Incidence of Stroke in Young Adults in Florence, Italy

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A population-based study specifically addressing stroke in young adults (aged 15–44 years) was conducted in Florence, Italy, from 1983 to 1985. We identified 47 cases of first stroke by means of a daily check of the medical facilities of the city and nearby towns and a review of death certificates. Patients were assessed by a neurologist shortly after the onset of the stroke, and computed tomography or autopsy was performed in 96%. The average annual incidence rate for all stroke (cases per 100,000 population per year) was 9.0 (95% confidence interval 5.8–13.4) for males and 8.7 (95% confidence interval 5.5–13.0) for females. The average annual incidence rates for the pathologic types of stroke were 3.4 for cerebral infarction, 3.2 for subarachnoid hemorrhage, and 1.9 for intracerebral hemorrhage. The case–fatality ratio was 23.4% at 1 month. Among patients with ischemic strokes, atherosclerosis and cardiac disease accounted for 50% of the cases. Based on angiography or autopsy findings, aneurysm or arteriovenous malformation were demonstrated in 88% of the patients with subarachnoid hemorrhage. In 50% of the patients with intracerebral hemorrhage, no cause of bleeding was detected. Our study may supply information about stroke pathologic types in an unselected series of young adults. (Stroke 1988;19:977–981)
TABLE 1. Average Annual Age- and Sex-Specific Incidence Rates of First Stroke in Young Adults, Florence, Italy, 1983-1985

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Male (no.)</th>
<th>Female (no.)</th>
<th>Incidence rate (no./100,000/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>331323</td>
<td>028580</td>
<td>Male Rate 3.2 95% CI 0.7-9.3</td>
</tr>
<tr>
<td>25-34</td>
<td>728477</td>
<td>628244</td>
<td>Male Rate 8.2 95% CI 3.3-16.9</td>
</tr>
<tr>
<td>35-44</td>
<td>1429151</td>
<td>1731424</td>
<td>Male Rate 16.0 95% CI 8.8-26.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Female Rate 0 95% CI 0-4.3</td>
</tr>
<tr>
<td>Total</td>
<td>2488951</td>
<td>2388248</td>
<td>Male Rate 9.0 95% CI 5.8-13.4</td>
</tr>
</tbody>
</table>

CI, confidence interval.

Each patient was assessed by a neurologist of the study group 24-72 hours after admission. To check on cases that could have been missed, we reviewed the hospital charts of all young patients whose discharge forms had diagnosis codes 430-438 according to the International Classification of Disease (ICD) (Eighth Revision in 1983-1984, Ninth Revision in 1985). The charts of all 15-44-year-old stroke patients admitted to the rehabilitation hospital between January 1, 1983, and February 28, 1986, were also checked for stroke cases not identified in the acute phase. Furthermore, we examined the death certificates of all young Florence residents who died between 1983 and 1985 and searched for their hospital records or autopsy findings, if any.

Stroke was defined according to criteria of the World Health Organization. The definition of different stroke types was based on criteria of the Oxfordshire Stroke Project.

Clinical and laboratory assessment included 1) in all patients: collection of historical data according to a standard form comprising questions about cardiovascular risk factors and trauma, neurologic and cardiovascular evaluation, standard biochemical blood and urine tests, standard electrocardiography (ECG), and computed tomography (CT scan) carried out ≤15 days after the onset of symptoms; 2) in hemorrhagic patients: selective four-vessel angiography; 3) in ischemic patients: two-dimensional (2-D) echocardiography, Doppler ultrasonography, selective conventional or digital intravenous angiography (except in patients with overt cardiac disease), 24-hour Holter monitoring (in selected cases), and immunologic and coagulation tests including antithrombin III and lupus inhibitor (in patients without pathologic findings on cardiac or angiography investigations).

A diagnosis of hypertension was based on at least two blood pressure recordings during admission with systolic pressure of >160 mm Hg or diastolic pressure of >90 mm Hg, history of hypertension, or previous/current antihypertensive treatment. Cerebrovascular atherosclerosis was considered a possible pathogenetic mechanism of ischemic stroke if angiography revealed stenosis or occlusion of the arterial branches appropriate to symptoms and if other potential causes were absent. Heart valvular diseases or cardiac rhythm disturbances, which are conventionally accepted as potential sources of emboli and were demonstrated here by 2-D echocardiography or ECG, were considered pathologic mechanisms of embolic stroke.

The frequency of stroke is expressed as incidence rate and mortality rate. Incidence rate was derived from the number of first episodes of stroke among the residents of Florence during 1983–1985, and mortality rate was derived from the number of deaths for first or recurrent stroke during the same period. The average of the populations living in Florence on January 1, 1983, and December 31, 1985, was the denominator of both rates. The rates were age-adjusted to the 1960 US population and 95% confidence intervals were computed.

Results

Seventy-six subjects were identified and registered as potential stroke cases. Of these, 17 (22.4%) were subsequently classified as having had TIAs, and eight (10.5%) were excluded because of other neurologic diseases diagnosed during hospitalization (multiple sclerosis in 3, epilepsy in 2, peripheral neuropathies in 2, and glioma in 1). Of the remaining 51 patients, 47 (61.8% of the total) were defined

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as having had a first stroke and four (5.3%) as having had a recurrent stroke.

The Young Stroke Register detected 41 (87%) of the 47 first strokes; the other six patients were identified by death certificates (three patients), rehabilitation hospital charts (two patients), and acute-care hospital discharge forms (one patient). The cases identified by death certificates had died before arriving at a hospital; for two the diagnosis was derived from necropsy examination, while the other was considered a stroke case on the basis of information supplied by his family physician. Within 24 hours after the onset of symptoms, 86% of the patients had been hospitalized. Forty-three of the 44 hospitalized patients had at least one CT scan, and 30 underwent angiography as well.

The average annual incidence rate of first stroke in the 15–44-year-old age group was 8.8/100,000 population. The age- and sex-specific incidence rates and the 95% confidence intervals are shown in Table 1. There was no difference between males and females. In both sexes, the risk of stroke increased with age ($\chi^2=8.0$, $p<0.02$ in males; $\chi^2=17.2$, $p<0.001$ in females).

Based on combined CT, angiography, and necropsy data, the 47 incident stroke patients were classified as follows: 18 (38.3%) cerebral infarction (CI), 17 (36.2%) subarachnoid hemorrhage (SAH), and 10 (21.3%) intracerebral hemorrhage (ICH). Two patients (4.2%) were considered to have had a stroke of uncertain type since no laboratory (CT or angiography) or necropsy data were available; however, the clinical data of both were strongly suggestive of SAH. The frequency of each stroke type except ICH was similar in the sexes; for ICH we found a higher, although not significantly higher, number of males. The age-specific incidence rates of CI, SAH, ICH, and uncertain type strokes are reported in Table 2.

Eleven of the 47 incident stroke patients died within 1 month, a case–fatality ratio of 23.4%. The 1-month fatality ratios were 6% for CI, 18% for SAH, 50% for ICH, and 100% for stroke of uncertain type. Two patients with recurrent stroke also died, increasing to 13 the number of young stroke patients who died. Consequently, the average annual mortality rate was 2.4/100,000 population.

The presumed pathologic mechanisms of ischemic stroke are listed in Table 3. Cardiac embolism was considered the possible pathogenesis in five (28%) of 18 CIs (incidence rate 0.9/100,000/yr) and atherosclerosis in four (22%) (incidence rate 0.8/100,000/yr). Neck trauma, fat embolism from long-bone fractures, complication of carotid endarterectomy in a TIA patient, migraine, and a presumed steal due to an arteriovenous malformation (AVM) were the other possible causes of ischemic stroke. In four patients with CI, etiology of the stroke remained uncertain due to AVM.

### Table 3. Pathogenetic Mechanisms of Ischemic Stroke in Young Adults, Florence, Italy, 1983–1985

<table>
<thead>
<tr>
<th>Case/age/sex</th>
<th>Angiography</th>
<th>Directional Doppler ultrasonography</th>
<th>Echocardiography</th>
<th>Electrocardiography</th>
<th>Possible pathologic mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/38/F</td>
<td>IC occlusion</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>2/39/F</td>
<td>IC occlusion</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>3/44/M</td>
<td>IC stenosis</td>
<td>CC turbulence</td>
<td>Normal</td>
<td>Normal</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>4/44/M</td>
<td>IC stenosis</td>
<td>IC stenosis</td>
<td>Normal</td>
<td>Normal</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>5/28/F</td>
<td>ND</td>
<td>Normal</td>
<td>Mitral valve prolapse</td>
<td>Normal</td>
<td>Heart valvular disease</td>
</tr>
<tr>
<td>6/38/M</td>
<td>ND</td>
<td>Normal</td>
<td>Prosthetic valve</td>
<td>LVH</td>
<td>Heart valvular disease</td>
</tr>
<tr>
<td>7/42/F</td>
<td>ND</td>
<td>Normal</td>
<td>Prosthetic valve</td>
<td>AF</td>
<td>Heart valvular disease</td>
</tr>
<tr>
<td>8/44/F</td>
<td>ND</td>
<td>Normal</td>
<td>Prosthetic valve</td>
<td>Normal</td>
<td>Heart valvular disease</td>
</tr>
<tr>
<td>9/44/M</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Arrhythmia</td>
<td>Sick sinus syndrome</td>
</tr>
<tr>
<td>10/36/F</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Unknown</td>
</tr>
<tr>
<td>11/39/F</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Unknown</td>
</tr>
<tr>
<td>12/41/M</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Unknown</td>
</tr>
<tr>
<td>13/42/F</td>
<td>ND</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Trauma: chiropractic</td>
</tr>
<tr>
<td>14/35/M</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Trauma: multiple fractures</td>
</tr>
<tr>
<td>15/20/M</td>
<td>ND</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Trauma: multiple fractures</td>
</tr>
<tr>
<td>16/41/M</td>
<td>IC stenosis</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Carotid surgery</td>
</tr>
<tr>
<td>17/44/M</td>
<td>AVM</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Steal due to AVM</td>
</tr>
<tr>
<td>18/30/F</td>
<td>Normal</td>
<td>ND</td>
<td>Normal</td>
<td>Normal</td>
<td>Migraine</td>
</tr>
</tbody>
</table>

F, female; M, male; IC, internal carotid artery; CC, common carotid artery; AF, atrial fibrillation; LVH, left ventricular hypertrophy; AVM, arteriovenous malformation; ND, not done.
unknown. One of these four had hypertension, diabetes mellitus, and dyslipidemia as risk factors but she did not undergo complete laboratory assessment. Among the 17 patients with SAH, angiography or necropsy revealed an aneurysm in 14 and an AVM in one. Hypertension was found in five of the 10 patients with spontaneous ICH; no ICH patient was on anticoagulants or amphetamine drugs.

Discussion

We studied a stable urban population whose age distribution was very similar to that of Italy as a whole according to the 1981 Italian census. Since the cerebrovascular pathology of infants and children differs from that of adults, our study was restricted to the 15-44-year-old age group. Ours was the first population survey specifically addressing stroke in young adults.

Our incidence rates might be underestimates because of our inability to identify some patients who were not referred to a hospital or who suffered a stroke while outside Florence; mild strokes had the highest probability of escaping our registration. Nevertheless, approximately 30% of our patients with ischemic stroke had complete recovery within 7 days after the onset of symptoms, and in approximately 35% of our patients with SAH the severity corresponded to Grades 1 or 2 of the Hunt and Hess criteria. Furthermore, since hospital care in Italy is completely free of charge and since access to hospitalization in an urban area like Florence is easy, it is likely that the majority of young subjects with stroke are hospitalized to receive the best possible evaluation and treatment. A recent survey in Great Britain reported a higher probability of hospitalization for young stroke patients than for older ones.

The annual incidence rate of first stroke in people up to the age of 44 years, as reported by studies worldwide, varied from 6 to 16 per 100,000 population (Table 4). These studies included the youngest group (aged 0-14 years), for which a rate of 2.5/100,000/yr was calculated in Rochester, Minnesota. Only a few studies report information limited to the 15-44-year-old age group (Table 4). The incidence of first stroke in Florence is lower than in Kuopio, Finland or Fargo, North Dakota. Different diagnostic criteria and the decline over time of stroke morbidity may explain this discrepancy. However, our rate appears close to those obtained in Goteborg, Sweden, during 1970-1975 (11/100,000/yr for those aged 15-44 years) or Rochester, Minnesota, during 1970-1974 (17/100,000/yr in our study compared with 20/100,000/yr in Rochester for the group aged 35-44 years; 5/100,000/yr in our group aged 15-34 years compared with 3/100,000/yr for all those aged <35 in Rochester).

In previous population studies, the classification of cerebrovascular disease in young adults has been based on clinical criteria. Our data, based on CT and necropsy findings, show a high incidence of hemorrhagic stroke in this age group. Moreover, our results confirm the higher incidence of SAH compared with spontaneous ICH. While the source of bleeding was identified in 88% of SAH patients, the cause remained unknown in 50% of ICH patients. These ICH patients were normotensive and had no evidence of malformation of the intracranial vessels. A high percentage of ICH of unknown cause was also reported in a clinical study on young adults. Moreover, Brott et al found that hypertension, though associated with a high relative risk for ICH, was present in only 56% of their patients of all ages.

Unlike some clinical series, our few incident cases do not allow us to identify some of the less common types of ischemic stroke. However, due to the completeness of laboratory assessment, our survey can provide the incidence rates of the most common pathologic stroke types. The rates of stroke due to atherosclerosis and to cardiac disease are low, but by comparison the rate of 0.8/100,000/yr for atherosclerosis in young adults is about twice that for myasthenia gravis or Huntington's disease in all ages. This observation may indicate the need for further effort in the prevention of stroke in young adults.

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**TABLE 4. Incidence Rates of Stroke in Young Adults**

<table>
<thead>
<tr>
<th>Population</th>
<th>Years</th>
<th>Age (yr)</th>
<th>No.</th>
<th>Crude (no./100,000/yr)</th>
<th>Age-adjusted* (no./100,000/yr)</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, Minnesota</td>
<td>1955-1969</td>
<td>0-44</td>
<td>41</td>
<td>9</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Rochester, Minnesota</td>
<td>1970-1974</td>
<td>0-44</td>
<td></td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>1975-1976</td>
<td>0-44</td>
<td>22</td>
<td>8</td>
<td>9</td>
<td>Retrospective hospital survey</td>
</tr>
<tr>
<td>Hiroshima, Japan</td>
<td>1950-1974</td>
<td>0-44</td>
<td>21</td>
<td>24</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Stockholm, Sweden</td>
<td>1973-1977</td>
<td>0-44</td>
<td>733</td>
<td>16</td>
<td>15</td>
<td>Retrospective hospital survey</td>
</tr>
<tr>
<td>Fargo, North Dakota</td>
<td>1965-1966</td>
<td>15-44</td>
<td>22</td>
<td>28</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Goteborg, Sweden</td>
<td>1970-1975</td>
<td>15-44</td>
<td>91</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kuopio, Finland</td>
<td>1978-1980</td>
<td>15-44</td>
<td></td>
<td>32</td>
<td></td>
<td>Prior stroke included</td>
</tr>
<tr>
<td>Florence, Italy</td>
<td>1983-1985</td>
<td>15-44</td>
<td>47</td>
<td>9</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

*1960 US population as standard; direct method of adjustment.
adults. We did not discuss potential risk factors, but the Italian case–control study on cerebral ischemia in young adults is investigating their role.

Acknowledgments

The authors thank Milton Alter, MD, PhD, for his helpful review of the manuscript and the CSPO of Florence, which provided the death certificate data.

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KEY WORDS • cerebrovascular disorders • epidemiology • Italy
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Stroke. 1988;19:977-981
doi: 10.1161/01.STR.19.8.977

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