Three-Year Survival and Recurrence After Stroke in Malmö, Sweden
An Analysis of Stroke Registry Data
A.M. Elneihoum, MD; M. Göransson, BS; P. Falke, MD, PhD; L. Janzon, MD, PhD

Background and Purpose—Data from the Malmö Stroke Registry were analyzed to determine whether any change in survival or nonfatal stroke recurrence rates had occurred during the 4-year period from 1989 through 1992 and whether prognosis was related to area of residence.

Methods—The series comprised 2290 patients, 1051 men and 1239 women, followed up for 3 years after their first stroke during the period 1989 through 1992.

Results—Of the series as a whole, 959 (43.4%) died and 137 (6%) suffered a second nonfatal stroke. Multivariate analysis showed age, type of stroke, severity of stroke, and the presence of diabetes mellitus or cardiac disease each to be an independent predictor of mortality, and the presence of diabetes, atrial fibrillation, and history of transient ischemic attacks each to be associated with increased risk of recurrence. Treatment for hypertension was associated with a protective effect. As compared to those with first stroke in 1989, those with first stroke in 1992 were characterized by a lower recurrence rate, which was reduced by 70% in the male subgroup (P=0.003) and by 80% in the female subgroup (P=0.006), the corresponding reduction in all-cause mortality being 30% (P=0.007) and 10% (P=0.5, NS). Recurrence-free survival rates differed markedly between the 17 residential areas studied.

Conclusions—The present study showed that survival rates after stroke have improved and recurrence rates have declined in this urban population. Further studies are needed to ascertain to what extent intraurban variation in the proportion of recurrence-free 3-year survivors is to be explained by differences in the severity of initial stroke and other prognostic markers, or in initial treatment and secondary preventive measures. (Stroke. 1998;29:2114-2117.)

Key Words: epidemiology □ mortality □ recurrence □ stroke

According to official statistics, the age-adjusted stroke mortality rate in Sweden has declined from approximately 9/10 000 to 7/10 000 during the 14-year period from 1980 through 1994.1 Findings in follow-up studies at some hospitals have suggested that this decline may be partly attributable to improvement in the acute survival rate.2,3 The beneficial effects of secondary preventive measures after stroke, such as antihypertensive, antiplatelet, or anticoagulant therapy and surgical treatment of severe symptomatic carotid artery stenosis, have been well established in clinical trials.4–6 However, little evidence is available as to whether the long-term survival rate after stroke has improved.

All patients residing in the city of Malmö who had their first-ever stroke after January 1, 1989, are registered in the Malmö Stroke Registry (STROMA), which was established in 1989.

The approximately 250 000 residents of the city live in 18 administrative areas, which differ widely from each other in sociodemographic, morbidity, and mortality profiles.

Data from this registry have been used to study survival and recurrence rate in relation to residential area and factors known to be associated with stroke outcome and to determine whether cases occurring during the 4-year period 1989–1992 were characterized by any change in 3-year survival or recurrence rates.

Subjects and Methods
Stroke was defined as rapidly developing clinical signs of local or global loss of cerebral function lasting for ≥24 hours (or leading to death before then) with no apparent cause other than cerebral ischemia or hemorrhage.8 By definition, cases of transient ischemic attack were excluded. Only patients with first-ever stroke after January 1, 1989, were included in STROMA. All recurrences were recorded, provided that the recurrent event occurred at least 4 weeks after the preceding event. Details of case retrieval and ascertainment have been reported previously.11 The present study series comprised 2290 patients, 1051 men and 1239 women, who had their first stroke during the 4-year period 1989–1992.

Prognostic Markers
Cardiovascular Risk Factors
Mortality and recurrence rates were studied in relation to the following prognostic markers: treatment for hypertension prior to...
stroke or within the first week after admission; the presence of diabetes mellitus (ie, previously diagnosed or repeat fasting blood glucose values of ≥6.5 mmol/L). The subgroup with cardiac disease included patients with ischemic heart disease, valvular heart disease, and heart failure. Patients with at least one prior serum total cholesterol value of ≥6.5 mmol/L were considered to have hypercholesterolemia. Smokers were defined as those smoking regularly at the onset of stroke and ex-smokers as those who had quit smoking at least 1 year before their stroke.

Stroke Severity
Stroke severity assessment, based on the Katz index, was performed for approximately 70% of patients by experienced occupational therapists.

Residential Area
The city of Malmö comprises 18 administrative areas, one of which (the harbor area) was not included in the analysis owing to its very small population.

Follow-Up
Survival and recurrent stroke data for the 3-year period after first stroke were obtained from the stroke registry for all 2495 patients, with each patient being followed up until second stroke, death, or the end of the 3-year follow-up period. Those who died were traced in the cause-of-death register, in which cause of death is classified according to the International Classification of Diseases, 9th Revision (ICD-9) codes.

Statistical Analysis
The Kaplan-Meier method was used to estimate the probability of survival and the Cox proportional hazards model to test the risk factors studied as independent determinants of survival and recurrence rates. Age adjustment was done with the direct method, using the entire population of Malmö as the standard population, with age distribution being averaged for the 4-year period 1989–1992. All statistical calculations were performed by computer, using SPSS software (Statistical Package for the Social Sciences; SPSS Inc). P values of <0.05 were considered statistically significant.

Results
The series as a whole (n=2290)−1051 men (mean±SD age, 72±12 years) and 1239 women (mean±SD age, 78±11 years)—account for a total of 2495 stroke events during the 4-year period 1989–1992. In the city of Malmö, the annual stroke incidence per 100,000 was 300 in 1989, 270 in 1990, 284 in 1991, and 286 in 1992.

In terms of stroke types, 68 (2.7%) of the 2495 stroke events were due to subarachnoid hemorrhage and 240 (9.6%) to intracerebral hemorrhage, 1388 (55.6%) as ischemic stroke and 799 (32%) as unspecified stroke. In terms of severity, which was assessed in about 70% of cases, 594 cases were classified as minor stroke (Katz Index grades A to B), 302 cases as moderate stroke (Katz grades C to E), and 689 cases as major stroke (Katz grades F to G).

Survival and Recurrence Rates
Of the series as a whole (n=2290), 959 (43.4%) died within 3 years and 137 (6%) had a new nonfatal stroke during the 3-year follow-up period. Three years after the first stroke event, 1158 (50.6%) of the patients were still alive, and had not had a second stroke (Figure 1 and 2).

Outcome Predictors
Age, the presence of diabetes mellitus or cardiac disease, severity of the stroke (Katz Index grade), and type of stroke were each found to be a significant independent predictor of mortality after stroke. Treatment for hypertension and hypercholesterolemia were each associated with an improved survival rate (Table 1).

Diabetes mellitus, atrial fibrillation and a history of transient ischemic attack were each found to be a significant independent predictor of recurrent stroke (Table 1).

Prognosis in Relation to Residential Area
The 17 residential area subgroups differed substantially with regard to the proportion of survivors who had not experienced a second stroke during the 3-year follow-up. The age-adjusted survival rates for the 17 residential areas are shown in Figure 3.

Time Trends
There was a trend toward improving prognosis after stroke with calendar time during the 4-year study period independent of other prognostic factors.
Compared to those with first stroke in 1989, those with first stroke in 1992 were characterized by a lower recurrence rate, which was reduced by 70% in the male subgroup ($P = 0.003$) and by 80% in the female subgroup ($P = 0.006$), the corresponding reduction in all-cause mortality being 30% ($P = 0.007$) and 10% ($P = 0.5$, NS) (Table 2).

**Discussion**

According to official statistics, there has been a continuous decline in age-adjusted stroke mortality in Sweden since 1980, a trend manifested in both the male and female subgroups. Findings in previous studies at some Swedish hospitals suggest that the decline has been caused in part by a decrease in immediate mortality. Evidence is also available which suggests that the same period has been characterized by a shift toward less severe stroke, with no concomitant decline in stroke incidence.

Although the improved survival rate in Malmö is consistent with the previously reported decrease in the immediate mortality rate, the declining recurrence independent of other risk factors suggests that the improved quality of secondary preventive measures may have contributed to the improved outcome. The smaller decline in the mortality rate among women may simply reflect the higher mean age of that subgroup compared with that of the men (78 versus 72 years).

Although it is well known that prognosis after stroke (in terms of both recurrence and survival) is related to a number of risk factors; prognosis in relation to place of residence has been investigated in few studies. In previous studies at Malmö, both incidence and mortality pattern of different diseases were shown to differ widely among the 17 residential areas, with the variation being related to a number of sociodemographic factors. The intraurban variation with regard to stroke-free survival found in the present study is consistent with these previous findings. Treatment after stroke is generally the responsibility of the primary health care provider; however, the role of the primary care physician is different in Malmö compared to the other areas. The severity of stroke at the time of treatment is an important factor in determining the outcome. The study is conducted in Malmö, a city with a well-developed primary care system, where patients are seen at the emergency department of the hospital and then referred to the stroke unit. The primary care physician plays a crucial role in the management of stroke patients, and the early referral to the stroke unit is an important factor in improving the outcome. The study is conducted in Malmö, a city with a well-developed primary care system, where patients are seen at the emergency department of the hospital and then referred to the stroke unit. The primary care physician plays a crucial role in the management of stroke patients, and the early referral to the stroke unit is an important factor in improving the outcome.

### Table 1. Influences of Different Prognostic Markers on All-Causes Mortality and Incidence of Nonfatal Recurrent Stroke

<table>
<thead>
<tr>
<th>Prognostic Marker</th>
<th>All-Cause Mortality</th>
<th>Nonfatal Recurrent Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>$P$</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.07 (1.06–1.08)</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>1.1 (0.9–1.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes mellitus (yes/no)</td>
<td>1.4 (1.1–1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension treatment (yes/no)</td>
<td>0.8 (0.7–0.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypercholesterolemia (yes/no)</td>
<td>0.7 (0.6–1.0)</td>
<td>0.053</td>
</tr>
<tr>
<td>Smoker (yes/no)</td>
<td>1.2 (1.0–1.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Ex-smoker (yes/no)</td>
<td>1.2 (1.0–1.6)</td>
<td>0.07</td>
</tr>
<tr>
<td>Atrial fibrillation (yes/no)</td>
<td>1.4 (1.2–1.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>1.2 (1.0–1.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.5 (1.2–1.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Multiple diagnosis</td>
<td>1.8 (1.5–2.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of TIA (yes/no)</td>
<td>0.9 (0.8–1.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Type of stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>Control</td>
<td>...</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>1.7 (1.4–2.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Unspecified stroke</td>
<td>1.3 (1.2–1.6)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Katz Index Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–E/A–B</td>
<td>1.4 (1.1–1.8)</td>
<td>0.007</td>
</tr>
<tr>
<td>F–G/A–B</td>
<td>3.0 (2.5–3.6)</td>
<td>$&lt;0.0001$</td>
</tr>
</tbody>
</table>

RR indicates relative risk; CI, confidence interval.
TABLE 2. Incidence and Relative Risk of Nonfatal Recurrent Stroke and All-Causes Mortality in Relation to Year of First Stroke

<table>
<thead>
<tr>
<th>Year of Stroke</th>
<th>No. of Cases</th>
<th>Follow-up, y</th>
<th>No. of Events (%)</th>
<th>Recurrence per 1000 Person-Years</th>
<th>RR (95% CI)</th>
<th>P</th>
<th>No. of deaths (%)</th>
<th>Deaths per 1000 Person-Years</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>Male 249</td>
<td>468.1</td>
<td>24 (9.6)</td>
<td>51.3</td>
<td>Control</td>
<td>Control 103 (41.4)</td>
<td>220.1</td>
<td>Control</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female 288</td>
<td>537.8</td>
<td>21 (7.3)</td>
<td>39.1</td>
<td>Control</td>
<td>Control 143 (49.7)</td>
<td>265.8</td>
<td>Control</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>Male 273</td>
<td>538.4</td>
<td>20 (7.3)</td>
<td>37.2</td>
<td>0.6 (0.4–1.2)</td>
<td>0.2</td>
<td>118 (45.2)</td>
<td>219.2</td>
<td>0.9 (0.7–1.2)</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>Female 310</td>
<td>525.8</td>
<td>24 (7.7)</td>
<td>45.7</td>
<td>1.2 (0.7–2.3)</td>
<td>0.5</td>
<td>149 (48.1)</td>
<td>238.4</td>
<td>1.2 (0.9–1.5)</td>
<td>0.2</td>
</tr>
<tr>
<td>1991</td>
<td>Male 260</td>
<td>550.5</td>
<td>10 (3.9)</td>
<td>18.2</td>
<td>0.3 (0.2–0.6)</td>
<td>0.001</td>
<td>100 (38.5)</td>
<td>181.8</td>
<td>0.7 (0.6–0.9)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Female 325</td>
<td>591.6</td>
<td>17 (5.2)</td>
<td>28.7</td>
<td>0.8 (0.4–1.5)</td>
<td>0.5</td>
<td>150 (46.2)</td>
<td>253</td>
<td>1.0 (0.8–1.3)</td>
<td>0.7</td>
</tr>
<tr>
<td>1992</td>
<td>Male 269</td>
<td>568.7</td>
<td>14 (5.2)</td>
<td>24.6</td>
<td>0.3 (0.2–0.7)</td>
<td>0.003</td>
<td>98 (36.4)</td>
<td>172.5</td>
<td>0.7 (0.5–0.9)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Female 316</td>
<td>597.2</td>
<td>7 (2.2)</td>
<td>11.7</td>
<td>0.2 (0.1–0.7)</td>
<td>0.006</td>
<td>143 (45.3)</td>
<td>239</td>
<td>0.9 (0.7–1.2)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

RR indicates relative risk; CI, confidence interval.

*P values determined by Cox regression analysis with adjustment for all significant risk factors.

Acknowledgments

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care physicians in the city. To what extent differences in stroke-free survival reflect differences regarding initial treatment and secondary prevention remains to be evaluated. In the analysis, we have with exception for age made no adjustment for the possibility that stroke victims from different areas of living may differ with regard to the exposure to risk factors related to survival and recurrence.

Questions may be raised regarding the validity of the estimates of recurrence and survival rates. Diagnosis of stroke was based on established clinical criteria and findings of CT and MRI. Malmö University Hospital is the only hospital for somatic disorders in the city, and all stroke patients are therefore referred to this hospital for evaluation. This includes patients belonging to the catchment area but initially admitted to a hospital outside the city. Although the annual outmigration rate from Malmö is about 1%, owing to computerized access to the national cause-of-death registry it is nonetheless possible to obtain complete follow-up data.

The relatively high percentage of cases (32%) in which the cause of stroke remained unclear merits comment. Most of these patients were elderly (mean±SD age, 82±9 years), many with very severe stroke. On clinical grounds it was felt that treatment was unlikely to be altered by access to more detailed knowledge of the underlying cause(s).

In summary, the present study showed survival rates following stroke to have improved and recurrence rates to have declined in this urban population. Further studies are needed to ascertain to what extent intraurban variation in the proportion of recurrence-free 3-year survivors is to be explained by differences in the severity of initial stroke and other prognostic markers or in initial treatment and secondary preventive measures.

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