Epidemiology of Acute Cerebrovascular Disease Before The Age of 55 in the Stockholm County 1973–77: I
Incidence and Mortality Rates
K. L. Mettinger, M.D., C. E. Söderström, M.D., and E. Allander, M.D.

SUMMARY The incidence and mortality rates of cerebrovascular disease (CVD) before age 55 were estimated for the Stockholm county between 1973 and 1977 using community based diagnosis and death statistics registers. Annual validation procedures concluded that less than 5% of hospitalized patients may have escaped registration. During the study period a diagnosis of CVD (initial stroke or TIA) was reported in 2,103 individuals, giving annual average crude incidence rates for stroke and TIA of 34 and 4 respectively per 100,000 inhabitants under age 55. Hemorrhagic lesions were reported in 45.4% of the cases, ischemic lesions in 33.1% and unclassified lesions in 21.5%. For all diagnostic categories a strong correlation to age is found, and for most categories the male:female ratio is high. The mortality rates are high for hemorrhagic lesions and low for ischemic and unclassified lesions. Incidence rates are higher than in Uppsala and Gothenburg, Sweden, but lower than in North Karelia, Finland. Mortality rates are similar to those reported by most other investigators.

Material and Methods
Location of the Study
Stockholm county had a total population of 1,485,587 in 1973 and 1,512,179 in 1977. The census is updated at two-week intervals. In 1973, 77% and in 1977, 76% of the inhabitants were in the age group under 55 years. For health administrative purposes the Stockholm county is divided into well defined catchment areas, each strictly served by an area community hospital or a teaching hospital with this function. Patients with acute stroke are almost always admitted to hospitals and in the age group under 55 they were, during the study period, in about 50% of the cases admitted immediately or later to the five neurological or neurosurgical clinics for specialist care.
### Table 1

**Review of Contemporary Stroke Incidence Studies (First Strokes per 1000 Inhabitants)**

<table>
<thead>
<tr>
<th>Ref. number</th>
<th>Place and time of study</th>
<th>No. of cases</th>
<th>Design</th>
<th>Au-topsy</th>
<th>Incidence rates age groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CT-scan</td>
<td>%</td>
<td>&lt;55</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>7,8</td>
<td>Gothenburg, Sweden</td>
<td>690</td>
<td>CP 0</td>
<td>30</td>
<td>0.2* 0.2 0.5* 0.3*</td>
</tr>
<tr>
<td>7,9</td>
<td>Fredriksberg, Denmark</td>
<td>556</td>
<td>CP 0</td>
<td>83</td>
<td>0.1 0.1 1.9 1.6</td>
</tr>
<tr>
<td>7</td>
<td>Copenhagen, Denmark</td>
<td>640</td>
<td>CP 0</td>
<td>12</td>
<td>0.2 0.1 2.0 2.3</td>
</tr>
<tr>
<td>7,10</td>
<td>Espoo, Finland</td>
<td>299</td>
<td>CP 0</td>
<td>30</td>
<td>0.4 0.3 1.2 1.3</td>
</tr>
<tr>
<td>7</td>
<td>North Karelia, Finland</td>
<td>774</td>
<td>CP 0</td>
<td>83</td>
<td>0.5 0.4 1.8 1.9</td>
</tr>
<tr>
<td>7</td>
<td>Zagreb, Yugoslavia</td>
<td>475</td>
<td>CP 0</td>
<td>12</td>
<td>0.3 0.3 1.2 0.8</td>
</tr>
<tr>
<td>7</td>
<td>Zerifin, Israel</td>
<td>778</td>
<td>HR 5</td>
<td>12</td>
<td>0.1 0.1 1.0 1.2</td>
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<tr>
<td>7</td>
<td>Akita, Japan</td>
<td>266</td>
<td>CP 0</td>
<td>30</td>
<td>1.1 0.5 2.9 2.3</td>
</tr>
<tr>
<td>7</td>
<td>Saku, Japan</td>
<td>546</td>
<td>CP 0</td>
<td>83</td>
<td>0.6 0.2 2.5 1.8</td>
</tr>
<tr>
<td>7</td>
<td>Fukuoka, Japan</td>
<td>108</td>
<td>CP 0</td>
<td>83</td>
<td>0.3 0.1 1.2 0.5</td>
</tr>
<tr>
<td>7</td>
<td>Osaka, Japan</td>
<td>103</td>
<td>CP 0</td>
<td>83</td>
<td>0.1 0.1 1.2 1.1</td>
</tr>
<tr>
<td>11</td>
<td>Tilburg, The Netherlands (1978-80)</td>
<td>152</td>
<td>CP 33</td>
<td>33</td>
<td>0.3 0.3 1.7 1.6</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>&lt;35 35-44 45-54 All ages</td>
</tr>
<tr>
<td>12</td>
<td>Dippoldiswalde, E. Germany (1972-73)</td>
<td>110</td>
<td>CP 0</td>
<td>?</td>
<td>0.0 0.0 1.5 1.0</td>
</tr>
<tr>
<td>12</td>
<td>Berlin-Lichtenberg, E. Germany (1972-73)</td>
<td>382</td>
<td>CP 0</td>
<td>83</td>
<td>0.0 0.2 0.8 1.0</td>
</tr>
<tr>
<td>13</td>
<td>National Survey of Stroke, USA (1975-76)</td>
<td>663</td>
<td>HR 5</td>
<td>12</td>
<td>0.0 0.2 1.1 1.0</td>
</tr>
<tr>
<td>14</td>
<td>Harlem, USA, 1971</td>
<td>328</td>
<td>HR 0</td>
<td>?</td>
<td>0.2 1.5 1.9 2.1</td>
</tr>
<tr>
<td>15</td>
<td>Melbourne, Australia, 1978-79</td>
<td>508</td>
<td>CP 0</td>
<td>?</td>
<td>0.0* 0.2 1.2 3.8*</td>
</tr>
<tr>
<td>15</td>
<td>Stockholm, Sweden 1973-77 (present study)</td>
<td>2.103*</td>
<td>HMR 25</td>
<td>75</td>
<td>0.1 0.5 1.5 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-29 30-39 40-49 All ages</td>
</tr>
</tbody>
</table>

*The Uppsala study only included patients under age 70 (subarachnoid hemorrhage excluded), the Gothenburg study only those under age 65 and the Stockholm study only those under age 55. The lower age-limit for the population at risk was 15 in Gothenburg, 20 in Shibata, Tartu and Soderhamn and 25 in Melbourne.

C = community based stroke register; H = hospital register; M = mortality register; P = prospective; R = retrospective.

### Case Detection

Since 1970 all inpatient care periods in the Stockholm county are reported to a computerized register using either an on-line system or a system of forms. For identification of each individual, a ten digit civic registration number is used. Inpatient care is registered in detail including diagnoses, dates of admission and discharge, nationality and home address. For all hospitals except the Karolinska Hospital, which until recently has been administered by the Swedish government, the registration also includes the use of x-ray investigations. Primary as well as secondary diagnoses are reported, coded according to the 1965 revision of the International Classification of Diseases. Details about this medical information system have been reported previously. The proportion of hospitalizations not reported are estimated annually: about 5% for all hospitals during the study period but only 3% for departments of internal medicine and less than 1% for departments of neurology.

The present material was compiled by selecting from this register data on all patients hospitalized under the age of 55 years, where the primary or one of the secondary diagnoses was 430.00-438.99, when the date of discharge was found in the five year interval from January 1, 1973 to December 31, 1977 and when the place of residence at that time was within the Stockholm county.
Furthermore, supplementary material was obtained by selecting from the Register for Death Statistics of the National Central Bureau for Statistics all individuals deceased during the same five year period and meeting the other criteria above. All subjects were evaluated separately with regard to consecutive hospitalization after the onset of the disease. The final material was derived from 2,082 hospitalizations that represented 1,855 patients. By including individuals who died before admission to hospital (n = 248) the final material consisted of 2,103 individuals.

Diagnostic Procedures

The diagnostic classification was based on neurological and neuroradiological examinations, examinations of the cerebrospinal fluid or the findings at operation or autopsy. The frequency of diagnostic methods could be estimated using the computerized codes for x-ray investigations and data from the Department of Neurology, Karolinska Hospital (Söderström et al, to be published). Computed tomography had been used in about 25% and isotope brain scan in another 25% and angiography of aortocranial arteries in 50% of the total material. In addition, the frequency of cerebrospinal fluid examination may be estimated to be about 40%, and was performed in almost all patients with subarachnoid hemorrhage and including spectrophotometry in 75% of the subjects admitted to the Department of Neurology, Karolinska Hospital. The autopsy frequency in the mortality register was about 75%.

The definitions and routines for diagnostic classification of CVD in Sweden during the study period essentially agree with those recommended by WHO4* and the Ad Hoc Committee on Cerebrovascular Diseases of the National Institute of Neurological Diseases and Blindness, USA.47 Transitory ischemic attack (TIA) is defined as rapidly developing signs of focal cerebral dysfunction of presumed vascular origin not lasting for more than 24 hours.47,48 Stroke is defined as rapidly developed signs of focal (or global) disturbance of cerebral dysfunction leading to death or lasting more than 24 hours with no apparent cause other than vascular.46 The term "global" mainly applies to cases of subarachnoid hemorrhage without focal neurological signs. Cases where further examination revealed nonvascular intracranial disease (e.g. neoplastic disease, trauma or infectious disease) were excluded from the study.

Table 2  Average Annual Incidence Rates of Initial Strokes per 100,000 Inhabitants Under Age 55 in Stockholm County 1973–77

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Observed person-years</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Number</td>
<td>Rate</td>
</tr>
<tr>
<td>&lt;25</td>
<td>1,266,489</td>
<td>1,240,690</td>
<td>71</td>
<td>6</td>
</tr>
<tr>
<td>25-34</td>
<td>674,315</td>
<td>657,789</td>
<td>99</td>
<td>15</td>
</tr>
<tr>
<td>35-44</td>
<td>446,639</td>
<td>426,318</td>
<td>225</td>
<td>50</td>
</tr>
<tr>
<td>45-54</td>
<td>445,324</td>
<td>465,280</td>
<td>723</td>
<td>162</td>
</tr>
<tr>
<td>&lt;55</td>
<td>2,833,767</td>
<td>2,796,077</td>
<td>1,118</td>
<td>39</td>
</tr>
</tbody>
</table>

Results

Crude Incidence Rates

A diagnosis of CVD (first stroke or TIA) was reported in 2,103 individuals under the age of 55 years, all residents of the Stockholm county, during the period January 1, 1973 to December 31, 1977. The crude average annual incidence estimate (attack rate) of first strokes per 100,000 inhabitants under age 55 is 34, if TIA is excluded, (39 for males and 28 for females, see table 2). The total number of hospitalizations may be used for an estimate of the attack rate of subsequent strokes, being 38 per 100,000. The number of patients discharged with a diagnosis of TIA may be used to estimate the annual incidence rate of TIA, then being 4 (5 for males an 3 for females per 100,000 inhabitants under age 55, table 3). The number of individuals with a diagnosis of CVD and incidence estimates by age group and sex are shown in table 2.

Incidence by Diagnostic Category

The incidence rates for each of diagnostic categories by age and sex are presented in table 4. Hemorrhagic lesions accounted for 45.4% of the total material: 26.3% with subarachnoid hemorrhage and 19.1% with intracerebral hematoma. Ischemic lesions were reported in 33.1%. A specific diagnosis was considered impossible to obtain in 21.5%.

Influence on Incidence by Age and Sex

The incidence for all diagnostic groups shows a strong correlation to age (r always >0.88).

The male/female ratios of incidence rates for each type of CVD by age group are shown in table 5. The sex ratio varies for each category. For subarachnoid hemorrhage under age 25 and above 45 as well as for ischemic lesions in the age group 25–34 there is a female preponderance. For intracerebral hemorrhage, ischemic and unclassified lesions there is a notable male preponderance in the age groups above 35, increasing with age.

Mortality Rates

The analysis of the accumulated case mortality rates six months after onset of disease demonstrates that the majority of deaths occurred during the first month. The mortality rates (table 6) are highest for intracerebral hemorrhage, 59%, as compared to 39% for subarachnoid hemorrhage, 21% for unclassified lesions and about 19% for ischemic lesions.
Discussion

The Swedish national health insurance system covers all inhabitants, subsidizing more than 95% of the patient’s total costs for hospital care and most of the costs for out-patient care. Thus, the availability of hospital care is high, particularly in an urban area like the Stockholm community. As a matter of fact, earlier community based epidemiological studies of stroke in Sweden have demonstrated that very few patients with acute stroke are treated outside hospitals. The occurrence of TIA has not been studied in Sweden, but it may be assumed that the majority of those under 55 years, who seek medical help would generally also be admitted to or referred to hospitals for specialist care.

The computerized inpatient care register of Stockholm county has been shown to be a useful tool for epidemiological studies. Even if the case ascertainment and the diagnostic accuracy is undefined in the present material, the high rate of specialist care and diagnostic procedures suggests that the classification, indeed, may be reliable, as compared to several other contemporary epidemiological studies of CVD (table 1).

The crude incidence rates for stroke before 55 (table 2) is higher than in the reports from Gothenburg and Uppsala in Sweden as well as Copenhagen and Fredriksberg in Denmark but lower than in Espoo and North Karelia in Finland. Sex ratios differ widely between reported series, but except for subarachnoid hemorrhage there is generally a male preponderance, increasing with age, as found in the present study.

The mortality rates specified by age, sex and type of stroke (table 3) are found to be almost identical to those reported by other investigators. However, the mortality rates in the present study may be slightly high since some of the diagnoses of CVD in death certificates may relate to onset of disease before the study period.

A reliable analysis of temporal trends is not possible in a study covering only five years. In a study of CVD in Uppsala, Sweden, 1967–71, a downward trend in the incidence of cerebral hemorrhage and infarction was observed during the study period as well as by comparison with incidence figures reported from the same hospital region in 1964. However, in the present study the annual incidence rates show a slight increase for subarachnoid hemorrhage and ischemic lesions, whereas mortality rates remain fairly stable. This is in agreement with a parallel increase in the incidence of acute myocardial infarction in the Stockholm county, shown in a recent study using the same methodology.

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Diagnostic Categorization of Stroke

The accuracy of a reported diagnosis depends by necessity on the sophistication and skill of each institution and is also partly disease specific: subarachnoid hemorrhage is found to be the most reliably diagnosed in most studies.\(^1\)\(^6\) The diagnostic reliability perhaps may be expected to be greater in several earlier studies, as the use of diagnostic methods and the performance of autopsy is high in the present material. Yet, the separation of hemorrhagic and ischemic lesions was considered impossible in 21.5% of the patients for the most part probably because many patients, especially those with minor strokes, may have been admitted too late to allow the optimal use of diagnostic methods.

The difficulty in the classification of stroke is not peculiar to the present material. The National Survey of Stroke in the U.S.\(^1\)\(^3\) found that 50.2% of the 1,846 patients from the study period 1971–76 were categorized as strokes of unspecified type. Also, in the WHO multicenter stroke project the validity and consistency of diagnoses were tested with 60 randomly chosen case reports assessed by European, Japanese and other centers.\(^2\)\(^5\) The distinction between types of strokes was found to be inconsistent in about 25% of the cases. Hence, incidence rates for specific categories of stroke should be interpreted with caution. The increasing use of CT-scan and CSF-spectrophotometry may be expected to further increase the diagnostic accuracy.\(^2\)\(^3\)\(^2\)\(^4\) in future studies of CVD before the senescence.

The portion of subarachnoid hemorrhage (26%) in the present material is higher than in young stroke patients in Tilbury, the Netherlands, (19%).\(^1\)\(^1\) It is also higher in these age groups than in materials from all ages, the same portion being about 8%.\(^3\) The ratio of intracerebral hemorrhage to cerebral infarction is about 0.1 in most age groups, which is in agreement with the findings in most community-based incidence studies, reporting a ratio in the range 0.1–0.2. Obvi-ously intracerebral hemorrhage, although heavily burdening mortality rates, is much more infrequent than cerebral infarction.

The age correlation, sex ratio as well as fatality rates shows a great variation between different categories of stroke. However, there is a notable agreement in the data for cerebral infarction and unclassified lesions, suggesting that the majority of these lesions really are infarctions. This hypothesis is also supported by the results of a pilot study in the National Survey of Stroke,\(^1\)\(^3\) where 95% of randomly selected unclassified cases fulfilled the criteria for thrombotic infarctions.

Regional Variation within Sweden

When the present results are compared to available data from the WHO study of Gothenburg, Sweden\(^8\) the age and sex specific incidence rates in this age group (table 7) are considerably higher for most diagnostic categories. This could partly reflect a better case-detection in the present study. In the Gothenburg investigation about 10% of hospitalized subjects were believed to be undetected, judging from retrospective validation procedures. However, the incidence rates in the age groups 15–44 and 45–54 is 2.2 and 1.6 times higher in Stockholm than in Gothenburg during five year periods which largely overlapped. Thus, it appears a reasonable conclusion that the incidence of CVD before age 55 is higher in Stockholm than in Gothenburg during the study period.

Various explanations for such a geographical variation in stroke incidence between two regions of Sweden have to be considered. It should be noted that no evident differences in the incidence of myocardial infarction were found in comparable studies of the two populations.\(^4\) This gives further support to the conclusion that the difference in stroke incidence is real and not an artefact due to systematic errors in methodology. The portion of immigrants (8 and 7% respectively) e.g. from Finland (3.9 and 2.5%) was slightly higher

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Subarachnoid hemorrhage</th>
<th>Intracerebral hemorrhage</th>
<th>Infarction</th>
<th>TIA</th>
<th>Unclassified lesions</th>
<th>Mean</th>
</tr>
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<tbody>
<tr>
<td>&lt;25</td>
<td>0.7</td>
<td>1.0</td>
<td>1.1</td>
<td>0.3</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>25–34</td>
<td>1.0</td>
<td>2.0</td>
<td>0.6</td>
<td>0.4</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>35–44</td>
<td>1.1</td>
<td>2.4</td>
<td>1.0</td>
<td>1.6</td>
<td>2.0</td>
<td>1.7</td>
</tr>
<tr>
<td>45–54</td>
<td>0.9</td>
<td>1.8</td>
<td>1.7</td>
<td>2.1</td>
<td>2.8</td>
<td>1.9</td>
</tr>
</tbody>
</table>

*Only one patient with TIA died.
in Stockholm than in Gothenburg county during the years 1973–75. A higher per cent of Finnish immigrants in Stockholm could have contributed to a higher stroke incidence since the Finns may be expected to run a higher stroke risk. Also climatological differences have to be considered. Future studies are needed to elucidate these questions.

References

Risk of Stroke in Patients With Mitral Annulus Calcification

ANTHONY J. FURLAN, M.D., ATANASE R. CRACIUN, M.D., ERNESTO E. SALCEDO, M.D.*
AND MARCELLO MELLINO, M.D.*

SUMMARY 63 patients with mitral annulus calcification (MAC) were followed for an average of 3.4 years. Two patients experienced TIA, both ipsilateral to a previous endarterectomy site, and IV-DSA demonstrated normal extracranial vessels. There were 3 strokes (5%), all fatal, but none could be attributed to embolism. Embolic stroke due to MAC is rare and difficult to prove due to coexistent atherosclerosis. Associated cardiac conditions such as atrial fibrillation, which might increase the risk of embolism, usually occur with MAC ≥ 5 mm. In many patients, MAC may be better viewed as a marker of generalized calcific atherosclerosis rather than as an immediate embolic source.

ALTHOUGH MITRAL ANNULUS CALCIFICATION (MAC) has been implicated as a cause of embolic stroke,1,2 no natural history studies have addressed this issue. We studied the frequency of cerebrovascular events in 63 patients with MAC diagnosed by echocardiography and cardiac catheterization.

Methods

Between 1977 and 1981, 65 patients with MAC demonstrated on echocardiography (M-mode or 2-dimensional) were seen at the Cleveland Clinic Foundation. The echocardiographic criteria for the diagnosis of MAC included the presence of a dense band of echoes behind the posterior cusp of the mitral valve, anterior to the posterior wall of the left ventricle, and moving in parallel with the left ventricular endocardium. Fifty six patients also underwent cardiac catheterization, which confirmed the presence of MAC. Follow-up data from the time of echocardiography and was accomplished using available medical records, telephone interviews and a standardized questionnaire.

Results

Follow-up averaged 3.4 years and was achieved in 63 patients (97%). There were 32 men and 31 women with a mean age of 65 years (range, 47–78 years).

Presenting symptoms included: angina pectoris, 50 patients (79%); congestive heart failure, 34 patients (54%); cardiac dysrhythmia, 22 patients (35%); syncope, 15 patients (24%). Associated medical conditions are given in table 1.

Four patients presented with amaurosis fugax and 2 with hemispheric transient ischemic attacks (TIA). All of these patients had hypertension and coronary atherosclerosis, 3 had left atrial enlargement, 5 had compensated congestive heart failure, and 1 had atrial fibrillation. Four of the patients with TIA underwent intravenous digital subtraction angiography (IV-DSA); none underwent intraarterial angiography. IV-DSA demonstrated mild irregularity of the internal carotid artery (ICA) origins in 2 patients. In 2 patients IV-DSA showed significant ulcerated stenosis of the ipsilateral ICA origin; both underwent carotid endarterectomy.
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K L Mettinger, C E Söderström and E Allander

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