Trends in Incidence, Case-Fatality Rate, and Severity of Stroke in Northern Sweden, 1985-1991

Birgitta Stegmayr; Kjell Asplund, MD; P.O. Wester, MD

Background and Purpose Incidence, case-fatality rate at 28 days, and severity of acute stroke were recorded for 7 years in a large population-based stroke register to understand the reasons for the decline in stroke mortality in northern Sweden.

Methods Within the framework of the World Health Organization MONICA Project, acute stroke was monitored in people aged 35 to 74 years in northern Sweden from 1985 through 1991 (target population in 1985, 238 948).

Results The annual incidence of stroke decreased by an average of 2.3% /y in men aged 35 to 64 years (P = .074) and increased significantly by 1.1% /y in men aged 65 to 74 years (P = .041). No significant changes in incidence occurred in either age group in women. The 28-day case-fatality rate in first-ever strokes (both sexes together) declined from 21.9% to 15.4% in patients aged 65 to 74 years (P = .02). Among survivors, the proportion with extensive motor deficits (at any time during the first 28 days) declined in patients younger than 65 years as well as in those older than 65 years (P = .007 and P = .019, respectively). In patients aged 35 to 64 years, the proportion with aphasia/dysphasia also decreased significantly (P = .032), but no such trend was seen in those aged 65 to 74 years.

Conclusions A shift toward higher ages has been noted in the occurrence of first-ever strokes in men, while incidence has remained unchanged in women. During the 7 years of observation, stroke has become a less severe disease. (Stroke. 1994;25:1738-1745.)

Key Words • cerebrovascular disorders • clinical trials • epidemiology • stroke outcome • Sweden

Stroke mortality, as reported in official statistics, has been declining markedly during the last 25 years in most countries in western Europe, North America, and eastern Asia, whereas it has increased in many eastern European countries. In Sweden the percentage decline per annum in the stroke mortality rate was 2.7% in men and 4.0% in women from 1970 to 1985.

Decreased mortality can be explained by decreased incidence (fewer stroke events occur) or a decrease in case-fatality (increased survival after the event) rate.

Studies from United States2 and the Scandinavian countries3-7 indicate that changes in stroke incidence during the last decade are insufficient to explain the reduced stroke mortality. Only a limited number of studies describe trends in case-fatality rates. In the Framingham Study, a declining case-fatality rate during three decades was observed in men aged 55 to 64 years but not in women.8 In Sweden, case-fatality decreased during the 1970s and early 1980s.9 10

Declining case-fatality rate in the acute phase of stroke can result from better case ascertainment in population-based registers, with more cases with good outcome being identified, but it can also result from a change in the natural history, with fewer severe strokes or better medical management.

Few studies elucidate the severity of stroke. The Framingham Study reported a decrease in the prevalence of unconsciousness and severe deficits, suggesting milder stroke events.8 In a hospital-based study in Pennsylvania, the proportion of stroke patients who were comatose on admission declined during the 1980s.11 In another study from the United States, improved survival and a decreased level of unconsciousness in hospitalized patients from 1970 to 1985 were observed.12 These studies suggest that the severity of stroke has diminished.

In the Northern Sweden MONICA Project, acute stroke events have been monitored since 1985. This study is a part of the multinational MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) collaboration, which was initiated by the World Health Organization (WHO) with the aim to relate changes over time in incidence and mortality in myocardial infarction and stroke to secular trends in population risk factor levels.13 Special efforts have been made to ensure that case-finding procedures do not change over time. The present report describes changes in incidence, case-fatality rate, and severity of stroke during the first 7 years of stroke registration in northern Sweden.

Subjects and Methods

The two northernmost counties in Sweden together constitute one of the 39 collaborating centers in the WHO MONICA Project. The total population in the Northern Sweden MONICA Project is 510 000 inhabitants, living in a sparsely populated area of 154 000 km2. All acute strokes in men and women aged 35 to 74 occurring in the years 1985 through 1991 were included in the present study. The study population (midyear) in 1985 was 238 948, of whom 189 099 were aged 35 to 64 years and 49 849 were aged 65 to 74 years. The midyear population had increased by 1991 to 243 662 persons.

Case Ascertainment

The case-finding of stroke is based mainly on three sources: discharge records from hospitals, reports from general practi-
Table 1. Yearly Average of Stroke Events by Subtype in Men and Women

<table>
<thead>
<tr>
<th>Age, y</th>
<th>ICD-9 Codes</th>
<th>Total</th>
<th>ICD-9 Codes</th>
<th>Total</th>
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<td>434</td>
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<td>19</td>
<td>78</td>
<td>32</td>
</tr>
<tr>
<td>65-74</td>
<td>6</td>
<td>31</td>
<td>179</td>
<td>115</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>59</td>
<td>293</td>
<td>153</td>
</tr>
</tbody>
</table>

ICD-9 indicates International Classification of Diseases, ninth revision (430, subarachnoid hemorrhage; 431, intracerebral hemorrhage; 434, brain infarction; and 436, unspecified stroke).

Stroke cases were registered in a standardized manner using the MONICA manual and defined by WHO criteria as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death) with no apparent cause other than a vascular origin." This definition excludes transient ischemic attacks (TIAs). Global clinical signs are accepted only in patients with deep coma or subarachnoid hemorrhage. Subdural hemorrhage, traumatic intracerebral hemorrhage, and lesions caused by brain tumor were also excluded. In this longitudinal project, special emphasis was placed on using uniform case ascertainment and diagnostic criteria throughout the study. Case-finding was therefore based on clinical presentation, and case subjects detected by brain imaging but not presenting with any acute symptoms of stroke were excluded. Information was abstracted from medical records, and the coders were the same throughout the study.

The subtypes of acute stroke, according to the MONICA manual, were based on the following examinations (ICD-9 codes in parentheses): subarachnoid hemorrhage (430); blood-stained cerebrospinal fluid and an aneurysm or an arteriovenous malformation found on angiography or positive finding on computed tomographic (CT) scan or necropsy; intracerebral hemorrhage (431); positive finding on CT scan or necropsy; brain infarction (434); no signs of hemorrhage on CT scan or at necropsy; and unspecified stroke (436): not investigated by CT scan or necropsy.

Each case was also described as "definite stroke," "unclassifiable," or "not stroke" based on available background information. The unclassifiable category was mainly used in fatal cases in which acute cerebrovascular disease was given as cause of death in the death certificate, but clinical information was too limited to classify the event as definitive stroke. The proportion of unclassifiable cases was 7.5% of fatal strokes and 1.4% of all strokes, with no important changes over time.

Fatal cases were subjects who died within 28 days from the onset of the stroke. In accordance with the terminology agreed on by the MONICA collaborators, "attack rate" describes all events whether or not the patients have had a previous event. "Incidence" relates to a first-ever stroke. When attack and incidence rates are provided, only cases classified as definite stroke have been included in data on nonfatal events, whereas data on fatal events also include cases coded as unclassifiable.

In patients with first-ever stroke, estimation of severity was obtained from medical records. Information on level of consciousness, extent of motor deficits, and presence of aphasia/dysphasia when first seen by medical staff or at any time during the first 28 days after onset was included. Lowered consciousness meant that the patient was somnolent (not fully alert), stuporous, or comatose. The term "extensive motor deficits" was used when there was a concomitant acute motor deficit in both arm and leg. The group with aphasia/dysphasia did not include patients with dysarthria or slurred speech.

In fatal cases, information about severity was missing in too many instances or was too unreliable to permit meaningful comparisons. Therefore, analyses of stroke severity were restricted to nonfatal cases.

Statistical Analysis

Because few events occurred in those in the younger age groups, two age groups (35 to 64 and 65 to 75 years) were selected for analysis. The age-specific rates in 35- to 64-year-old men and women were age standardized by the direct method to "world standard population" using 5-year age groups. Data in patients in the group aged 65 to 74 years were standardized to the 1988 population in northern Sweden. We calculated 95% confidence intervals according to the Poisson variation for the number of events within the age groups. A linear regression model was used for testing time trends. Moving averages have been used in the graphs. However, the linear regression analyses were based on the actual value from each single year.

With approximately 900 stroke events per year and assuming that trends were linear, the study had the power (at α = 0.05 and 1 - β = 0.80) to detect an overall annual change of 1.8% during the 7 years of observation in any of the variables.

Results

During the 7 years from 1985 through 1991, 8855 possible stroke events in the age range of 35 to 74 years were registered in the Northern Sweden MONICA stroke database. Of the 7204 nonfatal events, 2390 (33.2%), and of the 1422 fatal events, 151 (10.6%) were excluded because they did not fulfill the MONICA criteria for acute stroke events. Table 1 shows the yearly number (mean for 1985 through 1991) of events for the different subtypes of stroke.
The diagnosis of subarachnoid hemorrhage was based on autopsy (alone or in combination with CT scan,
years were analyzed separately, there was a tendency based on all strokes or on first strokes only (Fig 1). But the change reached statistical significance only for year variation in both men and women (due to a significant trends were observed, whether the estimates relatively small number of fatal events). No statistically significant trends in any sex or age group.

The distribution of different subtypes of stroke for separate years did not change in younger patients. In the older age group there was an increasing trend of use of CT scan in stroke patients aged 65 to 74 years, decreased (P=.008). This coincided with more frequent use of CT scan in stroke patients aged 65 to 74 years, with 42.3% being investigated in 1985 versus 74.6% in 1991 (P<.001).

The incidence of subarachnoid hemorrhage during the 7-year observation period is shown in Table 4. There were substantial variations from year to year, with no significant trends in any sex or age group.

**Severity of Stroke**

Because the numbers in some of the subgroups were small, particularly in women, and the trends were similar in the two sexes, men and women were analyzed together. Only patients with first-ever strokes were included.

For the years 1985 through 1991, information on level of consciousness was obtained in 3479 of 3566 (97.6%) of the first-ever stroke patients who survived for at least 28 days. Of the remaining (3479) patients, 253 (7.3%) were somnolent and 1723 of the remaining patients (48.9%) had paresis of both arm and leg, here denoted “extensive motor deficits.” Speech performance was known in 3452 patients (97.7%), of whom 1029 had aphasia or dysphasia (29.8%).

Fig 3 shows time trends in the proportion of surviving patients who had lowered consciousness, extensive motor deficits, or aphasia/dysphasia at any time during the first 28 days after stroke. In patients aged 35 to 64 years, the proportion with lowered levels of consciousness either when first seen by medical staff or during the acute phase (first 28 days) declined, although not significantly (P=.078). The proportion with extensive motor deficits declined significantly from 50.2% to 40.2% (P =.007), and the proportion with aphasia or dysphasia declined from 29.8% to 23.2% (P =.032).
In older patients aged 65 to 74 years, the proportion of patients with lowered consciousness showed a non-significant decrease from 14.1% to 10.9% during the 7-year observation period (P=.486) (Fig 3). The proportion with extensive motor deficits declined significantly from 50.5% to 46.1% (> =.019), whereas there was no change over the years in the proportion with aphasia/dysphasia (P=.540).

**Discussion**

The present data show that, in Sweden, stroke incidence rates tended to decline in men aged younger than 65 years during the years 1985 through 1991, whereas they increased in men aged 65 to 74 years and remained unchanged in women in both age groups. The 28-day case-fatality rate declined in stroke patients aged 65 to 74 years, possibly related to the fact that stroke seemed to become a less severe disease during the 7 years of observation, as suggested by a declining occurrence of several indicators of neurological deficits.

It has been suggested that differences in incidence of stroke observed within populations can mostly be attributed to registration differences. In the MONICA Project, the same diagnostic criteria are applied strictly throughout the study. More extensive use of brain imaging techniques does not influence case-finding,
Proportion with lowered consciousness

Proportion with extensive motor deficits

Proportion with aphasia or dysphasia

FIG 3. Line graphs show the proportion of patients (men and women together) in groups aged 35 to 64 years and 65 to 74 years with lowered consciousness, severe paresis, and aphasia or dysphasia from 1985 through 1991. Subarachnoid hemorrhages are excluded.

since identification of stroke cases relies solely on clinical presentation. Thus, patients with brain lesions detected by CT scan but without focal deficits are not included. The coders have been the same throughout the study. A validation of the Northern Sweden MONICA stroke register has been performed on two occasions, which indicated that the stroke register ascertained 96% or more of all stroke cases (fatal and nonfatal) in the population each year. Except in one subgroup (men aged 65 to 74 years), the incidence rates did not increase over time. It is unlikely that the changes in case-fatality rate and severity of stroke reported here are due to better case ascertainment over time.

During the period 1985 through 1991, the incidence of stroke tended to decrease in men aged younger than 65 years, whereas it increased in those aged 65 to 74 years. This would indicate that there has been a shift in the occurrence of first stroke in men toward higher ages. An increasing trend in stroke incidence among elderly men (but not in women) has previously been reported among people aged 65 to 74 years in Copenhagen, Denmark, where stroke incidence increased from 618/100 000 in 1972 through 1974 to 1190/100 000 in 1989 through 1990. Increasing stroke incidence rates in patients 40 years or older during the years 1974 through 1981 have also been reported from Stockholm, Sweden. In Finland no obvious trend was seen from 1983 through 1986, with a comparable high case-fatality. In women, we observed no changes in stroke incidence in either age group during the 7 years of observation, which is also consistent with earlier observations in the Stockholm area. This latter study was not community-based but relied on routine hospital statistics. In a validation of the MONICA register, we found that hospital discharge records poorly reflected the incidence of stroke, with a false-positive diagnosis of more than 30%. In Söderhamn, Sweden, a significant increase of stroke incidence in women aged 45 to 64 years was shown between the years 1975 through 1978 and 1983 through 1986. Taken together, previous results and ours indicate that, in Swedish and Danish populations, there is an ongoing shift in stroke incidence toward higher ages in men. A previous increase in incidence among middle-aged women may have halted, so that incidence rates are now fairly stable at all ages up to 75 years. In Finland the trend was unchanged between 1979 and 1986. Previous reports from United States, New Zealand, and Sweden have described a decline in case-fatality the first month or the first year after first-ever stroke. We confirmed a marked decline in 28-day case-fatality after first stroke events among men and women aged 65 to 74 years. The case-fatality in younger people did not change over the years, although there were few deaths in younger ages.

We used linear regression to monitor trends in incidence over time. The primary hypothesis was to test a linear model for trend. More complicated models such as U forms for incidence development by time have not been investigated. However, these must be seen as hypothesis generating and tested in a new data set. As an alternative, a logistic model could be used; in the present data set, however, the logistic model and the linear model provide nearly identical results.

An important explanation for the decrease in the case-fatality rate in first-ever strokes in persons aged 65 to 74 years is that stroke in this population has become a less severe disease during the observation period. In nonfatal patients younger than 65 years as well as those older than 65, the proportion of patients presenting with lowered consciousness or extensive motor deficits decreased over time.

In the MONICA registration procedure, maximal severity of symptoms during the first 28 days was based on information available in routine medical records. In the majority of cases, this reflects clinical presentation on admission to the hospital but also includes maximal deficits in patients deteriorating after admission to the hospital. The data on clinical symptoms and signs were collected retrospectively. Therefore, grading of motor deficits was based on extent of limb involvement (arm,
arm and leg) rather than on severity of paresis, for which data were regarded as less reliable and less uniformly described. Obviously, the extent of motor deficits depends not only on the size but also on the site of the brain lesion. A change in the mix of cortical versus subcortical lesions over time could possibly affect the occurrence of motor deficits.

Other changes were reported in the Framingham Study, in which a marked decline in severe deficits was shown in subjects aged 55 to 64 years.8 A study from Pennsylvania reported a reduced proportion of comatose stroke patients in hospital during a 10-year period (1971 through 1980).11 In Sweden, the proportion of patients with progressing stroke declined from 35% to 19% during the years 1978 through 1987.21 Thus, there are now several indications that the natural history of stroke is changing in industrialized countries, so that stroke is becoming a less severe disease than it used to be.

Another hypothetical explanation for the change in clinical presentation is that more cases with minor neurological symptoms have been recognized. As discussed above, case ascertainment procedures have been uniform throughout the MONICA study, and the reduced severity was present also in groups in which stroke incidence did not increase. The comparison of stroke symptoms did not include fatal cases because detailed information was missing in most fatal events occurring out of the hospital, and most patients dying in the hospital were comatose. The case-fatality rate either declined or was unchanged in the subgroups we analyzed. If anything, in time this would contribute to more patients with severe symptoms among the survivors, whereas we observed the opposite.

In the three American studies that measured stroke severity, great efforts were made to maintain uniform case-finding procedures throughout the study periods.8,11,12 Like the MONICA project, the Framingham Study is population based, but the studies of Ahmed et al11 and McGovern et al12 were hospital based, which warrants some caution when interpreting the results. Nevertheless, there are now indications that there is an ongoing decline in stroke severity, as presented in at least three studies.

Factors contributing to the decline in case-fatality rate and severity of stroke are unknown. A shift in the subtypes of stroke, with fewer intracerebral hemorrhages, would also result in a lower overall case-fatality rate in stroke.24 In our study there was no difference in the proportion of intracerebral hemorrhages between the beginning and the end of the study. Another factor contributing to the case-fatality rate might perhaps be improved management of patients during the hospitalization.

The present data do not provide any clue as a reason for the change in natural history. It may be that antihypertensive treatment not only lessens the risk of stroke but possibly also reduces the extent of brain lesions once they occur. However, calculations based on epidemiological data indicate that only a fraction of the decline in stroke mortality in the United States, New Zealand, and Finland can be explained by better control of hypertension in the community.25-28 It may also be that better control in diabetes, improved nutrition with higher intake of antioxidant vitamins, and more widespread use of aspirin among people at stroke-prone ages help to reduce not only stroke incidence but also the severity of stroke. Large brain infarcts have been associated with poor metabolic control in diabetes.29 Admittedly, such explanations for the reduced severity of stroke are, as yet, highly speculative.

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