

A Population Study of Stroke in West Ukraine

Incidence, Stroke Services, and 30-Day Case Fatality

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Background and Purpose—According to World Health Organization statistics, Ukraine has extremely high stroke mortality. No population-based prospective studies of stroke incidence have been performed yet in this European country with ≈50 million inhabitants. High reported rates of stroke mortality in official statistics conflict with some locally published incidence data in Ukraine. To obtain accurate data, we evaluated stroke incidence and 30-day case fatality in a prospective population study in the West Ukrainian city of Uzhgorod with a population of 126 000 inhabitants.

Methods—Case certification by neurologists and follow-up at 30 days after stroke for all patients identified by any level of the health service system were performed for a 12-month period.

Results—We identified 352 stroke cases. The age-standardized incidence was 341 and 238 of 100 000 and mortality was 83 and 69 of 100 000 with the use of the European or world standard population for standardization. Mean age of stroke patients was 63.4±12.5 years. Rate of hospitalization was 66%. Hospitalized patients were >10 years younger than those treated in their homes. The 30-day case fatality rates were 15.4% among hospitalized patients and 36.8% among those treated at home. Overall 30-day case fatality was 23.3%.

Conclusions—Stroke incidence and 30-day case fatality in this West Ukrainian city were similar to those of some West European countries and were much lower than what could be expected from World Health Organization statistics. The relatively low incidence rate seems accurate; because of the organization of local stroke services, it is not probable that a considerable proportion of patients with acute stroke could bypass all levels of the acute care health system. Local health statistics reported a much lower number of stroke cases and stroke deaths than found in our survey; thus, further study is needed to clarify the reason for the discrepancy between local data and the high reported stroke mortality in Ukraine. (*Stroke*. 2001;32:2227-2231.)

Key Words: case fatality ■ hospitalization ■ incidence ■ stroke, acute ■ Ukraine

According to the statistics of the World Health Organization (WHO), stroke mortality is extremely high in former Eastern block countries, including Ukraine.¹ Stroke mortality in Ukraine was constantly high in the 1981 to 1998 period, with a standardized mortality rate of >200 of 100 000.¹ In contrast to this high value, several local studies have reported relatively low stroke morbidity from the region, with numbers close to the data of some West European countries. For example, for 1992, the age-standardized death rate for cerebrovascular diseases (International Classification of Diseases [ICD]-9 430 to 438) was 305 for men and 225 for women in Ukraine,² whereas Pashkovskii³ reported that in 1992 to 1994, the incidence of cerebrovascular diseases, including ischemic and hemorrhagic strokes, ranged from 156 of 100 000 in the Western Cherniwtsi (Chernowitz) region to 213 of 100 000 in the southeastern region of Harkiv. The proportion of hemorrhagic strokes (intracerebral and sub-

arachnoid hemorrhages) was 15.9% in West Ukraine and 19.3% in the southeastern part, respectively.³ Although stroke mortality is not reported in the article by Pashkovskii, it is extremely improbable that stroke mortality (an average of 215 of 100 000 for 1992 to 1994 for Ukraine according to WHO data) would equal the incidence (224 of 100 000 for Ukraine for the same period), which should be the case if both the WHO data and the numbers reported by Pashkovskii are valid. The WHO data for cerebrovascular mortality seem too high even if we consider that in Ukraine the cause of death given on death certificates was erroneous in 5% to 40% of cases for cardiovascular diseases.^{4,5} Because both the mortality and incidence data were based on official reports and no prospective population-based study has been performed yet in this region, we performed a prospective epidemiological study in the West Ukrainian city of Uzhgorod to accurately evaluate stroke incidence, stroke services, and 30-day case fatality.

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Methods

Organization of Local Stroke Services

In the Uzhgorod health-care system, in most cases of suspected stroke, the emergency service is called either directly by the family or by the general practitioner (GP). According to local traditions and regulations, GPs are reluctant to treat stroke patients in the primary setting without first consulting either the emergency or the neurology outpatient service. If the emergency service is called and the information from the call is enough to indicate stroke, a special neurological emergency unit, available 24 hours a day, is sent to the patient. If accurate information is not available, regular emergency staff members see the patient first, and they call the special neurologist emergency team. This team decides whether the patient will be treated at home or admitted to a hospital.

If the decision is made to hospitalize patients, most patients are transferred to the county hospital, where CT and neurosurgical facilities are available. If cerebral hemorrhage is diagnosed by CT, the patient is admitted to the neurosurgical ward of the county hospital. If cerebral hemorrhage is excluded by CT, the patient is transferred to the stroke unit of the city hospital, or in a few cases, the patient is left at the neurological department of the county hospital. A few acute stroke patients from certain districts of the city are admitted to the hospital of the Ukrainian Railway Services. The stroke unit of the city hospital has a rehabilitation ward for postacute treatment. Patients from the neurosurgical and neurological units of the county hospital are also transferred to this rehabilitation unit after the acute phase.

Some patients with mild clinical signs might not call the emergency service but turn either to their family practitioner or, outside the GP's hours, directly to a neurological outpatient service. All such patients, even those with mild signs, are sent to the stroke unit of the city hospital. For these patients, CT is usually not performed, but a spinal tap is performed in some cases to exclude hemorrhage into the cerebrospinal fluid space.

The neurological emergency team sees most stroke patients. In some cases, they decide not to hospitalize the patient for different reasons (old age, condition that is too severe, refusal by the patient, etc). In these cases, either the GP or a neurologist of the city outpatient service will be in charge of the patient. The emergency service notifies both the GP and the city neurologist. The latter sees the patient on the first working day after the call and either decides to check the patient at least twice a week for the next 1 to 3 weeks (so called "home hospital," with a GP's nurse visit each day) or leaves the patient's care completely in the hands of the GP. If there are indications, patients might be referred to the rehabilitation ward of the stroke unit in the city hospital from the home hospital or the GP settings on recommendation of the neurologist.

Definitions and Case Identification

The study period lasted from October 1, 1999, to September 30, 2000. During this period, we intended to register all stroke cases in the city. Stroke was defined as rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting >24 hours or leading to death with no apparent cause other than that of vascular origin.⁶ Case fatality was defined as death caused by any reason within 30 days of stroke onset. Cases were identified from 7 sources: (1) hospital records prospectively collected for the study in all 4 hospitals where acute stroke patients were treated; (2) the registry of calls of the emergency neurology service; (3) the registries of the city's neurology outpatient service, including a registry of all neurologist home calls, a registry of outpatients seen at the city outpatient neurologist's office, and a separate registry for stroke cases; (4) the district registries of the GP zones (The 55 GP districts of the city are organized into 4 area zones, and each zone has its chief physician and a registry; all death cases in the zone are recorded in this registry); (5) the registry of the department of statistics at the city hospital, which keeps records of all deaths in the city and is updated monthly from the records of the city's Registrar's Office; (6) autopsy records of the hospitals and the county forensic department; and (7) for follow-up, regular personal contact with all

55 GPs and their nurses. According to local regulations, all stroke cases that meet the health-care system are supposed to be recorded in ≥ 1 of these registries. The registries were checked, and the GPs were contacted by 1 of the authors (Dr Mihálka). The age distribution of the population of Uzhgorod for men and women separately was obtained from the local census bureau. Values given for year 2000 were used in calculations.

Case Certification

Case certification for hospitalized patients was performed by the hospital neurologists or neurosurgeons. For those patients treated at home, 2 neurologists (1 from the neurological emergency team and 1 of the city's outpatient neurologists) clinically confirmed the stroke. Therefore, even for nonhospitalized stroke patients, ≥ 2 neurological examinations were performed. Case certification was basically performed by clinical examination. Results of CT and cerebrospinal fluid examination were recorded when performed. Quality of case ascertainment was checked according to the 5 key indicators given by Asplund et al.⁷

Recorded Data

Basic demographic data (age, sex), affected brain region, date of stroke, and date of death were recorded for all patients. For fatal cases, it was also noted whether autopsy was performed. For hospitalized patients, a standard data sheet—including risk factors, time from stroke onset to admission, clinical signs, diagnostic and therapeutic interventions, condition at discharge, and recommended secondary preventive measures—was filled out by the neurologist in charge.

Follow-Up

One of the authors (Dr Mihálka) kept track of all identified cases, hospitalized or not, and maintained personal contact with all 55 (later 52) GPs of the city, as well as with the emergency medical service and the city outpatient neurological service. The registries of the emergency service and city outpatient neurology service were regularly checked. The latter included all home calls for neurological reasons, and cases with calls for stroke were checked. Files of all stroke patients were checked at the GPs' offices to decide whether the patient was dead or alive on the 30th day after stroke independent of the actually registered cause of death.

Statistical Analysis

All patient data were entered into an electronic database. Incidence and mortality data were age standardized for the standard European and world population.⁸ Descriptive statistics was used to characterize age in several subgroups. Mean and SD are given. Normality of continuous variables was checked by the Saphiro-Wilk test. Analysis of variance (ANOVA) was used to compare continuous variables with normal distribution or Kruskal-Wallis ANOVA for variables with nonnormal distribution. Pearson's χ^2 test was applied to analyze cross-tabulated data. Statistica99 for Windows, version 5.5 (Stat-Soft), was used for data analysis. Statistical significance was assumed when $P < 0.05$.

Results

Characteristics of the Population and Patients

According to the Uzhgorod census office, in the year 2000, the city had 125 482 inhabitants. In the 20th century, there was significant migration into and out of the city, but there were no considerable migration and change in the ethnic structure of the population in the last 20 years. The current population is a mixture of Ukrainian, Russian, Hungarian, Polish, and Slovakian ethnicity; therefore, the city is not representative of the ethnic structure of Ukraine as a whole. The age distribution of the population and the number of total and fatal stroke cases are given in Table 1.

TABLE 1. Age Structure of the Population and of Patients by Sex and 30-Day Survival

Age Group, y	Men, n			Women, n		
	In Population	Stroke Cases	Fatal Cases 30 d After Stroke	In Population	Stroke Cases	Fatal Cases 30 d After Stroke
0–44	41 818	18	2	44 613	6	0
45–54	8 190	41	9	9 782	27	3
55–64	4 971	51	9	5 773	29	6
65–74	2 752	45	11	4 098	56	13
75–84	939	33	9	1 925	41	16
≥85	173	0	0	448	5	4
Total	58 843	188	40	66 639	164	42

During the 12 months of the study, 352 acute stroke cases were identified, 188 men and 164 women. Age-specific incidence and mortality data are shown in the Figure. Men were ≈ 6 years younger than women (60.8 ± 12.8 versus 66.6 ± 11.6 years, $P < 0.001$); 38% of women and 58% of men were < 65 years of age. In fatal cases, the age difference was even larger, ≈ 9 years (63.5 ± 12.4 versus 72.5 ± 10.4 years, $P = 0.001$). There were no women < 35 years of age and no men who were older than the limit of 85 years of age. The 30-day case fatality did not differ significantly between men and women. CT was performed in 145 of the 234 patients treated at hospital and in 0 patients treated out of hospital. Cerebrospinal fluid examination was performed in 43, ECG in 223, carotid Doppler in 12, and echocardiography in 10 of the 234 hospitalized patients. Of the 82 deaths, 27 had autopsies. Because only 41% of all stroke cases had CT examinations, it was not possible to reliably analyze stroke subgroups in this register.

Characteristics of Treatment Settings

Exactly two thirds of the patients were treated in hospital settings (Table 2). Those who are treated at home, either under the close supervision of the outpatient neurology service or in the care of the GP after an initial instruction by

a neurologist, were on average > 10 years older than those who were hospitalized ($P < 0.001$; Table 2). Four patients died either before the emergency service arrived or during transport by the ambulance.

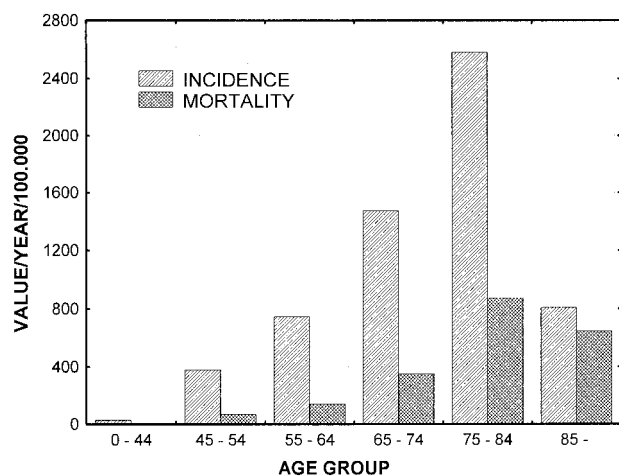
Thirty-Day Case Fatality in Different Settings

Case fatality was significantly higher in those subgroups that did not get hospital care ($P < 0.001$; Table 3). Overall 30-day case fatality was 23.3%, with the lowest values for hospitalized patients (15.4%) and highest values for those left in the care of the GPs. This difference in case fatality among the different settings probably reflects differences in prognostic factors at the time of the initial neurological examination when decisions for higher-level care were made for patients with more hopeful prognosis.

Evaluation of the Quality of Case Ascertainment

To evaluate the reliability of our study, we used the 5 criteria recommended by Asplund et al.⁷ The first indicator is the proportion of fatal cases identified by the study compared with that reported in official statistics. In our study, we found 352 stroke cases and 82 deaths within 30 days of stroke onset. For the year 2000, the official health statistics registered 228 stroke cases by ICD-10 codes as follows: I60 (subarachnoid hemorrhage), 14 cases; I61 (intracerebral hemorrhage), 42 cases; I63 (cerebral infarction), 144 cases; and I64 (stroke not specified), 28 cases. Of these, only 31 were recorded to have died of stroke. Similarly, in the previous year (1999), only 218 stroke cases (141 of them ischemic) and 30 stroke deaths were recorded. We found 2.6 times more stroke deaths and 54% higher stroke incidence than recorded by the official statistics. Because the ratio of stroke register to routine mortality is much higher than the limit of 0.75 set by Asplund et al.,⁷ identification of fatal cases seems acceptable in our register.

The second criterion is the proportion of fatal stroke cases not admitted to hospital. Although this proportion varies from country to country, depending on the local practice of stroke care, the proportion of fatal stroke cases not admitted to hospital should be $> 10\%$.⁷ In our register, 46 of the 82 deaths (56%) occurred outside hospital. Because 0 of the 21 Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) populations reported a higher proportion of



Age-specific incidence and mortality of stroke in Uzhgorod, West Ukraine, from October 1, 1999, to September 30, 2000.

TABLE 2. Age of Patients by Sex in Different Settings

Treatment Location	Men		Women		Total	
	Age, y	n	Age, y	n	Age, y	n
Hospitalized	57.9±12.3	138	61.9±10.7	96	59.6±11.8	234
Home neurology service	68.0±11.8	21	75.6±5.8	34	72.7±9.3	55
Home GP service	69.3±9.7	27	71.5±11.4	32	70.4±10.7	59
Died before getting to hospital	64.0±9.9	2	58.5±6.4	2	61.3±7.5	4

Values for age are mean±SD. The age of patients is significantly different in the hospital and home care settings (Kruskal-Wallis ANOVA, $P<0.0001$).

out-of-hospital than in-hospital fatalities,⁷ we believe that we found most stroke deaths that occurred outside hospital settings.

The third indicator suggested by Asplund et al⁷ is the case fatality rate; incomplete coverage of nonfatal events leads to overestimation of case fatality. With the 23% 30-day case fatality, our register would rank eighth among the 21 MONICA populations; therefore, we do not think that too many nonfatal events were missed in our register.

The fourth criterion is the proportion of surviving stroke patients cared for outside the hospital. If this proportion is low, it reflects less-than-optimal case ascertainment. This proportion ranged 0% to 16% in the 21 MONICA populations and was 20% in our register. Therefore, we assume that we identified most of those stroke survivors who were treated out of the hospital.

The fifth criterion is the proportion of fatal cases examined by a physician before death or subjected to autopsy in fatal cases. In our study, as well as in the MONICA study, stroke was defined by clinical investigation. Autopsy was performed in all 4 cases when death occurred en route to hospital. Therefore, all 82 fatal cases were subjected to medical investigation or autopsy. Because of local coding traditions, stroke deaths reported on death certificates are very low (31 per year). A large number of fatal cases in our register were coded as "death due to old age" in the official statistics, reflecting that in this region of Ukraine, stroke is not a preferred label for cause of death on death certificates. Therefore, in the region of study, underreporting, not over-reporting, of stroke cases might distort official statistics. This might be a problem in those cases in which the patient dies

without medical examination and autopsy. This could have happened in the oldest age group in our study because the age-specific crude incidence and mortality numbers (the Figure) were lower in the group of patients ≥ 85 years of age than expected. Although the low incidence and mortality found in this oldest age group might be due to chance because of the small number of old people in the population (Table 1), it also cannot be excluded that some stroke cases in this age group were not seen by the health-care system. However, even if stroke cases and stroke deaths were not recorded in this age group, they were not registered by the health system and fatal cases were not coded as death resulting from stroke in the death certificates.

Discussion

Because of conflicting information between WHO mortality data¹ and local stroke incidence reports for Ukraine, we set forth to perform a prospective, population-based survey of stroke incidence and 30-day case fatality in the West Ukrainian city of Uzhgorod. Such data are lacking for Ukraine; the available WHO data are based on death certificates; and to the best of our knowledge, no similar study has been performed yet in this East European country. Even a recent large-scale European survey of 22 countries does not include stroke incidence and case fatality data from Ukraine.⁹

The reliability of death certificates has long been debated, and questions were raised about the accuracy of studies dependent of such sources of information in general¹⁰ and specifically in Ukraine.^{4,5} Therefore, instead of an analysis of health authority reports, we chose to perform a 1-year survey of all levels of health care for stroke in a city of 126 000 inhabitants. Thorvaldsen et al¹¹ reported that there is systematic overreporting of stroke deaths in the official vital statistics of former USSR countries. Indeed, we found that stroke incidence was much lower than expected from WHO mortality data.

Theoretically, the low stroke incidence and mortality that we found in this West Ukrainian city might be due to the inadequate identification of stroke cases in the population. However, with the quality criteria of Asplund et al,⁷ it is not probable that insufficient case ascertainment is responsible for the low incidence and mortality data that we found. The only critical age group is the group >85 years of age. A disproportionate lack of older people might be suggested by the low frequency of cases >85 years of age (the Figure).

TABLE 3. Thirty-Day Case Fatality in Different Treatment Settings

Treatment Location	Surviving on Day 30, n	Dead by Day 30, n	30-d Case Fatality, %
Hospitalized	198	36	15.4
Home neurology service	37	18	32.7
Home GP service	35	24	40.7
Died before getting to hospital	0	4	100
Total	270	82	23.3

Case fatality differs significantly among the hospital and home care settings (Pearson's χ^2 square, $P<0.0001$).

However, this is true mostly for men (Table 1), and it is not probable that a large number of missed stroke cases in this age group could have significantly distorted our results. The relatively low representation of the age group >85 years of age (especially for men) might reflect the late effect of World War II; the current population that is 85 to 95 years of age was 25 to 40 years of age during the war. According to the data of the regional statistical bureau, in year 2000, only 173 men but 448 women were ≥ 85 years of age in Uzhgorod. The GPs see all patients, including stroke patients, in their districts, and in case of a suspected stroke, they have to call the emergency service or consult the city outpatient neurologist according to local traditions and for legal reasons. It cannot be excluded that in rare cases the GP may treat the stroke patient without consulting the neurologist. However, because the manager of the study (Dr Mihálka) kept in regular contact with all 55 GPs of the city, it is highly unlikely that a considerable number of stroke patients could have been lost to this survey. It is also possible that in some cases neither the GP nor the emergency service is called when stroke occurs in patients >85 years of age. Because in fatal cases in this age group the cause of death is usually coded other than stroke—even in patients seen before death by the health-care system—such cases are missed not only in our register but also in official statistics.

The 23.3% value for 30-day case fatality is similar to the values reported for Denmark (20% to 25%), Slovenia (21%), and the United Kingdom (20%).⁹ In our survey, 33% of stroke patients were not hospitalized, which is close to the reported numbers for Croatia (35%) and Oxfordshire (40%) but higher than the values reported for most European countries.^{9,12} The mean age of stroke patients in our survey (63.4 years) was similar to values reported for Switzerland (63 years), Turkey (65.5 years), Slovenia (63.2 years), and Estonia (64 years).

The crude stroke incidence of 280 of 100 000 in our register is close to values reported for several Western European countries like Austria (200 to 250 of 100 000) and Germany (170 to 250 of 100 000); somewhat higher than the numbers given for Belgium, Denmark, and Portugal (200 of 100 000); and lower than the number of 300 of 100 000 for Sweden and Croatia.⁹ Age-standardized incidence and mortality data are easier to compare; therefore, we calculated these numbers using the European and the world standard population as well. The incidence standardized for the European population was 341 of 100 000 in our survey, close to the values of Auckland, New Zealand (350 of 100 000); Perth, Australia (361 of 100 000); Rochester, Minnesota (362

of 100 000); Umbria, Italy (374 of 100 000); and Oxfordshire, England (379 of 100 000).¹² The mortality standardized for the world population was 69 of 100 000 per year in our study, a value comparable to those found for Eastern European MONICA populations.¹¹

From these comparisons, we conclude that for any of the above parameters, we could find ≥ 1 West European countries with parameters similar to those of Ukraine. Our results cast doubt on the accuracy of WHO data of high stroke mortality in Ukraine, as well as on the generalizability of the east-west gap of stroke epidemiological data, and support the assumption of Alter et al¹³ that much of the reported variation in stroke mortality and incidence rates between populations may be attributed to methodological issues.

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