Decreased Severity of Brain Infarct Can in Part Explain the Decreasing Case Fatality Rate of Stroke

Heikki Numminen, MD; Markku Kaste, MD; Kari Aho, MD; Olli Waltimo, MD; Mervi Kotila, MD

**Background and Purpose**—Case fatality rates for stroke have declined in most Western industrialized countries during recent decades. One possible explanation for this is a decrease in the severity of stroke symptoms. We therefore sought evidence for a change in stroke severity and its relationship with case fatality rates.

**Methods**—We compared the severity of symptoms among first-ever stroke patients in 2 population-based prospective stroke registers maintained during 1972 to 1973 and 1989 to 1991 in Finland. Patients who were evaluated by study assistants or the investigator during the first week after the onset of symptoms were included in the study, and their severity of symptoms was assessed with the use of comparable scales modified from the Scandinavian Stroke Scale.

**Results**—A total of 244 and 594 patients were registered, and a portion of them (155 [63.5%] and 360 [60.6%]) were included in the analyses in the registers for Espoo-Kauniainen from 1972 to 1973 and for 4 separate districts in Finland from 1989 to 1991, respectively. The death rates during the first week among those who were not included did not differ between the registers. The severity of symptoms decreased significantly between the registers in both patients with brain infarct or intracerebral hemorrhage but not in those with subarachnoid hemorrhage. The severity of symptoms was an independent factor of case fatality at 1 month.

**Conclusions**—The severity of symptoms of brain infarcts has decreased and can in part explain the decreased case fatality rate of stroke in Finland. However, the change in patients with intracerebral hemorrhage may be overestimated due to undiagnosed intracerebral hemorrhages in the first register resulting from the lack of brain CT. (Stroke. 2000;31:651-655.)

**Keys words:** cerebrovascular disorders ■ treatment outcome ■ mortality ■ prospective studies

The stroke mortality rate in Finland has declined steadily since 1965 in men and since 1955 in women,1 which is typical for most Western industrialized countries.2–5 This has occurred despite a stable incidence rate during the 1980s. The decreasing case fatality rates reported in the same studies3–5 are the most likely cause of this.

At least 3 explanations for the observed decrease in case fatality rates have been suggested: (1) enrollment bias during registration includes patients with milder strokes during subsequent years, (2) better supportive and rehabilitative care of acute stroke patients may have decreased the case fatality rate, and (3) the symptoms of acute stroke could have become milder, leading to increased survival rates.

To evaluate the impact of stroke symptoms, a valid method for the assessment of stroke severity is necessary. A retrospective method used in previous studies,6–11 which suggests that strokes are less disabling at the present than they were previously, may be too inaccurate or insensitive for this purpose. The present method, which is based on a prospectively used standard scale to evaluate the severity of symptoms modified from the Scandinavian Stroke Scale, avoids the difficulties involved in the previous studies. The aim of the present study was to compare the severity of stroke in 2 population-based registers during 1972 to 1973 and 1989 to 1991 in Finland and to determine the relationship between stroke severity and case fatality.

**Subjects and Methods**

The study area, population, case finding, and case ascertainment for the 2 registers have been published previously.5,12 The first register covered a semiurban area, Espoo-Kauniainen, from 1972 to 1973 (EK 72–73).12 The second register was maintained from 1989 to 1991 in 4 separate rural districts in Finland (FHA 89–91).5 The mean study population consisted of 113 100 and 134 804 inhabitants in the EK 72–73 and FHA 89–91 register regions, respectively. All patients with first-ever stroke and aged ≥15 years were registered and evaluated by the study assistants for the FHA 89–91 register or the investigator for the EK 72–73 register.12 The registers were maintained according to the guidelines of the World Health Organization (WHO) Stroke Register.13

The Scandinavian Stroke Scale14 was used for assessment of stroke severity in the FHA 89–91 register. It has a 4-grade scale for the evaluation of consciousness and a 5-grade scale for the evaluation of motor function in the arm and leg (Table 1). The WHO Stroke Register form, which assesses consciousness with a 4-grade scale,
was used in the EK 72–73 register. In addition, a 5-grade scale for the separate evaluation of motor function in the arm and leg was used in this register. It was possible to convert the raw data recorded in the EK 72–73 register to comparable values in the Scandinavian Stroke Scale (Table 1). In estimation of the severity of stroke, we used only level of consciousness, eye movements, and arm and leg power, which are known to correlate with case fatality. After these values were totaled, they constituted the score used to assess the severity of stroke. This severity score has a minimum of 0 points and a maximum of 22 points (from the most severe to the mildest stroke), which corresponds to the prognostic score used in the Scandinavian Stroke Scale. Only patients who were registered and evaluated during the first week after the onset of stroke symptoms were included in the analyses.

The severity scores are expressed as age-adjusted mean values and 95% CIs. We used $\chi^2$ tests with continuity correction (Statview; Abacus Concepts) and the exact test (Egret; Statistics and Epidemiology Research Corporation) to calculate differences in proportions. An ANOVA (SuperAnova; Abacus Concepts), with age as a covariate, was used to evaluate the differences in severity scores between the registers. The strength of association between the severity score and case fatality was analyzed with linear regression (Statview). Multiple logistic regression (Egret) was used to estimate the effect of various factors on case fatality rates. Factors used in these analyses included patient age and sex, severity score, subtype of stroke (infarct versus other types), and register (time period). Case fatality rates were also compared between the registers in subgroups of patients with brain infarcts (BIs): those with more severe symptoms (severity score 0 to 10), with moderate symptoms (severity score 10.5 to 19.5), and with milder symptoms (severity score 20 to 22).

In the FHA 89–91 register, conventional risk factors were recorded. Regression analysis was used to estimate the association of risk factors with the severity score. The available risk factors included treated hypertension, coronary heart disease, heart failure, atrial fibrillation, diabetes, and smoking. A combined factor, cardiovascular disease, was constituted if either hypertension, coronary heart disease, or heart failure was present. Other factors that were evaluated included age, sex, subtype of stroke, and the Rankin scale score to measure independence in activities of daily living before the onset of stroke.

### Results

A total of 244 and 594 patients with first-ever strokes were included in the EK 72–73 and FHA 89–91 registers, respectively, and a portion of them (155 [63.5%] and 360 [60.6%] patients, respectively) were investigated within 1 week after the onset of stroke and included in the analyses. Table 2 presents their number and case fatality according to stroke subtype and gender. The mean ages were 64.0 and 69.8 years for men and 64.5 and 75.3 years for women in the EK 72–73 and FHA 89–91 registers, respectively. In the EK 72–73 register, 15.2% (37 of 244) of the patients were excluded due to death during the first week and 21.3% (52 of 244) were excluded due to a delay in evaluation; respective values for the FHA 89–91 register were 11.3% (67 of 594) and 28.1% (167 of 594) (difference in death rates 3.9%, 95% CI 1.3% to 9.1%, $\chi^2=2.06$, $P=0.152$).

The severity score for all strokes has increased slightly (ie, strokes have become milder since 1973) (Table 3). The change was seen in BIs and intracerebral hemorrhages (ICHs)
but not in subarachnoid hemorrhages (SAHs). The increase in severity score is slightly less in females than in males with BI. The severity score is strongly associated with case fatality (slope 0.028, 95% CI 0.024 to 0.032, \(P = 0.001\), \(r^2 = 0.27\)) throughout the patient population (n = 515).

Table 4 presents the factors associated with case fatality rates for all strokes at 1 month after onset. In addition to the increase in severity score (ie, less severe stroke), low age, and having a stroke later (ie, included in the FHA 89–91 register) were independently associated with decreased case fatality rates. When only BIs were included in the analysis, having a stroke later (ie, included in the FHA 89–91 register) remained an independent factor even after adjustments to the severity score and patient age (Table 4). To analyze whether inclusion in the FHA 89–91 register had any effect on case fatality rates in different subgroups of patients with BIs, these patients were stratified according to their severity score. Case fatality rates for BI patients in the EK 72–73 register were 44% (34 of 77), 6% (6 of 96), and 2% (2 of 131). Despite the differences, the exact test did not show any significance in case fatality rate at 1 month between the registers (odds ratio 1.41, 95% CI 0.68 to 2.91, \(P = 0.41\)).

Because changes in stroke risk factors during recent decades have been associated with decreased stroke mortality rates, we wanted to analyze whether the presence of risk factors was associated with the severity of symptoms among patients in the FHA 89–91 register. However, only patient age (slope −0.12, 95% CI −0.17 to −0.07, \(P < 0.001\), \(r^2 = 0.06\)) and the Rankin scale score (slope −1.86, 95% CI −2.45 to −1.28, \(P = 0.001\), \(r^2 = 0.10\)) before the onset of stroke were significantly associated with the severity of stroke symptoms in a simple linear regression. Neither the stroke subtype nor the presence of cardiovascular disease or atrial fibrillation recorded at the onset of stroke was shown to be a significant factor.

**Discussion**

The severity of stroke symptoms among patients with their first-ever stroke has declined between 1973 and 1991 in Finland (ie, the essential signs of stroke, including motor hemiparesis, gaze paresis, and disturbed consciousness, are now milder than during previous decades); however, this change concerns only patients with BI and ICH. The change is overestimated in patients with ICH for methodological reasons discussed later. The results also show that the severity of stroke symptoms is a significant contributor to case fatality rate. In addition, the results indirectly support the hypothesis that better management of patients with BI could be another independent factor in case fatality rate.

Our results rely on the appropriate conversion of the severity scores into a modified Scandinavian Stroke Scale. We believe that the converted scores represent the original symptoms of patients as exactly as possible and thus are reliable, although the scales used were not originally the same. The assessment of stroke severity in both registers has occurred prospectively and simultaneously with the enrollment of patients by study assistants or the investigator. In addition, the conversion of scores was performed inflexibly with a microcomputer with the algorithm described in Table 1 without a review of medical records. The appropriate conversion of scales is supported by the observation that neither the severity score in patients with SAH in the present study nor case fatality rates throughout the study population of these patients changed. This is in agreement with the results of another Finnish study, in which the 3-week case fatality rates remained stable from the 1970s to the 1980s despite an intensified neurosurgical treatment policy that favored the hypothesis of a disastrous unchanged course in SAH, which was also observed at the Mayo Clinic.

One probable bias arose from the use of brain computed tomography, which was not available at the time of the EK 72–73 register, as a diagnostic tool. In the FHA 89–91 register, a CT scan was performed for 60% of patients. This naturally led to increased sensitivity in finding patients with a small ICH. Thus, the advent of cranial imaging might explain at least in part the changes in case fatality rates related to ICH. We argue, however, against the possibility that this

**TABLE 3. Age-Adjusted Mean of Severity Score (95% CI) According to Stroke Subtype and Gender and \(P\) Values for Significance of Difference Between Registers**

<table>
<thead>
<tr>
<th></th>
<th>EK 72-73</th>
<th>FHA 89-91</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI</td>
<td>13.3 (12.0–14.6)</td>
<td>15.5 (14.8–16.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Men</td>
<td>13.6 (11.9–15.4)</td>
<td>16.7 (15.6–17.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Women</td>
<td>13.1 (11.2–15.1)</td>
<td>14.6 (13.5–15.6)</td>
<td>0.198</td>
</tr>
<tr>
<td>ICH</td>
<td>7.5 (5.7–11.3)</td>
<td>14.9 (12.7–17.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Men</td>
<td>8.7 (7.1–16.4)</td>
<td>14.2 (11.8–16.7)</td>
<td>0.078</td>
</tr>
<tr>
<td>Women</td>
<td>6.5 (5.0–12.3)</td>
<td>16.4 (11.8–20.0)</td>
<td>0.008</td>
</tr>
<tr>
<td>SAH</td>
<td>17.1 (14.2–19.9)</td>
<td>14.6 (9.8–19.4)</td>
<td>0.358</td>
</tr>
<tr>
<td>Men</td>
<td>17.8 (12.5–23.2)</td>
<td>10.3 (0.0–21.2)</td>
<td>0.072</td>
</tr>
<tr>
<td>Women</td>
<td>16.8 (13.7–20.9)</td>
<td>16.1 (10.3–21.9)</td>
<td>0.818</td>
</tr>
<tr>
<td>NS stroke</td>
<td>16.6 (8.8–24.4)</td>
<td>3.5 (0.0–15.7)</td>
<td>0.025</td>
</tr>
<tr>
<td>Men</td>
<td>19.0 (5.4–32.6)</td>
<td>6.0 . . .</td>
<td>0.289</td>
</tr>
<tr>
<td>Women</td>
<td>10.0 . . .</td>
<td>2.0 . . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Total</td>
<td>13.4 (12.2–14.5)</td>
<td>15.4 (14.7–16.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Men</td>
<td>13.9 (12.3–15.5)</td>
<td>16.1 (15.1–17.1)</td>
<td>0.025</td>
</tr>
<tr>
<td>Women</td>
<td>12.9 (11.3–14.4)</td>
<td>14.9 (13.9–15.9)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

NS indicates nonspecific.

**TABLE 4. Effect of Various Factors on Case Fatality at 1 Month in Multiple Logistic Regression Analysis in All Patients and in Patients With BI**

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Patients With BI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>FHA 89-91</td>
<td>0.39</td>
<td>0.21–0.71</td>
</tr>
<tr>
<td>Age/1 y</td>
<td>1.03*</td>
<td>1.01–1.06</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.70</td>
<td>0.39–1.24</td>
</tr>
<tr>
<td>Stroke other than infract</td>
<td>1.91</td>
<td>0.95–3.83</td>
</tr>
<tr>
<td>Severity score/1 point</td>
<td>0.83*</td>
<td>0.79–0.86</td>
</tr>
</tbody>
</table>

*Change in the risk for death per unit change in the variable.
could also be the reason for the observed decrease in severity of symptoms among patients with BI, because patients with low severity scores (ie, severe stroke resulting from the ICH) were also most likely diagnosed in the first register, whereas the patients with slight symptoms and an undiagnosed ICH in the first register could have diluted the trend observed among patients with BI. The argument supporting this judgment is the fact that in the FHA 89–91 register, the mean severity score among patients with ICH was almost as high as the mean severity score among patients with BI. The BI results thus appear reliable, but those for ICH include bias due to the diagnostic differences between the registers.

Bias in patient registration is an unlikely reason for our results, because most of the patients enrolled in both registers were hospitalized during the acute phase of their stroke (89% and 86% in the EK 72–73 and FHA 89–91 registers, respectively), and in both time periods, all patients with severe strokes were hospitalized. The possibility, however, that more patients with mild strokes, especially BIs, were included in the FHA 89–91 register than in the EK 72–73 register cannot be ruled out. This is unlikely, however, because the incidence of BI in the FHA 89–91 register has not increased compared with the previous register; on the contrary, it has decreased slightly. In addition, the case fatality rates during the first week among the patients not included in the present analysis did not differ significantly between the registers, supporting the fact that mild strokes in both registers are registered with equal frequency within the first week after the onset of stroke.

In the few studies that evaluated trends in the severity of stroke, the assessment of symptoms was made retrospectively from medical records, which may have lead to either inaccuracy or insensitivity in the results compared with the present method. All of the investigators reached the same conclusion, however: the severity of stroke has declined during recent decades. The earliest observation is from the Framingham cohort, in which a significant increase in frequency of mild deficits was found from the 1950s to the 1970s. In the Minnesota Heart and Stroke Survey, the decreasing frequency in various stroke symptoms among hospitalized patients continued throughout the 1970s and 1980s. The WHO Monica project in northern Sweden also draws the conclusion that the proportion of patients with extensive motor deficits has declined during the late 1980s. Thus, the present prospective study confirms these earlier retrospective observations.

What are the reasons for the decreasing severity of symptoms? One possible explanation could be better general health of the population today than 2 decades ago. Reduction in the rate of stroke risk factors could be another reason. In all probability, changes in risk profile may in part be involved in the decreased mortality rates for stroke. In a recent publication from Finland, changes in conventional risk factors during the 1970s and 1980s could predict 71% of the observed fall in mortality rates for stroke in men and 54% of the fall in women. Although we were not able to compare changes between risk factors and case fatalities in the previous study, no association between the case fatality rate at 1 month and the cardiovascular risk factors could be found throughout the FHA 89–91 population, nor could any association be found in the present study between the cardiovascular risk factors and the severity of symptoms in all strokes. A similar conclusion could be drawn in a more detailed risk factor registration. Thus, the risk factors appear to play a minor role both in the case fatality rate and in the severity of symptoms when age, the subtype of stroke, and patient premorbid condition are accounted for.

Did medical treatment contribute to the decrease in stroke severity? To date, no evidence is available that any drug treatment, except thrombolytic therapy, which was not used among the registered patients, could influence stroke symptoms during the acute phase. There is some evidence, however, that aspirin treatment can contribute to a reduction in death and dependency caused by ischemic stroke in the long term, and the Chinese Acute Stroke Trial suggested that patients treated with aspirin could have a better early functional outcome. The use of aspirin before the appearance of SAHs could reduce the risk of ischemic complications. On the other hand, neither a population-based study nor a prospective survey that evaluated hospitalized stroke patients within 24 hours after admission could find any supportive evidence for the favorable effect of aspirin on the severity of stroke. The use of anticoagulant or antithrombotic treatment was not registered in the present study, and accordingly this question cannot be evaluated, but this possibility must be considered in future surveys.

The results of the logistic regression analysis show that in addition to the severity of symptoms among patients with BI, the time period of the register also exerted an independent positive effect on case fatality rates. Whether this effect is dependent on the above-mentioned possibilities of reducing the rate of stroke risk factors and medical treatments or on better prevention of complications and early rehabilitative care of acute stroke patients cannot be answered here. The lack of evidence for the association of stroke risk factors and case fatality, as well as medical treatments and case fatality, favors the assumption that better overall care of patients with BI could also influence case fatality rates.

Our conclusion is that the severity of ischemic BI has decreased and that this change could in part explain the decrease in case fatality rates observed in Western countries during the recent decades. Both the lack of any other evidence for the decrease in case fatality rates and the finding of the register time period as an independent factor contributing to the case fatality rate indirectly support the role of better patient care as another explanation for the decrease in case fatality rates, which tallies with the observation of the Stroke Unit Trialists’ Collaboration.

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References


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