Differences in Mortality and Cardiovascular Morbidity During a 3-Year Follow-up of Transient Ischemic Attacks and Minor Strokes

Pia Falke, MD, Lars Stavenow, MD, PhD, Marie Young, MD, and Folke Lindgärde, MD, PhD

We prospectively followed 78 patients with transient ischemic attacks (TIAs) from the carotid artery territory and 45 patients with minor ischemic strokes for 3 years. The mean±SD age of the patients in the TIA group was 66.9±7.9 years compared with 68.8±6.7 in the minor stroke group. Mortality among the TIA patients was significantly higher than that among minor stroke patients (18 of 78 compared with two of 45, p<0.01); mortality in the minor stroke group was not higher than that in the background population, whereas mortality in the TIA group was almost twice as high. The most common cause of death in the TIA group was myocardial infarction, and morbidity due to myocardial infarction and new TIA was higher in the TIA group than in the minor stroke group (35 events compared with seven), whereas no difference was found regarding stroke (five strokes compared with eight). Preexisting vascular disease implied an increased risk of mortality and morbidity in the TIA group. We conclude that carotid-territory TIA indicates a worse prognosis than minor stroke as mortality is higher in TIA patients at the same preexisting vascular disease prevalence and stroke frequency. (Stroke 1989;20:340-344)

The risk of stroke after a transient ischemic attack (TIA) is 6-10%/yr.1 Coronary heart disease is the most common cause of death in patients with TIA,1,2 and heart attacks are more frequent than stroke and are more often fatal. A worse prognosis for persons with TIA than for the general population has been reported.3 Factors negatively affecting prognosis after a definite stroke include intracerebral hemorrhage and embolic infarction, impaired consciousness on admission, high age, previous cardiac failure, diabetes mellitus, and male sex.4 Outcome after a minor stroke is less frequently studied. Wiebers et al5 retrospectively studied the incidence, prevalence, and long-term prognosis of 120 patients with reversible ischemic neurologic deficit (RIND) and found that the probability of a subsequent stroke or RIND was six times greater in RIND patients than in a control population; survival was not significantly different from that of the general population. In another study, Loeb and Priano6 studied 42 patients who had fully recovered from a stroke in 4–60 days; these authors found a mortality of 16.7% during a 4.25-year follow-up.6 In yet another study of 85 patients with minor stroke and 121 patients with TIA and protracted TIA (PTIA) from the carotid and vertebrobasilar territories, Loeb7 found that survival in patients with minor stroke was significantly greater than that in those with TIA and PTIA considered as a group.

In dealing with stroke patients, we have found that patients with carotid-territory TIA (including amaurosis fugax) were more severely affected by carotid atherosis than patients with minor strokes,8 and therefore we decided to test the hypothesis that TIA might be a more accurate marker for generalized complicated atherosclerosis than minor stroke. The purpose of our present study was to compare mortality and morbidity due to cardiovascular and cerebrovascular complications (myocardial infarction [MI], ischemic stroke, or TIA) in the two groups.

Subjects and Methods

We recruited patients with stroke from 96 patients in a trial of hemodilution therapy, the study protocol of which has been described.9 To compare 3-year mortality and morbidity with that for a group of patients with TIAs from the carotid territory, we selected a group of patients from these 96 patients. All stroke patients were examined using cerebral
computed tomography (CT) to exclude hemorrhage. An age interval of 40–78 years at the time of admission was decided upon, and patients with impaired consciousness, confusion, or the inability to walk by themselves, with or without walking aid, on Day 6 after admission were considered to have suffered a major stroke and were excluded. All patients included had a score of at least 44 on a 48-point scale according to Reference 9, and they could all return to their homes after a week, which was not the case for patients with major strokes. Thus, a minor sequela in one leg and a more pronounced weakness in one arm were not sufficient for exclusion. The decision to include or exclude patients was made on Day 7 as it was in some cases difficult to decide earlier whether a patient had suffered a major or a minor stroke. No minor stroke patient died during the first week after admission. Finally, we excluded all patients with strokes derived from the vertebrobasilar territory. We excluded 27 patients due to high age, 15 due to major stroke, and seven due to vertebrobasilar-derived symptoms; two were initially included but were later shown to have cerebral malignancies. Thus, we included 45 patients (28 men and 17 women); their mean±SD age was 68.8±6.7 years. After completing the hemodilution trial, 27 of the 45 minor stroke patients were given acetylsalicylic acid in low dosage, two received warfarin, and the remaining 16 were given no prophylactic therapy. The minor stroke patients were followed for 3 years, and mortality, new cerebrovascular disease (CVD), and MI were registered.

Patients with TIA from the carotid artery territory (defined as patients with complete recovery of symptoms within 24 hours) during 1982 and between June 1983 and March 1984 were followed for 3 years with regard to mortality and morbidity, as for the minor stroke group. The same age interval was used; the mean±SD age of the TIA patients (49 men and 29 women) was 66.9±7.6 years. After the diagnosis of carotid-territory TIA, 30 of the 78 TIA patients were given acetylsalicylic acid in low dosage and 13 received warfarin; nine TIA patients received no prophylactic therapy, and in 26 a prophylactic carotid endarterectomy was performed.

In Malmö, with 230,000 inhabitants, all patients with acute diseases are hospitalized in Malmö General Hospital and there was therefore no selection of patients other than as described above. The expected mortality for the two groups was calculated from the total mortality in Malmö. We used the following definitions:

**Preexisting vascular disease.** Knowledge of the following conditions before or on admission for the ischemic cerebral event: angina pectoris, MI, cerebrovascular event (ischemic stroke or TIA), intermittent claudication, or diabetes mellitus.

**Hypertension.** Treatment for hypertension, or blood pressure on two separate occasions of >180/100 mm Hg.

### Table 1. Vascular Disease and Mortality in Patients With Minor Stroke or TIA During 3-Year Follow-up

<table>
<thead>
<tr>
<th>Vascular disease</th>
<th>Minor stroke (n=45)</th>
<th>TIA (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no.</td>
<td>%</td>
</tr>
<tr>
<td><strong>Total mortality</strong></td>
<td>2</td>
<td>4.4</td>
</tr>
<tr>
<td><strong>Preexisting diseases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disease</td>
<td>20</td>
<td>44</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td><strong>Vascular diseases during follow-up</strong></td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Nonfatal cerebrovascular disease</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>TIA</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack.

*†‡§p<0.01, 0.05, 0.005, 0.025, respectively, different from minor stroke group.

**Diabetes mellitus.** Previously diagnosed disease, or fasting blood glucose level of >7.0 mmol/l on two separate occasions.

**Cardiac arrhythmia.** Potential embolicogenic arrhythmia such as chronic or intermittent atrial fibrillation or brady-tachy syndrome.

We used the χ² test with Yates’ correction for comparisons; p<0.05 was considered significant.

### Results

The results are shown in Table 1. Among the 45 patients with minor stroke, two died within 3 years, one of septicemia and the other of an unknown cause as he had moved from Malmö at the time of death. Among the 78 TIA patients, 18 were dead at follow-up, 12 of acute MI, two of major stroke, two of malignancies, one of subarachnoid hemorrhage, and one of an unknown cause. The difference in mortality was significant (p<0.01). Mortality in the minor stroke group was equal to or less than that in the background population, while that in the TIA group was almost twice as high (Figure 1).

Preexisting vascular disease occurred in 20 of the 45 minor stroke patients and in 43 of the 78 TIA patients (difference not significant). When the preexisting vascular diseases were divided into cardiovascular disease (angina pectoris and/or MI, CVD (ischemic stroke or TIA), and intermittent claudication (not shown), we found significantly more patients with intermittent claudication in the TIA group than in the minor stroke group (p<0.025). There were no significant differences between groups as to preexisting cardiovascular disease or CVD even though there was a predominance of CVD in the minor stroke group. The prevalence of preexisting hypertension was higher among the TIA patients (p<0.05), while that of preexisting diabetes mellitus was equal for the two groups.
In the TIA group, mortality among patients with preexisting vascular disease was higher than among those without (13 of 43 vs. five of 35); this difference was not significant, however. When mortality and morbidity due to CVD were taken together, these events occurred more frequently among TIA patients with preexisting vascular disease (nine of 43 vs. one of 35, p<0.025). Among the 43 TIA patients with preexisting vascular disease, 20 died or had nonfatal CVD, whereas among the 35 TIA patients without preexisting vascular disease only six died or had nonfatal CVD (p<0.01). When all unfavorable events (i.e., death, nonfatal CVD, nonfatal MI) were considered together, they occurred more frequently among the TIA patients with preexisting vascular disease than among those without (29 vs. 10, p<0.001). Some of these events, however, occurred in the same patient.

Morbidity due to new MI, TIA, or stroke was also higher in the TIA group than in the minor stroke group (35 vs. 7, Table 1; p<0.005). When this morbidity was subdivided into its components, there was still a difference between groups with regard to new nonfatal MI (13 vs. 1, p<0.025) and new TIA (14 vs. 1, p<0.025), while no difference was found between the groups regarding stroke (five of 45 vs. eight of 78). Three TIA patients had two MIs each, and two TIA patients that died had nonfatal strokes after their TIAs.

Table 2 shows the mortality and the number of patients with preexisting vascular disease in relation to different prophylactic treatments for the TIA group. Mortality among the 26 patients who underwent carotid endarterectomy appeared to be somewhat higher than that among the 52 medically treated patients, but no statistical comparisons could be made as the number of events was too small. There was also a difference among the treatment subgroups in relation to preexisting vascular diseases.

Discussion

Our study has demonstrated a clear difference in mortality and cardiovascular morbidity between TIA and minor stroke during a 3-year follow-up of patients of similar age. Differences in age, sex, and prevalence of preexisting vascular disease between the groups could not explain the difference in mortality. The most common cause of mortality in the TIA group was MI, while only two fatal strokes were registered. Mortality in the minor stroke group was equal to or less than that in the background population, while mortality in the TIA group was almost twice as high. The few deaths in the minor stroke group compared with the background population was probably mere chance, and we do not believe that having a minor stroke increases survival. Only one more death in this group would make the curves more parallel, and because of the
The most obvious explanation for the higher mortality and cardiovascular morbidity in the TIA group is that these patients are affected by generalized atherosclerosis to a higher degree than patients with minor strokes. It must once again be emphasized that TIA should be regarded as a marker for generalized vascular disease, and prophylactic measures concerning not only the brain but also the heart should be instituted. These patients should be attended by a clinical angiologist in cooperation with a surgeon and a neurologist. In support of the above finding, we have previously shown that ultrasound examination of the carotid arteries in TIA patients revealed significantly more advanced carotid artery lesions than in patients with minor strokes.

The minor stroke group, on the other hand, probably comprised many patients in whom thrombosis of the intracerebral large and small vessels constitutes the pathogenetic basis of the stroke. The better prognosis in this group might be due to less coronary atherosclerosis. The incidence of new strokes during follow-up seemed similar to that of the TIA group, although the incidence of new TIAs or MIs were lower. Therefore, in the minor stroke group it is urgent to concentrate therapeutic measures such as anticoagulation, platelet disaggregation, and careful antihypertensive therapy toward preventing new strokes.

We conclude that carotid-territory TIA and minor stroke are different expressions of atherosclerotic disease; the former is a generalized form with high mortality and cardiovascular morbidity during follow-up, whereas the latter is probably a less generalized form with a better prognosis, especially concerning coronary heart disease. Our findings should have therapeutic and diagnostic implications in clinical practice.

Acknowledgments

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References

8. Stavenow L, Bjerre P, Lindgärde F: Patients with reversible ischemic neurological deficit (RIND) have less severe carotid artery lesions than those with transient ischemic attacks (TIA) evaluated by duplex ultrasound. *Int Angiol* 1988;7:32-36


**KEY WORDS** • cerebral ischemia, transient • epidemiology • mortality • cerebral infarction
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