if they had not been admitted to our department in the acute phase); (2) functional disability (modified Rankin Scale); and (3) occupational status, categorized as workers (subjects having a part- or full-time
Total 215 4 (2) 27 (13) 184 (67) 2 (1) 8 (5) 6 (3)

TIA indicates transient ischemic attack.
Prospective Study

Four (2%) major stroke patients died acutely. Three had massive hemispheric infarcts, 1 due to carotid dissection, 1 on the first day before relevant etiologic information could be gathered, and 1 with both an appropriate carotid stenosis and a ventricular segmental akinesia due to an old myocardial infarction. The fourth death was due to brain stem infarction secondary to verteobasilar dissection.

Information on follow-up was available for 184 (87%) of the survivors. Follow-up information was obtained by direct observation in 79 and by mail or telephone interview in 106. Twenty-seven (13%) had moved to an unknown address and could not be reached by telephone. Mean duration of follow-up was 43.1 months (SD, 39.1 months; range, 1 to 228 months). Reliable information on occupational status and retirement could be gathered in only 140 (66%) of the subjects because some patients refused to answer those items, since they thought they could have social security or tax implications. Patients with and without follow-up information had similar age (mean age: with follow-up, 37 years; without, 38 years) and sex (men/women: with, 38/25; without, 38/25). In multivariate analysis, none of the other predictors significantly improved a multiple regression model of recurrence including only that variable.

Functional Recovery

At the end of the follow-up, 88 patients had a complete recovery, and only 21 were disabled (Rankin grade 4 or 5). Of those disabled, 13 had been included as major strokes and 7 as minor strokes. One patient had a TIA at inclusion but suffered a major stroke during follow-up. Disability at follow-up was more common among those included as major strokes (major stroke versus minor stroke/TIA, \( \chi^2 = 31, P < .0001 \)). In univariate logistic analysis (Table 3) severity at onset was the only significant predictor of disability (constant, -4; coefficient, 2.37). In multivariate analysis the introduction of any of the other three variables or their combinations did not improve the model including only that variable.

Occupational Status

At the end of the follow-up, 73% of the survivors were active (including full- or part-time workers, housewives, and students) (Table 4). Of the 25 patients who retired, 19 (76%) did so between the second and sixth year poststroke (the minimal bureaucratic delay for retirement due to illness is 2 years), and 6 (14%) retired between the sixth and the tenth year. Retirement was significantly more common among those drinking more between the sixth and the tenth year. Retirement was more common among those drinking more and those with a higher socioeconomic status at inclusion. Of those disabled, 13 had been included as major strokes and 7 as minor strokes. One patient had a TIA at inclusion but suffered a major stroke during follow-up. Disability at follow-up was more common among those included as major strokes (major stroke versus minor stroke/TIA, \( \chi^2 = 31, P < .0001 \)). In univariate logistic analysis (Table 3) severity at onset was the only significant predictor of disability (constant, -4; coefficient, 2.37). In multivariate analysis the introduction of any of the other three variables or their combinations did not improve the model including only that variable.
The incidence between 0.7% and 1.8%. These discrepancies rate from 1.7% to 20.6%, and the recurrent stroke death rate ranges from 2.6% to 12%, the annual death rate between 0.7% and 31%, the recurrent stroke method of follow-up was variable and, concerning long-term risk for recurrent vascular events, the mean period of follow-up (43 months) is short relative to the patient's life span. The methodological limitations of our study should, however, be considered. First, our series is hospital-based and could be biased toward severe cases or rare etiologies. This referral bias is less important, however, in young adult stroke because of the very high hospitalization rate. Moreover, systemic and other rare etiologies accounted for only 13% of the subjects in our series. Second, we lost a few subjects during follow-up. However, baseline characteristics and severity of the initial stroke, which was the best predictor of recovery, were identical in patients with and without follow-up. Although we included some patients with previous strokes, recurrences were similarly uncommon in patients with and without previous stroke. Third, the method of follow-up was variable and, concerning long-term risk for recurrent vascular events, the mean period of follow-up (43 months) is short relative to the patient's life span.

Only 13 series on young adult stroke investigated the recurrence of vascular events (Table 1). In these studies, the death rate ranges from 2.6% to 12%, the annual death rate between 0.7% and 31%, the recurrent stroke rate from 1.7% to 20.6%, and the recurrent stroke incidence between 0.7% and 1.8%. These discrepancies are related mainly to methodological differences: age limits for inclusion, type, setting and geographic location of the studies, and length of follow-up. Some studies were undertaken in the pre-CT era. In other series CT and/or MRI were not performed in all cases. Some series included both infarcts and hemorrhages. The prognosis of hemorrhage in the young adult should be studied separately because these patients have a higher mortality and a worse functional prognosis than those with infarcts. Long-term stroke prognosis can be adversely influenced if a series is biased toward systemic causes of stroke or includes many cases of valvular rheumatic heart disease. In our study there were only five cases of valvular rheumatic heart disease.

Information on the prognosis of TIA in young adults is scarce. In our series of 38 TIA, the prognosis was benign. This agrees with the reports of Levy, Tippin et al, and Johnson and Skre, who followed young adults who experienced a transient central nervous system deficit, amaurosis fugax, and presumed TIA from a population screening, respectively. The high rate of recurrence (5%) found by Marshall is probably due to a referral bias because in England many stroke patients are not referred to neurologists.

Although stroke of unknown cause occurs in a heterogeneous group of patients, our study confirms that its outcome is benign and that potentially dangerous preventive measures (such as long-term anticoagulation) probably should be avoided. As the number of subjects for each of the other etiologic categories was small, no firm conclusion can be drawn concerning the relative risk for stroke recurrence in each category. In accordance with other series and except for basilar artery dissection, dissection of either carotid or vertebral arteries had a favorable outcome and no recur-

Table 3. Univariate Logistic Regression for Disability (Rankin Scale Grade >3) and Retirement

<table>
<thead>
<tr>
<th>Dependent Variable Predictor</th>
<th>Disability</th>
<th></th>
<th></th>
<th></th>
<th>Retirement</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, &lt;30/30-40/&gt;40 y</td>
<td>0.71</td>
<td>0.37-1.39</td>
<td>.32</td>
<td>1.06</td>
<td>0.78-1.43</td>
<td>.72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex, female/male</td>
<td>0.55</td>
<td>0.19-1.59</td>
<td>.27</td>
<td>0.78</td>
<td>0.52-1.19</td>
<td>.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol, &gt;60/&lt;60 g daily</td>
<td></td>
<td></td>
<td></td>
<td>1.26</td>
<td>0.62-2.00</td>
<td>.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity at inclusion, major stroke/TI/minor stroke</td>
<td>10.71</td>
<td>3.75-30.59</td>
<td>&lt;.0001</td>
<td>1.5</td>
<td>0.84-2.68</td>
<td>.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etiology, unknown/known</td>
<td>0.74</td>
<td>0.17-3.29</td>
<td>.7</td>
<td>0.97</td>
<td>0.58-1.70</td>
<td>.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability at follow-up, Rankin &gt;3/&lt;3</td>
<td></td>
<td></td>
<td></td>
<td>1.6</td>
<td>0.75-3.40</td>
<td>.23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR indicates odds ratio; CI, confidence interval; and TIA, transient ischemic attack.

Discussion

Our data confirm the low acute mortality and the favorable long-term outcome of ischemic strokes in young adults; in fact, during follow-up no patient died of vascular causes, only a few had recurrent strokes, and more than two thirds returned to an active professional life. The methodological limitations of our study should, however, be considered. First, our series is hospital-based and could be biased toward severe cases or rare etiologies. This referral bias is less important, however, in young adult stroke because of the very high hospitalization rate. Moreover, systemic and other rare etiologies accounted for only 13% of the subjects in our series. Second, we lost a few subjects during follow-up. Although we included some patients with previous strokes, recurrences were similarly uncommon in patients with and without previous stroke. Third, the method of follow-up was variable and, concerning long-term risk for recurrent vascular events, the mean period of follow-up (43 months) is short relative to the patient's life span.

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Table 4. Follow-up: Occupational Status

<table>
<thead>
<tr>
<th>Status</th>
<th>TIA</th>
<th>Minor</th>
<th>Major</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Working</td>
<td>22 (68)</td>
<td>56 (64)</td>
<td>8 (40)</td>
<td>86 (61)</td>
</tr>
<tr>
<td>Housewife/student</td>
<td>2 (6)</td>
<td>12 (14)</td>
<td>2 (10)</td>
<td>16 (12)</td>
</tr>
<tr>
<td>Absent/ill/unemployed</td>
<td>4 (13)</td>
<td>7 (8)</td>
<td>2 (10)</td>
<td>13 (9)</td>
</tr>
<tr>
<td>Retired</td>
<td>4 (13)</td>
<td>13 (15)</td>
<td>8 (40)</td>
<td>25 (18)</td>
</tr>
</tbody>
</table>

TIA indicates transient ischemic attack.
ferences. Two subjects with lacunar infarcts suffered intracerebral hemorrhages during follow-up, a finding that is unusual in prospective lacunar series.33,34

The majority of the subjects regained full independence. The major predictor of independence was the severity of the initial stroke measured by the Rankin Scale at discharge. Figures on disability (available for only nine studies) are difficult to compare (Table 1) because the type of functional assessment is not specified1,2,5,9,10,11 or the categories of disability and dependency are not uniformly defined. The percentage of disabled survivors ranges from 2% to 38% and of dependents from 0% to 17% in different series. Few investigators addressed the question of the variables that influence recovery. Age and etiology were not found to affect it significantly. The severity of the initial strokes was found to be important by Haerer and Smith.2 Hemiplegia2 and aphasia33 are indicated by others to adversely affect independence but were not specifically addressed in our study.

Studies of stroke in young adults that investigated the ability to return to work show comparable figures (60% to 90%). Black-Shaffer and Osberg20 found a low Barthel Index score, aphasia, and alcohol consumption to be negative predictors. We could confirm the negative effect of heavy alcohol ingestion. Concerning the influence of disability, although we found that the proportion of retired people was higher among those with higher Rankin grades at discharge, this relation was less clear than for independence. Hindfelt and Nilsson9 also noticed that only 8 of their 17 retired patients had moderate or severe neurological handicaps. In our series some patients with TIAs and minor strokes were retired at the end of the follow-up period. The high retirement rate among young adults with TIAs or minor strokes may be related to misinformation concerning prognosis and recurrence risk as understood by general practitioners and doctors working for medicolegal institutions. Except in a few cases where stroke represents the first or one manifestation of a systemic disease, ischemic stroke in young adults is often a relatively benign episodic event. Functional recovery is good, even for subjects disabled at discharge from the hospital. Reassurance of the low risk of recurrence and encouraging early return to work appear to be important recommendations to improve the quality of life of young stroke survivors.

Appendix: Definitions

Vascular Risk Factors

Hypertension and diabetes were defined according to the World Health Organization criteria (hypertension: systolic blood pressure >160 mm Hg and/or diastolic blood pressure >95 mm Hg on two different occasions or subjects on antihypertensive treatment; diabetes: fasting glucose >140 mg/dL or random glucose >200 mg/dL). Hypercholesterolemia was said to be present if fasting cholesterol was >240 mg/dL; hypertriglyceridemia was present if fasting triglyceride levels were >200 mg/dL, and the hematocrit was high if >50%. Smokers were defined as patients who were current smokers at the time of the stroke. Alcohol abuse was considered consumption >120 mg/dL. Migraine was defined following the criteria of the International Headache Society.56

Etiologic Classification

A. Cardioembolic stroke was present if (1) a cardiac disease with a high emboligenic potential existed (mitral stenosis, prosthetic valve, dilated myocardopathy, atrial fibrillation, endocarditis, myxoma, intracardiac thrombus) or (2) if a cardiac disorder with a low emboligenic potential (mitral valve prolapse, atrial septal aneurysm, patent foramen ovale) was disclosed and extracranial or intracranial vessel pathology and a systemic cause of stroke were excluded.

B. Stroke due to large-vessel atheromatous disease was present if stenosis or occlusion of an appropriate extracranial or intracranial vessel was demonstrated by angiography or duplex or transcranial Doppler sonography. The finding of an isolated intracranial occlusion required the exclusion of cardioembolic disease.

C. Stroke related to single-perforator disease (lacunar infarction) was present if the patient presented with one of the recognized clinical lacunar syndromes (pure motor or pure sensory, sensory-motor, ataxic hemiparesis, and dysarthria clumsy-hand syndromes), normal intracranial and extracranial vessels, and either an appropriate lacunar infarction (<15 mm diameter) on CT/MRI or a normal CT.

D. Dissection was present if the symptomatic vessel presented the typical angiographic features of arterial dissection.

E. Systemic disease was present if stroke was symptomatic of arteritis, hematologic disease, or other systemic cause of stroke.

F. Mixed etiology was defined as any combination of the above.

G. Stroke of unknown cause was assigned if despite adequate investigation the etiology could not be ascertained; this group included patients with vascular risk factors, but no documented evidence of extracranial or intracranial arterial disease, and not fulfilling the criteria for single-perforator disease.

H. Nonspecific cause was assigned for patients who did not have a complete etiologic investigation (eg, vertebrobasilar distribution and lacunar strokes for which intracranial circulation was not studied by transcranial Doppler/angiography, low embolicigenic cardiac conditions without vessel studies, and intracranial occlusions without echocardiogram).

Events

TIA27 was defined as a focal neurological deficit occurring suddenly in a cerebrovascular territory, resolving within 24 hours, with causes other than vascular exclusion.

Stroke28 was defined as a focal neurological deficit occurring suddenly in a cerebrovascular territory and lasting more than 24 hours in surviving patients. For recurrent strokes an increase of handicap at the time of the event was required.

Myocardial infarction was defined as at least two of the following: typical pain, new electrocardiographic changes, and enzyme elevation.

References

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Stroke. 1994;25:1611-1616
doi: 10.1161/01.STR.25.8.1611

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