Stroke Incidence and 30-Day Case-Fatality in a Suburb of Tbilisi
Results of the First Prospective Population-Based Study in Georgia

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Background and Purpose—Although stroke is one of the main public health problems worldwide, no study of stroke incidence has been performed in Georgia, and therefore, a population-based registry was established to determine the incidence and case-fatality rates of first-ever stroke.

Methods—We identified all first-ever strokes between November 2000 and July 2003 in a defined population of 51 246 residents in the Sanzona suburb of Tbilisi, the capital of Georgia, using overlapping sources of information and standard diagnostic criteria.

Results—A total of 233 first-ever strokes occurred during the study period. The crude annual incidence rate was 165 (95% CI, 145 to 188) per 100 000 residents. The corresponding rate adjusted to the standard “world” population was 103 (95% CI, 89 to 117). In terms of stroke subtype, the crude annual incidence rate per 100 000 inhabitants was 89 (95% CI, 74 to 106) for ischemic stroke, 44 (95% CI, 34 to 57) for intracerebral hemorrhage, 16 (95% CI, 10 to 25) for subarachnoidal hemorrhage, and 16 (95% CI, 10 to 25) for unspecified stroke, and the corresponding case-fatality rates at 1 month were 19.2%, 48.4%, 47.8%, and 69.6%.

Conclusion—The overall stroke incidence rate in an urban population of Georgia is comparable to those reported in developed countries. As for the stroke subtypes, there is an excess of hemorrhagic strokes compared with other registries. Geographical and lifestyle variations may explain these findings, whereas inadequacy of the stroke care system in Georgia might contribute to the high case-fatality. (Stroke. 2004;35:2523-2528.)

Key Words: epidemiology incidence stroke

Stroke is a major public health problem worldwide because it is the second most common cause of mortality and the leading cause of adult long-term disability and represents an enormous socioeconomic burden for society. Despite this, there have not been many epidemiological studies on stroke incidence and mortality in industrialized countries that meet the requirements for an “ideal” epidemiological study, and information on stroke incidence and mortality in the developing world is even scarcer.

No study on stroke incidence and mortality has been performed in Georgia, a country with transition economy (ie, moving from a primarily state-planned to a market-based economic system) in the South Caucasian region, bordering the Black Sea (longitude 40° to 47° E, latitude 41° to 44° N), with an area of 69 700 km² and a population of 4.5 million inhabitants. Therefore, we have established a population-based registry to determine the incidence and case-fatality rates of first-ever stroke (FES) in a defined urban population of Georgia using modern methodological standards.

Subjects and Methods
This is a part of a large joint Swiss-Georgian prospective, population-based project aiming at estimating the major epidemiological and clinical patterns of stroke in Tbilisi, the Georgian capital.

The study population consisted of the population of the administratively defined Sanzona suburb of Tbilisi. This area is covered by the hospital involved in the study, the Sarajishvili Institute of Neurology and Neurosurgery (SINN). The suburb is located in the northeast part of Tbilisi, and its population (average 51 246 residents in 2000 to 2003; 53.6% women) is relatively stable and representative of the demographic structure of the Georgian population. The total population of Georgia in 2000 was 4 435 200 inhabitants, 53% urban and 47% rural, and the population of Tbilisi was 1 080 000 inhabitants. The gross national product per capita in Georgia was $3606 (US dollars) in 1999.

The study was approved by the ethics committee of the SINN. Oral informed consent was obtained from each participant before any interview or neurological examination was performed.

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Men No./Person y</th>
<th>Rate 95% CI</th>
<th>Women No./Person y</th>
<th>Rate 95% CI</th>
<th>Total No./Person y</th>
<th>Rate 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–44</td>
<td>9/44 251</td>
<td>20 9–39</td>
<td>2/47 069</td>
<td>4 0.5–15</td>
<td>11/91 320</td>
<td>12 6–21</td>
</tr>
<tr>
<td>65–74</td>
<td>46/5877 783</td>
<td>574–1043</td>
<td>49/7314</td>
<td>670 496–885</td>
<td>95/13 177</td>
<td>721 584–1371</td>
</tr>
<tr>
<td>All ages</td>
<td>104/65 418</td>
<td>159 130–193</td>
<td>129/75 522</td>
<td>171 143–203</td>
<td>233/140 926</td>
<td>165 145–188</td>
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<tr>
<td>WSR*</td>
<td>115 92–138</td>
<td>92 76–109</td>
<td>139 115–163</td>
<td>150 130–170</td>
<td>103 89–117</td>
<td></td>
</tr>
<tr>
<td>ESR†</td>
<td>163 130–196</td>
<td>139 115–163</td>
<td></td>
<td>150 130–170</td>
<td>103 89–117</td>
<td></td>
</tr>
<tr>
<td>ESR (45–84)‡</td>
<td>395 312–478</td>
<td>360 295–424</td>
<td></td>
<td>377 325–428</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*World standardized rate (WSR) age- and sex-adjusted to the world population by the direct method.
†European standardized rate (ESR) age- and sex-adjusted to the European population by the direct method.
‡ESR age- and sex-adjusted to the European population for the age group 45 to 84 years.

Case Ascertainment
We registered and analyzed all new cases of stroke in the study population between November 1, 2000, and July 31, 2003, including first-ever and recurrent strokes. Immediate notification of all new cases of stroke or alleged stroke and stroke mortality was achieved by: (1) daily checking of hospital registrations and hospital referrals in the SINN, the largest specialized neurological facility in Georgia, located in the Sanzona suburb; (2) daily checking of emergency medical service (EMS) calls (3 local centers and the central command station); (3) weekly checking of the outpatient data in the 3 polyclinics serving the district; (4) weekly checking of hospital registrations and hospital referrals and autopsy protocols in all 8 general hospitals serving the population of Tbilisi; (5) weekly checking of the death certificates in the central funeral bureau of Tbilisi for all deaths in the study region to identify persons with stroke (for those with “stroke,” “brain insult,” “myocardial infarction,” “sudden death,” “pneumonia,” “thromboembolism,” or “acute cardiovascular insufficiency” as cause of death, the clinical records were reviewed, if available, and the family members interviewed); and (6) daily rounds in the study region (field work), including door-to-door survey and contact with volunteers who kindly agreed to collect and share all relevant information on their neighbors’ health status (ie, cases of illness or mortality occurring in their neighborhood) to identify stroke patients without contact with any health care facility. On the basis of the information from the hospitals, polyclinics, EMS, and the field rounds, all patients with symptoms suggesting a possible cerebrovascular event (loss of consciousness, confusion, seizures, vertigo, hypertonic crises, and severe headache), including transient ischemic attack (TIA), were seen by study neurologists as soon as possible after the event. Regardless of whether the stroke patient was hospitalized, the information required by the standard study protocol was collected for each patient. Results of brain imaging, blood tests, ECG, transthoracic echocardiography, and extracranial and transcranial Doppler examination were obtained whenever possible.

For careful case ascertainment, all stroke patients identified using these overlapping sources of information were interviewed and examined (if it was impossible to interview the patient, the next of kin was interviewed) by specially trained cerebrovascular fellows supervised by senior neurologists. In doubtful cases, diagnosis was ascertained at the consensus meetings with the head of the clinic.

Subtypes of Stroke
Stroke was defined by the standard WHO criteria. Only FES were studied. The subtype of acute stroke was defined using well-accepted criteria: (1) definite ischemic stroke (IS) on the basis of computed tomography (CT), magnetic resonance imaging (MRI), or autopsy findings; (2) definite primary intracerebral hemorrhage (ICH), on the basis of CT/MRI or autopsy findings; (3) definite subarachnoid hemorrhage (SAH), on the basis of CT or cerebrospinal fluid (CSF) or autopsy findings; and (4) undetermined stroke (no CT/MRI or autopsy).

CT and MRI were performed within 30 days after stroke onset, but in cases when neuroimaging was performed >2 weeks after stroke onset, MRI was mainly used to avoid missing small ICHs, which are sometimes CT-negative at this time.

Using the Guy’s Hospital Stroke Diagnosis Score (GHSDS), subjects with undetermined stroke were further classified as having probable IS (GHSDS <4), probable ICH (GHSDS >25), or probable SAH (patients with a typical clinical picture of SAH but without confirmatory tests, including CT or CSF examination). Patients with a GHSDS of 4 to 25 and patients for whom the GHSDS was unavailable were classified as having unspecified stroke (US). The incidence and case-fatality rates were calculated for the IS (definite+probable), ICH (definite+probable), SAH (definite+probable), and US groups.

The etiologies for definite IS were determined using the criteria of the Lausanne Stroke Registry (LSR) as large artery disease (LAD), cardioembolism (CE), small artery disease (SAD), or other (undefined, mixed [OE]). IS clinicotopographical subtypes were defined using the Oxfordshire Community Stroke Project (OCSP) classification as total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), lacunar infarct (LACI), or posterior circulation infarct (POCI).

Data Analysis
The age- and sex-specific annual incidence rates of FES per 100 000 inhabitants were estimated and presented in 10-year age bands. The incidence rate was calculated as the number of cases divided by the population at risk. Age- and sex-specific incidence rates were adjusted by the direct method to the Segi standard world and European populations.

Results
Between November 1, 2000, and July 31, 2003 (140 926 person years), 363 patients with suspected stroke were identified, 55 of whom were excluded after detailed clinico-anamnestic and supplementary investigations because of having TIA (26 cases), subdural hematoma (7 cases), primary brain tumors (5 cases), neuroinfection (5 cases), brain meta-
cases (3 cases), migraine (3 cases), vascular dementia (3 cases), spinal cord disease (2 cases), or hypertensive encephalopathy (1 case). After exclusion of 75 cases with recurrent strokes, the remaining 233 patients (104 men and 129 women) with FES constituted the study subjects. No month-to-month variation in stroke incidence was noted; therefore, we used all the data collected during the study period (incomplete 3 years).

The mean age was 64.9 ± 11.5 years for men and 69.2 ± 9.2 years for women. CT or MRI was performed on 156 (66.7%) of the FES patients. No autopsy was performed. The patients who underwent CT or MRI were younger than those who did not (mean ages 65.5 ± 10.0 and 70.9 ± 10.4, respectively; P < 0.001). On the basis of the neuroimaging results, definite IS was diagnosed in 97 patients (42.6%), definite ICH in 41 (17.6%), and definite SAH in 18 (7.7%). In addition, 28 patients (12.0%) with a GHSDS <4 were diagnosed as having probable IS, 21 (9%) with a GHSDS >25 as having probable ICH, and in 5 patients (2.1%), the clinical picture indicated probable SAH. US was diagnosed in 23 patients (9.9%) with a GHSDS of 4 to 25 (12 patients) or when the GHSDS was not available (11 patients); the latter group comprised patients who died shortly after the index event without sufficient information to assign a GHSDS and who were mainly identified from death certificates. In total, there were 125 patients with IS, 62 with ICH, 23 with SAH, and 23 with US.

The hospitalization rate was 154 of 233 (66.1%). Eight patients were hospitalized but had no CT/MRI, and 10 patients were not hospitalized but had neuroimaging. Among nonhospitalized patients, 49 were identified from EMS or polyclinics, 9 from death certificates, and 21 patients were found during field work; 11 of them had had no previous contact with any health care service.

The crude annual incidence rate per 100 000 population was 165 (95% CI, 145 to 188) for all strokes, 89 (95% CI, 74 to 106) for IS, 44 (95% CI, 34 to 57) for ICH, 16 (95% CI, 10 to 25) for SAH, and 16 (95% CI, 10 to 25) for US.

Table 1 gives the number of FES cases and the age- and sex-specific incidence rates for the 10-year age bands, as well as the age-standardized rates for the world and European populations. In men, the stroke incidence rate increased steadily with each decade of age, including the ≥85 age group, whereas in women, this tendency was seen up to 85 years.

The age- and sex-specific incidence rates for the different stroke subtypes are given in Table 2. The IS incidence rate increased steadily with each decade of age, including the ≥85 age group, whereas for ICH, an increase was seen up to the age of 75 years, followed by a decrease. The incidence rate for SAH was higher in the
TABLE 3. Thirty-Day Case-Fatality Rates by Stroke Subtype

<table>
<thead>
<tr>
<th>Stroke Subtype</th>
<th>Died/Total No.</th>
<th>Case-Fatality Rate, %</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>24/125</td>
<td>19.2</td>
<td>12.7–27.2</td>
</tr>
<tr>
<td>ICH</td>
<td>30/62</td>
<td>48.4</td>
<td>35.4–61.4</td>
</tr>
<tr>
<td>SAH</td>
<td>11/23</td>
<td>47.8</td>
<td>26.8–69.4</td>
</tr>
<tr>
<td>US</td>
<td>16/23</td>
<td>69.6</td>
<td>47.1–86.8</td>
</tr>
<tr>
<td>All strokes</td>
<td>81/233</td>
<td>34.8</td>
<td>28.7–41.3</td>
</tr>
</tbody>
</table>

younger age categories, whereas for US, the incidence rate was maximal in the ≥85 age group.

Using the LSR etiology for definite IS (97 cases), there were 42 cases (43%) with LAD, 25 (26%) with CE, 15 (15%) with SAD, and 15 (15%) with OE. Using the OCSP classification of IS (125 cases), there were 17 cases (14%) of LACI, 32 (26%) of TACI, 54 (43%) of PACI, and 22 (18%) of POCI.

The 30-day case-fatality rates for the different stroke subtypes are shown in Table 3. The overall age- and sex-standardized case-fatality rate was 35.7% (95% CI, 29.3 to 42.2).

Discussion

Studying stroke epidemiology in developing countries using standardized and up-to-date methods is of great importance because it provides reliable data for planning adequate health care measures.

This is the first prospective population-based study on stroke incidence and 30-day case-fatality in Georgia. It is also an attempt to estimate the above-mentioned epidemiological patterns using the modern standards required for studies of stroke incidence. Careful case ascertainment was the most important issue in this study. The majority of cases were revealed using “hot pursuit” and multiple overlapping sources of information were used to detect every case of stroke in the study population. The application of this methodology was important because quite a high proportion of stroke victims are not hospitalized in Georgia. Frequently, in elderly patients with a mild stroke, the patient and family do not seek medical attention or the patient is treated at home, or, conversely, when the stroke is very severe, the family (with some degree of fatalism) decides not to upset the patient further by hospitalization and keep the patient at home under medical care or sometimes without it.

A potential limitation of our study is possible stroke subtype misclassification because of CT/MRI being performed in a slightly lower percentage of cases (67%) than the “ideal” rate of ≥70% because of the high cost of these investigations. However, our CT/MRI rate was much higher than those in other studies performed in post-Soviet countries. For those patients who did not undergo CT/MRI, we used the GHSDS, which, despite the known shortcomings, is recommended for epidemiological studies and has sufficient diagnostic accuracy for IS and ICH when considering only cases within the upper and lower 10% of the score.

Although strokes were more frequent in women, yielding higher crude incidence rates, after adjustment to the standard European and world populations, the overall stroke incidence was higher in men, as expected.

Figure 1. Age- and sex-standardized (to standard European population) annual incidence rates of first-ever strokes per 100 000 population in different registries.
The overall incidence rate for all strokes was not as high as expected for a country in transition with socioeconomical difficulties and shortcomings in medical care (eg, a high exposure of the population to vascular risk factors and a lack of preventive strategies). In fact, the rates were comparable to those in most industrialized countries and lower than in Oyabe, Japan, L'Aquila, Italy, Scandinavian countries, and post-Soviet republics (Figure 1). It was also striking that the incidence rate for IS was particularly low. The reason for the low overall incidence of stroke, which was attributable to the very low incidence of IS in our population, is not clear but might be explained as follows. First, it is possible that some cases of very mild stroke (especially IS) were missed despite the very careful case-finding procedure. We do not think that use of the GHSDS for diagnosis of stroke subtype overestimated ICH. It is possible that some ISs were in fact diagnosed as probable ICH, but this effect would be counterbalanced by diagnosing “pseudoischemic” ICH as probable IS. Second, it is likely that some genetic factors and the lifestyle of the Georgian population may play a role because the effect of such factors is well known. This may be related to the dietary habits of Georgians, who consume high quantities of vegetables and fruits, vegetable oils, and foods containing fibers (Mediterranean diet). Another dietary peculiarity of the Georgian population is the consumption, in rather large amounts, of Georgian wine (rich in flavonoids and tannins), mainly by men. All of these factors may have a protective effect against IS. The same hypothesis may explain the high frequency of ICH (Figure 2) because increased alcohol consumption, dietary protein deficiency, and high intake of polyunsaturated fatty acids derived from vegetable oils decrease the risk of IS but increase the risk of hemorrhage. Another factor contributing to the high incidence of hemorrhagic stroke might be the high prevalence of hypertension, which, in the majority of cases, is not managed at all or is managed improperly. These factors, together with the high prevalence of smoking in Georgia, mainly in men, which is considered the strongest risk factor for SAH, may also account for the high frequency of SAH (Figure 2).

The hypothesis that stroke-prone persons were eliminated by ischemic heart disease before reaching the age at which they would have experienced a stroke, which was proposed to explain the low stroke incidence rate in Warsaw, should also be considered for Georgia, especially for men because they are more prone to coronary heart disease, and the average life expectancy in men is rather low in Georgia (65.4 years).

The distribution of the etiological subtypes of definite IS and distribution of the main clinicopathological subtypes of IS according to the OCSP classification in our study do not differ markedly from those in other registries. The crude and standardized overall 30-day case-fatality rates of stroke in our population were 34.8% and 35.7%, respectively, which are among the highest rates reported. The case-fatality rate increased from IS to hemorrhagic stroke and was maximal for US, confirming the previous findings that this stroke subtype has the highest short-term mortality.

In summary, the overall stroke incidence rate in an urban population of Georgia is comparable to those reported in developed countries and lower than in most countries in transition. The incidence of IS is also rather low. Conversely,
we found a high proportion of hemorrhagic stroke compared with other registries. Geographical and lifestyle variations may explain these findings, whereas possible underascertainment of mild strokes or inadequacy of the stroke care system in Georgia, which includes the lack of an organized stroke service with specialized stroke units, might contribute to the high case-fatality.

Acknowledgments
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References
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