Ischemic Stroke
Impact of a Recent Myocardial Infarction

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Background and Purpose—The risk of ischemic stroke is increased after a myocardial infarction. We quantified the stroke risk and evaluated ischemic stroke characteristics after an acute myocardial infarction.

Methods—A case-control study including patients with first-ever stroke was undertaken. Cases (n=103) were recorded prospectively in the population-based Northern Sweden World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study. Two controls per case with a stroke but without a recent myocardial infarction were matched for age, sex, and year of stroke onset.

Results—The sudden onset of neurological symptoms (76.7% versus 54.9%, P<0.001), impairment of consciousness (35.0% versus 18.4%, P<0.01), and a progression in neurological deficits (19.4% versus 8.7%, P<0.01) were more common in cases, while the onset of stroke during sleep was rarer in cases (6.8% versus 21.4%, P<0.01). In cases and controls, the clinical subclasses of stroke were as follows: total anterior circulation infarcts, 51.5% versus 37.9% (P<0.05); partial anterior circulation infarcts, 28.2% versus 26.7% (P=NS); lacunar infarcts, 4.8% versus 27.2% (P<0.001); and posterior circulation infarcts, 15.5% versus 8.2% (P=0.051). During the first 28 days after myocardial infarction, the daily rate of stroke declined rapidly from ~9 to 1 stroke per 10 000 myocardial infarction patients compared with an age-adjusted average daily stroke rate of 0.14 per 10 000 in the MONICA population.

Conclusions—We conclude that the clinical characteristics of the stroke differ between patients with and without a recent myocardial infarction. The risk of a first-ever ischemic stroke is highest during the first few days after a myocardial infarction, but it then declines rapidly, and the absolute number of stroke events is low. (Stroke. 1999;30:997-1001.)

Key Words: case-control studies ■ myocardial infarction ■ stroke, ischemic

Several cardiac disorders, eg, atrial fibrillation, mitral valve disease, and acute myocardial infarction, are associated with an increased risk of ischemic stroke. Whether the underlying mechanism is an embolus from the heart is, however, almost impossible to determine, mainly because of coexisting atherosclerosis in the aorta and the cervical and cerebral arteries. Moreover, data from stroke registers indicate that individual neurological features are poor indicators of a cardiac cause of a stroke.

A subclassification of cerebral infarction based on clinical findings has been proposed, and it has been suggested that these subclasses provide pathophysiological, as well as prognostic, information.

The aims of the present study were to compare the clinical findings, subclasses, prognosis, and causes of death among patients with an ischemic stroke with and without a recent myocardial infarction. We also aimed to quantify the risk of first-ever ischemic stroke after an acute myocardial infarction.

Subjects and Methods
The 2 northernmost counties in Sweden constitute 1 of the centers in the World Health Organization (WHO) Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project. In this population-based study, all stroke events occurring in subjects aged 25 to 74 years have been prospectively recorded since 1985, and a specific code has been given to patients with a myocardial infarction within 28 days before the stroke. The area has a population of ~510 000 inhabitants, 310 000 of whom are between 25 and 74 years of age. The registry has been validated, and routine case-finding procedures identify 96% of all stroke events in the target population. The home care of patients with a suspected myocardial infarction is not practiced in Sweden.

The WHO definition of stroke was used: rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting for >24 hours (unless interrupted by surgery or death) with no apparent cause other than a vascular origin. The inclusion period was January 1, 1985, to December 31, 1994. Only patients with a first-ever stroke were included. Seven cases with a hemorrhagic stroke verified by CT, all occurring after thrombolytic therapy, were excluded from the study.

A diagnosis of myocardial infarction was based on typical chest pain, ECG findings, and a diagnostic elevation of cardiac enzymes. Two of 3 of the clinical criteria were required. A myocardial infarction occurring >28 days before the stroke was classified as old. Patients with a diagnosis of first-ever ischemic stroke but without a preceding myocardial infarction occurring within 28 days were used as controls. Two controls per case were matched for age, sex, and year of stroke onset.
A clinical subclassification of the cerebral infarctions in cases and controls was made according to Bamford et al. using data from the MONICA registry and medical records. Four subclasses were therefore defined: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI), and posterior circulation infarcts (POCI). The subclassification was made independently by 2 investigators, and disagreements were resolved by consensus in 9 cases.

The onset characteristics of stroke, course of neurological symptoms during hospital stay (regression, no change, progression), and the impairment of consciousness were recorded. The patients’ self-care performance before the stroke event and at discharge was recorded as independent, partly dependent, or fully dependent (or dead).7

Incidence and event rate were used to describe the daily occurrence of stroke in the MONICA population and the daily stroke rate within 28 days after myocardial infarction, respectively. Daily incidence was defined as the average number of first-ever strokes each day per 10 000 inhabitants aged 25 to 74 years during the observation period. Age adjustments were made with the myocardial infarction population as a standard population. The daily event rate was defined as the number of strokes each day per 10 000 inhabitants aged <75 years during the first 28 days after infarction.

During 1 year of follow-up from the initial stroke event, all new strokes were recorded in cases and controls. Mortality follow-up continued until June 30, 1996. After the assessment of death certificates and clinical records of all the deceased patients, the cause of death was classified as cardiac, cerebrovascular, or other.

**Statistical Analysis**

Data were analyzed with the use of STATISTICA 4.0 software modules (StatSoft Inc). Group data are expressed as the mean±SD for continuous variables and as rates for variables on a nominal scale. Differences between 2 means were assessed with Student’s t test for unpaired data or the Mann-Whitney U test when appropriate. Differences between proportions were analyzed with the χ² test. The null hypothesis was rejected for values of P<0.05.

**Table 1. Clinical Characteristics of Cases and Controls**

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=103)</th>
<th>Controls (n=206)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>65.4 (7.2)</td>
<td>65.5 (7.12)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>74.8%</td>
<td>74.8%</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>42.7%</td>
<td>47.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.3%</td>
<td>17.0%</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>12.6%</td>
<td>11.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>50.5%</td>
<td>28.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Old myocardial infarction</td>
<td>39.8%</td>
<td>15.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure during hospital stay</td>
<td>45.6%</td>
<td>6.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP, admission, mean (SD)</td>
<td>151.8 (29.5), n=94</td>
<td>169.5 (31), n=193</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP, admission, mean (SD)</td>
<td>92.1 (15.9), n=87</td>
<td>95.9 (14), n=190</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

BP indicates blood pressure.

An equation was fitted to the event-rate data by exponential regression to describe the risk of stroke after myocardial infarction. Kaplan-Meier curves were calculated for recurrent stroke events and survival in patients with and without myocardial infarction–related stroke and compared between groups with the log-rank test. The Cox proportional hazards model was used to identify predictors of death. A preceding myocardial infarction (within 28 days), hypertension, atrial fibrillation, diabetes, old myocardial infarction, impaired consciousness, and TACI subclass were included as variables, covering different aspects of risk.

**Results**

One hundred three cases with a first-ever stroke within 28 days of an acute myocardial infarction were identified from January 1, 1985, to December 31, 1994. These myocardial infarction–related strokes constituted 1.8% of all first-ever strokes. A CT, autopsy, or lumbar puncture was performed in 69 of 103 (67%), excluding hemorrhage. Of the remaining 34 patients, 6 were treated with thrombolysis. In this group of 6 patients, the strokes occurred 2 to 27 (median, 10) days after myocardial infarction onset. In the control group, a CT, autopsy, or lumbar puncture was undertaken in 201 of 206 (98%). During the 10-year period, 11 620 patients aged <75 years had a myocardial infarction, giving an overall event rate of first-ever ischemic myocardial infarction–related stroke of 0.9%.

**Table 3. Clinical Subclassifications, Self-Care Performance, and Death in Cases and Controls**

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=103)</th>
<th>Controls (n=206)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TACI</td>
<td>51.5%</td>
<td>37.9%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PACI</td>
<td>28.2%</td>
<td>26.7%</td>
<td>NS</td>
</tr>
<tr>
<td>LACI</td>
<td>4.9%</td>
<td>27.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>POCI</td>
<td>15.5%</td>
<td>8.2%</td>
<td>0.051</td>
</tr>
<tr>
<td>SCP before stroke event, independent</td>
<td>96.1%</td>
<td>94.7%</td>
<td>NS</td>
</tr>
<tr>
<td>SCP at discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>35.9%</td>
<td>55.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Partly dependent</td>
<td>11.7%</td>
<td>19.4%</td>
<td>0.08</td>
</tr>
<tr>
<td>Fully dependent</td>
<td>22.3%</td>
<td>18.4%</td>
<td>0.4</td>
</tr>
<tr>
<td>Dead during hospital stay</td>
<td>30.1%</td>
<td>6.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SCP indicates self-care performance, ns=not significant.
The clinical characteristics of the cases and controls are shown in Table 1. A higher prevalence of angina pectoris, a previous myocardial infarction, and congestive heart failure during the hospital period was observed in the cases.

A comparison of neurological features in cases and controls is shown in Table 2. The sudden onset of neurological symptoms, impairment of consciousness, and progression of neurological deficits were more common in cases, while the onset of stroke during sleep was considerably more common in controls. There were significant differences in clinical subclassification and self-care performance between cases and controls (Table 3). A large proportion of the cases (51.5%) had extensive neurological deficits corresponding to TACI, while only a few (4.9%) had infarctions of the LACI subtype. Accordingly, the cases had a poorer self-care performance at discharge.

Figure 1 shows the rate of first-ever ischemic stroke after myocardial infarction and the corresponding stroke occurrence in the MONICA population after age adjustments. During the month after myocardial infarction, the daily rate of stroke declined rapidly from \( \approx 9 \) to 1 stroke per 10,000 myocardial infarction patients, compared with an average age-adjusted stroke rate of 0.14 per 10,000 in the MONICA population.

Figure 2 shows recurrent strokes over 12 months after a first-ever cerebral infarction in cases and controls. Although there was a clear tendency toward a higher recurrence rate among myocardial infarction patients during the first 2 months, there was no statistically significant difference between the 2 groups over 1 year (\( P=0.29 \)).

Patients with a myocardial infarction preceding the stroke had high mortality during the hospital period (30.1% versus 6.3%, \( P<0.001 \)), mainly because of cardiac complications (18.4%...
versus 0.5%, \( P<0.001 \)). Furthermore, they died more frequently because of progressive stroke (11.6% versus 5.3%, \( P=0.047 \)) (Table 4).

Figure 3 shows the long-term survival in cases and controls \( (P<0.001) \). The mean follow-up time was 56 months. Patients with a stroke after myocardial infarction had a 70% cumulative survival at 28 days and a 57% cumulative survival at 1 year. The corresponding figures for patients without myocardial infarction were 94% and 88%. In the Cox regression model, a recent myocardial infarction, hypertension, diabetes, old myocardial infarction, and impaired consciousness were independently predictive of death, while a TACI subclass was not.

**Discussion**

Stroke is a rare but feared complication of an acute myocardial infarction.\(^8\) A hemorrhagic stroke during the first 24 hours is a well-known consequence of thrombolytic therapy.\(^9\) In most instances, however, a stroke after an acute myocardial infarction is ischemic in origin.\(^8\) We performed, for the first time, a total population study on stroke with identification of a preceding myocardial infarction within a defined period of time (28 days). Our data confirm the detrimental effect of a stroke after a myocardial infarction. The neurological deficit is more extensive, the clinical course more unfavorable, and the mortality higher compared with a stroke in patients without a recent myocardial infarction.

The clinical subclasses also differed in cases and controls. The TACI subclass was common and the LACI subclass was uncommon in the cases, a finding that agrees with previous reports of strokes associated with cardiac disease.\(^4\) Despite the differences in clinical characteristics and subclasses, no single clinical finding or combination of findings appears to be specific enough to differentiate between a cardiogenic and noncardiogenic stroke in the individual patient.

The pathophysiology of stroke after myocardial infarction is unclear. One hypothesis is that embolism from a left ventricular thrombus is a common mechanism.\(^1,10\) However, this has recently been disputed, and left ventricular thromboembolism can explain only a small fraction of myocardial infarction–related strokes.\(^11,12\) Other important mechanisms, which were suggested in the 1940s, may be in situ thrombosis and artery-to-artery embolism because of atherosclerosis and unfavorable hemodynamics.\(^13,14\) Moreover, an acute myocardial infarction is followed by increased fibrinogen levels\(^15\) and a pronounced sympathetic activation, which may facilitate thrombus formation in patients with atherosclerosis in the aorta and the cervical and cerebral arteries.\(^16,17\) Hypothetically, the prothrombotic mechanisms following a myocardial infarction may result in more dynamic and extensive thrombus formation, which at least in part may explain the differences in neurological features between cases and controls.

The present study provides important information about the time relationship between myocardial infarction and first-ever stroke (Figure 1). It is obvious that most strokes occur within the first few days after a myocardial infarction. The risk of stroke declines exponentially, and the equation fitted to the present data explained 74% of the variance. The right-hand part of the curve should, however, be interpreted with great caution because of few events. In the Survival And Ventricular Enlargement (SAVE) study, the rate of stroke during long-term follow-up of patients with ventricular dysfunction after myocardial infarction was 1.5% per year, corresponding to 0.41 stroke events per day.

### Table 4. Causes of Death in Cases and Controls

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=103)</th>
<th>Controls (n=206)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In hospital</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>18.5%</td>
<td>0.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Progressive stroke</td>
<td>11.6%</td>
<td>5.3%</td>
<td>0.047</td>
</tr>
<tr>
<td>Other</td>
<td>0%</td>
<td>0.5%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>After discharge</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>24.3%</td>
<td>19.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>4.8%</td>
<td>5.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Other</td>
<td>9.7%</td>
<td>10.2%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>All deaths</strong></td>
<td>68.9%</td>
<td>41.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Figure 3.** Cumulative survival during long-term follow-up in cases and controls \( (P<0.001, \text{log-rank test}) \).
per 10,000 subjects. Although the risk of a stroke after a myocardial infarction is much higher than the risk of a stroke in the population, the absolute numbers are still low. During a 10-year period, a first-ever ischemic stroke was diagnosed in 103 of 11,620 patients (0.9%) during the first 28 days after myocardial infarction.

The risk of a recurrent stroke was similar in cases and controls during 1 year of follow-up (13.6% versus 12.1%, \(P = 0.29\)) (Figure 2). The risk of a recurrent thromboembolic event after myocardial infarction has previously been estimated at between 30% and 50%. These data are based on heterogeneous and small studies, often autopsy series, making the results unreliable and probably not applicable to patients receiving modern myocardial infarction treatment.

The rate of recurrent stroke in the present control group agrees favorably with other epidemiological studies.

The mortality is high if a myocardial infarction is complicated by a stroke (Figure 3), but, after the first year, the Kaplan-Meier curves for cases and controls run almost parallel. As expected, cardiac disease predominated as the cause of death in the cases during the hospital stay. However, death from progressive stroke was also more common in cases, possibly reflecting the more extensive cerebral damage after myocardial infarction (TACI, 51.5% versus 37.9%).

After hospital discharge, cardiac death was almost as common in controls as in cases, underscoring the generalized vascular disease in patients who have suffered a stroke.

A recent myocardial infarction, old myocardial infarction, diabetes, and impaired consciousness were independent predictors of death, findings in agreement with other studies. As previously reported, simple clinical findings (ie, the level of consciousness) may be more important than the clinically defined subclass when prognosis is assessed after a stroke.

One limitation of the present study is that a pathological stroke diagnosis was lacking in 33% of the myocardial infarction patients. The stroke mechanism was often assumed to be embolic and the mortality was high, resulting in the less frequent use of CT compared with controls. This means that some hemorrhagic strokes may have been misclassified as ischemic. However, without thrombolytic treatment, an intracranial hemorrhage after myocardial infarction is very uncommon. In the 2 largest placebo-controlled trials of thrombolytic treatment after myocardial infarction, no hemorrhagic strokes were found in the placebo groups. Moreover, a hemorrhagic stroke after the administration of thrombolytics usually occurs within 24 hours, but the strokes in the 6 patients given thrombolytic therapy in the present study all occurred after 48 hours (median, 10 days).

Acknowledgments

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References

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