A Community-Based Study of Stroke Incidence after Myocardial Infarction

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Background: The rate of stroke after myocardial infarction (MI) remains unclear.

Objectives: To examine the rate of stroke after incident MI; compare it with that observed in the population of Rochester, Minnesota; determine how the rate of stroke after MI has changed over time; and examine the impact of stroke on survival after incident MI.

Design: Community-based cohort.

Setting: Olmsted County, Minnesota.


Measurements: Ischemic or hemorrhagic stroke in hospitalized and nonhospitalized patients that was identified by screening of the medical record for stroke diagnostic codes and subsequent stroke confirmation by physician review of the recorded event. Medical record review was used to ascertain baseline characteristics and death.

Results: A total of 2160 persons with incident MI were hospitalized between 1979 and 1998 and followed for a median of 5.6 years (range, 0 to 22.2 years). The rate of stroke was 22.6 per 1000 person-months (95% CI, 16.3 to 30.6 per 1000 person-months) during the first 30 days after MI, corresponding to a 44-fold increase (standardized morbidity ratio, 44 [95% CI, 32 to 59]) risk for stroke in the population of Rochester, Minnesota. The risk for stroke remained 2 to 3 times higher than expected during the first 3 years after MI. Older age, previous stroke, and diabetes increased the risk for stroke, which did not decline over the study period. Strokes were associated with a large increase in the risk for death after MI (hazard ratio, 2.89 [CI, 2.44 to 3.43]).

Coronary disease is the leading cause of death in the United States, and stroke is the third leading cause of death and the most common cause of disability (1). Both diseases share common risk factors (2–7) and treatments, such as antihypertensive agents, lipid-lowering agents, and aspirin (8, 9). Because the incidence of myocardial infarction (MI) is stabilizing and survival after MI is improving (10, 11), understanding the burden of morbidity after MI and how it may be changing over time becomes increasingly important in caring for the growing population of survivors. Several investigators, including our group, have reported declining recurrence of MI and heart failure after incident MI (10, 12–16). However, less is known about stroke after MI. Most studies that have reported rates of stroke after MI focused on short-term events that occurred during the patient’s hospital stay or within the first month after MI. They often addressed the question within the framework of clinical trials, which may not be fully representative of the experience of the community. Finally, the reported rate of stroke early after MI is difficult to interpret because of the lack of an appropriate reference population.

This study was conducted in Olmsted County, Minnesota, where residents receive medical care at a small number of facilities, including the Mayo Clinic. The characteristics of the study population mainly reflected those of U.S. white persons. The Rochester Epidemiology Project (17), a medical record linkage system, enables access to all aspects of an individual patient’s records from all sites in Olmsted County. These comprehensive medical records...
Community Study of Stroke after Myocardial Infarction

Context
After a myocardial infarction (MI), outcomes such as heart failure and recurrent MI are decreasing. What about stroke?

Contribution
This cohort study from Olmsted County, Minnesota, had a 44-fold increase in stroke rate during the first month after MI compared with the stroke rate in the general community. Stroke rates in the cohort declined markedly after the first month but exceeded the rates in the general community for 3 years. Strokes after MI were associated with increased risk for death, and their rate did not decline between 1979 and 1998.

Implications
Early after MI, risk for stroke is markedly increased. This risk has not declined over time.

—The Editors

allow the study of diseases over a prolonged period as they occur in an unselected, geographically defined population without many of the biases inherent in tertiary care settings. The appropriate institutional review boards approved all aspects of the study.

Identification of the Study Cohort
The procedures used to assemble the MI incidence cohort have been described previously (11). Briefly, all persons discharged from county hospitals between 1979 and 1998 with codes compatible with an MI were identified. The following target codes were included from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM): 410 (acute MI), 411 (other acute and subacute forms of ischemic heart disease), 412 (old MI), 413 (angina pectoris), and 414 (other forms of ischemic heart disease). All events coded 410 and samples of events coded 411 through 414 were reviewed (11). Trained abstractors verified patients’ residency status in Olmsted County and incident status of MI by complete review of the medical record and collected information on the presence of cardiac pain, creatine kinase values, and electrocardiograms, which were assigned a Minnesota Code by the Electrocardiogram Reading Center at the University of Minnesota (18). Standard criteria were applied to assign the diagnosis of MI on the basis of cardiac pain, enzyme values, and Minnesota Code. Comorbidity was measured by the Charlson index, a validated measure of comorbidity (19). Reperfusion therapy was defined as thrombolysis or percutaneous coronary intervention that was done during the hospitalization. Atrial fibrillation was recorded at any time during the patients’ medical histories before the stroke occurred.

In the Rochester Stroke Registry (20), all residents of Rochester, Minnesota, who had stroke diagnoses identified through the Rochester Epidemiology Project are validated by physician review and entered in the Registry. The ICD-9-CM codes used for case ascertainment include codes 430 through 438 (cerebrovascular disease), 781.4 (transient paralysis of a limb), 784.3 (aphasia), 362.34 (transient arterial occlusion, amaurosis fugax), and 368.12 (transient visual loss). Because the MI incidence cohort includes all of Olmsted County and the Stroke Registry includes only residents of the city of Rochester, there is incomplete overlap between the 2 registries. Thus, all strokes occurring before July 2003 in residents of Olmsted County that were not included in the Stroke Registry were identified by using the same aforementioned diagnostic codes and were validated by physician review.

Stroke Definitions
To avoid temporal changes in the ascertainment of stroke related to changes in imaging techniques and to be certain of the timing of stroke, strokes without a corresponding clinical event that were found only on imaging of the patient’s head (computed tomography [CT] or magnetic resonance imaging [MRI]) or at autopsy were not included. Transient ischemic attacks defined as focal neurologic symptoms lasting less than 24 hours; traumatic subdural hematoma; hemorrhage into abnormal tissue, such as tumor or inflammation; and isolated infarction of the retina, labyrinth, or cochlea were excluded.

Cerebral infarction was defined as the acute onset (minutes to hours) of a focal neurologic deficit persisting more than 24 hours, with or without CT or MRI documentation, and caused by altered circulation to a limited region of the cerebral hemispheres, brainstem, or cerebellum. Findings on CT, MRI, or autopsy (if available) did not show evidence of intracerebral hemorrhage.

Intracerebral hemorrhage was defined as the acute onset of a focal neurologic deficit associated with some or all of the following: headache, vomiting, altered level of consciousness, signs of meningeal irritation, or blood-stained cerebrospinal fluid. If done, CT, MRI, or autopsy showed a parenchymal hemorrhage.

Subarachnoid hemorrhage was defined as the abrupt onset of headache, with or without altered consciousness, with signs of meningeal irritation. A focal deficit may have developed acutely or with a delay of hours or days. Computed tomography, MRI, or examinations of cerebrospinal fluid examinations showed blood in the subarachnoid space.

Strokes were classified as “hospitalized strokes” if a hospital admission for stroke or stroke-related complications occurred within 30 days after the event. Follow-up was obtained by passive surveillance through community (inpatient and outpatient) medical records. More than 90% of the population of Olmsted County receives ongoing care at Mayo Clinic or Olmsted Medical Center, and...
96% of residents are seen, on average, every 3 years at Mayo Clinic (17). Ascertainment of death included death certificates filed in Olmsted County, autopsy reports, obituary notices, and electronic files of death certificates obtained from the State of Minnesota Department of Vital and Health Statistics.

Quality Control
The reliability of MI ascertainment has been reported previously (11) and indicates excellent interabstractor agreement. For stroke ascertainment, the study neurologist, in addition to the principal investigator, reviewed a sample of 25 randomly selected potential cases, of which 16 were ischemic strokes, 1 was a hemorrhagic stroke, and 8 were nonstrokes. The interobserver variability showed excellent agreement ($k = 0.93$; 95% CI, 0.79 to 1.00) between the 2 physicians, indicating excellent reliability for the ascertainment of stroke. Furthermore, previous work from our center indicated that the case-finding approach used in the current study yielded results similar to those reported for a cohort approach confirming the robustness of our method of ascertainment (20).

Statistical Analysis
The rate of stroke after MI was examined for all strokes (first and recurrent) and for incident (first-ever) strokes and was expressed per 1000 person-months. The incident stroke rate after MI was compared with the incident stroke rate in the population of Rochester, Minnesota, by using data from the Rochester Stroke Registry (21) to calculate standardized morbidity ratios. Expected stroke rates were calculated by applying sex-, age-, and period-specific stroke rates in the general population of Rochester to the person-time follow-up of the study population. The standardized morbidity ratio was calculated by dividing the number of observed strokes by the expected number of strokes over the duration of follow-up. Confidence intervals were calculated according to the Poisson distribution.

Proportional hazards regression was used to examine associations between patient characteristics and the occurrence of a stroke after MI and to examine the association between stroke and death after MI while adjusting for age, sex, Killip class, aspirin use, and warfarin use; stroke was analyzed as a time-dependent covariate. The correlation of the scaled Schoenfeld residuals with time was used to test the proportional hazards assumption. Except for family history of coronary artery disease (7.2%), anterior MI (15.8%), ST-segment elevation MI (12.8%), and presence of Q waves (21%), missing values did not exceed 5%. Because ST-segment elevation and presence of Q waves are both surrogates for MI severity, we elected to use peak creatine kinase ratio, defined as the ratio of the maximum creatine kinase value to the upper limit of normal, as the measure of MI severity. The peak creatine kinase ratio was missing in less than 5% of the observations. Fewer than 2% of persons had 1 or more missing variables for the predictors in the final multivariable models. Because the proportional hazards assumption was not met, strokes were divided into early strokes (occurring ≤ 30 days after MI) and late strokes (occurring > 30 days after MI). For late strokes, the proportional hazards assumption was met for all predictor variables ($P > 0.05$ for all variables). Results are reported as hazard ratios with 95% CIs. Analyses were done using the statistical software package SAS, version 8.2 (SAS Institute Inc., Cary, North Carolina).

Role of the Funding Source
The funding source supported the data collection, data analysis, and manuscript preparation.

RESULTS
Baseline Characteristics
Between 1979 and 1998, 2171 Olmsted County residents were hospitalized with incident MI. Stroke could not be ascertained as an outcome in 11 patients, resulting in a cohort of 2160 persons. The mean age (SD) at the date of index MI was 67 years (SD, 14), and 57% of the patients were men. Fifty-six percent of the patients had a history of hypertension, and 65% were current or former smokers. One hundred eighty-eight (9%) had a stroke before the index MI. Nearly all strokes that occurred before the MI were ischemic (174 [93%]), and the remaining 7% consisted of 7 intracerebral hemorrhages and 7 subarachnoid hemorrhages.

Occurrence of Stroke after MI
During a median follow-up of 5.6 years (range, 0 to 22.2 years), there were 273 strokes, of which 259 (95%) were ischemic; the remaining 5% consisted of 13 intracerebral hemorrhages and 1 subarachnoid hemorrhage. Eighty-three percent of the patients were hospitalized for evaluation within 30 days of the stroke. The occurrence of stroke was not equally distributed during the follow-up period; a large proportion of the strokes (18%) occurred within 30 days of the index MI followed by a gradual decline thereafter.

Table 1 shows the rates per 1000 person-months for all strokes (first and recurrent) and for incident (first-ever) strokes for the duration of follow-up. The rate was the highest during the first 30 days after MI, at 23.9 per 1000 person-months (CI, 17.6 to 31.6 per 1000 person-months) for all strokes, equating to 2.3% of all patients with MI. When only incident strokes after MI were considered, the observed rate of incident strokes during the first 30 days was 22.6 per 1000 person-months (CI, 16.3 to 30.6 per 1000 person-months). Compared with the expected rate, this represents a 44-fold increase in the risk for stroke (standardized morbidity ratio, 44 [CI, 32 to 59]).

In the second month of follow-up, the stroke rate declined to 2.3 per 1000 person-months without additional change during the remainder of the first year. The risk for stroke declined gradually as time from the index MI increased but remained 2 to 3 times higher than the expected...
rate during the 3 years after MI. Beyond year 3, the risk for stroke was no longer different from that in the general population of Rochester. The dynamic nature of the excess risk for stroke after MI is shown in the Figure, which depicts the gradual decline over time of the observed versus expected strokes (standardized morbidity ratio) from the time of the index MI throughout the follow-up.

The risk for stroke after MI did not decline in patients with more recent MIs. During the first decade of the study, after adjustment for age and sex, the risk for stroke increased by 74% (hazard ratio for stroke after an MI occurring in 1988 compared with that after an MI occurring in 1979, 1.74 [CI, 1.12 to 2.71]; P = 0.015). During the second decade, no additional change in the risk for stroke after MI was detected (hazard ratio for stroke after an MI occurring in 1998 compared with that after an MI occurring in 1988, 0.87 [CI, 0.54 to 1.41]; P = 0.57). The results were unchanged after adding previous stroke, hypertension, diabetes, smoking, hyperlipidemia, and obesity to the model.

Characteristics Associated with Stroke after Incident MI

Older age, female sex, greater comorbidity, hypertension, diabetes, atrial fibrillation, Killip class, and previous stroke were all univariately associated with stroke after MI (Table 2). No association was seen between stroke and peak creatine kinase ratio, location of MI, presence of Q waves, or ST-segment elevation. Regarding thrombolysis, there was no clinically significant difference between patients who had a stroke and those who did not, although patients who had a stroke were less likely to receive percutaneous coronary intervention.

When entered in a multivariable model, the factors independently associated with stroke after MI included older age (hazard ratio, 1.04 per year [CI, 1.03 to 1.05 per year]; P < 0.001); history of stroke (hazard ratio, 2.07 [CI, 1.44 to 2.97]; P < 0.001); and diabetes mellitus (hazard ratio, 1.68 [CI, 1.27 to 2.20]; P < 0.001). Adjusting for the use of aspirin, ß-blockers, angiotensin-converting enzyme inhibitors, statins, calcium-channel blockers, or diuretics at admission or at discharge did not change the results, nor did we detect an interaction between hypertension and any of these medications (data not shown). Because of the markedly higher excess risk for stroke early after MI, exploratory analyses were conducted to examine whether the association between any clinical variable and stroke differed by the timing of the stroke. Persons who had a stroke early after MI were older than those who had a stroke later (P < 0.001) and had a larger MI as measured by peak creatine kinase ratio (P = 0.030).

Survival after Stroke

At 1 year, follow-up was 99% complete and 402 patients had died. Patients who had a stroke at any time during follow-up had a markedly increased risk for death compared with patients who did not have a stroke (Table 3). Indeed, stroke was associated with a 2- to 3-fold increase in the risk for death, independent of age, sex, and Killip class. Similar results were found after adjusting for aspirin and warfarin use.

DISCUSSION

Patients with MI have a high risk for strokes, most of which are ischemic. The risk for stroke after MI is dynamic and declines as time from the index MI increases. However, the risk for stroke after MI did not decline during the 2 decades of the study period. The excess risk for stroke was no longer different from that in the general population of Rochester. The dynamic nature of the excess risk for stroke after MI is shown in the Figure, which depicts the gradual decline over time of the observed versus expected strokes (standardized morbidity ratio).
after MI is considerable compared with that expected in a population without MI, particularly in the first month after MI. The devastating impact of stroke after MI on survival and the increasing number of persons at risk because of improved survival constitute an important public health matter for persons with coronary disease.

**Risk for Stroke after MI**

Most studies considered strokes during the initial hospital admission for the MI or the first month thereafter and reported rates ranging between 0.75% and 4.6% (2, 4, 6, 7, 22–34). However, most of these are clinical trials that are not comparable with our study. Among cohort studies, stroke rates ranged from 1.1% to 1.5% in the first 30 days after MI (4, 35, 36). Several methodologic issues limit the inferences that can be made from these studies. These issues include, in particular, the exclusion of elderly individuals, the lack of long-term follow-up, reliance of the study design on registries from trials or national surveys, and small sample size.

Data on long-term risk for stroke after MI are also sparse. Stroke rates range from 3% at 6 months to 8.6% at 10 years after MI (22, 37–46). As is the case for studies reporting short-term stroke rates, many of these are clinical trials. Cohort studies providing long-term data are limited because they identified survivors through administrative databases (39) or through billing records (43). Also, they did not provide information on the background stroke rates in a similar population, except for 1 report from the Monitoring of Cardiovascular Disease (MONICA) study, where the rate of stroke within 28 days after MI was markedly higher than that expected in the general study population (4). This study, however, did not include older persons. Thus, our data extend these findings by including participants of all ages and providing a comparison population, which is essential to understand the magnitude of the excess risk for stroke conferred by MI. Finally, temporal trends in the risk for stroke after MI remain largely unknown with the exception of data from the Worcester Community Study of Stroke after Myocardial Infarction.

**Table 2. Characteristics of Patients with Myocardial Infarction by Occurrence of Stroke***

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MI without Stroke (n = 1887)</th>
<th>MI with Stroke (n = 273)</th>
<th>RR for Characteristic if Stroke Occurs (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, %</td>
<td>58</td>
<td>46</td>
<td>0.48 (0.38–0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean age at index MI (SD), y</td>
<td>67 (14)</td>
<td>71 (12)</td>
<td>1.05 (1.04–1.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbid conditions, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>44</td>
<td>33</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1 or 2</td>
<td>36</td>
<td>47</td>
<td>2.30 (1.75–3.02)</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>21</td>
<td>20</td>
<td>2.88 (2.03–4.07)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>54</td>
<td>64</td>
<td>1.93 (1.50–2.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>19</td>
<td>27</td>
<td>2.03 (1.55–2.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>30</td>
<td>25</td>
<td>0.55 (0.42–0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hyperlipidemia, %</td>
<td>33</td>
<td>28</td>
<td>0.81 (0.62–1.05)</td>
<td>0.114</td>
</tr>
<tr>
<td>Mean BMI (SD), kg/m²</td>
<td>27.0 (5.6)</td>
<td>26.8 (4.9)</td>
<td>0.98 (0.96–1.01)</td>
<td>0.22</td>
</tr>
<tr>
<td>Familial coronary disease, %</td>
<td>21</td>
<td>23</td>
<td>0.92 (0.68–1.23)</td>
<td>0.56</td>
</tr>
<tr>
<td>Clinical characteristics at index MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous stroke, %</td>
<td>8</td>
<td>14</td>
<td>3.20 (2.25–4.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Killip class 2, 3, or 4, %</td>
<td>35</td>
<td>35</td>
<td>1.50 (1.16–1.93)</td>
<td>0.002</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>12</td>
<td>14</td>
<td>1.58 (1.11–2.24)</td>
<td>0.011</td>
</tr>
<tr>
<td>Anterior location of the MI, %</td>
<td>35</td>
<td>34</td>
<td>1.11 (0.85–1.46)</td>
<td>0.45</td>
</tr>
<tr>
<td>STEMI, %</td>
<td>40</td>
<td>39</td>
<td>0.91 (0.70–1.19)</td>
<td>0.50</td>
</tr>
<tr>
<td>Q-wave MI, %</td>
<td>50</td>
<td>48</td>
<td>1.02 (0.79–1.34)</td>
<td>0.87</td>
</tr>
<tr>
<td>Peak CK ratio, %</td>
<td></td>
<td></td>
<td></td>
<td>0.95</td>
</tr>
<tr>
<td>Tertile 1</td>
<td>31</td>
<td>28</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tertile 2</td>
<td>32</td>
<td>33</td>
<td>1.03 (0.76–1.40)</td>
<td></td>
</tr>
<tr>
<td>Tertile 3</td>
<td>33</td>
<td>36</td>
<td>1.06 (0.78–1.43)</td>
<td></td>
</tr>
<tr>
<td>Reperfusion therapy, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>28</td>
<td>22</td>
<td>0.68 (0.51–0.90)</td>
<td>0.008</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>15</td>
<td>15</td>
<td>0.86 (0.62–1.21)</td>
<td>0.39</td>
</tr>
<tr>
<td>Aspirin†</td>
<td>67</td>
<td>65</td>
<td>1.12 (0.86–1.45)</td>
<td>0.41</td>
</tr>
<tr>
<td>Warfarin†</td>
<td>10</td>
<td>15</td>
<td>1.70 (1.22–2.36)</td>
<td>0.002</td>
</tr>
<tr>
<td>LMWH†</td>
<td>37</td>
<td>39</td>
<td>0.90 (0.70–1.15)</td>
<td>0.40</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>23</td>
<td>24</td>
<td>0.88 (0.66–1.16)</td>
<td>0.36</td>
</tr>
<tr>
<td>Calcium-channel blocker†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic†</td>
<td>54</td>
<td>62</td>
<td>1.82 (1.42–2.33)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* BMI = body mass index; CK = creatine kinase; LMWH = low-molecular-weight heparin; MI = myocardial infarction; PCI = percutaneous coronary intervention; RR = relative risk; STEMI = ST-segment elevation myocardial infarction.
† Includes use in-hospital and at discharge.
‡ Includes ticlopidine and clopidogrel use in-hospital and at discharge.

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Heart Attack Study, which suggested an increase in the risk for in-hospital stroke with time but lacked information about long-term follow-up (35).

As a result of these limitations, the magnitude and the dynamic nature of the risk for stroke after MI have not previously been recognized. Our study addresses this important gap in knowledge by showing that, within this geographically defined population, using rigorous definitions for MI and stroke and including strokes in patients who were not hospitalized, the observed rate of incident stroke after MI is high, largely exceeding that expected in a population without MI. Also, the risk for stroke after MI is dynamic and is markedly elevated early after MI. Indeed, compared with the expected incidence of stroke, the excess risk observed within 30 days after MI corresponds to a 44-fold increased risk for stroke. During the 2 decades of the study, no reduction in this risk was detected; however, an increase was apparent during the first decade with stabilization thereafter. These data suggest that contemporary management strategies for MI have not affected the subsequent risk for stroke compared with older therapies.

**Predictors of Stroke after MI**

Factors independently associated with an increased risk for stroke included older age, history of stroke, and diabetes, all of which are traditionally associated with stroke in the general population. However, the timing of stroke in relation to MI suggests that conventional cardiovascular risk factors do not fully explain the marked increase in the risk for stroke early after MI. Regarding acute treatment of MI, meta-analyses of the randomized trials of thrombolysis in acute MI eased the concern that thrombolysis increased the risk for stroke considerably (47, 48). Our study extends these reports by indicating that the rate of hemorrhagic stroke after MI in the community is low. Also, the stabilization of the rate of stroke in the second decade of the study, corresponding to the “thrombolytic era,” suggests that the use of thrombolytics, which increased over that period (49), did not coincide with an increase in hemorrhagic stroke.

The association between the size and severity of the MI and stroke remains controversial. Some authors suggest that severity is related to stroke (3, 4, 7, 25), whereas others failed to detect such an association. Our analyses suggest that larger size is associated with early occurrence of stroke after MI. Finally, the timing of the stroke in relation to the MI suggests that systemic inflammation, which plays an increasingly recognized role in MI and stroke, may partly explain the marked increase in the risk for stroke during the early period after MI (50).

**Implications**

These results have important implications. Our findings contrast with trends in cardiac outcomes after MI, such as heart failure (12) and recurrent MI (16, 51–53), which are declining over time. Stroke conversely exhibits no temporal decline, and therefore our data constitute proof of concept that the current therapies for acute MI do not confer adequate protection against stroke, particularly in the early phase after MI. The use of oral anticoagulation after acute MI remains controversial, despite increasing evidence that suggests a potential benefit in stroke prevention (48, 54, 55), because of the concern that the risk for bleeding associated with warfarin use outweighs its benefit. Notwithstanding this valid concern, our data suggest that the use of antithrombotic measures relying on different agents should be revisited. Our documentation of the dynamic nature of the risk for stroke after MI can further assist in determining the appropriate duration of such therapies. The strong association between stroke and death further underscores the need to aggressively pursue preventive approaches.

Several synergistic factors contribute to the increase in the absolute number of strokes after MI, including the increase in the number of MI survivors and the increased prevalence of 2 chief characteristics associated with stroke, namely older age and diabetes mellitus. These factors, along with the increased awareness of the importance of morbidity after MI in the growing and aging population of survivors of MI (56), indicate that increased attention should be dedicated to devising more effective stroke prevention strategies.

**Limitations**

The risk for stroke has increased in black and Hispanic persons (57). Although the population of Olmsted County is becoming more diverse, the population during the study period consisted primarily of U.S. white persons. Thus, these findings should be reexamined in different racial and ethnic groups. We do not have information on the distri-

### Table 3. Risk for Death after Myocardial Infarction Associated with Stroke*

<table>
<thead>
<tr>
<th>Risk for Death</th>
<th>Unadjusted RR for Death (95% CI)</th>
<th>P Value</th>
<th>RR for Death Adjusted for Age and Sex (95% CI)</th>
<th>P Value</th>
<th>RR for Death Adjusted for Age, Sex, and Killip Class (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke</td>
<td>3.94 (3.32–4.67)</td>
<td>&lt;0.001</td>
<td>2.85 (2.40–3.38)</td>
<td>&lt;0.001</td>
<td>2.89 (2.44–3.43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early stroke†</td>
<td>3.15 (2.27–4.37)</td>
<td>&lt;0.001</td>
<td>2.22 (1.60–3.09)</td>
<td>&lt;0.001</td>
<td>2.27 (1.63–3.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Late stroke‡</td>
<td>4.03 (3.33–4.89)</td>
<td>&lt;0.001</td>
<td>2.95 (2.43–3.58)</td>
<td>&lt;0.001</td>
<td>2.99 (2.46–3.62)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* RR = relative risk.
† Strokes occurring ≤ 30 days after myocardial infarction.
‡ Strokes occurring > 30 days after myocardial infarction.
bution of follow-up visits after MI and could only match the comparison population on the risk factors of age, sex, and year of diagnosis. Thus, we could not determine the proportion of the excess risk for stroke associated with MI that might be explained by traditional risk factors or MI alone. The observational design of our study did not allow us to determine whether anticoagulant or antiplatelet medications were prescribed to treat or to prevent stroke after MI, limiting our ability to draw conclusions regarding the use of such medications and stroke risk. Although subtyping of ischemic strokes in our cohort is not available, its impact on analysis would probably be minimal; many early strokes would have been classified as cardioembolic, because of their temporal association to the MI (58).

Conclusions

These data from a geographically defined population indicate that patients with MI have a high risk for stroke, which is not declining as treatment for MI improves. The excess risk for stroke after MI compared with that expected in a population without MI is considerable, particularly in the early phase. It is also dynamic and declines as time from the index MI increases. The devastating impact of stroke on survival and the increased number of patients at risk because of improved survival after MI constitute an important public health matter for persons with coronary disease.

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