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ORIGINAL COMMUNICATION

Michal Gostynski
Stefan Engelter
Susanna Papa
Vladeta Ajdacic-Gross
Felix Gutzwiller
Philippe Lyrer

Incidence of first-ever ischemic stroke in the Canton Basle-City, Switzerland

A population-based study 2002/2003

Abstract Our study sought to estimate the incidence rate of first-ever ischemic stroke (FEIS) in the geographically well-defined population of the Canton Basle-City, Switzerland. An one-year prospective population-based study among the permanent residents of the Canton Basle-City (188015 inhabitants, census 2002) was carried out. Multiple overlapping sources of information were used. Stroke was defined according to the WHO criteria. The diagnosis of FEIS was based on clinical assessment and neuroimaging findings. 269 patients (114 males; mean age 72.8, standard deviation (SD) ± 12 and 155 females; mean age 78.4, SD ± 11) with FEIS were identified. The overall crude incidence of FEIS amounted to 143 per 100000 population (95 % confidence interval (CI) 126 to 160) and it was higher among females (156; 95 % CI 132 to 181) than in males (128; 95 % CI 105 to 152). The age-specific incidence rates of FEIS approximately doubled with each decade of life, increasing from 17 (95 % CI 2 to 31) among 0–44 years old group to 1034 (95 % CI 774 to 1293) for those aged 85 or more years. The overall incidence rate of FEIS adjusted for age to the European standard population was 76 per 100000 inhabitants (95 % CI 66 to 86) and it was higher in males – 89, 95 % CI 72–106 – than in females – 66, 95 % CI 53–77. Moreover, in comparison with studies from other developed countries (e. g. Germany, Italy, Australia) – carried out in the middle of 1990s – the standardised incidence rates of FEIS were substantially lower in Switzerland. Our results indicate that the risk of ischemic stroke might be low in Switzerland. However, giving a major reduction in the age and gender specific stroke incidence over the past years our findings might – alternatively – mirror this favourable trend.

Key words ischemic stroke · incidence · epidemiology · population-based study

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M. Gostynski, MD, MPH (✉) · V. Ajdacic-Gross, DrSc · F. Gutzwiller, MD, DrPH
Institute of Social and Preventive Medicine
University of Zurich
Sumatrastrasse 30
8006 Zurich, Switzerland
Tel.: +41-1/634-4655
Fax: +41-1/634-4970
E-Mail: mjgost@ifspm.unizh.ch

S. Engelter, MD · S. Papa, MSc · P. Lyrer, MD
Neurological Clinic and Stroke Unit
University Hospital Basle, Switzerland

Introduction

Stroke is a considerable health problem, heavily influencing quality of life and costs of health care [1]. Despite the decline in mortality from stroke, cerebrovascular disease remains among the leading causes of death in developed countries [2]. According to the most recent estimate, the annual number of deaths due to stroke reached 5.54 million worldwide [3]. It is even likely that this clinical, social and economical burden will increase over the next years owing to the rapid rise in the elderly population [1].

During recent years, several population-based studies from developed countries provided data on the incidence of first-ever stroke [4–7]. There are, however, no data on the incidence of stroke derived from prospective population-based studies in Switzerland. Therefore, the present study sought to estimate the incidence rate of first-ever stroke in the geographically well-defined population of the Canton Basle-City, Switzerland to close this important information gap. Thereby we have fo-

cused on ischemic stroke as this stroke type makes up the majority of all strokes.

Subjects and methods

The study was conducted in the geographically well-defined area of the Canton Basle-City between 1 June 2002 and 31 May 2003. According to the 2002 census, the total population of the Canton Basle-City was 180015 (population at risk), of which 38873 (20.7 %) were 65 or more years old, compared with 15.5 % for the whole Swiss population. The population of the Canton Basle-City consists of 54285 (or 29 %) Non-Swiss persons of different origins. However, among subjects aged ≥ 65 years, where the overwhelming number of stroke cases occur, Non-Swiss persons made up only 5.4 % of the population.

Ascertainment of cases

Health insurance is compulsory for each permanent inhabitant of Switzerland and medical care is to a great extent free of charge, allowing unrestricted access to medical services. Although almost all acute stroke patients are admitted to hospitals, multiple overlapping sources of information were used to achieve completeness of case ascertainment, as recommended by Sudlow and Warlow [8].

Hospitalised stroke patients

The study area has been served by the following public and private hospitals: 1 University Hospital Basle with the only Stroke Unit of the whole region, 3 Rehabilitation Centres (one specialised in care of stroke patients), 4 General Hospitals, 2 Geriatric Hospitals and 1 Paediatric Hospital.

Stroke Unit at the University Hospital Basle

Patients with acute stroke are usually admitted to the emergency room of the University Hospital Basle. Predefined pathways and algorithms of the Stroke Unit determine the management of each stroke patient. This includes diagnostic procedures, treatment and internal transferral (e. g. to intensive care unit, neurological clinic or internal medicine ward).

Other hospitals

In order to identify acute stroke patients referred to other hospitals of the study area, a letter with a short questionnaire covering diagnosis and demographic data of stroke patients was sent to all acting hospitals (except the Pediatric Hospital). The letters were sent at the beginning of each three months interval and at the end of the study (i. e. altogether 5 times). The physician in charge of the study was asked to report prospectively the cases of first-ever ischemic stroke, diagnosed and treated within each of the three months intervals. The only Pediatric Hospital was contacted at the end of our study. None of the reported ischemic stroke cases there met, however, the study inclusion criteria (i. e. to be permanent residence of the study area).

Non-hospitalised stroke patients

Acute stroke patients are usually referred to hospital for early treatment and either patients' physicians or emergency physicians make the referral. However, some patients with acute stroke (mostly elderly subjects) might be managed in the community (at home or in the nursing homes) or have died prior to hospitalisation, and so they never emerged in hospital records. Hence, all medical practitioners of the study area who might potentially take care of stroke patients were contacted by letter. It should be stressed that the medical practitioners also offer their medical services to the institutionalised elderly (nursing homes or residential homes for elderly) so that our approach allowed us to identify events of ischemic stroke among the institutionalised elderly that were not followed by transfer to the hospital as well. Based on the physicians registry we identified 200 medical practitioners (primary care physicians, internists, neurologists, geriatricians, cardiologist and on call physicians including imaging and Doppler services) in the study area who were potentially eligible for a postal interview. They were contacted by letter at the beginning of each of the three months intervals and at the end of study period (i. e. 5 times altogether). An additional 6th letter was sent to all medical practitioners who had not reported at all over the whole period of study, reminding them to notify the cases from their practices. The letters contained an invitation, general information regarding the study structure and its objectives as well as a short questionnaire consisting of several questions covering diagnosis and demographic data of stroke patients. The medical practitioners were asked to report prospectively the cases of first-ever ischemic stroke, diagnosed within each of the three months intervals. Furthermore, they were asked about the mode of referral (e. g. hospital, nursing home, stay at home) and whether the patient had died from the stroke prior to hospital admission. This approach covers also the data source "death certificates" as it is required by law that all death certificates are to be filled in by the involved physicians.

Definitions

Stroke was defined according to WHO criteria, as "rapidly developing clinical symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin" [9]. First-ever ischemic stroke was defined as a stroke occurring in a patient without any prior stroke event. Only patients with first-ever ischemic stroke diagnosed during the study period were counted. Patients with hemorrhagic stroke and transient ischemic attack (TIA) were excluded from the analysis. All cases with hemorrhagic stroke were excluded for two reasons. First, to ensure comparability with previous epidemiological studies of first-ever ischemic stroke [4, 7, 10]. Second, to study a homogeneous population, taking into account that there are many differences between ischemic stroke and hemorrhagic stroke with regard to e. g. risk factors or age distribution (most striking for subarachnoid hemorrhagic stroke).

Diagnosis of first-ever ischemic stroke

Among hospitalised patients diagnosis of ischemic stroke was based on clinical signs and symptoms as well as corresponding findings on either computed tomography (CT) or magnetic resonance imaging (MRI), or both. In the Stroke Unit every patient with suspected stroke was entered in the stroke registry at patients' entry. Verification of the stroke diagnosis was made by a stroke neurologist after discharge using all available clinical and paraclinical information. For patients in the Stroke rehabilitation center, clinical data, neuroimaging findings and laboratory results were assessed by the same single stroke neurologist from the Stroke Unit (STE). Thus we took advantage of an established stroke care pathway between Stroke Unit and rehabilitation center. In other hospitals diagnosis was made by the treating physician from the initial findings.

For non-hospitalized patients i. e. patients managed at home or in a nursing home or who died before being admitted to hospital, the diagnosis of first-ever ischemic stroke was solely based on the information provided by physician in charge. No further verification of reported cases was undertaken. However, it should be stressed that

medical practitioners usually provide medical care for their patients for years, hence knowing their past medical records very well.

First-ever ischemic stroke rather than recurrent one was assumed in patients who fulfilled one of the following criteria:

- no history of previous stroke according to the patient, relatives or primary care physician

or

- no records on previous stroke in the stroke registry of the Stroke Unit that has been running since March 1995.

Ethics

The ethics committee of the Cantons Basle-City and Basle-Country approved of the study.

Data analysis

All ages were included in the analysis. Overall, gender- and age-specific incidence rates of first-ever ischemic stroke per 100000 population with 95% confidence intervals (CI) were calculated. To make our findings comparable with different population-based studies a direct standardization to the European standard population [11] was performed. Univariate analysis was carried out with the chi square test for dichotomous variables. Continuous variables were tested by the t test. Values of $p < 0.05$ (2-sided test) were considered as a statistically significant. Descriptive and inferential analyses were performed using the SPSS statistical package version 9 [12].

Results

We received 427 reports of "potential" stroke patients. After scrutinising all our medical records 158 cases were excluded. The majority of exclusions were due to prior ischemic stroke (n = 61), transient ischemic attacks (n = 33) and double records (n = 24) (Table 1). A final diagnosis of first-ever ischemic stroke was made in 269 patients (114 males and 155 females). Female patients were older (mean age 78.4, standard deviation (SD) ± 11, range 38.5 to 98.4) than male patients (mean age 72.8, SD ± 12, range 37.3 to 94.9) (mean age difference 5.6, 95% confidence interval (CI) 2.8 to 8.4). Table 2 presents the sources of referral for patients with FEIS. In general, there was an association between the sources of referral and gender (p = 0.016) with females less frequently referred to the Stroke Unit than to other hospitals. However, after adjustment for age this gender difference was statistically no longer significant (standardized coefficient 0.101, p = 0.094). Patients referred to the Stroke Unit were significantly younger (mean age 74.5, SD ± 12) than those admitted to other hospitals (84.3, SD ± 9) (mean age difference 9.8, 95% CI 5.8 to 13.6) or those managed by medical practitioners (77.8, SD ± 11) (mean age difference 3.5, 95% CI –10.6 to 3.6; difference not significant).

Table 1 Reasons for exclusion from the study

Reason for exclusion from study	No. (n = 158)	%
Prior ischemic stroke	61	39
Transient ischemic attacks	33	21
Double records	24	15
Hemorrhagic stroke	19	12
Misdiagnosis*	15	9
Unknown or missing past history of stroke	6	4

* This category includes: headache, migraine, vertigo, cancer, Parkinson disease, acute brain syndrome, and falls

Table 2 Source of referral for patients with first-ever ischemic stroke (FEIS)

Gender	Males		Females		Total	
Referral	n	%	n	%	n	%
Stroke Unit	100	88	119	77	219	81
Other hospitals	8	7	30	19	38	14
Medical practitioners	6	5	6	4	12	5
Total	114	100	155	100	269	100

The overall crude incidence rate of first-ever ischemic stroke amounted to 143 per 100000 population (95% CI 126 to 160) and it was higher among females (156; 95% CI 132 to 181) than in males (128; 95% CI 105 to 152) (Table 3). The age-specific incidence rates of FEIS approximately doubled with each decade of life, increasing from 17 (95% CI 2 to 31) among 0–44 years old group to 1034 (95% CI 774 to 1293) for those aged 85 or more years. The age-specific incidence rates of FEIS increased more progressively among males – especially among young ones – than among female subjects.

To make our findings comparable with different population-based studies a direct standardization to the European standard population was performed (Table 4). After adjustment for age by direct method the overall incidence rate amounted to 76 per 100000 population (95% CI 66 to 86) and it was higher in males (89; 95% CI 72 to 106) than in females (65; 95% CI 53 to 77) without significant difference.

Discussion

The present study provides for the first time in Switzerland the estimates of incidence rates of first-ever ischemic stroke derived from a prospective population-based study carried out in a geographically well-defined population. The overall incidence rate of FEIS adjusted for age was higher in males than in females and the age-specific rates increased substantially with advancing age in both genders. On average female patients with first-ever ischemic stroke were about 6 years older than male ones. Those findings are well in accordance with the results from previous incidence studies [4, 6, 7, 13] and they seem to be widely accepted.

Table 3 Incidence rates (IR) of first-ever ischemic stroke (FEIS) per 100000 population according to age and gender in Basel, Switzerland

	Males		Females		Total	
Age (years)	n/N	IR (95% CI*)	n/N	IR (95% CI)	n/N	IR (95% CI)
0–34	0/35743	0/35658	0/71401			
35–44	3/15329	20 (0–42)	2/14853	13 (0–32)	5/30182	17 (2–31)
45–54	11/12788	86 (35–137)	3/12744	24 (0–50)	14/25532	55 (26–84)
55–64	13/10584	123 (56–190)	14/11443	122 (58–186)	27/22027	123 (76–169)
65–74	33/7958	415 (273–556)	29/10782	269 (171–367)	62/18740	331 (248–413)
75–84	36/5059	712 (479–944)	64/9173	698 (527–869)	100/14232	703 (565–840)
85+	18/1509	1193 (642–1744)	43/4392	979 (686–1272)	61/5901	1034 (774–1293)
Total	114/88970	128 (105–152)	155/99045	156 (132–181)	269/188015	143 (126–160)

n number of first-ever ischemic stroke cases; *N* number of population; * 95% confidence interval

Table 4 Age-and gender-standardized incidence rates (SIR) of first-ever ischemic stroke per 100000 population with 95% confidence intervals for the group aged 0 to 85 and more, standardized to the European standard population

Study	Males SIR (95 % CI*)	Females SIR (95 % CI)	Total SIR (95 % CI)
Basle-Study	89 (72–106)	65 (53–77)	76 (66–86)
Erlangen-Study[a]	120 (98–142)	93 (78–108)	104 (92–104)
Italy (Foggia region)[b]	148 (93–202)	108 (68–148)	125 (93–158)
NEMESIS-Study[c]	132 (105–159)	97 (77–117)	112 (96–128)

* 95% confidence interval
[a] Kolominsky-Rabas PL, et al. (1998) Stroke 29:2501–2506
[b] Intiso D, et al. (2003) Eur J Neurol 10:559–565
[c] Thrift AG, et al. (2001) Stroke 32:1732–1738

Finally, our findings suggest that the risk of suffering from ischemic stroke appears to be noticeably lower in Switzerland than in several developed countries as e. g. Germany, Italy or Australia.

The comparison of international age- and gender-standardized incidence rates for ischemic stroke suggests a considerable heterogeneity of incidence rates between different studies that used the similar case-finding approach. For example, four out of eleven studies cited by Thrift at al. [10] determined the incidence rate between 300 and 350, 4 studies between 250 and 299, 2 studies between 200 and 249 and one study between 150 and 199 per 100000 population for the group aged 45 to 84 years. The incidence rate determined in Söderhamm, Sweden (349) was almost 2 times higher than in Dijon, France (183). Our incidence rate for first-ever ischemic stroke for the same age group adjusted to the European population amounted to 180 (95% CI 153 to 207) per 100000 population and it was slightly lower than that in Dijon. The comparison of age-standardised incidence rates of first-ever ischemic stroke for all age groups across different studies (Table 4) also indicates that the risk of suffering from ischemic stroke is lower in the Swiss population than in several developed countries. However, it should be stressed that we have made the comparison with the studies that were carried out in the middle of the 1990s. Since the most recent findings have shown a major reduction in the age and sex specific incidence of stroke over the past 20 years [14], it might be that our comparison reflects alternatively this trend. On the other hand, our finding seems to be consistent with mortality data according to which stroke mortality in Switzerland in males and in females aged 35–74 years is the lowest worldwide [15]. However, the low stroke mortality in Switzerland might be due to the low case-fatality. Interestingly, in the International Stroke Trial [16] two-weeks and six-months case-fatality rates turned out, however, to be higher among Swiss patients compared with patients in other centers. Moreover, it should be emphasised that life expectancy – a well-recognised indicator of current health and mortality conditions in the general population – is also higher in Switzerland (life expectancy at birth 80.31 years) than in Australia (80.26), Italy (79.54) or Germany (78.54) (www.indexmundi.com). Finally, it must be also said that the mortality rate due to coronary heart disease (CHD) is substantially lower in Switzerland than for example in Germany or Australia (www.heartstats.org). As ischemic stroke and CHD share several risk factors (e. g. high blood pressure, smoking, diabetes mellitus) the prevalence of these risk factors in the Swiss population might be low as well. Hence, the risk of sustaining the ischemic stroke might be in fact substantially lower in the Swiss population compared with the populations from several other developed countries.

The strength of the present study is that to achieve completeness of case ascertainment different and overlapping sources of information for stroke patients were used, as proposed by Sudlow and Warlow [8]. The major source of information for our study was the Neurological Clinic with its Stroke Unit. The Stroke Unit has been active in the study area since 1995, is very well established and provides medical care for patients within the acute phase of stroke. The second major source of infor-

mation was the Geriatric Hospitals that provide medical care for elderly patients (65 years or older) among others for elderly stroke patients. Having those medical centers, the medical practitioners in the study area rather tend to transfer their stroke patients to hospitals (younger patients to the Stroke Unit and older ones to Geriatric Hospitals) than providing medical care outside hospital. The admission rate among ischemic stroke patients amounted to 96 % and was roughly similar to those observed in other studies [4, 6, 7]. Moreover, it must be stressed that in the vast majority of cases verification of the stroke diagnosis was undertaken and performed by a single stroke neurologist. Finally, because the Canton Basle-City provides a high quality medical care for stroke patients (specialised Stroke Unit), it is rather unlikely that patients within the acute phase of stroke may seek medical attention outside study area.

Our study has several limitations. Firstly, the data were collected during one year. Thus, because of annual variation we might have missed some stroke cases especially among younger individuals (i. e. the group aged 0–34 years) where ischemic stroke occurs rarely. In a one-year prospective study among 133816 inhabitants in Australia Thrift et al. [10] have found for this age group three first-ever ischemic stroke cases (all among women). Intiso et al. [7] have reported for the group aged 0–54 years based on three-year retrospective study among the population at risk amounting to 41269 (i. e. approximately 125000 person-years of observation) five first-ever ischemic strokes compared with nineteen FEIS cases in our study. According to Erlangen study [4] one might expect about three cases of first-ever ischemic stroke in young individuals (i. e. aged 0–34 years) over the period of two years. Secondly, although medical practitioners were asked to report the cases of ischemic stroke among patients who died before admission to hospital (sudden death) or who died during medical care outside hospital, no such cases were reported. Hence, we have checked the official Swiss mortality statistics covering our study area. The check has disclosed 11 death cases (2 males and 9 females) in the study area, with ischemic stroke noted as either a primary or a secondary cause of death (according to International Classification of Diseases, 10th Revision, code I63). We could not discover if death was caused by first-ever or recurrent ischemic stroke. However, it is highly unlikely that all registered death cases were due to first-ever ischemic stroke. So if we have missed some first-ever ischemic stroke cases (among young population or among death cases) then they are very few and hence presumably without biasing our estimates. Thirdly, with regard to stroke patients managed only by medical practitioners the misdiagnosis of ischemic stroke is possible. Because all 24 double records in our data stemmed from medical practitioners we have checked the accordance between the admission diagnosis to hospital (made by medical practitioners) and final diagnosis (based on clinical data and neuroimaging findings). In 17 cases (71 %) we could confirm the medical practitioner's diagnosis and in 7 cases (29 %) there was discordance between the diagnoses (e. g. not first-ever ischemic stroke, haemorrhagic stroke or other disease). Based on this misclassification rate we would expect that about 3 to 4 out of 12 FEIS cases reported by medical practitioners without data verification could be presumably misdiagnosed. For the entire study population, possible misdiagnosis accounts for less than 1.5 % (4/269) which seems to be unlikely to cause significant alteration of our results.

In conclusion, our prospective population based study showed that the overall incidence rate of FEIS adjusted for age to the European standard population was 76 per 100000 inhabitants. This rate is lower than in several other developed countries, indicating that the risk of stroke might be low in Switzerland. Since the findings from other countries are several years older, our data might – alternatively – reflect merely the latest substantial reduction in the age and gender specific incidence of stroke.

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