Ten-Year Survival After First-Ever Stroke in the Perth Community Stroke Study

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Background and Purpose—Very few studies have provided information regarding long-term prognosis after stroke. We aimed to determine the absolute and relative survival over 10 years among patients with first-ever stroke from a population-based study in Perth, Western Australia.

Methods—For a 12-month period beginning February 1989, all individuals with a suspected acute stroke or transient ischemic attack who were resident in a geographically defined and representative region of Perth, Western Australia, were registered prospectively and assessed according to standardized diagnostic criteria. Patients with a definite first-ever stroke were followed up prospectively at 4 months, 12 months, 5 years, and 10 years after the index event.

Results—A total of 251 patients with first-ever stroke were registered, and 244 (97%) were followed up at 10 years, by which time 197 (79%; 95% confidence interval [CI], 74 to 84) had died. The major causes of death were the direct effects of the initial stroke (27%; 95% CI, 21 to 33) and cardiovascular disease (26%; 95% CI, 20 to 32). Among 1-year survivors of stroke, the average annual case fatality was 4.8%, which was 2.3 (95% CI, 1.9 to 2.7) times greater than for the general population of the same age and sex.

Conclusions—One in 5 patients with first-ever stroke survived to 10 years. The average annual case fatality was 4.8% between years 1 and 10 after stroke, which was twice that expected for the general population. Vascular disease is the major cause of death among long-term survivors of stroke. (Stroke. 2003;34:1842-1846.)

Key Words: Australia ■ stroke ■ survival

Stroke, with its attendant high morbidity and mortality, is a major global healthcare problem. According to the World Health Organization (WHO) Global Burden of Disease Study,1 stroke was the second-leading cause of death worldwide in 1990 (4.4 million, or 8.7% of deaths) and is expected to increase further in absolute terms, particularly in developing countries, as a result of rapid population restructuring and altered lifestyles. Although much has been published regarding the immediate and short-term prognoses for stroke, few population-based studies provide information regarding long-term survival of stroke. This is not too surprising, given the particular challenges in studying the incidence and outcome of stroke in a well-defined population and ensuring reliable and complete information on the vital status of a large number of patients many years after registration in a study. However, such information is important for healthcare planning and for estimating the opportunities for reducing the burden of stroke.

The Perth Community Stroke Study (PCSS) in Western Australia has reported case fatality figures for 28 days2,3 and 1 year,2,3 as well as a 5-year follow-up of patients registered in 1989 to 1990.4

The aims of the present study were (1) to describe 10-year survival after first-ever stroke in Perth, Australia; (2) to compare the observed survival with the expected 10-year survival of the age- and sex-adjusted general population; and (3) to determine the major causes of death during different time periods of follow-up.

Subjects and Methods

Study Design

The design of the PCSS has been reported in detail previously.2–6 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. Based on the Australian Bureau of Statistics 1986 Census, the estimated population of the study area (on June 30, 1989) was 138 708 persons (69 008 men, 69 700 women). Comparison with census figures for the remainder of Perth showed that the population of the study area contained proportions of elderly persons and those born overseas (particularly from southern European countries) that were slightly
Baseline Assessment and Follow-Up

All patients underwent a standardized neurological assessment by an author (C.A.). Information obtained at baseline included data on associated illnesses, risk factors for cardiovascular disease, and patterns of disability and social activity in the immediate premorbid period, as well as clinical features and physical signs at the onset of stroke.

All patients were followed up prospectively at 4 months, 12 months, 5 years, and 10 years. Vital status was initially ascertained by electronic linkage of PCSS records to mortality data supplied by the Registrar General of Births, Marriages and Deaths for Western Australia. The records of patients who did not respond to a postal survey, as part of another arm of the study, were electronically linked 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, and to the electoral roll in an attempt to detect any other deaths.

For patients who had died, we independently reviewed all the available clinical information and results of investigations obtained from records held by hospitals and doctors in private practice, as well as the findings at necropsy (if performed). We classified the causes of death into the 5 groups that were used as the findings at necropsy (if performed). We classified the causes of death using standardized diagnostic criteria for stroke, recurrent stroke, myocardial infarction, other vascular death, and nonvascular death as outlined below.

Definitions

Initial strokes were defined according to the WHO criteria 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.” As outlined elsewhere, 80% of patients registered in the PCSS 1989 to 1990 study had objective evidence for the pathological basis of their stroke from neuroimaging or necropsy.

Like others,9,10 we defined a recurrent stroke using the above definition2 in which (1) there was clinical evidence of the sudden onset of a new focal neurological deficit without an apparent cause other than that of vascular origin (ie, the deficit could not be ascribed to an intercurrent acute illness, seizure, or toxic effect) occurring at any time after the index stroke or (2) there was clinical evidence of 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 neuroimaging performed within 28 days of the ictus or necropsy. Hemorrhagic stroke includes both primary intracerebral hemorrhage and subarachnoid hemorrhage.

We classified the causes of death into the 5 groups that were used in the Oxfordshire Community Stroke Project:10 (1) deaths resulting from first-ever stroke were due to the direct effects of the brain lesion or complications of resulting immobility, including deaths from bronchopneumonia even if they occurred several years after the stroke if stroke-related disability was thought to be contributory; (2) deaths resulting from recurrent stroke were due directly to the brain lesion or complications of immobility;8,10 (3) deaths caused by cardiovascular events were those definitely or probably from myocardial infarction, ruptured aortic aneurysms, peripheral arterial disease, or sudden death when there was no alternative explanation; (4) deaths from nonvascular events were those not due to any stroke-related disability and included such illnesses as cancer, injuries, or suicide; and (5) deaths of undetermined cause were those in which there was insufficient information to establish a cause.

Statistical Analysis

The Kaplan-Meier product-limit technique was used to generate survival probabilities and survival curves based on the 197 deaths within 10 years. In addition, we compared the cumulative incidence of deaths over 10 years of follow-up (observed deaths) with the expected incidence of deaths in the general population (expected deaths) derived from the age- and sex-specific rates of death from the official mortality statistics for Western Australia11 and calculated with the SAS macro Survexp.12 The ratio of observed to expected frequency of deaths was calculated from the Poisson distribution and reported with 95% confidence intervals (CIs). Outcomes of patients with hemorrhagic and ischemic stroke subtypes were compared as odds ratios (ORs), and the 95% CIs were calculated using the probability distribution of the natural logarithm.

Results

Overall, the PCSS included 328 patients with acute stroke during the 12-month recruitment period in 1989 to 1990, among whom 251 (77%; 95% CI, 72 to 81) had had a first-ever stroke. Cerebral infarction accounted for 69% (95% CI, 63 to 75) of all strokes; primary intracerebral hemorrhage, 13% (95% CI, 9 to 17); and subarachnoid hemorrhage, 4% (95% CI, 2 to 6).

There were 251 patients (mean ± SD age, 72.7 ± 13.9 years; median, 76.0 years) with first-ever stroke who served as the denominator for the survival analyses. The vital status of only 7 of these patients was not known after 10 years of follow-up; all were male and relatively young (mean age, 59 years; range, 23 to 80 years at time of first-ever stroke). However, these patients were known to be alive at the 5-year follow-up point and contribute to the Kaplan-Meier calculations at time points before loss of contact.

Survival at 10 Years

Of the 251 patients with first-ever stroke, 197 were known to have died within 10 years: 56 within the first 30 days and 141 subsequently.

Table 1 shows that the 10-year cumulative risk of death was 79% (95% CI, 74 to 84). Case fatality was greatest in the first year after stroke (36%; 95% CI, 30 to 41) and particularly in the first 30 days after stroke (22%; 95% CI, 17 to 28). Among 1-year survivors of stroke, the average annual case fatality over the next 9 years was 4.8%, 6% between years 1 and 5 and 4% between years 6 and 10.

Figure 1 shows survival curves for the stroke subtypes. Patients with hemorrhagic forms of stroke had higher case fatality at 30 days than patients with ischemic stroke (38% [95% CI, 23 to 53] versus 9% [95% CI, 5 to 13]; OR, 6.0; 95% CI, 2.7 to 13.5) but over 10 years had a better chance of survival (31% [95% CI, 17 to 45] versus 23% [95% CI, 17 to 29]; OR, 1.5; 95% CI, 0.7 to 3.1).

For the 10 years of follow-up, all patients with a first-ever stroke had an ~3-times-greater risk of dying compared with individuals of the same age and sex in the general population of Western Australia (Table 2). Patients had a 9-fold (95% CI,
7.1 to 10.8) greater risk of death in the first year after stroke and then a 2-fold increase in risk in each of the subsequent years. Closer examination showed that the 2-fold (95% CI, 1.9 to 2.7) excess risk of death over 10 years was apparent as soon as 30 days after the index stroke, the overall figure for the first year reflecting the high case fatality in the first month.

Table 3 shows that the risk of dying over the next 10 years relative to individuals of the same age and sex in the general population was far greater in younger patients.

Causes of Death
Patients with hemorrhagic strokes were much more likely to die as a direct result of the stroke than those with ischemic strokes. Those patients dying of a recurrent stroke were more likely to have had a primary intracerebral hemorrhage as their first-ever stroke (Figure 2).

Figure 3 shows the causes of death during different time intervals from the onset of first-ever stroke. During the first 30 days, ~80% of deaths were due to the direct neurological effects of the first-ever stroke. Among 30-day survivors, the average proportion of patients dying of recurrent stroke in each time interval was 22% (range, 9% to 38%). Over 10 years, as many patients died from other cardiovascular causes (26%; 95% CI, 20 to 32) as died from their initial stroke (27%; 95% CI, 21 to 33). Between 5 and 10 years, nonvascular deaths were most common (44%; 95% CI, 30 to 58), but cardiovascular events and recurrent stroke still accounted for 33% (95% CI, 20 to 46) and 23% (95% CI, 11 to 35) of deaths, respectively.

Discussion
In this population-based study, we have shown that the cumulative risk of death at 10 years after first-ever stroke was 79%, which represents an ~2-fold overall excess risk of death in these patients compared with that of the general population of the same age and sex. Death is most commonly due to direct cerebral damage in the first month after the onset of stroke. However, having survived 30 days, ~1 in 4 patients will die of a recurrent stroke event, and 1 in 3 will die of a cardiovascular event.

The strengths of this study include its large sample size, the uniform and strict diagnostic criteria, and its population-based design. Stroke events were diagnosed prospectively with standardized criteria, and only 3% of patients were lost to follow-up over 10 years. Among those lost to follow-up at 10 years, the likelihood that they died from a cardiovascular event is low. Given their age, on average 13 years younger than the total study population, and other data from our group showing that few deaths from vascular disease among residents of Western Australia occur outside of the state,14 it is


<table>
<thead>
<tr>
<th>Time Interval</th>
<th>At risk, n</th>
<th>Deaths, n</th>
<th>Cumulative deaths, n</th>
<th>Risk, %</th>
<th>95% CI</th>
<th>Cumulative risk, %</th>
<th>95% CI</th>
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<tr>
<td>&lt;30 d</td>
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<td>56</td>
<td>56</td>
<td>22</td>
<td>17–28</td>
<td>22</td>
<td>17–28</td>
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<tr>
<td>1 to 6 mo</td>
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<td>23</td>
<td>79</td>
<td>12</td>
<td>7–16</td>
<td>32</td>
<td>26–37</td>
</tr>
<tr>
<td>6 to 12 mo</td>
<td>172</td>
<td>10</td>
<td>89</td>
<td>11</td>
<td>6–16</td>
<td>36</td>
<td>30–41</td>
</tr>
<tr>
<td>1 to 2 y</td>
<td>162</td>
<td>18</td>
<td>107</td>
<td>11</td>
<td>9–17</td>
<td>43</td>
<td>37–49</td>
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<tr>
<td>2 to 3 y</td>
<td>144</td>
<td>16</td>
<td>107</td>
<td>11</td>
<td>9–17</td>
<td>49</td>
<td>43–55</td>
</tr>
<tr>
<td>3 to 4 y</td>
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<td>15</td>
<td>107</td>
<td>13</td>
<td>10–18</td>
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<tr>
<td>4 to 5 y</td>
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<td>16</td>
<td>113</td>
<td>13</td>
<td>12–20</td>
<td>80</td>
<td>74–88</td>
</tr>
<tr>
<td>5 to 6 y</td>
<td>100</td>
<td>16</td>
<td>116</td>
<td>16</td>
<td>13–22</td>
<td>97</td>
<td>90–100</td>
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<tr>
<td>6 to 7 y</td>
<td>84</td>
<td>11</td>
<td>116</td>
<td>15</td>
<td>12–22</td>
<td>99</td>
<td>92–102</td>
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<td>7 to 8 y</td>
<td>71</td>
<td>9</td>
<td>115</td>
<td>12</td>
<td>11–20</td>
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<td>92–102</td>
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<tr>
<td>8 to 9 y</td>
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<td>5</td>
<td>110</td>
<td>10</td>
<td>11–20</td>
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<td>92–102</td>
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<tr>
<td>9 to 10 y</td>
<td>59</td>
<td>4</td>
<td>106</td>
<td>8</td>
<td>8–19</td>
<td>99</td>
<td>92–102</td>
</tr>
<tr>
<td>All</td>
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<td>195</td>
<td>79</td>
<td>74–84</td>
<td>79</td>
<td>74–84</td>
</tr>
</tbody>
</table>

Table 2. Number of Deaths in Each Calendar Year After the First-Ever Stroke versus Expected Number of Deaths 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>
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<tr>
<td>1</td>
<td>251</td>
<td>89</td>
<td>9.9</td>
<td>9.0</td>
<td>7.1–10.8</td>
</tr>
<tr>
<td>2</td>
<td>162</td>
<td>18</td>
<td>8.2</td>
<td>2.2</td>
<td>1.2–3.2</td>
</tr>
<tr>
<td>3</td>
<td>144</td>
<td>16</td>
<td>7.8</td>
<td>2.1</td>
<td>1.1–3.1</td>
</tr>
<tr>
<td>4</td>
<td>128</td>
<td>11</td>
<td>7.1</td>
<td>1.5</td>
<td>0.6–2.5</td>
</tr>
<tr>
<td>5</td>
<td>117</td>
<td>15</td>
<td>6.6</td>
<td>2.3</td>
<td>1.1–3.4</td>
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<tr>
<td>6</td>
<td>100</td>
<td>16</td>
<td>5.9</td>
<td>2.7</td>
<td>1.4–4.1</td>
</tr>
<tr>
<td>7</td>
<td>84</td>
<td>11</td>
<td>4.9</td>
<td>2.3</td>
<td>0.9–3.6</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>8</td>
<td>4.1</td>
<td>2.0</td>
<td>0.6–3.3</td>
</tr>
<tr>
<td>9</td>
<td>63</td>
<td>4</td>
<td>3.4</td>
<td>1.2</td>
<td>0.6–2.3</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
<td>9</td>
<td>3.1</td>
<td>2.9</td>
<td>1.0–4.8</td>
</tr>
<tr>
<td>All</td>
<td>251</td>
<td>197</td>
<td>61.0</td>
<td>3.2</td>
<td>2.8–3.7</td>
</tr>
</tbody>
</table>

(30-d survivors)
likely that the few patients who were unable to be contacted from the PCSS cohort at 10 years were a healthier and more mobile subgroup.

Our findings compare favorably with the few other well-designed studies conducted over the last few decades. These show that the risk of dying over 10 years after a first-ever stroke ranges from 65% (95% CI, 60 to 70) in the Framingham study14 (up to 93% at 20-year follow-up)15 to 76% (95% CI, 75 to 77) in the Danish Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) study.16 It should be noted, however, that these studies were conducted during different time periods and are prone to some selection bias, the Framingham cohort involved volunteers and excluded those with pre-existing coronary artery disease, whereas the MONICA Project excluded very old patients. Two other community-based studies provide outcome data over shorter periods of follow-up: a study in Moscow8 found a 77% frequency of death over 7 years, and the Oxfordshire Community Stroke Project 10 showed a 51% risk of dying over 6 years after a first-ever stroke. Among hospital-based studies with long-term follow-up, Eriksson and Olsson17 reported a 65% 10-year mortality in Sweden, but this study included only patients admitted to a stroke unit, which represented about two thirds of all those admitted to hospital with stroke and excluded subarachnoid hemorrhage.

Our findings regarding the ongoing excess mortality from vascular disease after the first 12 months after stroke are in keeping with data from the Oxfordshire study, which was conducted in the mid-1980s.10 However, both studies suffer from imprecision of the estimates in the younger age groups because of small numbers of events, as is reflected in the wide CIs.

A previous report from the PCSS18 indicated that the most important predictors of poor outcome at 5 years after stroke (death, institutionalization, or disability) were increasing age, prestroke disability, severe stroke-related deficits at onset (severe hemiparesis, urinary incontinence), the presence of risk factors for recurrent stroke (current smoking, intermittent claudication), and the occurrence of recurrent stroke. Thus, the only modifiable factors for long-term outcome were prestroke levels of activity, smoking, and recurrent stroke. Unfortunately, the present study did not provide enough outcome events to refine these estimates with repeat analyses for a longer period of follow-up.

For 1-year survivors of stroke, the most common cause of death during the first 5 years was a cardiovascular event, but beyond this point, nonvascular deaths were more common.
Even so, taken together, recurrent stroke and other cardiovascular events still accounted for more than half of all deaths between 5 and 10 years after stroke.

The ongoing burden of fatal vascular disease in long-term survivors of stroke emphasizes the likely importance of vigilant long-term control of atherogenesis and atherothrombosis. Randomized controlled trials with long-term follow-up may help to establish the cumulative benefits, hazards, adverse effects, and costs of these interventions, as well as the subgroups of patients most and least likely to benefit.

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References

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