Quality of hospital care and health outcomes after stroke
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IMPACT OF STROKE TYPE ON
SURVIVAL AND
FUNCTIONAL HEALTH
ABSTRACT

Background and purpose
In a cohort of 760 consecutive stroke patients (23 hospitals in the Netherlands), we studied prognosis in relation to stroke type and focused on (a) short-term and long-term mortality, and (b) long-term functional health.

Methods
Based on clinical and CT data, we distinguished infratentorial strokes from supratentorial strokes (lacunar infarctions, (sub)cortical infarctions and intracerebral hemorrhages).

Results
Cumulative mortality for all stroke patients was 34% at 6 months, 51% at 3 years, and 62% at 5 years. Short-term mortality could be explained by stroke type, whereas long-term mortality could not. Of all survivors, 55% was in poor functional health at 6 months, 49% at 3 years and 42% at 5 years. Long-term functional health outcomes were associated with stroke type.

Conclusion
We conclude that the impact of stroke type on mortality is limited to the first 6 months whereas the type of stroke influences the long-term functional health.
6.1 Introduction

The prognosis of stroke patients is generally expressed in terms of mortality. The studies show a high mortality during the first weeks after the onset of stroke and an increased risk of death until at least 5 years thereafter. Factors associated with a higher mortality are older age, severe stroke and concomitant cardiovascular diseases. Mortality also differs between the various pathophysiological stroke types. Patients with an intracerebral hemorrhage are more likely to die within the first weeks than those with a cerebral infarction, whereas patients with a lacunar infarction are less likely to die than patients with (sub)cortical infarctions. Yet, only a few large studies specifically focus on the relationship between stroke type and long-term survival.

Stroke not only reduces the life expectancy, but has also a major impact on the patients' functional health. The majority of the prognostic studies on functional outcomes focus on basic daily activities and were often performed in rehabilitation centers. Consequently, the results of these studies are not representative for the total stroke population. Moreover, data on the relationship between stroke type and long-term functional health outcomes are rare.

The objective of this study was to analyze the impact of stroke type on (a) the mortality within the first 6 months, and between 6 months and 5 years, and (b) functional health status 5 years after stroke.

6.2 Patients and methods

Hospital data
The study group comprised 760 patients consecutively admitted for stroke (within 1 week after onset) to 23 Dutch hospitals, which were randomly selected from an urban (n=17) and a rural (n=6) region after stratification for hospital size. Patients were considered to have had a stroke if there was a focal neurological deficit of sudden onset that lasted at least 24 hours with no known alternative to a vascular cause. Included were first and recurrent strokes. Excluded were patients with a transient ischaemic attack (symptoms < 24 hours) or a subarachnoid hemorrhage.
After hospital discharge, trained research assistants evaluated the patients' medical and nursing records for stroke type, stroke severity, age, sex, previous strokes, and cardiovascular and non-cardiovascular co-morbid diseases.

Stroke type was determined by Computed Tomography (CT) (available for 681 patients; 90%) and by clinical features.\textsuperscript{15,16} We used the evaluations of local radiologists to interpret the CT scans. Furthermore, all CT data were checked by a neurologist (M.L.). We distinguished infratentorial strokes from supratentorial strokes. The latter were subdivided into lacunar infarctions, (sub)cortical infarctions and intracerebral hemorrhages. Stroke severity upon admission was defined by the Glasgow Coma Scale.\textsuperscript{17} A patient was considered to have suffered a severe stroke if the score on the Eyes or Motor component was less than maximal. Because of possible aphasia, we did not use the Verbal component of the instrument. Cardiovascular co-morbid diseases were present if one or more of the following diseases were noted on the patients' charts: cardiac disease (atrial fibrillation, heart failure or myocardial infarction); hypertension (defined as 2 recordings of diastolic blood pressure > 100 mmHg within the first 24 hours after hospital admission or previously diagnosed); peripheral vascular disease and diabetes mellitus. Non-cardiovascular co-morbidity was defined as: musculoskeletal diseases, chronic obstructive pulmonary disease and mental decline. Hospital data was collected between June 1991 and August 1992. The study was approved by the medical ethical committees of the participating hospitals. All patients or their proxies gave informed consent.

Follow-up data
All patients were contacted for a structured face-to-face interview 6 months, 3 years, and 5 years after stroke. In all, seven patients were lost to follow-up. In case of death, the date was retrieved via a family member, the GP or a Registry Office. Of all 502 six months survivors, 17 declined to participate in the follow-up interview. At three years, 9% of the surviving patients declined to participate (34/372), and at 5 years 11% declined (32/289). Data about the functional health of the survivors were collected with the Rankin Scale, ranging from 0 (no symptoms) to 5 (totally
dependent).\textsuperscript{18,19} Patients with a Rankin score of 3, 4 or 5 (not able to live a fully independent life) were considered to have a poor functional health.

\textit{Statistical analyses}
Survival curves for all patients and for the different stroke types were estimated by the Kaplan-Meier method. Survival was compared with an age-matched cohort from the Dutch population, using the Dutch death probabilities over the period 1990 to 1994 (data: Statistics Netherlands, The Hague).\textsuperscript{20} We analyzed the association between stroke type and time to death with the Cox proportional-hazards model; patients without CT data were excluded. Because of the shapes of the survival curves, the impact of stroke type on mortality was analyzed separately for two periods. Short-term mortality (up to 6 months) was analyzed in the first model and long-term mortality (6 months to 5 years) in the second. First, an unadjusted analysis (only stroke type) was performed, then we added age, sex, previous strokes and (cardiovascular and non-cardiovascular) co-morbidity to the Cox model. Finally, in the full model we included stroke severity. In all models, ties were handled according to the Efron's method.\textsuperscript{21} Relative risks (RR) were calculated with their 95% confidence intervals (CI). Similarly, the association between stroke type and long-term poor functional health in the 5-years survivors was analyzed with logistic regression. First, we performed an unadjusted analysis (only stroke type), then a logistic model adjusting for age, sex, previous strokes and co-morbidities, and finally the full model which included stroke severity. Effect sizes were expressed in odds ratios (OR) with their 95% confidence intervals (CI). After adjusting for stroke types, we also assessed the impact of the other prognostic factors (age, sex, previous stroke, co-morbidities, stroke severity) on long-term mortality (6 months-5 years) and long-term functional health (5-years survivors). For these analyses, we also used Cox proportional-hazards and logistic regression.

6.3 Results
The mean (SD) age of the 760 patients was 73.0 years. (11.8), and 48% was female (Table 1).
## Table 1. Characteristics of 760 hospitalized stroke patients according to type of stroke

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients N=760</th>
<th>Infrastructural stroke n=89</th>
<th>Lacunar infarction n=107</th>
<th>(sub)Cortical infarction n=373</th>
<th>Intracerebral Hemorrhage n=112</th>
<th>No. CT n=79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>73.0 (11.8)</td>
<td>69.3 (11.5)</td>
<td>69.9 (10.4)</td>
<td>73.3 (11.9)</td>
<td>73.5 (12.4)</td>
<td>79.2 (9.4)</td>
</tr>
<tr>
<td>Median</td>
<td>75.0</td>
<td>72.7</td>
<td>70.3</td>
<td>75.0</td>
<td>75.9</td>
<td>79.8</td>
</tr>
<tr>
<td>Female</td>
<td>366 (48%)</td>
<td>39 (44%)</td>
<td>51 (48%)</td>
<td>186 (50%)</td>
<td>50 (45%)</td>
<td>40 (51%)</td>
</tr>
<tr>
<td>Previous strokes</td>
<td>147 (19%)</td>
<td>27 (30%)</td>
<td>12 (11%)</td>
<td>71 (19%)</td>
<td>17 (15%)</td>
<td>20 (25%)</td>
</tr>
<tr>
<td>Cardiovascular co-morbidity*</td>
<td>558 (73%)</td>
<td>69 (78%)</td>
<td>73 (68%)</td>
<td>287 (77%)</td>
<td>75 (67%)</td>
<td>52 (66%)</td>
</tr>
<tr>
<td>Non-cardiovascular co-morbidity†</td>
<td>319 (42%)</td>
<td>32 (36%)</td>
<td>39 (36%)</td>
<td>160 (43%)</td>
<td>51 (46%)</td>
<td>37 (47%)</td>
</tr>
<tr>
<td>Severe stroke‡</td>
<td>185 (24%)</td>
<td>23 (26%)</td>
<td>2 (2%)</td>
<td>75 (20%)</td>
<td>52 (46%)</td>
<td>33 (42%)</td>
</tr>
</tbody>
</table>

*Presence or history of: cardiac disease (atrial fibrillation, heart failure or myocardial infarction), hypertension, peripheral vascular disease, or diabetes mellitus; †presence or history of: musculoskeletal disease, chronic obstructive pulmonary disease, or mental decline; ‡defined as a less than maximal score on the Eyes or Motor component of the Glasgow Coma Scale

CT data were not available of 79 patients, foremost because of death shortly after admission. Eighty-nine of the 681 patients suffered an infratentorial stroke and 592 a supratentorial stroke (lacunar infarction 107, (sub)cortical infarction 373, intracerebral hemorrhage 112).

**Stroke type and mortality**

The cumulative mortality was 34% (258/760) at 6 months, 51% (388/760) at 3 years, and 62% (471/760) at 5 years. The mortality during the first six months was 11 times higher than that of the general Dutch population of the same age and sex. After the first 6 months and up to 5 years, the mortality was about twice as high (Figure 1).
Figure 1  Five-year survival after stroke (n = 760, 366 women and 394 men), and five-year survival for an age-matched cohort from the Dutch population.

Mortality markedly differed for the various stroke types (Figure 2).

Figure 2  Five-year survival after stroke in relation to stroke type: lacunar infarction, infratentorial stroke, (sub)cortical infarction and intracerebral hemorrhage.
The differences in mortality according to stroke type were most prominent during the first 6 months after stroke (Figure 2). During this period, 8% of the patients with a lacunar infarction died (reference group), 28% of the patients with an infratentorial infarction (unadjusted RR = 4.1; 95% CI 1.9-8.7), 33% of the patients with a (sub)cortical infarction (unadjusted RR = 4.6; 95% CI 2.3-9.0), and 46% of the patients with an intracerebral hemorrhage (unadjusted RR = 7.8; 95% CI 3.8-15.9) (Table 2). After adjusting for age, sex, previous strokes and co-morbidity, the mortality differences between stroke types hardly changed. When we added the stroke severity to the model, the differences in short-term mortality between various stroke types became smaller (Table 2).

Table 2. Association between stroke type and short-term mortality (onset to 6 months) for 681 patients with CT data; and between stroke type and long-term mortality (6 months to 5 years) for 465 patients with CT data who survived the first 6 months*

<table>
<thead>
<tr>
<th>Short-term mortality</th>
<th>Adjusted for Age, sex, previous strokes, and co-morbidity</th>
<th>Adjusted for Age, sex, previous strokes, co-morbidity, and stroke severity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of stroke</strong></td>
<td><strong>Unadjusted</strong></td>
<td><strong>Adjusted</strong></td>
</tr>
<tr>
<td>Lacunar infarction</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>Infratentorial stroke</td>
<td>4.1 (1.9-8.7)</td>
<td>4.0 (1.9-8.7)</td>
</tr>
<tr>
<td>(sub)Cortical infarction</td>
<td>4.6 (2.3-9.0)</td>
<td>4.0 (2.0-7.8)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>7.8 (3.8-15.9)</td>
<td>7.0 (3.4-14.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long-term mortality</th>
<th>Adjusted for Age, sex, previous strokes, and co-morbidity</th>
<th>Adjusted for Age, sex, previous strokes, co-morbidity, and stroke severity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of stroke</strong></td>
<td><strong>Unadjusted</strong></td>
<td><strong>Adjusted</strong></td>
</tr>
<tr>
<td>Lacunar infarction</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>Infratentorial stroke</td>
<td>1.0 (0.6-1.7)</td>
<td>0.9 (0.5-1.5)</td>
</tr>
<tr>
<td>(sub)Cortical infarction</td>
<td>1.6 (1.1-2.3)</td>
<td>1.2 (0.8-1.9)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>1.5 (0.9-2.5)</td>
<td>1.2 (0.7-2.0)</td>
</tr>
</tbody>
</table>

* Relative Risk (RR) and 95% Confidence Interval (CI)
The 6 months survivors showed only a moderate association between stroke type and mortality up to 5 years in the unadjusted analyses. Patients with (sub)cortical infarctions (RR = 1.6; 95% CI 1.1-2.3) were more likely to die than those with lacunar infarctions (reference group). After adjusting for the other prognostic factors (age, sex, previous stroke, co-morbidity, and stroke severity), we found no significant independent impact of stroke types on the long-term mortality (Table 2).

*Stroke type and long-term functional health*

Six months after stroke 55% (277/502) of the survivors had a poor functional health. After 3 and 5 years respectively 49% (184/372) and 42% (122/289) of the survivors reported poor functional health. Of the patients who survived up to five years, those with (sub)cortical infarctions (unadjusted OR = 3.2; 95% CI 1.7-6.3) and intracerebral hemorrhages (unadjusted OR = 2.4 95% CI 1.0-5.8) had a higher risk of long-term poor functional health than patients with lacunar infarctions (Table 3). These odds ratios remained unchanged after adjusting for age, sex, previous stroke and co-morbidities. After adding stroke severity (full model), the OR of patients with hemorrhages decreased to a statistically non-significant OR of 2.1 (95% CI 0.7-6.3) (Table 3).

Table 3. Association between stroke type and long-term (5 years) poor functional health for 235 patients with CT data who survived up to 5 years*

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Unadjusted</th>
<th>Adjusted for age, sex, previous strokes, and co-morbidity</th>
<th>Adjusted for age, sex, previous strokes, co-morbidity, and stroke severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacunar infarction</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>Infratentorial stroke</td>
<td>0.8 (0.3-1.9)</td>
<td>0.6 (0.2-1.6)</td>
<td>0.5 (0.2-1.4)</td>
</tr>
<tr>
<td>(sub)Cortical infarction</td>
<td>3.2 (1.7-6.3)</td>
<td>3.7 (1.8-7.8)</td>
<td>3.4 (1.6-7.4)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>2.4 (1.0-5.8)</td>
<td>2.9 (1.0-8.1)</td>
<td>2.1 (0.7-6.3)</td>
</tr>
</tbody>
</table>

*Odds ratio (OR) and 95% confidence Interval (CI)*
Impact of other prognostic factors on mortality and functional health

The impact of the other prognostic factors on the long-term mortality and functional health of the patients, after adjusting for stroke types, is summarized in Table 4.

Female stroke patients were less likely to die than men (adjusted RR = 0.8; 95% CI 0.6-1.0), but more female survivors were in a poor functional health (adjusted OR = 1.8; 95% CI 1.0-3.5). Older age, previous stroke and co-morbidities had about the same impact on mortality and poor functional health. Stroke severity was the main prognostic factor for a poor functional outcome (adjusted OR = 7.0; 95% CI 1.7-28.8).

Table 4. For stroke type adjusted predictors of long-term mortality (6 months survivors) and long-term poor functional health (5-years survivors).

<table>
<thead>
<tr>
<th></th>
<th>Mortality RR (95% CI*)</th>
<th>Poor functional health OR (95% CI†)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=465</td>
<td>n=235</td>
</tr>
<tr>
<td>Age per 10 year increment</td>
<td>2.1 (1.7-2.4)</td>
<td>2.1 (1.6-2.9)</td>
</tr>
<tr>
<td>Females</td>
<td>0.8 (0.6-1.0)</td>
<td>1.8 (1.0-3.5)</td>
</tr>
<tr>
<td>Previous strokes</td>
<td>1.4 (1.0-2.0)</td>
<td>2.3 (0.9-6.4)</td>
</tr>
<tr>
<td>Cardiovascular co-morbidity</td>
<td>1.1 (0.8-1.5)</td>
<td>1.2 (0.6-2.4)</td>
</tr>
<tr>
<td>Non-cardiovascular co-morbidity</td>
<td>1.5 (1.1-1.9)</td>
<td>2.0 (1.0-3.9)</td>
</tr>
<tr>
<td>Stroke severity</td>
<td>1.6 (1.1-2.5)</td>
<td>7.0 (1.7-28.8)</td>
</tr>
</tbody>
</table>

* Relative Risk and 95% Confidence Interval (Cox proportional-hazards model)
† Odds Ratio and 95% Confidence Interval (logistic regression model)

6.4 Discussion

With our Dutch multicentre study of 760 hospitalized patients, we could confirm the overall poor prognosis after stroke. After 5 years, 62% of the cohort had died, whereas 42% of the survivors was in a poor functional health.

Stroke type and mortality

A marked contrast in mortality was observed between patients with different stroke types in the first 6 months. Patients with lacunar
Stroke type, survival and functional health

Infarction had the lowest risk to die, 92% of them were still alive at 6 months. We found the highest mortality in patients with hemorrhage; about 55% was alive at 6 months. About 70% of patients with infratentorial infarction and (sub)cortical infarction was alive at 6 months. Our 6 months mortality for patients with a lacunar infarction was comparable to that found by Bamford and colleagues, but was somewhat higher than described by the research group of Salgado (mortality after 1 year: 5%). Salgado, however, also included patients treated on an outpatient basis. These patients are likely to be healthier. Our high mortality for patients with an intracerebral hemorrhage compare well with those reported by others.

Our results indicate that differences in short-term mortality were primarily explained by the combination of stroke type and stroke severity. However, in the patients who survived the first 6 months, we could not demonstrate an independent impact of stroke type on the mortality up to 5 years. Older age, male gender, previous stroke, the presence of pre-existent conditions and the severity of stroke largely explained the long-term survival.

Stroke type and poor functional health

A different picture emerged from the analysis of functional health. We found an independent association between stroke type and poor functional health status at 5 years. Especially, patients with (sub)cortical infarction and, to a lesser extent, patients with hemorrhages were more likely to be in a poor functional health than those with lacunar infarction. Cognitive disturbances in stroke types which involve the cortical regions, appear to be the most likely explanation for this finding. Although the mortality after intracerebral hemorrhage is high, the health of the survivors is not worse than for patients who survive a large (sub)cortical infarction. In an earlier study, we demonstrated this for the functional outcomes up to 6 months, in the present study we observed this effect up to 5 years.

Furthermore, a poor functional health was significantly associated with older age, non-cardiovascular co-morbidity, and stroke severity. The impact of these factors on the functional health of the patients was more or less similar to the impact on the mortality. An interesting finding was the difference between male and female stroke patients. In our cohort, women
had a lower mortality than men. However, women were more likely to be in a poor functional health. This might suggest that more men with an initially poor functional health status died, leading to a group of male patients in a relatively good health. Another explanation may be related to our definition of functional health in terms of the ability to live independently. This means that household activities play a dominant role. In this older cohort, women may encounter these problems more often.

Methodological considerations
The first issue to be considered is selection bias. Are our results representative for the whole population of stroke patients? About 20-35% of all stroke patients in the Netherlands is not admitted to a hospital\textsuperscript{26,27}, these either concern patients with a very poor prognosis or with a rapidly reversible stroke. However, the mortality we found was remarkably similar to other community-based studies. Moreover, compared to the general population, the excess mortality risk\textsuperscript{1,3,7,8} we found in our stroke population was also in agreement with other studies.\textsuperscript{1,6,28,29} These findings suggest a limited selection bias in our study.

In our analyses on stroke type and long-term functional health we studied all patients who survived the first 6-months, including those who were already functionally impaired. Repeated analysis with only the healthy 6 months survivors (n = 121; data available upon request) demonstrated that the association between the type of stroke and the long-term functional health was even more pronounced. Although the results were not statistically significant (small number of patients studied), they support our conclusion that the type of stroke influences the long-term health outcomes.

We achieved a high rate of CT scanning, 90% of our stroke patients. The most common reason for the absence of a CT scan in our study was that patients died shortly after hospital admission. It is likely that the majority of these patients had a large infarction or a hemorrhage. This means that the prognosis for patients with a large infarction or hemorrhage is probably even worse than demonstrated in our stroke type analysis.

Various authors used different ways to classify stroke subtypes. Some based their classification on the presumed causal mechanisms of
stroke. As mentioned by Bamford and colleagues, a disadvantage of this approach is that it needs a detailed investigation that is not always feasible. Furthermore, even after a detailed investigation, the causal mechanism remains obscure in as many as 40% of the infarcts. Therefore, we largely defined our stroke subtyping according to the Oxfordshire Community Stroke Project criteria.

In conclusion, we found that the impact of stroke type on mortality is limited to the first 6 months after stroke, whereas the type of stroke influences the long-term functional health of the patients.

6.5 References


