Trends in Stroke Incidence and Mortality in Hawaiian Japanese Men

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Background and Purpose Vital statistics show a sharp decline in stroke incidence since the mid-1960s. It is not clear whether this has been associated with a decline in stroke mortality.

Methods Since 1966 the Honolulu Heart Program has monitored the incidence and mortality of coronary heart disease and stroke in a target population of 11,136 men of Japanese ancestry living on Oahu. Trends were analyzed from January 1, 1969, through December 31, 1988.

Results Of 7,893 men aged 45 to 68 years and free of stroke at entry examination, 530 developed first episodes of stroke in the period 1969 to 1988 (389 cases of thromboembolic stroke, 124 cases of hemorrhagic stroke, and 17 cases of stroke of unknown type). Age-adjusted annual stroke incidence declined from 5.1 per 1,000 person-years in 1969 to 1972 to 2.4 in 1985 to 1988. The incidences of thromboembolic stroke, hemorrhagic stroke, and total stroke decreased 3.5%, 4.2%, and 4.4% per year, respectively. The 1-month case-fatality rates for thromboembolic stroke decreased moderately; those for hemorrhagic stroke fell dramatically.

Conclusions These findings suggest that the decline in stroke mortality in the past two or three decades results from a decline in both incidence rates and early case-fatality rates in thromboembolic and hemorrhagic stroke and stroke of unknown type. The decreases may be related to changes in risk factors, such as the decline in blood pressure and the decrease in cigarette smoking, as well as improvements in diagnosis and treatment. (Stroke. 1994;25:1170-1175.)

Key Words: incidence • mortality • subarachnoid hemorrhage
for review. Computed tomography (CT) scans became available in 1976 and have been widely used since 1978. Attending physicians were contacted regarding their outpatient records when testing was done outside of a hospital or when patients were not hospitalized for their strokes.

The diagnosis of hemorrhagic stroke required the finding of blood in the cerebrospinal fluid or on CT scan. Subarachnoid hemorrhage was differentiated from cerebral hemorrhage by clinical findings as well as the results of either nuclear or CT scans or angiography. Thromboembolic strokes were diagnosed by intra-axial lesions in the absence of blood in the cerebrospinal fluid or on CT scan. CT diagnosis of infarction was limited to lesions that were clearly new and/or caused a clinical shift or mass effect. CT readings were compared with readings from prior hospitalizations and/or prior stroke. Periventricular white matter lesions, old lacunar white matter lesions, and leukoaraiosis were not considered new infarctions. Lacunes developing in the correct location for symptoms and signs during the hospitalization and clearly not present on admission CTs were considered infarcts. We could not consistently distinguish embolic from thrombotic strokes. Nuclear brain scan or flow studies performed late enough in the patient’s course to allow blood-brain barrier breakdowns were major diagnostic criteria for hemorrhagic and ischemic infarctions until the advent of CT scanning. Findings on all tests were combined when no single test was definitive. A single neurologist (J.F.) characterized and classified all the material to achieve optimal consistency.

Some associated conditions led to the exclusion of a stroke as a study stroke. These included the following: (1) precipitating conditions (eg, uremia); (2) mimics (eg, migraine, Todd’s paralysis, hypoglycemia); (3) bleeding (eg, blood dyscrasias, anticoagulant therapy); (4) trauma (especially cranial); (5) malignancies (eg, metastases, nonbacterial endocarditis, brain tumor); and (6) surgical strokes (eg, endarterectomy, coronary artery bypass graft, aortic aneurysm surgery, intracranial surgery, angiography). Strokes due to arteriovenous malformations, aneurysms, and other congenital abnormalities of the vascular apparatus were considered study strokes; subdural hematomas were not.

Men who had existing stroke at the time of the initial examination were included in the calculation of mortality rates but not in the calculation of incidence rates or case-fatality rates. For the calculation of case-fatality rates, the denominator consisted of all first-event strokes occurring within a given 4-year period. The numerator consisted of all deaths occurring within 30 days, 1 year, and 5 years after the date of stroke onset.

The nonexamined men had a higher stroke mortality than the examined men in the period from 1965 to 1968.6 The examined men in the population at risk for stroke incidence thus represented a relatively low-risk group for stroke incidence and mortality. This was caused by the disease- and self-selective elimination from the population at risk of those men who developed a stroke after the mailing of the questionnaire but before the end of the first examination in November 1968 and who did not come in for an examination, or of those men who developed a stroke between January 1965 (the time of the mailing of the questionnaire) and November 1968 and who came in for examination but had had the stroke before the examination. They thus fell into the category of stroke prevalence and were no longer eligible for the category of incidence of first episode of stroke. The healthy participant effect operating at a maximum through the first examination period makes it problematic to use the stroke data during that early period for analysis of trend. We have elected, therefore, to begin our trend analysis starting January 1, 1969.

We have used two statistical methods to calculate trends. The study subjects were classified into age-date categories of 1 year each, with each subject’s contribution to a given year based on his birthdate, and person-years at risk were calculated. Incident cases were tabulated by age and date of onset of the first event; fatal cases were tabulated by age and date of death. Age-adjusted rates for each year were calculated by an iterated proportional fitting process.7 Incidence rates were expressed as rates per 1000 person-years at risk. Estimation of the change in incidence over time was by standard yearwise logistic regression analysis of the probability of having a stroke during a calendar year among subjects at risk at the start of the year.8 Each subject contributed one record per year of observation until death, stroke, or the end of the follow-up, with the variable “age” for each record being the subject’s age at the start of that year. Presence or absence of an incident stroke was registered on calendar year and subject’s age that year, using a logistic regression model.

### Results

During the follow-up period there were 530 episodes of stroke among the 7893 men who were free of stroke at the initial examination (389 cases of thromboembolic stroke, 124 cases of hemorrhagic stroke, and 17 cases of stroke of unknown type).

Age-adjusted incidence rates for total stroke declined during the period of follow-up, from 5.1/1000 person-years in 1969 to 1972 to 2.4/1000 person-years in 1985 to 1988 (Fig 1). The trends for age-specific rates varied. The decline in rates was steeper for men younger than 70 years at the time of onset (Table 1). Rates increased at ages older than 80 years.

In the categories of type-specific stroke, incidence rates for thromboembolic stroke paralleled those for total stroke. Age-adjusted rates fell from 3.5/1000 person-years in the first 4-year period to 1.9/1000 person-years in the fifth period (Fig 1). As was true in the case of total stroke, the declining incidence trend for thromboembolic stroke was steeper for men younger than 70 years, and rates increased at ages 80 to 88 (Table 1).

Age-adjusted incidence rates for hemorrhagic stroke fell from the first follow-up period to the fifth period. The rates for the first and fifth periods were 1.1/1000 person-years and 0.6/1000 person-years, respectively (Fig 1). Age-specific rates did not show consistent trends (Table 1).
The distribution of stroke by subtype varied during the period of observation (Table 2). There was no change in the proportion of strokes due to intracerebral hemorrhage. There was a fall in the proportion of cases of subarachnoid hemorrhage from a high of 13% in 1973 to 1976 to a low of 0.8% in 1985 to 1988. Thromboembolic stroke increased from 69% in 1969 to 1972 to 80% in 1985 to 1988. The changes in the proportions of thromboembolic stroke and subarachnoid hemorrhage may reflect the changes in incidence associated with an aging cohort. It is well recognized that there is an increase in the proportion of thromboembolic stroke with increasing age, and the peak occurrence of rupture of berry aneurysms is among persons in their 50s. By 1980 none of our cohort was aged younger than 60 years.

Case-fatality rates also changed during the period of observation (Table 3). Death rates during the first 30 days after stroke occurrence fell from 29.9% in the first period to 16.4% in the fifth period. For thromboembolic stroke the corresponding figures were 12.9% (1969 to 1972) and 10.4% (1985 to 1988). For hemorrhagic stroke death rates were 74.8% in the first follow-up period and 28.7% in the fifth period (Fig 2).

Cumulative 1-year fatality rates for stroke consistently fell from 39.2% in 1969 to 1972 to 25.3% in 1985 to 1988. The corresponding rates for thromboembolic stroke were 23.7% and 19.6% for thromboembolic stroke and 76.5% and 34.8% for hemorrhagic stroke.

Cumulative 5-year mortality rates for total stroke were 61.1% for strokes occurring in 1969 to 1972 and 40.8% for strokes occurring in 1985 to 1988. Corresponding rates for thromboembolic stroke were 55.2% and 36.8%; the rates for hemorrhagic stroke were 79.2% and 54.2%. In long-term follow-up, there was a shift in causes of death from stroke to CHD and other causes.

The major improvement in survival after hemorrhagic stroke occurred within the first month after onset (Fig 2). For hemorrhagic stroke, improvement was greatest in the final 4-year follow-up period. For thromboembolic and total stroke the greatest improvement in 1-year survival occurred in the fourth follow-up period.

Stroke mortality rates were higher for nonexamined than for examined men in the period from 1965 to 1968; and this pattern persisted during the periods 1969 to 1972 and 1973 to 1976 (Fig 3), although this difference was not statistically significant. The rates were equivalent by 1977, and surveillance of nonexamined men was discontinued after 1982.

The trend in stroke mortality for Hawaiian Japanese men in our target population, combining examined and nonexamined men, paralleled the decline among US white men aged 60 to 69 years during the same follow-up period (Fig 4).

Logistic regression analysis revealed an age-adjusted mean annual decrease of 4.4%/y ($P<.0001$) for total stroke incidence, 3.5%/y ($P<.005$) for thromboembolic stroke incidence, and 4.2%/y ($P<.05$) for hemorrhagic stroke incidence.

Similarly, 30-day case-fatality rates decreased at an average annual rate of 7.3% for total stroke ($P<.001$), 3.6% for thromboembolic stroke ($P$=NS), and 8.7% for hemorrhagic stroke ($P<.005$).

The 1-year case-fatality rates fell at an annual rate of 7.3% for total stroke ($P<.0002$), 5.7% for thromboembolic stroke ($P<.05$), and 7.4% for hemorrhagic stroke ($P<.02$).
TABLE 2. Distribution of Strokes by Subtype

<table>
<thead>
<tr>
<th>Years of Follow-up</th>
<th>Total</th>
<th>Thromboembolic</th>
<th>Intracerebral Hemorrhage</th>
<th>Subarachnoid Hemorrhage</th>
<th>Unknown Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1969-1972</td>
<td>96</td>
<td>66 (69)</td>
<td>16 (17)</td>
<td>8 (8)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>1973-1976</td>
<td>100</td>
<td>65 (65)</td>
<td>17 (17)</td>
<td>13 (13)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>1977-1980</td>
<td>98</td>
<td>71 (72)</td>
<td>18 (18)</td>
<td>7 (7)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>1981-1984</td>
<td>112</td>
<td>88 (79)</td>
<td>18 (16)</td>
<td>4 (4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>1985-1988</td>
<td>124</td>
<td>99 (80)</td>
<td>22 (18)</td>
<td>1 (0.8)</td>
<td>2 (2)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>530</strong></td>
<td><strong>389 (73)</strong></td>
<td><strong>91 (17)</strong></td>
<td><strong>33 (6)</strong></td>
<td><strong>17 (3)</strong></td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.
TABLE 3. Stroke Case-Fatality Age-Adjusted Rates in the Honolulu Heart Program Examined Cohort

<table>
<thead>
<tr>
<th>Years</th>
<th>No. of Cases</th>
<th>Cumulative Fatality</th>
<th>No. of Cases</th>
<th>Cumulative Fatality</th>
<th>No. of Cases</th>
<th>Cumulative Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 d</td>
<td>1 y</td>
<td>5 y</td>
<td>30 d</td>
<td>1 y</td>
<td>5 y</td>
</tr>
<tr>
<td>1969-1972</td>
<td>66</td>
<td>12.9</td>
<td>23.7</td>
<td>55.2</td>
<td>24</td>
<td>74.8</td>
</tr>
<tr>
<td>1973-1976</td>
<td>65</td>
<td>12.6</td>
<td>27.7</td>
<td>45.3</td>
<td>30</td>
<td>53.2</td>
</tr>
<tr>
<td>1977-1980</td>
<td>71</td>
<td>10.9</td>
<td>19.9</td>
<td>45.8</td>
<td>25</td>
<td>40.8</td>
</tr>
<tr>
<td>1981-1984</td>
<td>88</td>
<td>6.7</td>
<td>13.9</td>
<td>44.8</td>
<td>22</td>
<td>37.3</td>
</tr>
<tr>
<td>1985-1988</td>
<td>99</td>
<td>10.4</td>
<td>19.6</td>
<td>36.8</td>
<td>23</td>
<td>28.7</td>
</tr>
</tbody>
</table>

Values are percentages.

One problem in the interpretation of trends in typespecific stroke incidence and mortality was the introduction of new diagnostic technology during the study period. In particular, CT scanning came into use in 1976 (it was used in 6 of 28 cases that year), and in succeeding years its use rose to approximately 95% of hospitalized cases.

Although the advent of CT scans in the mid-1970s was an advance for subtype classification, there was no substantial change in our ability to determine stroke incidence. Because the majority of CT scans were performed too early in the patients' course for conclusive evidence of cerebral infarction, the major impact was to increase somewhat the specificity of the diagnoses of cerebral and subarachnoid hemorrhage and to reduce somewhat the proportion of stroke of unknown type.

During the current study there has been a change in risk factors in the cohort. An examination of a 30% subsample 15 years after the initial examination showed a significant decrease in blood pressure levels among treated hypertensive subjects. There was also a significant decrease in the percentage of men who smoked cigarettes. In addition, there were changes in dietary habits, with declines in the intakes of animal protein and cholesterol and an increase in the intake of vegetable protein. There was also a nominal but statistically insignificant decrease in both saturated and polyunsaturated fatty acid intake, an increase in monounsaturated fatty acid intake, and an increase in carbohydrate intake.

Another piece of evidence supporting the hypothesis that the fall in stroke mortality is the result, at least in part, of a decline in incidence is supplied by the findings of a decline in severity of atherosclerosis in the circle of Willis between 1967 and 1982 among those who died and were autopsied.

Although we may derive satisfaction from the trends in stroke incidence (probable) and mortality (certain), it is not clear who, if anyone, can claim credit for their occurrence. Is the decrease part of a change (perhaps cyclical) in the natural history of cardiovascular disease in general and of stroke in particular such that both the frequency and severity of stroke have declined without any relation to change in human societal behaviors? Is the change attributable to a general improvement in the standard of living among developed nations in recent decades, including better housing and better nutrition?

Alternatively, the epidemiological research and public health communities can lay claim to the elucidation of risk factors for CHD and stroke and for the promotion of more healthful behaviors to modify these risk factors, including improved nutrition, decreased cigarette smoking, improved control of high blood pressure, and a resultant decrease in the frequency, and perhaps severity, of stroke.
In addition, the medical community can claim its contribution to promoting a healthier lifestyle, to improved treatment of high blood pressure, and when these do not succeed in preventing stroke, to improved diagnosis and treatment, leading to improved case-fatality rates and overall mortality.

These speculations are complicated by the fact that other studies, although confirming a decline in mortality, do not all confirm a decline in incidence. As noted above, studies in Rochester, Framingham, Finland, Sweden, and Denmark do not agree on trends in stroke incidence. Other studies analyzed morbidity data, including recurrent events, whereas the Rochester and the Honolulu studies counted only first events for incidence.

The current study can only contribute to the formulation of a model describing the contribution of a decline in incidence to the decline in mortality. Further studies, both of a data-gathering and of a synthesizing nature, are required to achieve such a formulation.

We cannot yet know whether we have reached the nadir of stroke mortality, or whether further improvement is in store.

Acknowledgments

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References

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