A Comparison of Risk Factors and Prognosis for Transient Ischemic Attacks and Minor Ischemic Strokes
The Oxfordshire Community Stroke Project

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In a community-based study of transient ischemic attack and stroke, we identified 184 cases of transient ischemic attack and 213 cases of first-ever minor ischemic stroke. A comparison of age, sex, and prevalence of coexistent vascular diseases and risk factors revealed no major differences between the two groups. The risk of further stroke and of further stroke and/or death was greater in patients with minor ischemic stroke although the difference was significant only for the latter. The apparent differences in prognosis could largely be accounted for by the favorable prognosis of patients with amaurosis fugax among those with transient ischemic attack. Although for some purposes it may be useful to distinguish transient ischemic attacks from minor ischemic strokes, the similarity of the two groups suggests that in many situations, including in clinical trials of treatments for the secondary prevention of strokes, the arbitrary distinction between them could be dispensed with. (Stroke 1989;20:1494-1499)

It has been argued that the distinction between transient ischemic attacks (TIAs) and minor ischemic strokes is arbitrary and has now outlived its usefulness. Indeed, if TIAs and minor ischemic strokes affected the same types of people with similar risk factors, similar underlying pathologies, and similar prognoses for survival and further vascular events, then the distinction could be abandoned. On the other hand, it makes sense to distinguish patients with disabling stroke from those with nondisabling stroke since the latter need little rehabilitation, are less likely to die, and may have more to gain from secondary preventive measures. It is, of course, useful to distinguish patients with hemorrhagic stroke, who may have different risk factors, different underlying pathologies, a worse prognosis, and different treatment requirements from those with cerebral infarction. However, the question remains whether ischemic events with symptoms lasting <24 hours (TIAs) differ in any fundamental way from ischemic strokes that cause symptoms lasting >24 hours but do not result in long-term disability. Unfortunately, there have been very few studies directly comparing these two groups of patients. Almost all the studies have been hospital-based so that observed differences between patients with TIAs and those with minor strokes may have resulted from selection bias. The reasons for hospital admission may be different for these two groups of patients. In this community-based study we have been able to compare the groups of patients, which were not biased by hospital admission status and probably represent almost all of the patients consulting a doctor in a defined population.

Subjects and Methods

This study formed part of a larger study of acute cerebrovascular disease in Oxfordshire (the Oxfordshire Community Stroke Project [OCSP]) described in detail elsewhere. Between November 1, 1981, and October 31, 1986, in a population of approximately 105,000 we registered all new cases of TIA that were seen by a doctor, and for 4 of these 5 years we registered all patients with a first-ever stroke. The population was not geographically defined but was based on the age/sex registers of approximately 50 general practitioners. We ensured complete case ascertainment by a variety of methods discussed elsewhere.

Following notification to the study, patients suspected of having had either a stroke or a TIA were examined by one of us as soon as possible after the event, and the clinical features of each case were
discussed at a weekly consensus meeting. At the initial examination, details of coexistent vascular diseases and risk factors were recorded and subsequently checked with the general practitioner’s and hospital records, and the patient’s prestroke handicap was assessed using the modified Rankin Scale. A range of investigations including a blood cell count, random blood sugar and cholesterol concentrations, electrocardiogram (ECG), and a computed tomogram (CT scan) of the brain were performed on every patient, if possible.

Each case diagnosed as a first-ever stroke or incident TIA was followed up at 1 month, at 6 months, at 1 year, and then yearly from the date of the initial event. The follow-up, performed by research nurses in the patient’s place of residence, was designed to determine whether the patient had suffered any further cardiovascular or cerebrovascular events. The follow-up included an assessment of handicap using the modified Rankin Scale. If the research nurse suspected that a further TIA or stroke had occurred, the patient was reexamined.

A TIA was defined as an acute loss of focal cerebral or ocular function with symptoms lasting <24 hours and which, after adequate investigation, was presumed to be due to embolic or thrombotic vascular disease. A more complete description of the types of attack counted as TIAs and the types regarded as “incident” cases has been published elsewhere.

A stroke was defined as rapidly developing symptoms and signs of focal or, in patients with deep coma or those with subarachnoid hemorrhage, global loss of cerebral function lasting >24 hours or leading to death and apparently of vascular origin. A cerebral infarction was diagnosed when CT was not available or when CT was performed >28 days after the event that showed no hemorrhage or when confirmed at autopsy. Probable cerebral infarction was diagnosed when CT was not available or when CT was performed >28 days after the event and the Guy’s Hospital Stroke Diagnosis Score was <4, indicating a 90% probability that the stroke was due to cerebral infarction. A detailed account of this definition appears elsewhere.

A minor ischemic stroke (definite or probable) was one in which the score on the Rankin Scale 1 month later was 0 or 1 in which the score was the same as or lower than that estimated for the period immediately before the stroke. If the patient died or had a recurrent stroke before the 1-month follow-up, a judgment of whether the first stroke was disabling, based on neurologic deficit at the initial examination, was made. This was essential to avoid excluding patients with minor strokes who died or who had a recurrent stroke before the first follow-up since this would have biased the group and resulted in a misleadingly low estimate of the risk of early death or recurrence following minor ischemic stroke. In fact, only one patient died before the 1-month follow-up.

Hypertension was defined two ways: first, by history (if the patient or his medical records gave such a diagnosis) and, second, if there were two blood pressure recordings in the patient’s records with both a systolic pressure of ≥160 mm Hg and a diastolic pressure of ≥90 mm Hg. A previous myocardial infarction was diagnosed if the patient had a history of anterior chest pain and pathological Q waves on an ECG and/or an accompanying 50% rise in the concentrations of cardiac enzymes. Atrial fibrillation was diagnosed if it was confirmed by an ECG either before the initial event or at the initial examination. Peripheral vascular disease was diagnosed if the patient had more than one absent foot pulse or if femoral artery bruits were heard. Diabetes mellitus was diagnosed if the patient gave a history of diabetes that was confirmed in his medical records. Also included as diabetics were patients with a random blood sugar concentration of ≥11 mmol/l at the initial examination. Hypercholesterolemia was diagnosed if a random cholesterol level was ≥7.8 mmol/l.

Based on these definitions, the patients were grouped into those with TIs and those with minor ischemic strokes. We compared these two groups using SPSS X and a FORTRAN program for survival analysis. wurden und on the other hand specific exclusions patients who were notified to the study after already suffering a stroke. All probabilities are expressed as two-tailed values.

Results

During the study period, 184 incident cases of TIA (described elsewhere) and 675 patients with a first-ever stroke (described elsewhere) were registered. Of the 675 strokes, 213 (32%) were categorized as minor ischemic strokes; 207 of these 213 (97%) had a CT scan, and in 20 of the 207 (10%) CT was performed >28 days after the stroke. Therefore, of the 213 patients with minor ischemic strokes, 187 (88%) had a definite cerebral infarction and 26 (12%) had a probable infarction. Seven patients were included in both the TIA and minor ischemic stroke groups since they were initially notified to the study with a TIA and then had a minor ischemic stroke. The age of patients with TIs (mean 69.4, SD 12.2, range 24–100 years) and those with minor ischemic stroke (mean 70.8, SD 12.3, range 23–100 years) did not differ significantly (p=0.27). The proportion of men in the two groups also did not differ (103 of 184 with TIA [56%] compared with 119 of 213 with minor ischemic stroke [56%]). Because
TABLE 1. Prevalence of Coexistent Vascular Disease and Risk Factors in Patients With Transient Ischemic Attacks and Minor Ischemic Strokes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Transient ischemic attack (n=184)</th>
<th>Minor ischemic stroke (n=213)</th>
<th>Two-tailed probability level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient history</td>
<td>86</td>
<td>46.7</td>
<td>97</td>
</tr>
<tr>
<td>Blood pressure ≥160/90 mm Hg</td>
<td>91</td>
<td>49.5</td>
<td>118</td>
</tr>
<tr>
<td>twice ever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of angina pectoris</td>
<td>34</td>
<td>18.5</td>
<td>43</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>17</td>
<td>9.2</td>
<td>28</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>26</td>
<td>14.1</td>
<td>28</td>
</tr>
<tr>
<td>History of intermittent claudication</td>
<td>21</td>
<td>11.4</td>
<td>26</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(absent pulses and/or femoral bruits)</td>
<td>31</td>
<td>16.8</td>
<td>44</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td>50</td>
<td>27.2</td>
<td>41</td>
</tr>
<tr>
<td>Cigarette smoker at any time</td>
<td>126</td>
<td>68.5</td>
<td>135</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>12</td>
<td>6.5</td>
<td>18</td>
</tr>
<tr>
<td>Random cholesterol concentration ≥7.8 mmol/l</td>
<td>43</td>
<td>23.6†</td>
<td>34</td>
</tr>
<tr>
<td>Hematocrit ≥0.50</td>
<td>29</td>
<td>15.8</td>
<td>29</td>
</tr>
<tr>
<td>Cervical bruits</td>
<td>38</td>
<td>20.7</td>
<td>37</td>
</tr>
</tbody>
</table>

*No smoking history for 1 patient.
†No cholesterol concentration for 2 patients with transient ischemic attack and for 9 patients with minor ischemic stroke.
‡No hematocrit for 4 patients.

of the very similar age and sex distributions in the two groups, we made no adjustments for these variables in our comparisons of risk factor prevalence and prognosis.

The prevalence of vascular disease and risk factors in the two groups are compared in Table 1 and Figure 1. There were no significant nor very great differences between groups. Of course, with a relatively small sample size the CIs were quite wide and Type II errors are possible. However, it is unlikely that a larger sample would reveal important differences since the ORs (Figure 1) are close to unity for all variables studied.

The mean±SD hematocrit of patients with TIAS (44.4±5.3%) and minor ischemic stroke (44.0±5.1%) did not differ significantly (p=0.4). The mean±SD random blood sugar levels also did not differ significantly (5.57±1.88 mmol/l for TIASs, 5.84±2.58 mmol/l for minor ischemic stroke; p=0.24). Although the prevalence of hypercholesterolemia was similar in the two groups, the mean cholesterol levels were higher in the TIA patients than in those with minor ischemic stroke (6.9 and 6.5 mmol/l, respectively; p=0.006).

The survival rate and risk of further stroke in the two groups are compared in Figures 2 and 3. There was a trend for patients with TIAS to have a lower risk of death (OR 0.72, 95% CI 0.45–1.16) and stroke (OR 0.65, 95% CI 0.41–1.04) during follow-up. In neither instance was the difference in prognosis between groups significant, although when the groups' risks of either dying and/or having a stroke are compared (Figure 4), the patients with TIAS did
significantly better than those with minor ischemic strokes (OR 0.64, 95% CI 0.44–0.92; \(p=0.01\)).

However, it may not be valid to compare the two groups this way. Our definition of a TIA included patients with amaurosis fugax; 32 of the 184 patients with TIA (17%) had only ocular attacks. Patients with retinal infarction were not included among those with minor ischemic strokes, nor were retinal infarctions counted as stroke events during follow-up although retinal infarction could be considered as a stroke equivalent in patients with amaurosis fugax. There is also some evidence that patients with amaurosis fugax have a lower risk of subsequent strokes than those with transient cerebral ischemic attacks.\(^1^3\) In Figure 5, we have excluded patients with amaurosis fugax from the TIA group. The difference in prognosis for death and/or stroke between the two groups was less marked and is no longer significant (OR 0.74, 95% CI 0.51–1.08; \(p=0.11\)).

Discussion

Our study shows that patients who suffer TIAs and minor ischemic strokes are very similar in terms of age and sex. Previous hospital-based studies\(^1^4,1^5\) have also shown that the ages of patients with TIAs and those with minor strokes are similar. However, probably due to the bias resulting from hospital admission, the patients in those studies were much younger (mean ages 58\(^1^4\) and 64.5\(^1^5\) years) than those in ours. In both those studies the male:female ratio among patients with TIAs and minor strokes was almost 3:1, whereas in our study there was only a very small excess of men. This difference is probably due to exclusion of elderly patients (who are less commonly hospitalized) and therefore women from the other studies since the risk of having a stroke or TIA is greater in middle-aged men than in women of the same age.\(^4,5\)
We have shown that the prevalence of coexistent vascular disease and risk factors was very similar in the two groups. The only significant difference was in cholesterol levels; patients with TIAs had higher levels. During an acute illness, particularly myocardial infarction, cholesterol levels may be depressed and may not regain preillness values for several weeks. If the depression of cholesterol level were proportional to the severity of the illness, then one might expect cholesterol concentration to remain higher in patients with TIAs than in patients with minor ischemic stroke. Gambina et al demonstrated no difference in cholesterol levels in their patients, but in the majority of patients blood was taken ≤24 hours after stroke onset, perhaps before any depression of cholesterol level occurred.

In their hospital-based study, Harrison and Marshall showed that atrial fibrillation occurred in 1.6% of patients with TIAs and in 5.6% of patients with stroke. We found a much higher proportion with atrial fibrillation, 14.1% of patients with TIAs and 13.1% of those with minor ischemic stroke. This was probably because we included many older patients in our series, patients who are not normally hospitalized and are therefore excluded from hospital-based studies. Kannel et al have shown that the prevalence of atrial fibrillation increases with age. On the basis of the lower prevalence of atrial fibrillation in patients with TIAs, Harrison and Marshall concluded that atrial fibrillation was more likely to be associated with completed strokes, possibly because of the size of the resulting emboli.

The results of our study, in which atrial fibrillation occurred with equal frequency in patients with TIAs and those with minor ischemic strokes, suggest that this is not the case. Gambina et al demonstrated that patients with TIAs and reversible ischemic neurologic deficits (RINDs) differed significantly with respect to smoking and hematoctrit, findings that we were unable to confirm. In our study, more patients with TIAs than with minor ischemic strokes were current smokers, although the proportions of each who had smoked previously were similar. It appeared that patients with minor ischemic strokes were more likely to have given up smoking than those with TIAs.

We have shown that patients with TIAs appear to have a lower risk of dying or having a stroke than those with minor ischemic strokes but that much of the apparent difference was due to the good prognosis in patients with amaurosis fugax. In a retrospective community-based study, Wiebers et al found that patients with TIAs and attacks lasting ≤7 days had very similar risks of both death and later stroke. However, patients with strokes and complete recovery but in whom symptoms lasted >7 days had a significantly lower risk of subsequent stroke than those with shorter-duration attacks. In our study, the trend was for a longer duration of symptoms to be accompanied by an increased rather than a decreased risk of subsequent stroke. There are no obvious methodologic reasons to explain the different findings of these studies.

There are a number of reasons for maintaining the distinction between TIAs and minor strokes even if differences in risk factors, underlying pathology, and prognosis cannot be demonstrated. First, the differential diagnosis of focal neurologic symptoms that last only minutes or hours is quite different from that of longer-lasting attacks. Second, as the duration of the symptoms increases, so does the chance that they are due to intracranial hemorrhage rather than to ischemia. Cases of intracerebral hemorrhage have been described in which symptoms have lasted only 48 hours, and it is possible that some intracerebral hemorrhages have the temporal profile of a TIA. However, it is probably fairly safe to assume that an event with symptoms that completely resolve within 24 hours (the patient should be questioned carefully about residual symptoms) is ischemic, so treatment with aspirin or even warfarin can be started without a CT scan. Otherwise, if there is any doubt, a CT scan should be done ≤14 days after the event to exclude a hemorrhage. Lastly, stroke epidemiologists are struggling to detect changes in stroke incidence with time and in different geographic locations. Such changes, if they exist, may provide important clues to the etiology of stroke, and in the future such changes may be useful in measuring the effects of stroke prevention programs. The methodologic problems involved in measuring stroke incidence are great enough already, but if one were to include all patients suffering attacks lasting only a few seconds, minutes, or hours, then accurate studies would become almost impossible. Patients with brief attacks are probably more likely to ignore or forget them and consequently are less likely to report them to a doctor. For epidemiologic purposes, it would therefore seem sensible to maintain the distinction between stroke and TIA, although as we have previously pointed out it is important to detect TIAs in studies of stroke incidence to ensure complete case ascertainment (in the OCSP 7% of strokes were incorrectly labeled as TIAs by the referring doctor).

The results of our study suggest that TIAs and minor ischemic strokes affect people of similar age and sex and with similar underlying diseases and risk factors. This supports the use of TIAs as a surrogate for ischemic stroke in case–control studies. The prognosis of patients with TIAs may be better, although the differences are probably small if one excludes patients with amaurosis fugax, but this warrants further study. Certainly, when planning trials of secondary preventive measures, it would be an advantage to include patients with minor ischemic strokes as well as those with TIAs for two reasons. First, patients with TIAs may contribute more major events and thus increase the power of the study. Second, the incidence of minor ischemic stroke is greater than that of TIAs, and
patients with minor ischemic stroke have at least as much to gain from treatment; it is therefore important to show that treatment benefits patients with minor ischemic stroke also. In conclusion, it would seem sensible for most practical purposes, except those mentioned above, to reduce the emphasis placed on the distinction between TIA and minor ischemic strokes. Perhaps the term reversible ischemic attack could be used to encompass both groups of patients.

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References

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