Poor Outcome After First-Ever Stroke
Predictors for Death, Dependency, and Recurrent Stroke
Within the First Year

Peter Appelros, MD; Ingegerd Nydevik, MD, PhD; Matti Viitanen, MD, PhD

Background and Purpose—The purpose of this study was to define predictors of poor outcome after a first-ever stroke. We studied risk factors and stroke severity at baseline in relationship to death, dependency, and stroke recurrence within a year after the event.

Methods—The study included a community-based cohort of first-ever stroke patients. Subarachnoid hemorrhage was not included. All patients (n=377) were subjected to investigations regarding risk factors. Stroke severity was evaluated with the National Institutes of Health Stroke Scale, and dependency was defined according to the modified Rankin Scale. Multivariate regression models were used to analyze predictors of survival, dependency, and stroke recurrence. The following independent variables were used: age, sex, cohabitation status, cigarette smoking, dementia, hypertension, ischemic heart disease, heart failure, atrial fibrillation, diabetes mellitus, transitory ischemic attack, peripheral atherosclerosis, and stroke severity.

Results—The 1-year mortality was 33%. After 1 year, 37% of the survivors were dependent; 9% of survivors had a recurrent stroke within a year. Dementia, age, stroke severity, and atrial fibrillation were associated with death within a year. Dependency was associated with age, stroke severity, and heart failure. Stroke recurrence was predicted by age and dementia.

Conclusions—In addition to age and stroke severity, heart diseases and dementia before the stroke seem to have an impact on mortality and recurrence after 1 year. Finding and, when possible, treating these prestroke conditions may affect stroke morbidity and mortality favorably. (Stroke. 2003;34:122-126.)

Key Words: atrial fibrillation ■ cognitive disorders ■ heart failure, congestive ■ prognosis ■ stroke

In the last decades, in Sweden, as well as in many other Western countries, stroke seems to have become a less severe disease. The reasons for this are not clear, but it has been suggested that a reduction in the population level of blood pressure, diminished smoking, reduced intake of saturated fats, and better stroke care in dedicated units may contribute. One way of affecting stroke morbidity and mortality might be to further reduce the impact of factors that increase stroke severity. Several authors have studied prognostic factors for long-term survival after stroke, stroke recurrence, and functional outcome or dependency. Although few of these studies used population-based materials, it is well established that old age and severe impairment after stroke predict poor outcome. Few studies have considered the impact of prestroke dementia, which is now recognized as a risk factor for stroke. Dementia after stroke is also known to have a negative impact on long-term survival. We have previously shown that heart failure, atrial fibrillation, and dementia are associated with more severe strokes. The purpose of this article is to demonstrate the impact of prestroke risk factors on the outcome of patients who survived the acute phase of a stroke. We designed the present study to compare 3 different domains of poor stroke outcome, with special attention given to whether risk factors other than age and stroke severity play a role.

Subjects and Methods
All cases of first-ever stroke were registered in Örebro, Sweden, during a 12-month period, from February 1, 1999, through January 31, 2000. The study population was 123 503. The World Health Organization (WHO) definition of stroke was used. Cases were found inside and outside the hospital. Multiple overlapping sources and “hot pursuit” techniques were used in the process of case ascertainment to fulfill the requirements of an “ideal” stroke incidence study. Patients with subarachnoid hemorrhage (n=11) were not included in the present study because of their different etiologies and prognoses. Case ascertainment and the definition of stroke types have been discussed in detail.

A year after the stroke event, each patient was offered a free follow-up consultation. Optional to the patient, the investigator either saw the patient at the consulting room or visited the patient...
Stroke severity at baseline was assessed with the National Institutes of Health Stroke Scale (NIHSS). The assessment was performed within 24 to 48 hours after the event, except if a patient’s general health was rapidly declining; in this case, the assessment was performed within the first 24 hours. At the follow-up after 1 year, dependency was assessed with the modified Rankin Scale (MRS). Functionally dependent was defined as an MRS score of 3, 4, or 5. The MONICA criterion for stroke recurrence was adapted: “every stroke event must have its apparent onset . . . more than 28 days from any preceding stroke event.” At the follow-up, the incidence of new stroke events was verified in 1 of 3 ways. First, some stroke events could be verified directly by the study doctor at the time of the new stroke. Second, clear documentation in medical records of new focal signs that had lasted >24 hours was accepted. Third, some patients did not seek medical help when they had their second stroke but told the study doctor and showed signs of it at the 1-year follow-up visit. If a patient died within the year of follow-up, the cause of death was researched in hospital or primary care medical records.

Strokes were divided into the following main types according to the WHO criteria: brain infarction (BI), intracerebral hemorrhage (ICH), and stroke of undetermined pathological type (UND). Risk factors were evaluated at the time of stroke diagnosis. A structured interview was done to map the relevant medical history of each patient. When appropriate, the next of kin was interviewed. Previous hospital medical records and, when relevant, primary care records were reviewed. Assessment of prestroke dementia was based on interviews with the patient and a knowledgeable informant. We required the presence of memory impairment and deficits in at least 1 other cognitive ability. The presence of prestroke dementia was established if these disabilities were severe enough to interfere with everyday activities for at least 6 months or if there had been a confirmed diagnosis of dementia according to medical records. First-hand information was gained from a relative in 75% of patients. This relative was most often the patient’s spouse, son, or daughter. The diagnosis of dementia was based entirely on clinical grounds, and both etiological main groups of dementia—vascular and primary degenerative—were included. For a comprehensive definition of risk factors, we refer to our previous article.

Population statistics were used to ascertain whether a patient was still alive 1 year after the stroke event.

Statistical Analysis

The Kaplan-Meier method was used to estimate the probability of survival 1 year after the stroke event. Assuming binominal distribution, CIs for proportions were calculated with STATA, version 7.0. Cox’s regression and multiple logistic regression were used to calculate which factors contributed to each outcome. We used SPSS, version 11.0.

The regression analyses were performed as follows. All variables except age and stroke severity were dichotomized. The 13 explanatory variables were first tested 1 by 1 against the dependent variable for the presence of a significant association ($P < 0.05$). Variables for which no significant association was found were removed from the model. Thereafter, the remaining variables were cross tabulated to assess for multicollinearity. In no cases were 2 variables correlated at $>0.25$ with each other, which was acceptable for the subsequent analysis. The regression analysis was then performed. Finally, the logistic regression models were examined for goodness of fit. Hosmer-Lemeshow statistics were calculated to analyze how well the model fit each case. The relative influence of individual observations was analyzed by Cook’s influence statistic. In all cases, it was concluded that the model fit was adequate, and experimental removal of outliers did not violate the model.

Ethics

Before entering the study, patients were asked orally for consent and received written information. When a patient’s ability to communicate was restricted, consent was obtained from the next of kin. The

### Results

Three hundred seventy-seven patients were found to have had a first-ever stroke in Örebro during the study period. Nineteen were included retrospectively when the hospital discharge records and death certificates were scrutinized. Two hundred nine patients (55%) were female, and 168 were male. The overall 28-day case fatality was 18.3% (95% CI, 14.7 to 22.5). The baseline characteristics of the study population are given in Table 1. A CT of the brain was performed at baseline in 84% of the patients. At the 1-year follow-up, 6 patients denied consent to take part in the consultation visit but agreed to answer questions in a telephone interview.

### One-Year Mortality

After 1 year, 124 patients had died. The overall 1-year probability of death was 0.33 (95% CI, 0.28 to 0.38). The survival probability for different stroke subtypes was as follows: ICH, 0.36 (95% CI, 0.22 to 0.52); nonlacunar type of BI, 0.29 (95% CI, 0.23 to 0.36); lacunar type of BI, 0.06 (95% CI, 0.02 to 0.14); and UND, 0.78 (95% CI, 0.65 to 0.88). No significant differences were seen between men and women. Ninety-seven deaths (78%) were stroke related. Other causes of death were heart disease (n=9), malignant tumor (n=7), infection (n=6), and other disease (n=5).

### Functional Outcome

At baseline, the median NIHSS score for all 377 patients was 6 (interquartile range, 3 to 12). The mean value was 9.2, which indicates a positive skewness. For survivors, the median score was 1.0 after 1 year (interquartile range, 0 to 3; mean value, 2.2). No patient with a baseline NIHSS score of $\geq 30$ survived the first year. These patients often had lowered consciousness at the time of admission.

The frequency of different MRS scores at 1 year was as follows: 42 (16%) scored 0, 58 (23%) scored 1, 60 (24%) scored 2, 40 (16%) scored 3, 25 (10%) scored 4, and 28 (11%) scored 5.

<table>
<thead>
<tr>
<th>TABLE 1. Baseline Characteristics of the Study Population</th>
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<tbody>
<tr>
<td>No. of subjects</td>
</tr>
<tr>
<td>Age, average (range)</td>
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<tr>
<td>Male sex, n (%)</td>
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<tr>
<td>Main types of stroke, BI/ICH/UND, n</td>
</tr>
<tr>
<td>Living alone, % (95% CI)</td>
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<tr>
<td>Arterial hypertension, % (95% CI)</td>
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<tr>
<td>Ischemic heart disease, % (95% CI)</td>
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<td>Whereof myocardial infarction</td>
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<tr>
<td>Heart failure, % (95% CI)</td>
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<td>Atrial fibrillation, % (95% CI)</td>
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<td>Diabetes mellitus, % (95% CI)</td>
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<td>TIA, % (95% CI)</td>
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<tr>
<td>Cigarette smoking, % (95% CI)</td>
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<tr>
<td>Peripheral atherosclerosis, %</td>
</tr>
<tr>
<td>Prestroke dementia, % (95% CI)</td>
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</tbody>
</table>

*Human Ethics Committee of the Örebro County Council and the local Data Inspection Board approved the study.*
Stroke January 2003

TABLE 2. Hazard Ratios and Odds Ratios for Death, Dependency, and Stroke Recurrence Within 1 Year After First-Ever Stroke According to Different Prestroke Risk Factors and Stroke Severity (95% CIs)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Univariate Model</th>
<th>Multivariate Model</th>
<th>Univariate Model</th>
<th>Multivariate Model</th>
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<th>Multivariate Model</th>
<th>Univariate Model</th>
<th>Multivariate Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.07 (1.04–1.09)</td>
<td>1.05 (1.02–1.07)</td>
<td>1.07 (1.04–1.10)</td>
<td>1.08 (1.05–1.12)</td>
<td>1.12 (1.06–1.18)</td>
<td>1.11 (1.05–1.18)</td>
<td></td>
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<tr>
<td>Male gender</td>
<td>0.7 (0.5–0.9)</td>
<td>1.1 (0.7–1.8)</td>
<td>1.2 (0.7–2.0)</td>
<td>1.2 (0.6–2.6)</td>
<td>0.5 (0.2–1.0)</td>
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<tr>
<td>Living alone</td>
<td>1.5 (1.1–1.2)</td>
<td>1.2 (0.3–1.1)</td>
<td>2.1 (0.7–6.4)</td>
<td>5.1 (2.2–12.2)</td>
<td>3.0 (1.2–7.2)</td>
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<tr>
<td>Cigarette smoking</td>
<td>0.5 (0.3–0.9)</td>
<td>0.6 (0.3–1.1)</td>
<td>0.7 (0.4–1.2)</td>
<td>0.9 (0.4–2.1)</td>
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<tr>
<td>Prestroke dementia</td>
<td>4.0 (2.6–6.1)</td>
<td>1.9 (1.2–3.1)</td>
<td>1.6 (0.9–2.8)</td>
<td>2.5 (1.2–5.3)</td>
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<tr>
<td>Hypertension</td>
<td>0.8 (0.5–1.2)</td>
<td>0.7 (0.4–1.2)</td>
<td>3.2 (1.3–7.7)</td>
<td>3.0 (1.1–8.0)</td>
<td>1.5 (0.5–4.4)</td>
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<tr>
<td>Ischemic heart disease</td>
<td>1.2 (0.8–1.6)</td>
<td>1.6 (0.8–3.1)</td>
<td>1.6 (0.8–3.1)</td>
<td>2.1 (1.0–4.8)</td>
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<tr>
<td>Heart failure</td>
<td>2.2 (1.4–3.5)</td>
<td>3.2 (1.3–7.7)</td>
<td>2.4 (1.6–3.6)</td>
<td>3.0 (1.1–8.0)</td>
<td>1.5 (0.5–4.4)</td>
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<tr>
<td>Atrial fibrillation</td>
<td>2.7 (1.8–3.9)</td>
<td>2.4 (1.6–3.6)</td>
<td>1.6 (0.8–3.1)</td>
<td>2.1 (1.0–4.8)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.0 (0.6–1.7)</td>
<td>1.6 (0.8–3.1)</td>
<td>1.6 (0.8–3.1)</td>
<td>2.1 (1.0–4.8)</td>
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<tr>
<td>TIA</td>
<td>1.1 (0.7–1.9)</td>
<td>1.4 (0.7–2.8)</td>
<td>1.4 (0.7–2.8)</td>
<td>1.0 (0.4–3.0)</td>
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<tr>
<td>Peripheral atherosclerosis</td>
<td>1.3 (0.5–3.2)</td>
<td>3.0 (0.7–12.7)</td>
<td>2.0 (1.2–3.6)</td>
<td>2.5 (0.6–10.5)</td>
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<tr>
<td>Stroke severity (per NIHSS unit)</td>
<td>1.15 (1.12–1.17)</td>
<td>1.15 (1.12–1.17)</td>
<td>1.26 (1.16–1.37)</td>
<td>1.33 (1.21–1.46)</td>
<td>1.06 (0.99–1.12)</td>
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</tbody>
</table>

**Stroke Recurrence**

Of the 310 survivors, 27 had a new stroke within the year of follow-up. The overall 1-year probability of recurrence was 0.09 (95% CI, 0.06 to 0.12). The probabilities for different stroke subtypes were as follows: ICH, 0.09 (95% CI, 0.02 to 0.23); nonlacunar type of BI, 0.10 (95% CI, 0.05 to 0.14); lacunar type of BI, 0.03 (95% CI, 0.003 to 0.09); and UND, 0.29 (95% CI, 0.11 to 0.46). No significant differences were seen between men and women. Half of the patients (n=13) did not seek medical help for their recurrent stroke, which was recorded in the follow-up examination.

**Risk of Death**

To evaluate which risk factors were independent predictors of death within 1 year, Cox’s proportional-hazards regression analysis was used. The following explanatory variables were included: (1) age, (2) sex, (3) living alone, (4) cigarette smoking, (5) dementia, (6) hypertension, (7) ischemic heart disease, (8) heart failure, (9) atrial fibrillation, (10) diabetes mellitus, (11) previous transitory ischemic attack (TIA), (12) peripheral atherosclerosis, and (13) stroke severity as measured with the NIHSS. Because of obvious covariation between dementia and items 1b and 1c in the NIHSS (questions and commands), these items were excluded from this calculation.

The results of both the univariate analysis and the final Cox’s model (with 95% CIs and probability values) are shown in Table 2. Hypertension, diabetes, ischemic heart disease, and TIA variables were removed from the model because of a lack of significant association. The following variables were identified as the best predictors of death within 1 year: stroke severity, age, atrial fibrillation, and dementia. Because of the heavy impact of stroke severity on mortality, the model was also tried without stroke severity as an explanatory variable. Then, heart failure, in addition to age, atrial fibrillation, and dementia, was significant.

To further validate the model, age was divided into 4 categories (<72, 72 to 77, 78 to 84, >84 years), and stroke severity was dichotomized into mild stroke (NIHSS score <6) and severe stroke (NIHSS score ≥6). Obviously, this changed the numerical values of the hazard ratios, but it did not change which predictors were significant.

Cox’s regression was also performed on different stroke subtypes. Stroke severity, atrial fibrillation, and dementia were significant in patients with both BI and ICH, whereas age and heart failure were significant only in patients with BI. Although differences between sexes were small, the impact of age seemed somewhat larger on women, whereas atrial fibrillation and dementia had a larger impact on men.

**Risk of Dependency**

Logistic regression was used to determine the risk of dependency, defined as an MRS score ≥3, 1 year after a first-ever stroke in 253 survivors. The explanatory variables listed above were used. The results of both the univariate and the multivariate analysis (with 95% CIs and probability values) are shown in Table 2. Sex, hypertension, diabetes, ischemic heart disease, TIA, and peripheral atherosclerosis were not included in the multivariate model because of a lack of significant association in the univariate model. The following combination was identified as the best predictor of dependency after 1 year: stroke severity, age, heart failure, and dementia.

In a logistic regression model performed for BI only, diabetes mellitus, in addition to age and stroke severity, was a significant predictor of dependency. When logistic regression was performed on the sexes separately, heart failure was a significant predictor only in men, whereas age and stroke severity were significant in both sexes.

**Risk of Having a Recurrent Stroke**

Cox’s regression was used to evaluate which risk factors could predict a recurrent stroke within a year from the first stroke. The results are shown in Table 2. In the first step, all variables except age, ischemic heart disease, and dementia were removed because of a lack of significant association.
Age and dementia were identified as the best predictors of recurrence.

Discussion
This community-based stroke study has shown that prestroke dementia has an impact on outcome 1 year after stroke in terms of mortality and recurrence. Furthermore, atrial fibrillation affects mortality, and heart failure is associated with dependency after 1 year. Although our study is small compared with some longitudinal or multicenter studies, it has the advantage of a complete case ascertainment, including even cases managed outside the hospital, and a single investigator who evaluated patients at both baseline and the 1-year follow-up.

We have previously shown that prestroke dementia is a risk factor for initial stroke severity and for 28-day case fatality.27 Others have shown that dementia after stroke increases the risk of long-term stroke recurrence25 and shortens long-time survival26 and that patients with cognitive impairment have an increased risk of a first stroke.24,25 From the present study, it is also evident that prestroke dementia is a risk factor for death and stroke recurrence within 1 year. To the best of our knowledge, this has not been shown before. The common denominator between stroke and dementia may be apolipoprotein E 

Poprotein E

, which is linked to both sporadic and late-onset Alzheimer’s disease,26 as well as dementia with stroke.23 Patients expressing this apolipoprotein may be more vulnerable to a vascular insult.38 This has been discussed in more detail elsewhere.27 Because patients with dementia are at an elevated risk of having a first stroke,24,25 they may well be susceptible to a second stroke. However, it was not possible to show that prestroke dementia had any influence on dependency, although there was a tendency in that direction.

Atrial fibrillation is perhaps the most well-recognized cardiac risk factor. Atrial fibrillation increases stroke severity and early mortality,27,29 as well as late mortality, as this and other studies9–13 have shown. Atrial fibrillation is also associated with increased risk for a second ischemic stroke.16 The latter was not shown in the present study, which may be explained by the fact that 38% of the patients were on warfarin after the stroke compared with only 7% before. Also, the number of patients with recurrent stroke in this study was small, which negatively affects precision.

The negative impact of heart failure on late mortality5,6,10–12 is well documented. Prestroke heart failure is associated with more severe strokes,27 but the impact of heart failure on 1-year mortality in the present study was significant only in univariate analysis and when stroke severity was excluded from the multivariate analysis. The reason that heart failure is associated with more severe strokes remains unclear, although it may predispose to cardiac embolism, which gives rise to larger infarcts.40 Recently, it has been shown that the administration of an angiotensin-converting enzyme inhibitor (ramipril) to patients at high risk of cardiovascular events reduces the relative risk of stroke by 32%.41 There are also proposals for 2 studies comparing warfarin and antiplatelet agents in patients with low ejection fraction.40 The relationship between heart failure and stroke is certainly interesting because it may open new possibilities for prophylactic treatment. A more aggressive attitude toward investigation and treatment of heart diseases may already have had a part in lowering stroke mortality and morbidity in Western countries. Ryglewicz and coworkers45 found that ischemic strokes were more severe in Poland than in the United States. They also found that cardiac diseases (coronary disease, myocardial infarction, atrial fibrillation, and heart failure) were more frequent in Poland than in the United States, while the prevalence of hypertension, smoking, and diabetes mellitus was similar in the both countries.

Within a community-based study design, we have confirmed that age and stroke severity are risk factors for mortality and dependency within the first year after a first-ever stroke. We have also shown that ischemic heart disease, heart failure, and atrial fibrillation have adverse influence on long-term prognosis in different ways. The adverse effect of prestroke dementia on stroke severity and short-term survival27 continues to influence long-term survival. It seems that effective treatment of heart diseases, especially atrial fibrillation and heart failure, before and after a stroke may improve outcome. Further studies are needed to confirm the impact of dementia on stroke outcome, and the causal connection remains to be explored.

Acknowledgments
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References


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