Differences between coronary disease and stroke in incidence, case fatality, and risk factors, but few differences in risk factors for fatal and non-fatal events

Lars Wilhelmsen1*, Max Köster2, Per Harmsen1, and Georg Lappas1

1 Section of Preventive Cardiology, The Cardiovascular Institute, Göteborg University, Drakängan 6, SE-412 50 Göteborg, Sweden; and 2 Centre for Epidemiology, National Board of Health and Welfare, Stockholm, Sweden

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Aims To compare incidence and mortality of coronary and stroke events, and risk factors for non-fatal and fatal events, respectively.

Methods and results Incidence and mortality were compared in all coronary (n = 559 341) and stroke (n = 530 689) events in Sweden from 1987 to 2001. Data from 28 years of follow-up of a random sample of 7400 men aged 47–55 and free of disease at baseline were used to compare risk factors. Incidence and 28 days of case fatality were considerably higher for coronary disease than for stroke, especially for men. Incidence of coronary disease decreased, especially for men (P = 0.0001 for both sexes), and mortality declined for both men and women during 1987 –2001 (P = 0.0001 for both sexes). Stroke incidence declined slightly (P = 0.0001 for both sexes), and there was a decline of mortality (P = 0.0001 for both sexes). Out-of-hospital mortality during the first 28 days was higher than in-hospital mortality for coronary events, whereas for stroke, in-hospital mortality was higher (in men) or the same (in women) as out-of-hospital mortality. High serum cholesterol was a strong risk factor for coronary events, but not for stroke. High blood pressure was a stronger risk factor for stroke. About 50% of men with both stroke and coronary disease died from coronary disease.

Conclusion Several differences regarding incidence, mortality, prognosis, and risk factors for stroke and coronary disease point towards different pathologies.

KEYWORDS Coronary disease; Stroke; Incidence; Mortality; Risk factors; Pathology

Introduction

Myocardial infarction and sudden coronary death (in the following denoted as coronary disease) and stroke are common causes of disability and death and are often discussed as two diseases of the same family and caused by atherosclerotic arterial disease. If there were major similarities between coronary disease and stroke, declining trends in the incidence of coronary disease would be expected also for stroke. Alternatively, decreasing incidence of coronary events could lead to risk of stroke in more people.1 If the two diseases had similar background and pathology, one would also expect similar risk factors. Elevated serum cholesterol is a strong risk factor for coronary disease, but in most prospective studies, it has not been associated with increased risk for stroke.2,3 However, lipid-lowering therapy with statins has reduced the incidence of both thrombotic stroke and coronary disease.4,5

Owing to the suggested similarities of the two diseases and their great impact on public health, they were analysed together in the recently published SCORE project.6 The project was forced to restrict the analysis to fatal events because of differences in criteria for non-fatal events in the contributing prospective studies. Against this background, it would be of interest to study further to what extent risk factors are similar for stroke and coronary disease and whether risk factors are the same for non-fatal and fatal events.

In the present paper, we have analysed mortality and morbidity data from the countrywide Swedish Acute Myocardial Infarction register, which contains data on incidence and mortality from 1987 until 2001 with a total of 340 721 male and 218 620 female non-fatal and fatal coronary events. A similar registration of non-fatal and fatal stroke events included 261 357 male and 269 332 female events.

In addition, data on 28 years of follow-up of 7400 men, free of these diseases at baseline, were used to compare risk factors for non-fatal and fatal coronary and stroke events.

Methods

Registration of events

A national hospital register of diagnoses at discharge has been in operation since 1972 in Sweden and includes all hospitals in the
country since 1987. The quality of the register during the period 1987–95 has been checked and found to be good. A file of the men of the population study described subsequently was also checked against this register and it was found that the register had missed only 3% of hospitalizations for myocardial infarction, atrial fibrillation (AF), or heart failure.

The Swedish Causes of Death Register has been operating since 1961 and found to miss only single events. In the present study, record linkage of the Hospital Discharge Register and the Causes of Death Register was performed. An event (non-fatal or fatal) that occurred within 28 days was considered to be the same event and was counted as one event.

In 1987, there was a change from the eighth to the ninth revision of the International Classification of Diseases (ICD) and in 1997, there was a change to ICD-10. These changes were taken into account in the present analyses. The ICD-8 codes were changed to ICD-9.

For coronary disease, ICD-9 code 410 and ICD-10 codes I21 and 22 were used; for stroke, ICD-9 codes 431, 434, and 436 and ICD-10 codes I60, 61, 63, and 64 were used.

Population study of men

The Multifactor Primary Prevention Study was started in Göteborg in 1970 and was intended as an intervention trial against smoking, hypercholesterolaemia, and hypertension at pre-defined levels in an intervention group comprising 10 000 men, a random third of all men in the city (n = 30 000) who were born between 1915 and 1925, but not in 1923. The remaining two-thirds of the population constituted two control groups of 10 000 men each. A first screening examination took place between 1970 and 1973 and the data from this screening examination are used in the present study. After 10 years of follow-up, 20% men surviving and still living in the area, according to the population census from the intervention group and one control group, were re-examined. Out of 1805 invited men in the control group, 1473 participated, and of 1803 invited controls, 1404 participated. After these 10 years of follow-up, risk factor values had decreased in the intervention group, but there were no significant differences in serum cholesterol, smoking, and blood pressure, or outcome between the intervention and control groups. Thus, any changes brought about by the intervention took place in the general population as well, as revealed in the randomly selected control group, and the present study group is considered to be representative of the background population.

Those men who responded to a postal questionnaire were invited to a screening examination in hospital, in which 7495 men (75% of the sample) took part. The questionnaire contained questions about history of myocardial infarction and stroke among mothers, fathers, and brothers/sisters, previous myocardial infarction, stroke, diabetes mellitus as well as chest pain and dyspnoea on exertion, smoking habits, psychological stress (defined as feeling tense, irritable or filled with anxiety, or having sleeping difficulties as a result of conditions at work or at home during the preceding 1–5 years), and physical activity at work and during leisure time.

Screening examinations were performed in the afternoon. Blood pressure was measured after 5 min rest to the nearest 2 mmHg, with the subjects seated. These afternoon blood pressures were found to be considerably lower when checked later at a more relaxed situation in a subsample; 175/115 mmHg is comparable with 165/95 at resting conditions. Body height was measured to the nearest centimetre and body weight to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kg)/height (m²). Serum cholesterol concentrations (from a sample taken after fasting for at least 2 h) were determined according to standard laboratory procedures. Details of the procedures have been published previously.

The follow-up extended through the year 1998. The endpoints were registered from several sources. Non-fatal and fatal myocardial infarction and stroke up to 65 years of age were recorded according to specific criteria in special registers. The national hospital discharge register, which included all ages, was also used. For the present analyses, the following principal or contributory diagnoses at hospitalization or death were used:

(i) Non-fatal myocardial infarction (ICD-9 code 410; ICD-10 code I21).
(ii) Death from coronary disease (ICD-9 codes 410, 411, 412, and 414; ICD-10 code I21).
(iii) Non-fatal and fatal stroke (ICD-9 codes 430–434, 436, and ICD-10 codes I60, 61, 63, and 64. I60 (subarachnoidal bleeding) was included in this analysis, but not in the national register of events.

The study was conducted according to the Declaration of Helsinki rules and was approved by the Ethics Committee of Göteborg University.

Statistical methods

Incidence and mortality rates were calculated with the mid-year Swedish population in the respective age groups as denominator. When age-standardization was performed, the Swedish mid-year population of the year 2000 was used as standard. Ages were categorized in 5-year age groups. Differences over time in incidence and mortality were tested with logistic regression. Owing to the large number of events, significant differences are to be expected for some time trends that do not seem impressive. Differences between discrete variables and differences between continuous variables were tested with χ² analysis and t-test, respectively. Two-sided test with P-values <0.05 are considered as significant.

Results

Incidence, mortality, and case fatality of coronary disease and stroke in Sweden

The age-standardized incidence of non-fatal and fatal myocardial infarctions during 1987–2001 among men and women is shown in Figure 1. The incidence was about two times higher for men compared with women, and there was a decline in incidence for men from about 1000/100 000 of the population per year in 1987 to about 800 in 2001 (P = 0.0001); for women, the incidence was around 400/100 000 and there was a slight decline (P = 0.00021). There is a slight increase in incidence for 2001, which can be attributed to change of criteria for myocardial infarction; elevated levels of plasma troponin T became accepted as criterion for the diagnosis. The declining incidence among men was seen for all age groups, except for men aged >80. Among men aged ≥90, the incidence increased (data...
not shown). For women, the incidence declined between ages 60 and 84 years, but it increased in the highest age groups (data not shown).

Mortality from coronary disease declined during the same period for both men ($P = 0.0001$) and women ($P = 0.0001$) (Figure 2). This was evident for all age groups of both men and women, except those aged ≥90. These trends reflected in declining age-standardized case fatality (including deaths in hospital and outside hospital within 28 days) from 50.5% in 1987 to 33.8% in 2001 among men ($P = 0.0001$) and from 46.7% in 1987 to 31.9% in 2001 among women ($P = 0.0001$).

The number of coronary deaths outside hospital exceeded that of in-hospital deaths, especially for men (all numbers for mortality within 28 days) (Figure 3). During the entire period of 1987–2001 and for all ages, there were 145,345 deaths within 28 days among men and 61.5% of these occurred outside hospital. For women, there were 103,484 deaths and 56.3% of these occurred outside hospital.

Incidence and mortality for stroke are shown in Figures 4 and 5. The age-standardized incidence was just above 700/100,000 for men and just above 500/100,000 for women. Thus, the sex difference for stroke was smaller than that for coronary disease. For both sexes, there was a moderately declining incidence over the period ($P = 0.0001$). The 28 days of case fatality among men declined slightly from 180/100,000 to just over 160/100,000 from 1987 to 2001 ($P = 0.0001$) and declined among women from about 145/100,000 to just over 130/100,000 during the same period ($P = 0.0001$).

The number of deaths in hospital and outside-hospital from stroke appears in Figure 6. For men, in-hospital deaths were higher than out-of-hospital deaths for the entire period of 1987–2001, and was about 1.3 times higher than out-of-hospital deaths. For women, the numbers were similar for the two types of death.

Tables 1 and 2 give the number and incidence for coronary disease and stroke among men and women per 10-year age groups during the year 2001 (data available for the last year). Incidence of coronary disease was higher for men compared with women for all age groups, with the ratio 4.6 for the age group 35–44 years, declining to 1.5 for the
group >85 years. For stroke, the men/women ratio was lower; 1.4 for the lowest age group decreasing to 1.1 for those aged >85. Thus, for both diagnoses and in all age groups, the incidence was higher for men than for women. However, the absolute number of women with strokes was higher in the two highest age groups because of the higher number of women in the population in these ages.

Tables 3 and 4 show the case fatality for men and women, respectively, who died during the first 28 days from onset and those who died between 29 days and 5 years. The results are based upon the entire period 1987–2001.

The pattern was very similar for men and women; 28 days case of fatality was about twice as high for coronary disease (24–75%) compared with stroke (15–44%), whereas case fatality for stroke tended to be higher for the long-term follow-up (6–24% for coronary disease vs. 9–44% for stroke). Thus, for age groups over 55 years, long-term (29 days to 5
years) case fatality from stroke increased to about twice as high compared with that for coronary disease.

Risk factors for coronary disease and stroke among men in Göteborg

The original sample of men included 7495 aged between 47 and 55. Myocardial infarction or stroke had occurred before baseline in 95 men, and 7400 remained for the present analyses. During up to 28 years of follow-up, 1150 men suffered primarily non-fatal myocardial infarction and 554 men fatal coronary disease. Out of the fatal events, 278 (50%) had diagnoses for myocardial infarction or coronary atherosclerosis. Primarily non-fatal strokes occurred in 855 men and fatal events in 150 men. Out of these, 179 men had a diagnosis of subarachnoidal bleeding or intracerebral bleeding.

Using Cox regression analyses, independent risk factors for the combination of non-fatal and fatal events have been published previously2,12 (Harmsen et al. has submitted for publication). Independently significant risk factors for coronary disease (non-fatal and fatal) during 28 years of follow-up were age, myocardial infarction in mothers, fathers, and siblings, chest pain on exercise, diabetes mellitus, smoking, low social class, psychological stress, high serum cholesterol, and high blood pressure (in spite of treatment), but not low physical activity during leisure time or high BMI.

For stroke (non-fatal and fatal), independent risk factors were age, previous transient ischaemic attacks, AF, diabetes mellitus, psychological stress, smoking, high blood pressure, and high BMI, but not high serum cholesterol or low physical activity during leisure. Table 5 lists risk factors that differed between coronary disease and stroke. Coronary disease and stroke events during 28 years of follow-up by serum total cholesterol are shown in Figure 7.

Table 6 gives baseline data for primarily non-fatal and fatal events within 28 days among those who suffered coronary events and stroke events, respectively, as well as for those who did not suffer any of these diseases during the following 28 years. Taking into consideration that multiple tests were performed, only P-values less than 0.01 may be considered important. Only few differences were found. Men with fatal coronary events tended to be older (P = 0.013) and had diabetes more often (P = 0.006). They tended to have a family history of stroke more often among mothers (P = 0.036) compared with men who suffered non-fatal events. Men who suffered fatal strokes tended to report chest pain (P = 0.011) and dyspnoea on effort (P = 0.027) more often than men with non-fatal strokes, but the baseline age did not differ. None of the other baseline factors as mentioned in Methods differed between non-fatal and fatal events for either coronary disease or stroke.

Out of the 1150 primarily surviving men with coronary disease, 676 (59%) died during 12 483 person-years of follow-up. Of these men, 68% died from coronary disease, 5% from stroke, and 27% from other diseases (Figure 8). Out of the 855 surviving men with stroke, 478 (56%) died during 8315 person-years of follow up. Causes of death were coronary disease (52%), stroke (13%), and other causes (35%) (Figure 8). Thus, a considerable proportion of the men with stroke died from coronary disease.

Discussion

When comparing coronary disease and stroke, we found that incidence and short-term case fatality of coronary disease were considerably higher than that of stroke, especially for men. Incidence of coronary disease decreased especially for men, and mortality declined for both men and women during 1987–2001. For stroke, there was a less marked decline regarding incidence and there were slight declines in mortality. Out-of-hospital mortality during the first 28 days from occurrence was higher than in-hospital mortality for coronary events, whereas for stroke, in-hospital mortality was higher (in men) or the same (in women) as out-of-hospital mortality. The 28 days of case fatality from coronary disease was nearly three times higher for men and at least two times higher for women compared with case fatality of stroke during that period. It is known that a substantial proportion of these early coronary deaths are instantaneous and are caused by fatal cardiac arrhythmias. Longer-term (29 days to 5 years) case fatality was higher for stroke than for coronary disease.

There were well-known differences in risk factors between coronary disease and stroke: serum cholesterol being a strong risk factor for coronary events, but not for stroke, not even

![Figure 7](image-url)  
**Figure 7** Coronary and stroke events by serum total cholesterol at baseline during 28 years of follow-up of 7322 men free of any of these diseases at baseline.

<table>
<thead>
<tr>
<th>Table 5 Differences between coronary disease and stroke for independent risk factors among men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
</tr>
<tr>
<td>-------------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Coronary disease in father</td>
</tr>
<tr>
<td>Previous TIA</td>
</tr>
<tr>
<td>AF</td>
</tr>
<tr>
<td>Serum cholesterol (mmol/L)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>BMI</td>
</tr>
</tbody>
</table>

A 28 years of follow-up of 7400 men aged 47–55 at baseline. TIA, transitory ischaemic attack; n.s., not significant.
when only pure thrombotic strokes are analysed, a finding that is contrary to what was published by Lawlor et al.\textsuperscript{13} High blood pressure and high BMI were more important risk factors for stroke than for coronary events. However, 50\% of both stroke and coronary disease men died from coronary disease, suggesting similar background pathology for the two diseases.

The changing incidences for stroke and coronary disease are of interest. It has been hypothesized that decreasing coronary incidence might lead to increased stroke incidence because of the higher number of surviving coronary patients at risk for stroke. However, death from stroke was not common among the post-infarct men of the present study. On the basis of statistical calculations, Peeters et al.\textsuperscript{1} denied that increased coronary survival could lead to increased stroke incidence. The declining coronary mortality is, to some extent, due to the better hospital treatment, but it is noteworthy that out-of-hospital coronary mortality also declined. The autopsy rate was previously high, especially among out-of-hospital deaths, and it was earlier shown that this mortality was mainly caused by coronary disease.\textsuperscript{14} It has been shown that the declining coronary incidence is primarily due to primary preventive achievements regarding smoking, serum cholesterol, and blood pressure.\textsuperscript{14} The previous decline in mean blood pressure in the population seems to have halted recently,\textsuperscript{15} and that may be part of the reason for the considerable decline of stroke incidence. Increased body weight, which is not of strong importance for coronary disease (yet) according to our studies,\textsuperscript{12} but is important for stroke,\textsuperscript{16} is another factor that may have played a part. The different stroke subtypes have different pathological background—athero-thrombosis vs. haemorrhages. Since 1983, at least 90\% of stroke diagnoses were based upon CT scan,\textsuperscript{2} and only 18\% of the strokes were due to any type of haemorrhage. When we analysed risk factors for thrombotic/occlusive strokes separately, we came to the same risk factor pattern. Thus, athero-thrombotic pathology is the main background for most stroke events, and the risk factor difference against coronary disease seems to be due to differences in pathology for different vascular beds. In another study, we found increased fibrinogen levels to be strongly associated with both stroke and coronary disease, whereas coronary disease, but not stroke, was associated with high total plasma cholesterol in that study.\textsuperscript{17} We studied only men in the present study because comparable long-term results on risk factors from the same population and with a great number of events were available. In an earlier study of women, we found risk factors for coronary disease to be high serum cholesterol and triglycerides, smoking, diabetes, as well as high blood pressure, and for stroke, triglycerides and high blood pressure, but the number of endpoints was limited to 67 and 66 events.\textsuperscript{18} Puddu et al.\textsuperscript{19} discussed the possible different pathologies between stroke and coronary disease and concluded that they are two aspects of the same disease, but that the

<p>| Table 6 Baseline factors for men who suffered primarily non-fatal and fatal coronary disease and stroke, respectively, as well as for men who did not suffer any of these diseases during 28 years of follow-up (Primary Prevention Study, Göteborg) |</p>
<table>
<thead>
<tr>
<th>Factor</th>
<th>Coronary events</th>
<th>Stroke events</th>
<th>No disease (n = 4691)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-fatal (n = 1150)</td>
<td>Fatal (n = 554)</td>
<td>Non-fatal (n = 855)</td>
</tr>
<tr>
<td>Age</td>
<td>51.9</td>
<td>52.2</td>
<td>52.0</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>6.74</td>
<td>6.66</td>
<td>6.48</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>153.1</td>
<td>154.9</td>
<td>153.8</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>97.4</td>
<td>97.4</td>
<td>99.0</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>79.3</td>
<td>79.6</td>
<td>79.2</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>175.0</td>
<td>175.0</td>
<td>174.9</td>
</tr>
<tr>
<td>Smoking (yes)</td>
<td>58</td>
<td>58</td>
<td>54</td>
</tr>
<tr>
<td>Physical activity during leisure (%)</td>
<td>14</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Psychological stress (%)</td>
<td>18</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Chest pain on effort (%)</td>
<td>18</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Dyspnoea on effort (%)</td>
<td>24</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>3</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Myocardial infarction in father (%)</td>
<td>19</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Myocardial infarction in mother (%)</td>
<td>11</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Stroke in father (%)</td>
<td>19</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>Stroke in mother (%)</td>
<td>18</td>
<td>22</td>
<td>20</td>
</tr>
</tbody>
</table>

P-values for difference between non-fatal and fatal events are given in the text.

Figure 8 Cause of death during follow-up among primarily surviving men with coronary disease (n = 1150) and stroke (n = 855).
reactivity of the coronary and cerebral arteries is different. Falk proposed that the ulceration of atherosclerotic plaques is important in coronary occlusion, but not in intracranial cerebral arteries. It is also known that individuals with familial hypercholesterolaemia develop myocardial infarction at a young age, but they do not develop stroke. The coronary atherosclerotic plaque had higher lipid content, whereas the cerebral plaque had higher content of fibrous tissue, which in turn is more strongly affected by high blood pressure.

An important practical question is whether the predictions in the SCORE project, which was based upon fatal coronary and stroke events, can also be used for non-fatal disease. In the present analyses, diabetes was a stronger risk factor for fatal events when compared with non-fatal events, but diabetes was not included in the SCORE diagram. Thus, it would not make a difference. A problem is, however, that out of the three risk factors used in SCORE, serum cholesterol, blood pressure, and smoking, there are quantitative differences regarding cholesterol and blood pressure. In the present study, the relative risk for coronary events with 1 mmol/L increase of total serum cholesterol was 1.220, but was insignificant for stroke. The risks associated with increase of blood pressure were more similar. Risk for stroke increased with 1.026 and for coronary risks associated with increase of blood pressure were more similar. Risk for stroke increase with 1.026 and for coronary with 1.020 for 1 mmHg increase of diastolic blood pressure.

The results regarding coronary events agree with other prospective studies summarized by Dobson et al. When using SCORE, risk of coronary events are somewhat overestimated by blood pressure values, but underestimated by serum cholesterol values, and vice versa for stroke events.

References