A prospective study of acute cerebrovascular disease in the community: the Oxfordshire Community Stroke Project—1981–86

2. Incidence, case fatality rates and overall outcome at one year of cerebral infarction, primary intracerebral and subarachnoid haemorrhage

J Bamford, P Sandercock, M Dennis, J Burn, C Warlow

Abstract

The age and sex specific incidence rates for cerebral infarction, primary intracerebral haemorrhage and subarachnoid haemorrhage in a population of approximately 105,000 are presented. Over four years 675 patients with a first-ever stroke were registered with the Oxfordshire Community Stroke Project. The pathological diagnosis was confirmed by computerised tomography (CT) scan, necropsy or lumbar puncture (cases of subarachnoid haemorrhage only) in 78% of cases and a further 17% were diagnosed according to the Guy’s Hospital Stroke Diagnostic Score. The proportion of all first-ever strokes by pathological type was: cerebral infarction 81% (95% confidence interval 78–84), primary intracerebral haemorrhage 10% (8–12), subarachnoid haemorrhage 5% (3–7), and uncertain type 5% (3–7). These proportions are similar to other community-based studies. The overall 30 day case fatality rate was 19% (16–22), that for cerebral infarction being 10% (7–13), primary intracerebral haemorrhage 50% (38–62) and subarachnoid haemorrhage 46% (29–63). One year post stroke 23% (19–27) with cerebral infarction were dead and 65% (60–70) of survivors were functionally independent. The figures for primary intracerebral haemorrhage were 62% (43–81) dead and 68% (50–86) of survivors functionally independent and for subarachnoid haemorrhage were 48% (24–72) dead and 76% (56–96) of survivors functionally independent. There are important differences between these rates and those from other sources possibly due to more complete case ascertainment in our study. Nevertheless, the generally more optimistic early prognosis in our study, particularly for cases of cerebral infarction, has important implications for the planning of clinical trials and for the expected impact that any treatment might have on the general population.

If our understanding and management of cerebrovascular disease in the community is to advance then pathologically homogeneous groups of patients need to be identified and studied. Recently a number of large multicentre trials of acute stroke treatment and secondary stroke prevention have been undertaken and more are being planned. There is also increasing interest in hospital-based stroke data banks which can record the multiple physical examinations and detailed investigations which are only possible when patients are in hospital. Accurate population-based data about the incidence and outcome of the commonly diagnosed pathological types of stroke are needed to plan trials and to determine the relevance of the findings from hospital-based stroke data banks to the generality of patients with stroke. By using more detailed epidemiological data, trial designers may be able to predict which inclusion or exclusion criteria might lead to successful recruitment, whilst failure to do so will “virtually assure future therapeutic uncertainty”. The value of these types of data in the planning of a clinical trial of secondary stroke prevention in patients with non-valvular atrial fibrillation was reported recently.

Whilst community-based studies must provide information about the commonly diagnosed stroke types if they are to be of value, concern has been expressed about the accuracy of pathological diagnoses in such studies. The Oxfordshire Community Stroke Project (OCSP) aimed to determine accurately the pathological type of first-ever stroke by CT and necropsy examination in an unbiased and representative sample of patients. We present the incidence and outcome after one year for cerebral infarction (CI), primary intracerebral haemorrhage (PICH) and subarachnoid haemorrhage (SAH).

Methods

The methodology of the OCSP has been reported in detail previously. In summary, all patients in a population of approximately...
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Table 1 Modified Rankin Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>Minor symptoms which do not interfere with lifestyle</td>
</tr>
<tr>
<td>2</td>
<td>Minor handicap—symptoms which lead to some restriction in lifestyle but do not interfere with the patient's capacity to look after themselves.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate handicap—symptoms which significantly restrict lifestyle and prevent totally independent existence.</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe handicap—symptoms which clearly prevent independent existence though not needing constant attention.</td>
</tr>
<tr>
<td>5</td>
<td>Severe handicap—totally dependent requiring constant attention night and day.</td>
</tr>
</tbody>
</table>

Functionally independent = Grades 0, 1, 2
Functionally dependent = Grades 3, 4, 5

105,000 who presented for medical attention with their first-ever stroke during a four year period were registered with the study. The patients were assessed as soon as possible after the event by a study neurologist, who decided whether or not they were admitted to hospital, and we attempted to obtain a CT scan or necropsy examination in all cases.

Strokes were classified into the following pathological types (for full definitions see appendix): cases with diagnostic CT and/or necropsy findings were classified as definite CT or definite PICH. Cases with a history of actue non-febrile headache and meningism typical of SAH were classified as definite SAH if supported by diagnostic CT, necropsy or CSF findings or as probable SAH if confirmatory tests were lacking. For other cases lacking diagnostic CT or necropsy data, the Guy's Hospital Stroke Diagnostic Score (GHSDS) was calculated. This is a clinical scoring system which has been validated using two independent data sets. The score yields a probability of a stroke being due to cerebral infarction or intracranial haemorrhage using a combination of clinical signs and symptoms. It is more accurate than an unstructured clinical diagnosis. If the GHSDS indicated that the stroke had a greater than 90 probability of being due to PICH or a greater than 90 probability of being due to CI, it was classified as probable PICH or probable CI respectively. All remaining cases were considered to be of uncertain (UNC) pathological type.

All patients were followed up by our research nurses who visited survivors at their place of residence one month, six months and one year after the first-ever stroke. If a patient died all hospital and general practitioner records relating to the death were examined. At each visit overall handicap was assessed using a modification of the Rankin scale (table 1). Further papers will report the functional outcome in more detail but for the purposes of this report the scale has been collapsed into two categories: functionally independent (corresponding to grades 0, 1, 2) and functionally dependent (corresponding to grades 3, 4, 5).

Table 2 Method of making pathological diagnosis

<table>
<thead>
<tr>
<th>Classification</th>
<th>Method of Diagnosis</th>
<th>Number</th>
<th>( \alpha )</th>
<th>95% Conf. Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarction</td>
<td>CT positive infarct &lt; 28 days</td>
<td>181</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT no relevant lesion &lt; 28 days</td>
<td>226</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No CT, infarct at necropsy</td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>439</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Probable&quot;</td>
<td>GHSDS &lt; 4, CT non-specific</td>
<td>57</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GHSDS &lt; 4, CT wedge shaped lesion</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GHSDS &lt; 4, CT, no necropsy</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>545</td>
<td>(81)</td>
<td>[78-84]</td>
</tr>
<tr>
<td>&quot;Definite&quot;</td>
<td>Primary intracerebral haemorrhage</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT positive</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Necropsy, no CT</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Probable&quot;</td>
<td>GHSDS &gt; 25</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>66</td>
<td>(10)</td>
<td>[8-12]</td>
</tr>
<tr>
<td>&quot;Definite&quot;</td>
<td>Subarachnoid haemorrhage</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT positive</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CT negative, LP positive</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LP positive, no CT</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Necropsy, no CT, no LP</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Probable&quot;</td>
<td></td>
<td>32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>Uncertain</td>
<td>31</td>
<td>(5)</td>
<td>[3-7]</td>
</tr>
</tbody>
</table>

Results

Over the four years, 675 patients with a first-ever stroke were registered with the study. The characteristics of these patients, the study population and the time from onset of the stroke to assessment by the study neurologist, as well as the age and sex specific incidence rates, have been described previously.

CT was performed on 542 (80%) of 675 patients and 467 (69%) were within 28 days of the onset of symptoms. Amongst these 467 the median time from onset of symptoms to CT was seven days with an inter-quartile range of four–12 days. Necropsy examinations were obtained on 77 of the 208 (37%) patients who have died so far, of which 54 were in cases where there had not been a CT scan within 28 days of onset. In seven cases of SAH the diagnosis was made by lumbar puncture (LP) alone though in a further five cases with no abnormality on CT scan an LP was the first diagnostic test. Thus the pathological type of stroke was determined definitely in 528 (78%) of 675 patients (table 2).

Two patients were considered to have had “probable” SAH. One, a 17 year old female, died rapidly with an acute illness with the clinical features of SAH but without confirmatory investigations. The second presented with a definite SAH confirmed by LP but gave a clear history of an event one month earlier which had the clinical features of SAH but was misinterpreted as migraine by the GP. We considered the earlier attack to have been the
"incident" event. The GHDS was calculated for the remaining 145 (22%) patients. In 106 (16%) the score was less than 4, that is, there was a greater than 90% probability of the stroke being due to cerebral infarction, and in eight (1%) it was greater than 25, that is, there was a greater than 90% probability of the stroke being due to intracranial haemorrhage.

In the remaining 31 (5%) the GHDS was either between 4 and 25 or the clinical details were insufficient to calculate it, and these cases were considered to be of uncertain pathological type. Of the patients classified as "probable CI, 70 of 106 (66%) had had CT performed at some time after 28 days from the onset of symptoms and in 13 (19%) there was a wedge shaped low density area extending to the cortex which appeared typical of an arterial occlusion. The other scans either showed no relevant abnormality or low density areas which could equally have been infarcts or the residua of previous haemorrhage.

Table 3 shows the numbers of cases and incidence rates in each pathological group according to age and sex. In view of the small numbers in some groups further analyses for both sexes have been combined. Figure 1 shows the proportion of each stroke type by age. The overall proportions are compared with other community-based studies in fig 2. Figure 3 shows the age specific incidence rates (using the previously published denominator) according to pathological type of stroke (definite and probable cases combined).

The 30 day and one year case fatality rates are shown in table 4. There were significantly fewer deaths among patients with CI than those with intracranial haemorrhage both at 30 days (Odds ratio 0.12, 95% confidence interval 0.08-0.20) and at one year (Odds ratio 0.22, 0.10-0.43).

One year after their stroke 305 of 467 survivors (65%, 95% confidence interval 61-69%) were functionally independent, the number of those with CI being 272 of 420 (65%, 60-70), with PICH 17 of 25 (68%, 50-86) and with SAH 13 of 17 (76%, 56-96). There was no significant difference in functional status between CI and all intracranial haemorrhage (Odds ratio 0.74, 0.37-1.48) or between CI and SAH alone (Odds ratio 0.57, 0.18-1.77).

Discussion

Before the development of computed tomography (CT), epidemiological studies relied on clinical features to distinguish the two main pathological types of stroke, cerebral infarction (CI) and primary intracerebral haemorrhage (PICH). These clinical features had been derived from necropsy studies such as that of Aring and Merritt and therefore were most likely to predict the pathological type accurately for large, fatal strokes. Subsequent CT studies, particularly of non-fatal stroke, showed that the clinical features do not reliably differentiate CI and PICH. There is evidence that both community and hospital-based studies which have not used CT extensively and have underestimated the incidence of small PICH and therefore may have reported an unduly poor prognosis for PICH.

Subarachnoid haemorrhage (SAH) has always been easier to distinguish because of its distinctive clinical features though CT detects any additional intracerebral haematoma. This has blurred the distinction between SAH and PICH somewhat and some studies have reported combined figures for "intracranial haemorrhage". Therefore, it seems reasonable to include SAH in epidemiological studies of stroke.

Even though it is widely available in developed countries, CT remains a hospital-based facility and its use in community-based studies of cerebrovascular disease has been limited. Consequently, concern continues to be expressed about the accuracy of the pathological diagnoses in community studies and hence the interpretation of outcome data based on them. This would be of no consequence if patients admitted to hospital were always similar to those remaining at home but we have
shown that patients with a severe neurological deficit, which is more common in strokes caused by intracranial haemorrhage, are more likely to be admitted to hospital.13,14 Therefore, hospital-based studies are likely to underestimate the number of mild strokes, particularly cases of CI, that have most to gain from proven treatments of secondary stroke prevention. Alternatively, if there is any delay before being admitted to hospital those patients who die very rapidly will not be included. Phillips et al15 reported that 8% of patients suffering a SAH in Rochester died before receiving any medical attention. The factors influencing admission and case mix vary unpredictably between institutions and certainly between different countries making it difficult to compare hospital-based series. The potential magnitude of this case mix variation is shown in the recent report of the Stroke Data Bank16 in which the proportion of patients with PICH in each of the four institutions varied from 7% (95% confidence interval 4–10) to 19% (95% confidence interval 15–23). Until recently our knowledge of the incidence and outcome of the major pathological types of stroke came either from hospital-based series which might have had a biased case mix due to local admission practices, or from community-based series where the pathological diagnosis may have been inaccurate in a significant proportion of cases. Exceptions to this are the two major community-based studies, Rochester21,22 and Hisamatsu,23,24 which have provided vital time-trend data.25 These studies maintained a fairly high necropsy rate which are now complemented by CT data. Large community-based epidemiological studies face logistical problems in obtaining CT and necropsy examinations on all patients but recent reports have shown the proportion of cases with such examinations is increasing.26

We recognise that a few very small haemorrhages may not have been visible on CT scans performed more than two weeks after the onset of stroke.27 However, we considered that the 28 day limit for making a definite diagnosis of pathological type was a reasonable compromise28 and, in fact, 75% of the “diagnostic” scans were performed within 12 days of onset. We cannot be quite as confident about the accuracy of the pathological diagnosis in patients classified using the GHSDS but this has been shown to be more accurate than an unstructured clinical diagnosis29 and should be sufficiently accurate for epidemiological if not clinical decision making purposes. Furthermore, by accepting only cases within the upper and lower 10% of the score it is likely that the predictive value is even greater than that for the overall score. We considered that more bias was likely to be introduced by categorising all such cases as “uncertain pathology” than by using the GHSDS. This view was supported by the finding of areas of low density typical of infarction within a single arterial territory (that is, they were unlikely to be the residua of PICH) on 19% of CT scans performed after 28 days from the onset of symptoms all of which had GHSDS scores less than 4 and had therefore been categorised as “probable in- forks”. There remained a few cases where we were unable to categorise the type of stroke with confidence. They were, for the most part, very elderly (fig 1) and we were reluctant to transport very frail, elderly people to hospital to have a CT scan, particularly if death was imminent and the scan was unlikely to influence management. There was also a reluctance to request necropsies in such patients. Other community-based studies have had similar difficulty with very elderly patients27,30,31 and therefore outcome data for each separate pathological type of stroke in this age group need to be interpreted with caution. The high CFR among patients without CT or necropsy suggests that such strokes were more likely to have been due to intracranial haemor-
rhage than ischaemia and, if so, this might account for the apparent decline in the incidence of haemorrhagic strokes in the most elderly group whilst the incidence of CI continued to rise steeply with age.

We emphasise that to be an incident case in our study a patient had to have had a first-ever in a lifetime stroke. This is particularly important when considering pathological types of stroke since the survival rates and therefore the proportion of patients who remain at risk of a recurrent stroke are so different. Harmsen and Wilhelmsen20 reported a 30% higher CFR for recurrent strokes and Aho et al33 noted a higher CFR among more disabled people which would have included those with residual deficits from previous strokes. Many trials will only include patients having their first clinically apparent stroke and therefore it is important to know the natural history of these patients. Figure 2 shows that the distribution of the pathological types of first stroke has been similar in the North American and European community-based studies.22 23 26–28 34 Although the data are not ideal, it does appear that the proportion of haemorrhagic strokes amongst the Japanese is greater than in Western countries. The interpretation of the figures from Hisayama24 24 where the rate of confirmation of stroke type was high is difficult because of the small number of cases involved. In the Shibata study34 37 the rate of pathological confirmation was not as high (though the authors attempted to assess the likely degree of accuracy) but the case ascertainment was very thorough.

Whilst the proportion of each pathological type of stroke is similar in western community-based studies, there is a wide variation in the reported CFR. If the results from Rochester are compared with the OCSP, the overall 30 day CFR was about 28% compared with 19%. This difference was mirrored among those with CI (19%, and 10%) and with PICH (84%, and 50%), though for those with SAH the CFRs were similar (52%, and 45%). There are a number of possible explanations for these results. Firstly there are potential methodological differences between the two studies. It seems likely that at least some of the lower CFR in the OCSP with PICH reflected the more accurate diagnosis of small haematomas with a good prognosis by CT scan. However, this would not explain the lower overall CFR or that for CI and one would need to infer that there had been a relative failure to detect cases of mild ischaemic stroke in Rochester. Whilst the chances of this occurring are greater because the Rochester studies were based on retrospective casenote reviews and our data were collected prospectively, the Mayo Clinic record system is well established and validated and therefore it seems unlikely that this would account for all of the difference. A second possibility is that there has been a genuine decline in CFR over the last 20 years (since the mid-point of the Rochester study was 1962).

In favour of this explanation would be the observation by Matsumoto et al22 that there was a trend towards increasing survival after CI over their study period. The fact that the overall 30 day CFR in the South Alabama study,28 which was performed at about the same time as the OCSP, was 22% also supports this hypothesis. However, our results do not support the hypothesis of Gross et al26 that the lower CFR in South Alabama compared with European studies (specifically Tilburg, Netherlands27) might be due to “modern aggressive medical and surgical management” since the OCSP patients have a similar CFR to those in South Alabama yet were managed in very conventional ways, over 40% of them entirely at home. A more likely explanation is that the rather high CFRs in Tilburg were for all strokes in the study period rather than just lifetime first-ever strokes. A further explanation might be that as part of the presumed overall declining incidence of stroke,25 26–28 there has been a disproportionately large drop in the incidence of fatal or severely disabling strokes, perhaps of cardio-embolic origin. At present, there is little detailed data concerning the incidence and outcome of subtypes of cerebral infarction though we will be publishing this in the future.39

It is difficult to compare most outcome measures reported in the literature, especially for haemorrhagic stroke when the numbers are usually small. However, the most recent data from Rochester report the outcome according to the original Rankin scale. With this, 48% of survivors at one year were in some way dependent on others compared with only 35% in the OCSP. Again, this suggests that there might have been more complete detection of mild cases in the OCSP or that there has been a decline in the incidence of severe ischaemic strokes. Whatever the reasons, there seem to be significantly more patients who might benefit from secondary preventive measures than might have been predicted from previous studies. Many of these, in the United Kingdom at least, are currently being managed purely by general practitioners. Whilst further epidemiological studies of stroke which are able to obtain a high proportion of definite pathological diagnoses would be of value, particularly if they are in different parts of the world, attention should now be given to delineating the epidemiology of homogeneous subgroups of the major pathological types of stroke.

Appendix

DEFINITIONS OF PATHOLOGICAL TYPES OF STROKE

Definite cerebral infarction

Cases of stroke (defined by clinical criteria described previously—paper 1) with:

(a) CT performed on or before the 28th day from the onset of symptoms which shows an area of low attenuation in a region compatible with the clinical symptoms and signs, or

(b) CT performed on or before the 28th day from the onset of symptoms which shows no abnormality in any region compatible with the clinical symptoms and signs, or
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(c) CT performed on or before the 28th day from the onset of symptoms which shows an area of irregular high attenuation within an area of low attenuation, considered to be due to haemorrhagic infarction by a consultant neuroradiologist, in a region compatible with the clinical symptoms and signs, or
(d) An adequate necropsy examination which shows an area of cerebral infarction, either pale or haemorrhagic, in a region compatible with the clinical symptoms and signs.

Probable cerebral infarction
Cases of stroke who do not have a CT scan on or before the 28th day of the onset of symptoms or an adequate necropsy examination, but in whom sufficient clinical details are available to derive the Guy's Hospital Stroke Diagnostic Score (GHSDS) and the score is less than 4 (that is, there is a greater than 90% chance that the stroke is due to cerebral infarction).

Definite primary intracerebral haemorrhage
Cases of stroke with:
(a) A CT scan which shows an area of uniform high attenuation unrelated to tumour or trauma, in a region compatible with the clinical symptoms and signs, or
(b) An adequate necropsy examination which shows an intracerebral haemorrhage of an age and in a region compatible with the clinical symptoms and signs.

Probable primary intracerebral haemorrhage
Cases of stroke who do not have a CT scan on or before the 28th day from the onset of symptoms or a necropsy examination, but with sufficient clinical details to derive a GHSDS which must be greater than 24, that is, there is a greater than 90% chance that the stroke is due to intracranial haemorrhage.

Definite subarachnoid haemorrhage
Cases with a typical history of acute onset of headache, meningism, photophobia, sometimes with loss of consciousness, not associated with trauma, with:
(a) A CT scan which shows subarachnoid blood, or
(b) An adequate necropsy examination showing a spontaneous subarachnoid haemorrhage, or
(c) An atraumatic lumbar puncture with greater than 2 x 10^6/litre red blood cells and/or a xanthochromic supernatant.

In cases where subarachnoid and intracerebral haemorrhage coexist, the primary site of bleeding must be considered to be subarachnoid by a neuroradiologist or neuropathologist.

Probable subarachnoid haemorrhage
Cases with the clinical features of subarachnoid haemorrhage but without confirmatory investigations.

Uncertain types
Cases of stroke without adequate confirmatory investigations and in whom the GHSDS score is between 4 and 24 or for whom clinical details are insufficient to derive the score.

31. Scmidt EV, Smirnov VE, Ryabova VS. Results of the seven-
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