Incidence of Transient Ischemic Attacks in Oxfordshire, England

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The Oxfordshire Community Stroke Project is a prospective register of all new cases of stroke and transient ischemic attack (TIA) in a population of 105,000 residents of Oxfordshire, England. Between November 1, 1981, and October 31, 1986, 184 patients presented for the first time to a general practitioner or hospital with a TIA. The crude annual incidence rate was 0.35/1000, 0.42/1000 standardized to the 1981 population of England and Wales. We estimate that each year approximately 21,000 patients in England and Wales (about half of whom are >70 years old) consult a doctor for the first time with a TIA. Approximately 80% of our 184 patients had TIA in the carotid distribution; the remainder had TIA in the vertebrobasilar distribution or TIA of uncertain vascular distribution. The incidence of TIA increased sharply with increasing age, and the overall incidence in men was very similar to that in women (incidence ratio 1.3). However, in middle age, men were much more likely to suffer a TIA than women (odds ratio 2.6), which probably explains the marked male predominance in most hospital-based studies and treatment trials in which the elderly, and thus women, are underrepresented. This has important implications for the design and interpretation of clinical trials of treatments for TIA. (Stroke 1989;20:333–339)

There have been relatively few community-based studies of the incidence of transient ischemic attacks (TIAs), only one in Great Britain. It is important to measure the incidence of TIAs for several reasons. First, reliable incidence data allow one to calculate the contribution of treatments for TIAs to the primary prevention of stroke, bearing in mind that TIAs may increase the risk of stroke sevenfold and may precede stroke in 9.4% to 26% of cases. Second, if carotid angiography and carotid endarterectomy can be shown to be worthwhile in the investigation and treatment of TIAs, accurate incidence data will allow us to estimate the cost of providing these procedures. Third, one cannot plan trials of treatment for TIAs without knowing the untreated natural history of the disease, the number of patients likely to be available, and in particular the number of patients likely to fulfill entry criteria; only then can fundamental decisions, such as whether the trial should be performed in one center (e.g., the Newcastle Carotid Surgery Trial), in several centers in one country (e.g., the UK-TIA Aspirin Trial), in one continent (e.g., the European Carotid Surgery Trial), or even in several continents (e.g., the EC/IC Bypass Study), be made. Of course, for these purposes one does not need to know the incidence of all TIAs but rather the incidence of TIA patients who seek medical attention and whose subsequent strokes are at least potentially preventable. Persons who have had a TIA but do not seek medical attention (and there is evidence that these may form a large percentage of the total; see below) are of less interest in these respects, although if such persons could be encouraged to seek medical help, the opportunities for primary stroke prevention would be greatly enhanced.

Our study was designed to measure the incidence of TIA in the population whose TIAs come to the attention of a doctor; it was based on primary-care as well as hospital physicians so that persons who were not normally admitted or referred to hospital clinics could be counted. Our study was designed to overcome many of the methodologic problems, including incomplete or biased case ascertainment (which tend to occur in retrospective or hospital-based studies) and a lack of precision in defining a TIA and more particularly an incident case, of previous studies.
Subjects and Methods

Our study of the incidence of TIAs formed part of a larger study of the epidemiology of acute cerebrovascular disease, the Oxfordshire Community Stroke Project (OCSP), the overall design of which has been described in detail.9-11

The study population comprised approximately 105,000 people who were fully registered (i.e., not temporary residents) with 50 general practitioners (GPs) working from 10 health centers distributed throughout urban and rural Oxfordshire. The denominator for the incidence rates was calculated by averaging the number of people in each 10-year age band on the age/sex registers (ASRs) of the GPs at the beginning and end of the study. The population increased by approximately 6% during the study period. The figures obtained from the ASRs were validated against records held by the Oxfordshire Family Practitioners Committee (FPC), which are generally considered to be more accurate than ASRs since they form the basis for remuneration of GPs.12 It was impractical to use the FPC figures themselves since these records are not computerized, are stored alphabetically, and are split into only three age bands (0–65, 65–75, and >75 years).

In the 5 years between November 1, 1981, and October 31, 1986, the collaborating GPs agreed to notify the OCSP of all patients suspected of suffering a TIA. We also scrutinized hospital admission and discharge records to detect patients who had come directly to a casualty department. Each patient was assessed by one of us, in the patient’s home if necessary. A set of basic investigations (including computed tomography) was performed to exclude other causes of transient symptoms (e.g., intracranial tumors, hypoglycemia, etc.). We examined each patient’s GP’s and hospital records to exclude patients with previous (known to their doctor) TIAs and strokes as well as to provide data on vascular risk factors collected prior to the TIA.

A TIA was defined as an acute loss of focal cerebral or ocular function with symptoms lasting <24 hours and that, after adequate investigation, was presumed to be due to embolic or thrombotic vascular disease.13 We classified attacks of unilateral motor or sensory symptoms, dysphasia, or transient monocular blindness as carotid-distribution TIAs while attacks of vertigo, diplopia, hemianopsia, or bilateral (during a single attack) motor or sensory symptoms were classified as vertebrobasilar-distribution TIAs. Dysarthria was not used to classify the vascular distribution of a TIA. We excluded patients with isolated vertigo, diplopia, bilateral blindness, or drop attacks since such symptoms occurring alone may result from either diffuse cerebral ischemia or from nonvascular pathologies. We also excluded patients with only nonfocal symptoms (such as loss of consciousness) as well as patients with features suggesting migraine (i.e., progressive onset or a typical positive visual phe-

omena even if headache was absent), epilepsy, or transient global amnesia.

In studies of the epidemiology of stroke in which accurate measurements of incidence are required, it is important that only new (or incident) cases are registered and that patients with previous strokes are not included.14 Furthermore, in studies of natural history it is important to include cases at an early and uniform point in the course of their disease.15 These considerations are even more important in the study of the epidemiology of TIAs, yet no previous study has attempted to provide a rigorous definition of an incident case. We define an incident case as a patient whose first TIA that led to consultation with a doctor occurred during the study period. TIAs occurring before the study period that the patient had not brought to a doctor’s attention were ignored; if a patient suffered a further TIA during the study period that led him or her to consult a doctor, then the most recent attack was counted as the incident TIA. Patients who suffered attacks prior to the study period that, after consultation with a doctor, were diagnosed as TIAs were classified as prevalent cases. Occasionally patients had seen a doctor prior to the study period with attacks that were not diagnosed as TIAs but then presented with a definite TIA during the study period; if the previous attacks were identical to the present episode, then the patient was classified as a prevalent case. Therefore, we did not rely upon the diagnostic skills of GPs. We excluded patients who presented to a doctor during the study period with their first TIA but who had already suffered a stroke either before or after the TIA.

We excluded patients who had a TIA but did not seek medical advice until after a stroke had occurred since their inclusion would inevitably have biased the prognosis and may have distorted the age/sex-specific incidence of TIA if the risk of stroke after a TIA is influenced by age or sex. This rather complex definition is necessary to avoid ambiguity because, unfortunately, patients with TIAs often do not consult a doctor with their first TIA if, indeed, they consult a physician at all. Some of the more important features of our definition of an incident case are illustrated in Figure 1.

Several authors have shown that the interobserver reliability of the diagnosis of TIAs is poor.16,17 We attempted to optimize interobserver reliability by first discussing, using simple language17 at a weekly meeting that at least two of us attended, the clinical features of every patient referred. Second, we kept the delay between the attack and our assessment of the patient as short as possible (median 5 days) to obtain the most accurate history from the patient. Third, we applied our definitions strictly, and to ensure their uniform interpretation throughout the study period, after all cases had been notified to the OCSP one of us reviewed the notes of every patient notified to and assessed by the OCSP.

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FIGURE 1. Diagram illustrating some important parts of our definition of incident transient ischemic attack (TIA). Included, counted as incident case in this study; TIA's occurring before study period (prevalent cases) or patients who already had a stroke (S) at the time of medical contact were not included. ●, first TIA; ○, incident TIA, arrow, medical contact.

We calculated 95% confidence intervals (CIs) of incidence rates and the approximate 95% CIs of odds ratios (ORs) using standard methods.18,19 Pooled ORs (see Figure 4) with 95% CIs were obtained by the method described by Yusuf et al.20

Results

The age and sex structure of the study population is shown in Table 1. The totals obtained from the ASRs were slightly lower (~1.1%) in 1981 and slightly higher (2.3%) in 1986 than those from the FPC. Such small discrepancies made little difference in the calculated incidence rates.

During the study period, 512 patients were referred by their GPs or presented at a hospital with transient symptoms. Following our assessment, we included 184 as incident TIAs; the remainder fell into a variety of other diagnostic categories (Figure 2). The mean age of the 184 incident cases was 69.4 (range 20–100) years; 103 were men and 81 were women. The number of cases is shown by sex and 10-year age band in Table 1 along with the age/sex-specific incidence rates and 95% CIs. The age/sex-specific incidence is shown graphically in Figure 3, which illustrates that the incidence of TIAs rose sharply with increasing age in both men and women, although there was a tendency for the incidence to decrease in men >85 years old.

The overall incidence of TIAs was slightly greater in men than in women (incidence ratio 1.3); however, during middle age the difference in incidence between the sexes increased. This is illustrated in Figure 4, in which the ORs (i.e., the odds of a man suffering a TIA divided by the odds of a woman suffering a TIA) with their approximate 95% CIs are shown for 10-year age bands. Only between 55 and 74 years of age does the difference between men and women reach the conventional level of significance (p<0.05).

Our study population was slightly younger than that of England and Wales21 so, although the crude incidence of TIAs in our study was 0.35/1000/yr (95% CI 0.3–0.4/1000/yr), the age/sex-adjusted incidence (standardized by the direct method to the 1981 population of England and Wales21) was greater (i.e., 0.42/1000/yr). If our incidence rates are applied to the 1981 England and Wales population,21 approximately 21,000 people, about 50% of whom would be >70 years old, are likely to present for the first time to doctors each year with a TIA.

One hundred sixteen patients (63%) had cerebral attacks in the carotid distribution (two of these also had episodes of amaurosis fugax) and 32 (17%) had amaurosis fugax only; approximately 80%, therefore, had a carotid-distribution TIA. The remaining 36 patients suffered either vertebrobasilar-distribution TIAs or TIAs of uncertain vascular distribution (e.g., isolated dysarthria).

Table 1. Age/Sex-Specific Incidence Rates for Transient Ischemic Attacks in Oxfordshire, England, November 1, 1981, to October 31, 1986

<table>
<thead>
<tr>
<th>Age band (yr)</th>
<th>5-year study period</th>
<th>Annual incidence/1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td></td>
<td>Cases At risk</td>
<td>Cases At risk</td>
</tr>
<tr>
<td>&lt;15</td>
<td>0 9754</td>
<td>0 9215</td>
</tr>
<tr>
<td>15–44</td>
<td>3 27,953</td>
<td>2 25,871</td>
</tr>
<tr>
<td></td>
<td>0.02 0.02–0.04</td>
<td>0.02 0.00–0.04</td>
</tr>
<tr>
<td>45–54</td>
<td>7 5595</td>
<td>7 5396</td>
</tr>
<tr>
<td></td>
<td>0.26 0.12–0.39</td>
<td>0.26 0.07–0.45</td>
</tr>
<tr>
<td>55–64</td>
<td>29 4752</td>
<td>15 4789</td>
</tr>
<tr>
<td></td>
<td>0.92 0.45–1.33</td>
<td>0.63 0.31–0.94</td>
</tr>
<tr>
<td>65–74</td>
<td>40 3297</td>
<td>17 3770</td>
</tr>
<tr>
<td></td>
<td>1.87 1.20–2.03</td>
<td>1.88 1.20–2.03</td>
</tr>
<tr>
<td>75–84</td>
<td>23 1528</td>
<td>28 2446</td>
</tr>
<tr>
<td>≥85</td>
<td>1 285</td>
<td>12 835</td>
</tr>
<tr>
<td></td>
<td>0.87 0.67–1.09</td>
<td>0.87 0.67–1.09</td>
</tr>
<tr>
<td>Total</td>
<td>103 53,164</td>
<td>81 52,312</td>
</tr>
<tr>
<td></td>
<td>0.31 0.24–0.38</td>
<td>0.31 0.24–0.38</td>
</tr>
</tbody>
</table>

Cl, confidence interval.
During 4 of the 5 years of our study, stroke patients were also registered, and 76 (11%) of 675 patients who presented with a first-ever stroke also gave a history of definite preceding TIAs. Fifty (66%) of these 76 patients had TIAs during the study period, and of these 50, 27 (54%) had not seen a doctor about the TIA, 19 (38%) had been referred to the OCSP with TIAs previously and were included as incident cases, and four (8%) had seen a doctor with a TIA but had not been referred to the OCSP. Therefore, it appears that at least 54% (95% CI 40-68%) of patients suffering TIAs did not consult a doctor until their stroke occurred. Of course, we do not know how many persons had a TIA and failed to consult a doctor but did not suffer a stroke and as a consequence did not come to our attention. If the 31 patients presenting to the OCSP with a stroke but giving a history of a definite previous TIA occurring during the study period are included, the crude incidence of TIA is increased from 0.35 to 0.41/1000/yr.

Discussion

Studies of TIA incidence have been performed in Britain, Europe, the United States, and Asia. However, problems arise when one tries to compare the results of these studies. First, many studies give incidence rates for only limited and differing age ranges; other studies give only crude incidence rates so that differences between studies may simply reflect the differing age and sex structures of the study populations. Most studies investigated only small populations and consequently identified very few cases so that their estimates of incidence rates lack precision. Only two studies quote 95% CIs for their rates. Several studies were hospital-based and therefore presumably failed to count an unknown, but probably significant, number of cases remaining in the community. Certain studies used survey techniques (i.e., questionnaires and interviews by nonmedical personnel) to detect all persons with a
TIA whether they saw a doctor or not27,28,31–34 while other studies counted only those persons who consulted a doctor.1,3,22–26,29,30 The former are clearly more likely to produce higher incidence rates but may include patients who did not have definite TIs. In the first incidence study, Acheson and colleagues1 defined a TIA as an attack lasting <1 hour and might therefore be expected to produce lower incidence rates than the other studies. However, more subtle differences in the definitions of a TIA and an incident case and differences in the methods of case ascertainment may also contribute to the differences in the results of these studies. The importance of using standard methods to measure the incidence of stroke has recently been highlighted by Malmgren and colleagues,14 but many of their comments apply equally to the estimation of the diagnostic index has recently revealed that the diagnostic index of crude incidence rates is the comparison of age/sex structures of the study populations.

More interesting than this very rough comparison of crude incidence rates is the comparison of age-specific rates (Figure 5). This is possible for only the three studies that published such rates3,22,29 for all ages. Direct comparison is hampered by the different age bands used, but in Figure 5 we have adjusted our age bands to match those of the other studies. There appears to be little difference between them, especially if one notes the fairly wide 95% CIs around these age-specific rates (shown only for the OCSP). Certainly in one study,3 and perhaps in the other two,22,29 patients were included even if they presented with a stroke, and this would tend to inflate the incidence rates. These studies were all retrospective and relied upon diagnostic indexes to detect cases. J.P. Whisnant (personal communication) has recently revealed that the diagnostic index at the Mayo Clinic may have failed to detect up to 50% of cases of TIs presenting to that institution, and Whisnant et al3 may therefore have underestimated the TIA incidence. In the OCSP GPs may have failed to refer some patients with TIs, but the small number of cases who came to our attention via other routes (i.e., hospital records) or perhaps after they had gone on to suffer a stroke indicated that this was probably not a major problem. A very much more important problem is that so many patients with TIs simply do not report them to a doctor. The size of this problem may vary between populations, depending on several factors such as how stoic the people are, their awareness of health matters, and perhaps the cost of medical care.

The higher relative odds of a TIA in men of middle age (Figure 4) is interesting since it could explain differences in the sex ratios observed in community-based incidence studies compared with hospital series and treatment trials. In the former, the overall male:female incidence ratio is usually approximately 1.0 (0.98–1.26; Table 2), while in the latter, ratios of 2:1 and even 3:1 are not uncommon, presumably because in hospital-based studies and treatment trials young and middle-aged people predominate to the exclusion of the elderly. This hypothesis is supported by the fact that the average age of patients in our study was 69.4 years while in most hospital studies it is around 60 years and in some37 it is as low as 49 years. This underrepresentation of the elderly, and thus women, in treatment trials may be important, especially as 50% of patients with TIs are >70 years old. The results of randomized controlled trials would be more precise and generalizable to women if they included more elderly (and thus female) subjects. Older patients are bound to contribute more events (such as vascular deaths and strokes) in trials so that differences between treatment groups might be identified more easily. This would be an argument for basing future trials of medical treatment for TIs in the community rather than in hospitals.

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References

FIGURE 5. Graphs of age-specific incidence and 95% confidence intervals for transient ischemic attacks in Oxfordshire Community Stroke Project (OCSP) compared with incidences from three studies that provided such information for all age groups. Top left: Rochester, Minnesota; top right: Tartu, Estonia, USSR; bottom left: Lehigh Valley, Pennsylvania. Note different age bands used in each graph. These studies did not publish 95% confidence intervals.

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