Acute and Long-Term Increase in Fracture Risk After Hospitalization for Stroke

John Kanis, MD; Anders Oden, PhD; Olof Johnell, MD

Background and Purpose—The aims of this study were to determine the magnitude of the increase in fracture risk after hospitalization for stroke, and in particular to determine the time course of this risk.

Methods—The records of the Swedish register of patients admitted during 1987–1996 were examined to identify all patients who were admitted to the hospital for stroke. Patients were followed for subsequent hospitalizations for hip and all fractures combined. We analyzed 16.3 million hospitalizations, from which 273,288 individuals with stroke were identified. A Poisson model was used to determine the absolute risk of subsequent fractures and the risk compared with that of the general population.

Results—After hospitalization for stroke, there was a >7-fold increase in fracture risk, including that for hip fracture within the first year after hospitalization for stroke. Thereafter, fracture risk declined toward, but did not attain, the baseline risk except in men and women aged ≥80 years.

Conclusions—The high incidence of new fractures within the first year of hospitalization for stroke suggests that such patients should be preferentially targeted for treatment. It is possible that short courses of treatment at the time of stroke would provide important therapeutic dividends. (Stroke. 2001;32:702-706.)

Key Words fractures, spontaneous ■ hip fractures ■ prospective studies ■ stroke

StROKE is a well-documented risk factor for hip fracture. Population studies suggest that the risk of fracture is increased approximately 2- to 4-fold.1–5 Hip fracture occurs most commonly on the paretic side and is usually trochanteric, most likely due to a high risk of falling on the affected side.3 Although less extensively studied, an increase in risk is seen in men as well as in women.5,6 A gap in our epidemiological knowledge of relevance to treatment is whether the risk of fracture is highest in the months after stroke or remains consistently increased.

We have shown in a previous study that the risk of all fractures, including that of hip fracture, increases markedly after hospitalization for vertebral fracture. The increase in risk was particularly evident in the first year immediately after a vertebral fracture, and rates declined thereafter toward that of the general population.7 The increase in risk was much greater than that likely on the basis of changes in bone density, suggesting that other factors associated with hospitalization were important for the transient increment in risk.

The aims of the present study were to examine whether stroke might be associated with a transient increase in risk after the acute event. If a high but transient risk of fracture occurred, this might suggest that interventions could be offered to cover this acute period of risk rather than for the remaining lifetime of individuals. The aim of the present study was therefore to determine the time course of any increase in fracture risk after stroke.

Subjects and Methods
We studied 16.3 million admissions to Swedish hospitals during 1987–1996. Our source was the National Swedish Register (the patient register of the National Board of Health and Welfare), which documents each hospital admission. A unique personal identifier permitted the tracking of individuals for multiple admissions. All patient records were examined to identify individuals who were admitted to the hospital for a stroke during the 10-year interval. Patients with International Classification of Diseases codes 430 to 436 were included. In cases in which an individual had ≥1 separate admission for stroke during 1987–1996, the patient was followed from the first event.

After hospitalization for stroke, we followed each patient by code concordance to identify fractures from the event up to 1996. Fractures at the time of first admission to the hospital in association with stroke were not included. Subsequent fractures were categorized according to site. For the purposes of this report we include the subsequent risk of any fracture requiring hospitalization and of hip fracture.

We calculated the risk function of a fracture, judged indirectly by hospitalization for a fracture, over a period of 10 years. The probability of fracture within a specified period was calculated by the hazard function and the death hazard. Hazard function estimates were made for age, sex, and site of new fracture. The relative risk and incidence of fractures were calculated with allowance for a different change of risk with change of age above and below 65.
years. The incidence of fractures was compared with the incidence of the same fracture or group of fractures in the entire population of Sweden (patient register of the National Board of Health and Welfare).

The hazard function of a new fracture after the stroke was estimated in men and in women separately by the use of a Poisson model. The hazard function was estimated as follows:

$$
\exp(\beta_0 + \beta_1 \text{min}(\text{age}, 65) + \beta_2 \text{max}(\text{age}, 65) + \beta_3 \text{min}(\text{time}, 1) \\
+ \beta_4 \text{max}(0, \text{min}(\text{time} - 1.2) + \beta_5 \text{max}(0, \text{time} - 3))
$$

where time is time period (years) since the patient was admitted to the hospital for the stroke. Truncation to the left was applied at the time when the patient left the hospital after the stroke. Censoring to the right was applied if the patient died without a previous fracture or if the patient survived to the last day of December 1996 without a fracture. The function was continuous as a function of age and time period and allowed different rates of increase and decrease in different intervals. The model also included an additional variable “days in hospital” to examine the possible importance of the duration of hospitalization on fracture risk. The technique of calculation and the interpretation of the $\beta$ coefficients are the same as for the Cox model, but the Poisson model made it possible to assess the effect of time period since the stroke.

**Results**

The baseline risk of all fractures and for hip fractures in 1992 is shown in Table 1 for the general population. Of 16.3 million hospitalizations, we identified 273,288 patients hospitalized for a stroke during 1987–1996 (Table 2). Nine percent had subsequent fracture (8875 men and 15,791 women), and 14,263 had a hip fracture (52%) (4988 men and 9275 women). The mean duration of follow-up was 2.54 years, with a maximum of 10 years.

The incidence of all fractures and hip fractures in stroke patients by age compared with the general population is shown in Figure 1. For any fracture requiring hospitalization, the risk ratio (RR) was greatest in the younger age groups (RR, 2.38 to 4.69) and declined with age but was still increased in the population aged ≥95 years (RR, 1.43 to 2.64). Risks were higher in women than in men. Thus, the highest risks were seen in young women. The increase in risk was most marked immediately after the stroke, intermediate at 6 months, and lowest at 4 years.

For hip fracture, a pattern of risk was observed with regard to age, sex, and time after stroke that was similar to that observed for all fractures (Figure 1). The RR were, however, much higher for hip fracture. For example, the risk of any fracture requiring hospitalization immediately after stroke was 3.72 in women aged 50 to 54 years, and the risk for hip fracture was 11.75.

With the use of the Poisson model, the incidences of hip fracture and any fracture were compared at specific ages according to time after stroke (Figure 2). At all ages and in both sexes, there was a marked increase in risk within the first year compared with that of the general population. Therefore, the risk decreased but did not approach that of the general population except in the elderly. The difference between the acute increase in risk was therefore most marked in the younger patients. At the age of 72 years, the excess risk for hip fracture (stroke population risk/population risk) was increased by >300% at the time of stroke and remained 23% higher 8 years after the event (Table 3).

For both hip fracture and all fractures, the risk was related to the duration of hospital stay for stroke ($P<0.0001$) except for hip fracture among women ($P>0.30$). The relationship between fracture risk and hospital stay differed between sexes. In men the risk of any fracture increased by 2.3% for every additional 10 days in hospital, and for hip fracture the risk increased by 4.0%. In contrast, the risk decreased in women with duration of hospital stay by 1.1% for all fractures, but there was no correlation for hip fracture.

**Discussion**

The present study confirms the finding of many other studies indicating an increase in fracture risk after a stroke. The
present study shows, however, that the excess risk is not uniform with time and differs according to age. For all fractures as well as for hip fractures, the excess risk was most marked in the year after stroke and declined thereafter. Risk declined to an asymptotic value that paralleled that of the general community. The older the population, the lower was the relative risk, but the relative risk still substantially increased at all ages.

The limitations of this study include errors of coding for both stroke and fracture. Fractures were not verifiable by x-rays or other independent assessment. Errors of coding would, however, tend to minimize any apparent difference in risk between patients with stroke and the general population. An additional limitation is that we assessed only events that required hospitalization. Whereas most subjects with hip fractures are admitted to the hospital, subjects with many other fractures, including forearm and vertebral fractures, are not hospitalized.

An additional limitation is that we included all patients characterized as having stroke irrespective of whether this was associated with hemiplegia. The risk of hip fracture is likely to be higher in patients with hemiplegia. In a previous case-control study in southern Europe, stroke with hemiplegia was associated with a significant increase in relative risk of 2.42; in contrast, stroke without residual hemiplegia was associated with a much lower increase in risk (RR, 1.51; \( P_{\text{NS}} \)), as was transient ischemic attack. These findings suggest that the inclusion of all strokes would diminish differences in risk between patients and controls and that the risks in patients with hemiplegia would be much greater than reported here.

The strength of this study is that it covers the National Patient Register for the whole country, and the register itself is known to have high validity. A very small minority of patients may be lost to follow-up by leaving the country. The

Figure 1. Relative risk of any fracture (top) and hip fracture (bottom) in men and women by age at the times shown (0, 6 months, and 4 years) after a stroke.

Figure 2. Time course of fracture risk in men and women aged 62, 72, and 82 years after a stroke requiring hospitalization and in the general population.
Our findings relate only to events that come to hospital attention. The risks of fracture or hip fracture that we describe relate to patients who are admitted to the hospital for stroke. Thus, the pattern of acute and long-term risk that we describe may not pertain to individuals with stroke who are not admitted to the hospital. Indeed, it is likely that those admitted to the hospital have excess comorbidity and more severe lesions, and this may have contributed to the acute as well as the residual increase in fracture risk. In addition, the need for hospitalization implies that a degree of immobility occurred, and this too may have contributed to an increase in risk that may not pertain to individuals with stroke who are not admitted to the hospital.

Similarly, our data on fracture risk relate only to fractures requiring hospitalization. Since not all subjects with fractures are admitted to the hospital, the absolute risk will have been underestimated. In the case of hip fracture, ascertainment would be nearly complete, but for distal forearm fractures it has been estimated that <20% of subjects are hospitalized.9,10

Stroke is a well-recognized risk factor for hip fracture. The average increase in risk is approximately 2-fold. In our study patients hospitalized for stroke had a >4-fold increase in risk of having a hip fracture in the immediate poststroke period compared with the general population; in men or women aged 50 to 54 years, the risk was increased as much as 8- to 12-fold. Thereafter, the risk decreased to that observed in other studies. The time course of the pattern of risk for hip fracture and other fractures may be related to comorbidity or to immobilization. Both have been associated with a significant increase in fracture risk.2,9 Rates of bone loss as great as 2% per week have been observed during prolonged bed rest and would be expected to also have consequences for trabecular connectivity of cancellous bone.15–17 Destruction of normal skeletal architecture may be irreversible and contribute to persistent osteopenia, particularly in adults.11,18–20

Table 3. Risk and Excess Risk of Hip Fracture in Women Aged 72 Years at Time of Stroke

<table>
<thead>
<tr>
<th>Time, y</th>
<th>Fracture Incidence, Rate/1000</th>
<th>Population Fracture Risk, Rate/1000</th>
<th>RR</th>
<th>Excess Risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>28.7</td>
<td>6.2</td>
<td>4.63</td>
<td>363</td>
</tr>
<tr>
<td>0.5</td>
<td>23.2</td>
<td>6.9</td>
<td>3.36</td>
<td>263</td>
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<tr>
<td>1</td>
<td>18.8</td>
<td>7.6</td>
<td>2.47</td>
<td>147</td>
</tr>
<tr>
<td>2</td>
<td>18.5</td>
<td>9.0</td>
<td>2.06</td>
<td>106</td>
</tr>
<tr>
<td>3</td>
<td>18.3</td>
<td>10.3</td>
<td>1.78</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>19.3</td>
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</tr>
<tr>
<td>8</td>
<td>23.7</td>
<td>19.3</td>
<td>1.23</td>
<td>23</td>
</tr>
</tbody>
</table>

Aged 72 Years at Time of Stroke

There are several clinical implications of these findings. First, the magnitude of the acute risk is such that all patients with stroke requiring hospital attention should receive treatment. Falling is the major cause of hip fracture. Approaches to treatment include functional exercises and improvements to the environment to prevent falls. Whereas these measures may decrease the risk of falling, the magnitude of the effect and their effect on hip fracture risk have been disappointing.21,22 Another approach is to decrease the impact of falling with the use of hip protectors. Controlled trials suggest that hip protectors confer considerable protection against hip fracture risk, but compliance is a problem.23,24 An additional possibility is pharmaceutical intervention to strengthen bone. Current clinical guidelines suggest that patients with risk factors such as stroke should be referred for bone density measurements, and only those patients with osteoporosis should be treated. Second, it is possible that the acute increment in risk in the first few years after stroke might be amenable to therapeutic intervention. If this were so, then short-term treatments, rather than a commitment to treatment for many years, may provide worthwhile clinical dividends.

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References


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