Long-Term Prognosis of Infratentorial Transient Ischemic Attacks and Minor Strokes

Claus R. Hornig, MD; Catrin Lammers; Thomas Büttner, MD; Oskar Hoffmann, PhD; and Wolfgang Dorndorf, MD

Background and Purpose: This study was performed to gather information about long-term prognosis after infratentorial transient ischemic attacks and minor strokes and about the factors influencing it.

Methods: We included 226 patients with transient ischemia and 169 patients with a minor stroke of the brain stem/cerebellum consecutively admitted to a neurological department. Medical records and the findings of computed tomography, Doppler ultrasonography, and angiography were evaluated retrospectively. Follow-up information was gathered from the patients and their physicians by questionnaires. Complete follow-up information was available for 381 patients.

Results: During a mean follow-up of 3.9 years, 15.7% of the 381 patients suffered a stroke and 6.8% a myocardial infarction; 15% died. Kaplan-Meier estimates revealed a cumulative stroke rate of 5.1% within the first year and a risk of stroke, myocardial infarction, or death of any cause of 9.8%. In a proportional hazards model, the time-dependent risk of stroke was significantly increased by increasing age (p=0.018), minor stroke (p=0.0005), hypertension (p=0.022), previous stroke (p=0.0006), and carotid artery occlusive disease (p=0.0065). The probability of stroke, myocardial infarction, or death was influenced by age (p=0.0001), minor stroke (p=0.006), diabetes (p=0.015), previous stroke (p=0.002), infarct on a computed tomogram (p=0.041), and carotid artery disease (p=0.032).

Conclusions: Long-term prognosis after brain stem/cerebellar transient ischemic attacks and minor strokes is significantly influenced by age, diabetes, hypertension, previous stroke, and concomitant carotid artery disease. Patients with transient ischemic attacks have a better prognosis than those with minor stroke. (Stroke 1992;23:199–204)

From 20% to 34% of all transient ischemic attacks (TIAs) affect the vertebrobasilar territory.1–5 Although the risks of stroke after carotid TIA and vertebrobasilar TIA seem to be similar, little is known about factors influencing the long-term prognosis following brain stem or cerebellar TIA. The aim of this study was to identify patients with an increased risk of stroke, myocardial infarction (MI), or death following an infratentorial TIA or minor stroke. Patients with minor stroke were included in the study because they were expected to be fairly comparable with TIA patients concerning stroke-free survival.6

Subjects and Methods

Medical records of 630 consecutive patients with infratentorial ischemia treated in the Department of Neurology of the University of Giessen between 1983 and 1990 were evaluated retrospectively concerning functional outcome. The university hospital has the only neurological department in an area of 235,000 inhabitants. Most patients with vertebrobasilar ischemia are referred to this department. Nevertheless, a few patients will have been treated as outpatients by resident neurologists or in local general hospitals. Infratentorial ischemia was diagnosed based primarily on clinical criteria and was assumed if at least two of the following signs or symptoms had suddenly occurred: vertigo/nystagmus, diplopia, gaze palsy, internuclear ophthalmoplegia, motor or sensory disturbances, dysarthria, dysphagia, cranial nerve palsy, and ataxia. Patients with motor or sensory signs combined with ataxia or dysarthria and those with
ataxia and dysarthria were included only if they had additional symptoms or if computed tomography (CT) or magnetic resonance imaging showed an infratentorial infarct. Bilateral motor or sensory signs during a single event were classified as infratentorial ischemia. We excluded patients with hemianopsia, drop attacks, transient amnesia, and isolated vertigo or diplopia.

Of the 630 patients, 226 (35.9%) suffered a TIA, 169 (26.8%) a minor stroke, and 160 (25.4%) a major stroke; 75 (11.9%) died during hospitalization. Minor stroke was assumed if the functional deficit did not exceed 2 points on a modified Rankin disability scale at discharge. Nearly all patients with minor stroke were admitted on the day of the event, none later than 1 week after the stroke. All patients with TIA were admitted within 2 weeks after the event.

Medical records of the 395 patients with TIA or minor stroke were evaluated retrospectively concerning risk factors, previous strokes, clinical signs, and symptoms. Patients with a definite history of hypertension or a diastolic blood pressure above 90 mm Hg on repeated measurements were categorized as hypertensive. CT was performed in 316 patients, direct continuous-wave Doppler sonography of the carotid arteries in 252, and angiography of the vertebrobasilar circulation in 236.

Most patients (73.4%) received aspirin for stroke prevention after discharge from the hospital. The daily dose was 1 gr until 1986, 0.5 gr until 1989, and 300 mg since then. Seven percent of the patients were anticoagulated with dicumarol for 6 months, followed by aspirin. No continuous antithrombotic therapy was performed in 19.2% of the patients after discharge from the hospital.

Follow-up information was gathered by questionnaires sent to the patients, their relatives, and their physicians. They were asked about recurrent stroke, MI, medication, and death and its cause. In case of insufficient or contradictory answers, complete information was obtained by telephone interviews if possible. Sufficient follow-up information was finally gathered on 381 patients. Fourteen patients were lost to follow-up immediately after discharge from the hospital and thus were not considered in the statistical analysis. Follow-up ranged between 1 and 8 years, with a mean of 3.9 years.

The follow-up results were evaluated statistically by use of Kaplan-Meier survival estimates and the Mantel-Haenszel $\chi^2$ test (log-rank test) as well as a proportional hazards model for multivariate analysis.

Results

About 56% of the patients with infratentorial TIA or minor stroke were younger than 60 years; mean±SEM age was 59.5±11.1 years. There was a slight preponderance of men (64.3%).

The most frequent risk factor was hypertension (50.1%), followed by hypercholesterolemia (48.6%), cigarette smoking (34.2%), coronary heart disease (29.1%), and diabetes (18.5%). In 4.6% of the patients a potential cardiac source of emboli, predominantly nonvalvular atrial fibrillation (33.3%), could be identified.

Of the 395 patients 19 (4.8%) had already suffered a cerebral infarction. It involved the carotid territory in 10 cases, the vertebrobasilar territory in four cases, and was of unknown origin in five cases. Previous TIs were frequent and had occurred in 130 patients (32.9%). Symptoms could be related to the vertebrobasilar territory in 117 cases and to the carotid territory in eight. The origin remained indefinite in 15 cases.

Doppler sonography of the carotid arteries revealed a pathological finding in 22 patients (8.7%). The most common finding was unilateral stenosis (11), followed by unilateral occlusion (five); six patients had bilateral occlusive disease of the carotid arteries. An infraclinoidal cerebral infarct was visible in 54 of 316 CT scans (17.1%) (Table 1). In particular, 16 of 163 patients with a TIA (9.8%) and 38 of 153 patients with a minor stroke (24.8%) had an infratentorial infarct on CT. Only 17 of the 42 patients with infarcts in the anterior circulation had suffered a previous TIA or stroke. Of the 236 patients who underwent angiography of the vertebrobasilar circulation, 90 had a pathological finding exceeding minor atherosclerotic wall irregularities (Table 2).

During follow-up 15.7% of the 381 patients suffered a stroke (7.9% a minor stroke, 5.6% a disabling stroke, and 3.1% a fatal stroke). An MI occurred in 6.8% of the patients, and it was fatal in 2.6%. Fifty-seven patients (15%) died during follow-up. The cause of death was stroke in 12 patients, MI in 10, other cardiovascular reasons in six, and nonvascular complications in 17; the cause of death was uncertain in 12 patients. Kaplan-Meier estimates revealed a rather linear decreasing probability of survival following infratentorial TIA or minor stroke for stroke, for MI, for death, and for the combination of stroke, MI, and death (the main end point) (Table 3, Figure 1). Outcomes after TIA and minor stroke differed. Kaplan-Meier survival estimates revealed a significantly increased risk of stroke (particularly
increasing age, diabetes, previous TIA or stroke, and minor stroke (Table 5).

In subgroup analyses of those patients who had CT, an infarct on CT was a significant risk factor for the main end point (Table 5), but not for stroke alone. Univariate analysis showed that only the demonstration on CT of supratentorial infarcts, not infarcts within the vertebrobasilar circulation, significantly increased the time-dependent risk of the main end point following TIA or minor stroke (Table 6). Patients with carotid artery stenosis or occlusion demonstrated by Doppler ultrasonography had a significantly increased risk for stroke and for the main end point (Tables 4 and 5).

**TABLE 3.** Cumulative Risk of Stroke, MI, and Death After Infratentorial TIA or Minor Stroke (Kaplan-Meier Estimates)

<table>
<thead>
<tr>
<th>End point</th>
<th>6 mo Risk (%)</th>
<th>1 yr Risk (%)</th>
<th>2 yrs Risk (%)</th>
<th>5 yrs Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>After TIA or minor stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major/fatal stroke</td>
<td>0.9</td>
<td>1.6</td>
<td>3.2</td>
<td>7.5</td>
</tr>
<tr>
<td>All strokes</td>
<td>2.7</td>
<td>5.1</td>
<td>9.2</td>
<td>18.6</td>
</tr>
<tr>
<td>MI</td>
<td>0.3</td>
<td>2.2</td>
<td>3.2</td>
<td>7.2</td>
</tr>
<tr>
<td>Death of any cause</td>
<td>2.1</td>
<td>4.8</td>
<td>8.2</td>
<td>18.6</td>
</tr>
<tr>
<td>Stroke, MI, or death</td>
<td>4.5</td>
<td>9.8</td>
<td>15.3</td>
<td>32.9</td>
</tr>
<tr>
<td>After TIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major/fatal stroke</td>
<td>0.5</td>
<td>1.4</td>
<td>3.0</td>
<td>7.0</td>
</tr>
<tr>
<td>All strokes</td>
<td>1.4</td>
<td>4.3</td>
<td>6.9</td>
<td>15.0</td>
</tr>
<tr>
<td>Stroke, MI, or death</td>
<td>4.2</td>
<td>9.8</td>
<td>13.9</td>
<td>27.3</td>
</tr>
<tr>
<td>After minor stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major/fatal stroke</td>
<td>2.5</td>
<td>4.4</td>
<td>8.4</td>
<td>18.2</td>
</tr>
<tr>
<td>All strokes</td>
<td>4.3</td>
<td>6.2</td>
<td>12.3</td>
<td>24.0</td>
</tr>
<tr>
<td>Stroke, MI, or death</td>
<td>4.9</td>
<td>9.9</td>
<td>17.1</td>
<td>41.4</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; TIA, transient ischemic attack; n, number of patients under observation.

Probability of stroke (major stroke in particular) is significantly increased after minor stroke compared with TIA (log-rank test: all strokes, \( p<0.0387 \); major stroke, \( p<0.0063 \)).
Table 4. Parameters Significantly Increasing Risk of Stroke After Infratentorial TIA or Minor Stroke in Proportional Hazards Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(\beta)</th>
<th>(\exp(\beta))</th>
<th>95% CI</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.03</td>
<td>1.03</td>
<td>1.01-1.06</td>
<td>0.0180</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.62</td>
<td>1.87</td>
<td>1.09-3.19</td>
<td>0.0224</td>
</tr>
<tr>
<td>Previous TIA or stroke</td>
<td>0.95</td>
<td>2.58</td>
<td>1.50-4.42</td>
<td>0.0006</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>0.97</td>
<td>2.64</td>
<td>1.53-4.56</td>
<td>0.0005</td>
</tr>
<tr>
<td>Carotid disease</td>
<td>1.16</td>
<td>3.19</td>
<td>1.38-7.37</td>
<td>0.0065</td>
</tr>
</tbody>
</table>

\(\beta\), regression coefficient; \(\exp(\beta)\), relative risk; CI, confidence interval of relative risk; TIA, transient ischemic attack.

Parameters tested in forward-selection stepwise manner for entire group of 381 patients included age, sex, TIA or minor stroke, hypertension, diabetes, serum cholesterol, coronary heart disease, cigarette smoking, previous TIA or stroke, previous vertebrobasilar TIA, somnolence at admission, ataxia, nystagmus, Horner's syndrome, motor paresis, dysarthria, and dysphagia. In subgroup of 252 patients with Doppler investigation parameter "carotid disease" (pathological findings on Doppler investigation) was tested together with factors found significant for entire group.

No angiographic parameter significantly increased the time-dependent risk of the main end point or of stroke in the proportional hazards model. In univariate analyses patients with unilateral vertebral artery occlusion or bilateral vertebral artery occlusive disease, but not those with unilateral vertebral artery stenosis or basilar artery disease, had an increased risk of stroke and of the main end point (Table 6). All 24 patients with basilar artery stenosis or occlusion received anticoagulants for 6 months (on average) followed by aspirin. The patients were followed up for 3.2 years (on average). Five of these patients (20.8%) suffered a recurrent stroke, and three (12.5%) died.

Discussion

Of 630 patients with vertebrobasilar ischemia, 395 suffered a TIA or minor stroke. Compared with patients suffering ischemic strokes in general, as documented in recent stroke data banks,8-10 these patients were younger and more often male. About 15% of all ischemic strokes are due to embolism from the heart,11 but only 5% of our patients had a potential cardiac source of emboli.

The cumulative rate of stroke after infratentorial TIA or minor stroke in this study was 5.1% within 1 year, 9.2% within 2 years, and 18.6% within 5 years. Thus the risk of stroke after infratentorial TIA or minor stroke seems to be similar to the stroke rate after cerebral ischemic events in general and under treatment with aspirin. The probability of stroke after TIA, reversible ischemic deficit, or minor stroke is variable in different studies even with the same kind of medication for stroke prevention, probably reflecting differences in the risk profile of the study populations. During 1 year of observation the stroke rate of medically treated TIA patients varied between 3.3% and 11.8%.6,12 In three large trials with a follow-up of approximately 2 years, 7%, 15.3%, and 16.8% of aspirin-treated patients suffered a stroke.4,13,14 An even lower overall stroke risk for aspirin-treated patients of 8.3-13% during 3-4 years of observation was reported in three trials.5,15-17

Similar risks of stroke following vertebrobasilar and carotid TIs have been assumed previously.20,21 At most, nonsignificantly increased risks of stroke after vertebrobasilar reversible ischemic deficit and of early recurrence after stroke within the posterior circulation compared with the anterior circulation have been reported.5,22 The latter could not be verified by comparing the 9.2% stroke risk within 2 years for our patients with the risk reported in studies

Table 5. Parameters Significantly Increasing Risk of Stroke, Myocardial Infarction, or Death as Main End Point After Infratentorial Transient Ischemic Attack or Minor Stroke in Proportional Hazards Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(\beta)</th>
<th>(\exp(\beta))</th>
<th>95% CI</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.04</td>
<td>1.04</td>
<td>1.02-1.06</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.53</td>
<td>1.71</td>
<td>1.11-2.62</td>
<td>0.0149</td>
</tr>
<tr>
<td>Previous TIA or stroke</td>
<td>0.63</td>
<td>1.87</td>
<td>1.26-2.79</td>
<td>0.0020</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>0.57</td>
<td>1.76</td>
<td>1.18-2.64</td>
<td>0.0057</td>
</tr>
<tr>
<td>Infarct on computed tomogram</td>
<td>0.45</td>
<td>1.56</td>
<td>1.02-2.39</td>
<td>0.0410</td>
</tr>
<tr>
<td>Carotid disease</td>
<td>0.79</td>
<td>2.22</td>
<td>1.07-4.62</td>
<td>0.0322</td>
</tr>
</tbody>
</table>

\(\beta\), regression coefficient; \(\exp(\beta)\), relative risk; CI, confidence interval of relative risk. Parameters tested for entire group of 381 patients and subgroup of 252 patients who underwent Doppler sonography are listed in Table 4. In subgroup of 316 patients with computed tomography parameters "infarct on computed tomogram" and "brain stem or cerebellar infarct on computed tomogram" were tested together with factors found significant for entire group.
concerning hemispheric TIA. In the Joint Study 15.9% of 88 aspirin-treated patients and 22.2% of 90 placebo-treated patients with hemispheric TIA or amaurosis fugax suffered a stroke or retinal infarc
tion within 2 years. In another study the cumulative stroke rate within 5 years was 26.3% for patients with hemispheric TIA.

The probability of survival after carotid TIA is assumed to be less than that after vertebrobasilar TIA. The cumulative survival rate following TIAs of various territories has been estimated to be 95–99% after 1 year and 80–90% after 5 years in two large series. This is in accordance with the cumulative fatality rate of our patients of 4.8% within 1 year and 18.6% within 5 years.

In a proportional hazards model significant risk factors for stroke after infratentorial TIA or minor stroke were age, minor stroke, arterial hypertension, previous TIA or stroke, and concomitant carotid artery disease. The probability of stroke, MI, or death was significantly increased by increasing age, minor stroke, diabetes, previous TIA or stroke, concomitant carotid artery disease, and infarcts on CT. This is in accordance with the results of a community-based study comparing patients with recurrent or single strokes. Recurrent strokes were significantly associated with prior TIA, MI, arterial hypertension, and diabetes. However, the results concerning risk factors for recurrence in follow-up studies of patients with TIA or stroke are conflicting. An increased risk of stroke for hypertensive patients was found in the joint study of carotid TIA, in an Italian study of reversible ischemic attacks, and in the North American Stroke Data Bank, but hypertension did not influence the probability of stroke after TIA in two other studies. Diabetes increased the risk of recurrent stroke in the Stroke Data Bank and of multiple ischemic events in the Italian study of reversible ischemic attacks. Other studies did not find any risk factors for stroke after TIA. The probability of survival after TIA was significantly decreased by increasing age, smoking, previous stroke, ischemic heart disease, and diabetes in a proportional hazards model and by the coincidence of TIA, hypertension, heart disease, and peripheral arterial disease in another study.

A further prognostic criterion in this study was concomitant carotid artery disease demonstrable by Doppler ultrasonography. In accordance, univariate analysis showed that only infarcts in the anterior circulation on CT, not ischemic lesions in the posterior territory, increased the time-dependent risk of stroke, MI, or death following vertebrobasilar TIA or minor stroke. Stenosis or occlusion of the vertebrobasilar arteries did not significantly influence the long-term prognosis after infratentorial TIA or minor stroke in the proportional hazards model. Nevertheless, in univariate analysis the probability of stroke, MI, or death was significantly increased for patients with unilateral vertebral artery occlusion or bilateral vertebral artery occlusive disease, but not for those with unilateral vertebral artery stenosis. In previous studies the prognosis of patients with proximal vertebral artery stenosis has been assumed to be better than that of patients with distal stenosis. Further statistical differentiation with regard to the site of obliteration was not possible in our study because of the limited number of cases. The long-term prognosis of patients with basilar artery stenosis or occlusion did not differ from that of other patients, although both types of patients were followed up for comparable times. Of course, this may not reflect the natural course of vertebrobasilar occlusive disease because all these patients were receiving antithrombotic treatment.

References


Long-term prognosis of infratentorial transient ischemic attacks and minor strokes.
C R Hornig, C Lammers, T Büttner, O Hoffmann and W Dorndorf

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