Ten-Year Risk of First Recurrent Stroke and Disability After First-Ever Stroke in the Perth Community Stroke Study

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Background and Purpose—Limited information exists on the long-term prognosis after first-ever stroke. We aimed to determine the absolute frequency of first recurrent stroke and disability and the relative frequency of recurrent stroke over 10 years after first-ever stroke in Perth, Western Australia.

Methods—For a 12-month period beginning February 1989, all individuals with suspected acute stroke or transient ischemic attack who lived in a geographically defined and representative region of Perth were registered prospectively. Patients with a definite first-ever stroke were followed up 10 years after the index event.

Results—Over 10 years of follow-up, the cumulative risk of a first recurrent stroke was 43% (95% confidence interval [CI], 34 to 51). After the first year after first-ever stroke, the average annual risk of recurrent stroke was ∼4%. Case fatality at 30 days after first recurrent stroke was 41%, which was significantly greater than the case fatality at 30 days after first-ever stroke (22%) (P=0.003). For 30-day survivors of first-ever stroke, the 10-year cumulative risk of death or new institutionalization was 79% (95% CI, 73 to 85) and of death or new disability was 87% (95% CI, 81 to 92).

Conclusions—Over 10 years of follow-up, the risk of first recurrent stroke is 6 times greater than the risk of first-ever stroke in the general population of the same age and sex, almost one half of survivors remain disabled, and one seventh require institutional care. Effective strategies for prevention of stroke need to be implemented early, monitored frequently, and maintained long term after first-ever stroke. (Stroke. 2004;35:731-735.)

Key Words: Australia ■ cerebrovascular accident ■ epidemiology ■ morbidity

Despite improvements in public health, stroke remains a leading cause of death worldwide.1 Given that those most at risk from stroke, the elderly, constitute the fastest-growing segment of many populations,2 the burden of stroke will continue to be an important healthcare problem unless the incidence of first-ever and recurrent strokes and their disabling sequelae are reduced. However, effective planning and monitoring of prevention strategies for stroke requires reliable data on incidence and outcome of stroke.

Although the incidence of stroke has been well documented, albeit predominantly in Western populations, limited information exists on the long-term prognosis after stroke. Moreover, results of the only population-based study to examine the risk of recurrent stroke over 10 years may not be applicable today because it was conducted several decades ago,3 when prevention strategies for stroke were poorly developed.

The present study was undertaken to extend information from earlier follow-up analyses of patients registered in the Perth Community Stroke Study (PCSS) of 1989 to 1990.4,5 We aimed (1) to determine the absolute and relative risks of recurrent stroke in the 10 years after first-ever stroke, (2) to compare the 30-day case fatality of recurrent stroke in the 6-to 10-year period with that during the first 5 years after first-ever stroke, (3) to compare the 30-day case fatality from recurrent stroke with that for first-ever stroke, and (4) to describe the frequency of disability among survivors 10 years after first-ever stroke.

Subjects and Methods

Study Design

The design of the PCSS has been reported in detail previously.4–7 The study registered all episodes of possible acute cerebrovascular disease among residents of a geographically defined segment of Perth, Western Australia, over 18 months in 1989 to 1990. The PCSS was repeated for 13 months in 1995 to 1996 and for 12 months in 2000 to 2001, but those data are not reported here. Because the 10-year outcomes from the 1989 to 1990 cohort were collected with comparison with the 1995 to 1996 cohort in mind, only those patients whose first-ever stroke occurred during the first 12 months of the study, beginning February 1989, are included here.
The study was approved by the Committee for Human Rights at the University of Western Australia and by the Confidentiality of Health Information Committee of the Health Department of Western Australia. Patients or their next of kin gave permission for review of their medical records pertaining to suspected vascular events occurring during follow-up.

Baseline Assessment and Follow-Up

At baseline, all cases underwent standardized interviews and neurological assessment by one of the authors (C.A.). Information obtained included data on associated illnesses, risk factors for vascular disease, and patterns of disability and social activity in the immediate premorbid period, as well as clinical features at the onset of stroke. Premorbid and baseline levels of physical disability were based on self-report or proxy sources (ie, caregiver or medical records for those patients who were deceased or disabled) and categorized according to the modified Rankin Scale (mRS).8,9

Patients were followed up prospectively at 4 months, 12 months, 5 years, and 10 years. At 4 months and 12 months, only vital status was collected. Vital status was ascertained by electronic linkage of PCSS records to mortality data supplied by the Registrar General of Births, Marriages and Deaths for Western Australia. All surviving patients were interviewed in person at the 5-year follow-up. At the 10-year follow-up, all surviving patients were invited to complete a postal questionnaire and participate in a structured telephone interview. The interview sought any new stroke that had occurred during the preceding 5 years, current living arrangements, and level of disability. If a patient was unable to take part in the interview because of disability, the information was obtained from a caregiver or other reliable proxy.

Recurrent stroke events were detected by a number of overlapping methods. Admissions to hospital for possible stroke during the period of follow-up were identified by electronic linkage to the Hospital Morbidity Data System, a computerized, name-identified register of all admissions to hospitals in Western Australia that is maintained by the State Health Department. In addition, we searched by hand the medical records of all PCSS patients at the 2 major hospitals in Perth. All patient-described episodes of possible recurrent stroke were investigated by review of hospital and general practice medical records and the results of neuroimaging when available. Finally, efforts were made to locate all survivors by checking their most recent address available from the Hospital Morbidity Database or the electoral roll.

Definitions

Initial strokes were defined according to the World Health Organization criterion as "rapidly developing symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin."10

As in other studies,11,12 we also used this criterion to define a recurrent stroke as one in which (1) there was clinical evidence of the sudden onset of a new focal neurological deficit with no apparent cause other than that of vascular origin (ie, the deficit could not be ascribed to an intercurrent acute illness, epileptic seizure, or toxic effect) occurring at any time after the index stroke or (2) there was clinical evidence of the sudden onset of an exacerbation of a previous focal neurological deficit with no apparent cause other than that of vascular origin occurring >21 days after the index stroke. Each recurrent stroke was classified as ischemic, hemorrhagic, or of undetermined nature on the basis of a CT or MRI scan performed within 28 days of recurrence or examination at autopsy.

Institutional care was defined as residence in a nursing home or private hospital where full-time care was provided. Disability was defined as a score of at least 3 of 5 on the mRS.8,9

Statistical Analysis

The Kaplan-Meier product limit technique was used to generate survival probabilities and survival curves based on first recurrent strokes within 10 years. The cumulative incidence of recurrent strokes over 10 years (observed) was compared with the incidence of first-ever strokes in the general population (expected), derived from the age- and sex-specific rates of stroke in the PCSS,7 and calculated with the SAS macro Survexp.13 Rate ratios and 95% confidence intervals (CIs) of the observed to expected frequency of recurrent strokes were calculated from the Poisson distribution. Comparisons of proportions were made with the χ² test or Fisher’s exact test as appropriate.

Results

Overall, the PCSS included 328 patients with acute stroke during the 12-month recruitment period in 1989 to 1990, of whom 251 (77%; 95% CI, 72 to 81) had experienced their first-ever stroke. Cerebral infarction accounted for 69% (95% CI, 63 to 75) of first-ever strokes; primary intracerebral hemorrhage, 13% (95% CI, 9 to 17); and subarachnoid hemorrhage, 4% (95% CI, 2 to 6).
These 251 patients (mean±SD age, 72.7±13.9 years; median, 76.0 years) with first-ever stroke served as the denominator for the survival analyses (Figure 1). Although the vital status of 7 of these patients (mean age, 59 years; range, 23 to 80 years at baseline) was unknown at 10 years, they were known to be alive at the 5-year follow-up and contribute to the Kaplan-Meier calculations at time points before loss of contact.

Recurrent Stroke
Ten years after a first-ever stroke, 64 patients had suffered a first recurrent stroke, of whom 41% (95% CI, 29 to 53) had died within 30 days. Four patients suffered a second recurrent stroke, and 1 patient had a third recurrent stroke. There were 142 patients who were censored because of death (ie, death occurred before a recurrent stroke) of a total of 197 deaths.

Table 1 and Figure 2 show that the 10-year cumulative risk of first recurrent stroke was 43% (95% CI, 34 to 51). The risk of recurrent stroke was greatest in the first 6 months after first-ever stroke at 9% (95% CI, 5 to 14), but the average annual risk was ≈4% after 1 year.

Over the 10 years of follow-up, the risk of first recurrent stroke among the PCSS cohort was 6 times greater than the risk of first-ever stroke in the general population, adjusted for age and sex (Table 2). However, in those survivors <45 years of age at baseline, the risk of first recurrent stroke was 38 times greater than the risk of first-ever stroke in a similar group in the general population (Table 3).

The pathological subtype of the first recurrent stroke was determined in 63% of cases; most (56%) were due to cerebral infarction, with 89% of recurrent ischemic strokes (32 of 36) occurring in patients who had suffered an initial ischemic stroke. Among the 4 patients with a recurrent stroke caused by primary intracerebral hemorrhage, 2 had suffered an intracerebral hemorrhage as the index event (Table 4). Overall, 87% of the patients (34 of 39) had the same verified pathological basis for their index and recurrent stroke events.

Case fatality at 30 days after first recurrent stroke was 41% (95% CI, 29 to 53), which was significantly greater than the case fatality at 30 days after first-ever stroke of 22% (P=0.003). However, there was no significant difference (P=0.16) between the case fatality at 30 days after recurrent stroke in the 0-to-5-year (20 of 54, 37%) and 6-to-10-year (6 of 10, 60%) periods after first-ever stroke.

Disability
Of 195 patients who survived to 30 days after stroke, 150 had been free of disability before the onset of their first-ever stroke. Seven patients were lost to follow-up, and 2 patients survived 10 years after stroke but died just before being interviewed. Thus, complete information regarding form of residence was known for the 47 survivors at 10 years, 45 of whom responded to the follow-up inquiry regarding disability.

Of the 47 patients who survived to the 10-year follow-up, 7 were new residents of a nursing home. Thus, the cumulative risk of new institutionalization in 10-year survivors of a first-ever stroke was 15% (7 of 47; 95% CI, 5 to 25). Confining the analysis to those patients who were not living in a nursing home at the time of their first-ever stroke and

### Table 2. Number of First Recurrent Strokes in Each Calendar Year After First-Ever Stroke Compared With the Expected Number of Strokes in the Same Population

<table>
<thead>
<tr>
<th>Year</th>
<th>At Risk, n</th>
<th>Observed, n</th>
<th>Expected, n</th>
<th>Observed/Expected</th>
<th>95% CI of Observed/Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>251</td>
<td>30</td>
<td>1.9</td>
<td>15.5</td>
<td>10.0–21.1</td>
</tr>
<tr>
<td>2</td>
<td>144</td>
<td>4</td>
<td>1.5</td>
<td>2.7</td>
<td>0.1–5.3</td>
</tr>
<tr>
<td>3</td>
<td>131</td>
<td>10</td>
<td>1.5</td>
<td>6.9</td>
<td>2.6–11.2</td>
</tr>
<tr>
<td>4</td>
<td>113</td>
<td>4</td>
<td>1.2</td>
<td>3.3</td>
<td>0.1–6.4</td>
</tr>
<tr>
<td>5</td>
<td>99</td>
<td>6</td>
<td>1.1</td>
<td>5.5</td>
<td>1.1–9.9</td>
</tr>
<tr>
<td>6</td>
<td>81</td>
<td>4</td>
<td>0.9</td>
<td>4.3</td>
<td>0.1–8.5</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>2</td>
<td>0.8</td>
<td>2.6</td>
<td>−1.0–6.1</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>2</td>
<td>0.7</td>
<td>2.9</td>
<td>−1.1–7.0</td>
</tr>
<tr>
<td>9</td>
<td>49</td>
<td>0</td>
<td>0.6</td>
<td>0</td>
<td>0–0</td>
</tr>
<tr>
<td>10</td>
<td>47</td>
<td>2</td>
<td>0.5</td>
<td>3.9</td>
<td>−1.5–9.4</td>
</tr>
<tr>
<td>All years</td>
<td>251</td>
<td>64</td>
<td>10.7</td>
<td>6.0</td>
<td>4.5–7.5</td>
</tr>
<tr>
<td>30-day survivors (all years)</td>
<td>195</td>
<td>63</td>
<td>10.7</td>
<td>5.9</td>
<td>4.5–7.4</td>
</tr>
</tbody>
</table>
TABLE 3. Number of First Recurrent Strokes in Each Calendar Year After First-Ever Stroke Compared With the Expected Number of Strokes in the Same Population by Age

<table>
<thead>
<tr>
<th>Age, y</th>
<th>At Risk, n</th>
<th>Observed, n</th>
<th>Expected, n</th>
<th>Observed/Expected</th>
<th>95% CI of Observed/Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>13</td>
<td>1</td>
<td>0.03</td>
<td>37.5</td>
<td>−36.0 to −110.9</td>
</tr>
<tr>
<td>45–54</td>
<td>12</td>
<td>2</td>
<td>0.1</td>
<td>14.7</td>
<td>−5.7 to −35.1</td>
</tr>
<tr>
<td>55–64</td>
<td>29</td>
<td>6</td>
<td>0.7</td>
<td>9.2</td>
<td>1.8 to −16.5</td>
</tr>
<tr>
<td>65–74</td>
<td>57</td>
<td>15</td>
<td>2.6</td>
<td>5.8</td>
<td>2.9 to −8.7</td>
</tr>
<tr>
<td>75–84</td>
<td>99</td>
<td>33</td>
<td>5.2</td>
<td>6.3</td>
<td>4.2 to −8.5</td>
</tr>
<tr>
<td>&gt;84</td>
<td>41</td>
<td>7</td>
<td>2.0</td>
<td>3.4</td>
<td>0.9 to 6.0</td>
</tr>
<tr>
<td>All ages</td>
<td>251</td>
<td>64</td>
<td>10.7</td>
<td>6.0</td>
<td>4.5 to 7.5</td>
</tr>
</tbody>
</table>

who survived ≥30 days indicates that the cumulative risk at 10 years of death or new institutionalization was 79% [(141+7)/188; 95% CI, 73 to 85].

Among the 47 patients who survived to 10 years after stroke, information on level of disability was available for 45, 2 of whom were disabled before their first-ever stroke, whereas 21 patients were disabled at the end of follow-up. Thus, the cumulative risk of new disability was 44% (19 of 43; 95% CI, 29 to 59).

Among the one hundred fifty 30-day stroke survivors who were not disabled at the time of their stroke, 105 had died, 19 were newly disabled at 10 years, and 7 were lost to follow-up. Thus, the cumulative risk of death or new disability was 87% (124 of 143; 95% CI, 81 to 92) among 30-day survivors of stroke.

### Discussion

The principal findings of this study are that (1) the cumulative 10-year risk of a first recurrent stroke was ≈40%; (2) after the first year after first-ever stroke, the average annual risk of recurrent stroke was ≈4%; (3) ≈40% of recurrent stroke events were fatal within 30 days, which is nearly twice the 30-day case fatality of a first-ever stroke; (4) about one seventh of 10-year survivors of first-ever stroke require institutional care; and (5) almost one half of 10-year survivors of stroke are disabled.

The strengths of this study lie in its careful design that conforms to the “ideal” criteria outlined by Sackett et al for prognostic studies. The PCSS had a large, well-defined, population-based inception cohort identified prospectively and assessed early with standardized diagnostic criteria. Outcome events were carefully defined and assessed with well-validated, reliable instruments, and only 3% of patients were lost to follow-up over 10 years.

There are several limitations of the study. The first is that objective verification of the pathological basis of the recurrent strokes was possible in only two thirds of cases. Although this proportion exceeds that in previous long-term follow-up studies, it is less than in our own and other studies of first-ever stroke. The reason is that a greater proportion of patients with recurrent stroke die at home because of the higher early case fatality, and a greater proportion of patients, particularly those who live in institutional care as a result of their first-ever stroke, are not referred to hospital for further investigation. A second limitation of our study was that recurrent stroke events were not ascertained prospectively at frequent intervals (eg, 6 months) during the 10 years of follow-up. Recurrent strokes self-reported by survivors accounted for 14% of all recurrent strokes; 45% were first identified by electronic linkage, 23% by hand-searching hospital records, and 18% by other means such as notifications from general practitioners. It is therefore possible that nondisabling, nonfatal strokes, which did not result in admission to hospital, may have been forgotten by patients and not ascertained at subsequent interview or by the hospital-based surveillance mechanisms. Hence, we may have underestimated the overall risk of recurrent stroke and overestimated the proportion of recurrent strokes that were fatal. The third limitation is that we did not have the resources to assess the impact of medical management on modifying vascular risk and outcomes during the 10 years of follow-up. This task would have been particularly complex and resource intense, complicated further by the structure of the Australian

TABLE 4. Pathological Subtype of First Recurrent Stroke According to Pathological Subtype of Initial Stroke

<table>
<thead>
<tr>
<th>Initial Stroke</th>
<th>Cerebral Infarction</th>
<th>Primary Intracerebral Hemorrhage</th>
<th>Undetermined</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral infarction (n=168)</td>
<td>32</td>
<td>2</td>
<td>13</td>
<td>47</td>
</tr>
<tr>
<td>Large-artery occlusion (n=116)</td>
<td>23</td>
<td>1</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td>Lacunar (n=15)</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Cardioembolic (n=28)</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Boundary Zone (n=9)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Primary intracerebral hemorrhage (n=30)</td>
<td>3</td>
<td>2</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage (n=10)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Undetermined (n=36)</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total (n=244)</td>
<td>36</td>
<td>4</td>
<td>24</td>
<td>64</td>
</tr>
</tbody>
</table>
healthcare system, which makes discontinuity of primary care common.

The key finding of an average annual risk of recurrent stroke of $\approx 4\%$ beyond the first year after a first-ever stroke is similar to other studies conducted over 7 years of follow-up in Moscow \cite{11} and over 5 years in the Oxfordshire Community Stroke Project (OCSP) \cite{12} but exceeds that reported from Rochester (Minn) in which there was a 29\% cumulative risk of recurrent stroke over 10 years. \cite{3} Possible explanations for these differences may relate to an indistinct definition of recurrent stroke in the last study or true differences in the natural history of stroke and background risk of vascular disease in these populations.

Conversely, our finding of a 2-fold excess 30-day case fatality after first recurrent stroke compared with first-ever stroke is higher than that seen in other population-based studies. The Moscow study \cite{11} found a 21-day risk of death after recurrent stroke over 7 years of 56\%, which was 1.5 times greater than for the initial stroke, whereas in Oxford, \cite{12} the 30-day risk of death after first recurrent stroke within 5 years of 17\% was not significantly different from the 19\% 30-day case fatality for first-ever stroke.

Although new, more sensitive instruments for assessing disability have been developed over the last 15 years, we continued to assess disability by means of the mRS because it is valid, simple, reliable, and consistent and facilitates longitudinal comparison with the original baseline disability data collected in 1989. The pattern of disability in our patients at 5 years \cite{16} was in keeping with findings from other population-based studies, \cite{17,18,19} namely that about one third of survivors of stroke were disabled. At 10 years, however, almost half of the survivors of the PCSS 1989 to 1990 cohort were disabled, and one seventh required institutional care. There are no published studies with 10-year follow-up with which to compare these results.

The major implication of this study is that recurrent strokes are an ongoing health concern among survivors of stroke, with risks continuing to accumulate in the long term at almost the same rate as that in the first few years after first-ever stroke. Although this partly reflects the natural history of the chronic process that is cerebrovascular disease, it presumably also indicates incomplete efficacy of preventive interventions. In a previous report from our group, \cite{16} we indicated that the most important predictors of poor outcome (death, institutionalization, or disability) at 5 years after stroke were increasing age, prestroke disability, severe stroke-related deficits at onset (severe hemiparesis, urinary incontinence), presence of risk factors for recurrent stroke (current smoking and intermittent claudication), and occurrence of recurrent stroke. Thus, once a stroke has occurred, the only modifiable factors for functional outcome are continued smoking and recurrent stroke. Unfortunately, the present study did not provide us with enough power to repeat the earlier multiple regression analysis for predictors of outcome.

However, our data do show that patients who survive an acute stroke have a continuing high risk of recurrent stroke, which itself carries twice the case fatality as the index stroke and is a predictor of poor functional outcome. Further studies are required to identify strategies to maximize lifelong use of medical therapies aimed at preventing recurrent strokes and subsequent disability.

Acknowledgments

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References

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