Stroke in Spain: Epidemiologic Incidence and Patterns; A Health Sentinel Network Study

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Introduction: Cerebrovascular disease is among the 4 main causes of mortality in Spain. The objective of this study was to estimate the incidence of stroke and to describe the principal risk factors and other clinical and epidemiologic patterns found in patients. *Methods:* Doctors from the Spanish sentinel health network recorded the episodes of acute cerebrovascular diseases in 2005 in a population of 201,205 inhabitants older than 14 years. The information of the patients (age and sex) and the episode (e.g., duration, symptoms, origin, medical attention, risk factors) was collected on a standard form. *Results:* The estimated incidence rate of stroke was 141 cases per 100,000 inhabitants (confidence interval [CI] 95%: 125-158), 134 (95% CI: 112-157) in women and 148 (95% CI: 124-172) in men. The incidence increases significantly from the age of 65 years and men younger than this have higher rates than women. In all, 12% of patients with stroke die within the first 24 hours. *Conclusions:* Incidence of cerebrovascular disease in Spain is below that recorded in other countries. There is no difference according to sex, but incidence among young and middle-aged men is greater than that among women. Significant variations from some population groups to others are observed, maybe because of the difference in the prevalence of risk factors. **Key Words:** Stroke—incidence studies—Spain.

Stroke is among the 4 principal causes of mortality in developed countries. In 2005, 14,611 men and 20,139 women died in Spain of cerebrovascular disease, with rates of 68 and 91 per 100,000 inhabitants, respectively. In ageing populations, such as in the interior regions of our country, mortality is more than 90 cases per 100,000 inhabitants for both sexes, higher than acute myocardial infarction, heart failure, lung cancer, or breast cancer in women.[1]

In addition, patients who survive a stroke have significant neurologic sequelae that bring on differing levels of disability with public health,[2,3] social,[4] and economic consequences.

Measures for control of risk factors put into practice in recent years appear to have reduced the incidence and mortality of this serious health problem, mainly in the groups at particular risk of thromboembolism and in very elderly patients. However, the accumulated risk has not decreased the same way,[5] possibly as a result of increased life expectancy. Nor is there evidence that this

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reduction has occurred at middle age. On the contrary, it is suspected that in certain age groups, mainly in men younger than 65 years, the number of strokes is above what is expected. It seems that this group shows high levels of cardiovascular risk factors that are not currently diagnosed or controlled.[6-8]

Existing information on cerebrovascular morbidity in Spain is limited and almost always refers to hospitalized cases with particular characteristics. The search for information on the population does not result in more than partial and highly localized data[9,10]; therefore, there are no valid estimates or clinical epidemiologic information on this disease based on population reference. In addition, there is, without doubt, a need for necessary resources that permit correct planning and evaluation of preventive and therapeutic measures (e.g., the demand for data to understand the variations that have occurred in recent years related to preventive anticoagulation). In this respect, the information that primary care professionals have available is the most complete and reliable, although collection and analysis difficulties demand special study methods.

All these approaches related to the lack of information, together with the need to complete the clinical information with epidemiologic and public health data, led the RECENT[11] project work group to propose multicenter research into this significant health problem.

The first objective of this study was to estimate the incidence of stroke based on 3 heterogeneous Spanish population groups, all of which are different from a demographic, social, and public health point of view. The second objective put forward was to set out the main risk factors by age group and sex, and other clinical and epidemiologic characteristics of these patients in our country.

Methods

Sentinel physicians belonging to 3 Spanish health sentinel networks from the autonomous regions of Castilla y León (CYL), Extremadura (EXT), and Comunitat Valenciana (CVA), a total of 206 doctors, recorded episodes of stroke occurring in patients older than 14 years who were under observation in 2005. This population, obtained from the national health number registers, came to a total of 201,025 people (2.4% of the population of the 3 regions), of whom 48,346 were aged 65 years or older.

A sentinel network is an information and epidemiologic research system based in a random sample of general practitioners who, voluntarily, participate in several research studies along 1 year. In Spain, population under surveillance of a sentinel network is representative of the population at regional level.[12]

Inclusion Criteria

A common inclusion criteria, the International Classification of Primary Care 2 Defined (Spanish version),[13] was used by all participants.

Stroke was defined as a neurologic deficiency (symptoms and signs of cerebral dysfunction), whether localized or not, secondary to a vascular pathology (thrombosis, embolism, hemorrhage), excluding other causes, and with a duration of more than 24 hours or which led to the death of the patient.

Episodes that were not initially diagnosed by the patient's doctor, but were noticed later, were also recorded. That is the situation where cases occurred during a holiday or went directly to the emergency department of a hospital. Doctors always received medical discharge information from hospital for each patient in their list, including death certificate or circumstances of death. In addition, these patients or their relatives had to visit their physician to get the death certificate, receipts, and any complementary treatment.

The following criteria for the definition of variables were established:

1. Hypertension when recorded in the patient's medical history or when blood pressure levels were equal to or more than 140/90 mm Hg before the episode.
2. Dyslipidemia when recorded in the patient's medical history or when total cholesterol was equal to or more than 250 mg/dL.
3. Diabetes when recorded in the patient's medical history or when basal glucose was equal to or more than 126 mg/dL.
4. Obesity when the body mass index was equal to or more than 30.
5. Physical inactivity when physical work derived from sport or daily life (e.g., aerobic exercise including walking, running, swimming, habitual work on physical requirements, housework) was less than 3 hours per week.
6. Heart disease, peripheral arterial disease, anticoagulation, and excess alcohol consumption when recorded in the patient's medial history.
7. Smokers who smoked one or more cigarettes a day and ex-smokers who smoked more than 100 cigarettes throughout their life and currently did not smoke.
8. Recent surgical operation during the 30 days before the episode.

The participating doctors used a standard form to collect the information on the characteristics of the patient (age and sex) and the episode (e.g., duration, symptoms, possible ischemic or hemorrhagic origin, medical attention, risk factors) on a weekly basis.

Data Management and Analysis

The information collected on the standard forms was sent to the coordination facilities where they were validated and computerized. A homogeneously structured

database was set up from each network for the recorded cases and the reference population. The joint database set up in MS Access (Microsoft Corp., Redmond, WA) was debugged and analyzed with the SAS statistical module (SAS Institute, Cary, NC). There were 285 valid entries for analysis.

Incidence rates were estimated for the total and each one of the 3 population groups under study, and for each age group and sex. A 95% confidence interval was calculated approximating normal distribution. The rates were adjusted by age considering the European standard population. The comparison of the numeric estimators was carried out with Student *t*, whereas the categorical distributions were compared with the Chi squared test.

Results

Incidence Estimates

The estimated total incidence rate was 141 cases of stroke per 100,000 inhabitants (95% confidence interval: 125-158). No significant differences were found according to sex, but there were differences according to age, reaching a maximum in patients aged 75 years and older with an incidence of more than 0.6% (Table 1). The risk of having an acute episode of stroke after 75 years of age was two times greater than between ages 65 and 74 years, and 6.6 times greater than between ages 55 and 64 years. Men had a significantly higher risk than women in the 55- to 64-year age groups, 3.6 times more.

The incidence in each of the 3 reference populations under study reflected significant variations. CYL presented the highest crude rate with 167 episodes per 100,000 inhabitants, whereas in EXT and CVA it was 93 and 129, respectively. Adjusted rates by the European age standard population show a total estimate rate of 83 per 100,000 inhabitants and reduced the differences among the 3 regions. Age-adjusted rates confirm the statistically significant higher risk of men (99/100,000) than women (66/100,000) (Table 2).

Descriptive Study

Stroke episodes occurred earlier in men, among which 19% occurred younger than 65 years, whereas for women this percentage was 8%. These differences in the onset of strokes by sex are statistically significant ($P < .05$) (Table 3).

One of 3 episodes (32.6%) occurred in people with a history of the disease, with a higher occurrence among older people but without significant differences, as was the case for sex or hemorrhagic or ischemic origin.

The most frequent clinical symptoms that could be found in a stroke episode were speech disorders, paresis, and consciousness disorders. There was little difference by sex and age groups, although significant differences were appreciated in the presentation of paresis, which was higher in men (61.5%) than in women (45.3%) ($P < .05$). Consciousness disorders were more common in women (49.6%) than men (37.2%) ($P < .05$). By age group, the relative frequency was comparably distributed with the exception of paralysis, incontinence, and consciousness disorder, all of them more frequent in patients aged 75 years and older with differences statistically significant ($P < .05$) (Table 4).

The most frequent risk factor for all sexes and age groups was hypertension, more than 50%. Smoking in middle-aged men and physical inactivity in women were also present in one of two patients. There were also statistically significant differences between age groups for dyslipidemia, diabetes, alcohol consumption (more frequent in middle age), and obesity and physical inactivity (more frequent in elderly patients). Anticoagulation was found more frequently at aged 75 years and older (Table 5).

Table 1. *Incidence of acute episodes of stroke by sex and age*

	Total	Women	Men
Total	141 (125-158)	134 (112-157)	148 (124-172)
15-54 y	12 (6-18)	9.6 (2-17)	15 (5-24)
55-64 y	96 (57-135)	42 (5-78)	150 (80-219)
65-74 y	308 (229-387)	270 (168-371)	352 (228-476)
≥75 y	634 (544-725)	572 (460-685)	721 (572-871)

Rates (95% confidence interval) per 100,000 inhabitants.

Table 2. *Incidence of stroke by sex and region*

	Rate (95% CI)	Adjusted rate* (95% CI)
Total	141 (125- 158)	83 (72-94)
Women	134 (112-157)	66 (53-80)
Men	148 (124-172)	99 (81-117)
Castilla y León	167 (140-195)	83 (65-101)
Extremadura	93 (51-134)	54 (28-81)
Comunitat Valenciana	129 (106-152)	96 (78-114)

Abbreviation: CI, confidence interval.
Crude and adjusted rates per 100,000 inhabitants.
*European age-standardized rates.

Table 3. *Distribution of acute episodes of stroke by sex and age*

Age groups	Women (n = 137) cases (%)	Men (n = 148) cases (%)
15-54 y	6 (4.4)	10 (6.8)
55-64 y	5 (3.6)	18 (12.2)
65-74 y	27 (19.7)	31 (20.9)
≥75 y	99 (72.3)	89 (60.1)

Chi squared test $P < .05$.

Table 4. *Deficiency symptoms in acute episodes of stroke by sex and age group*

Symptoms	Sex			Age group		
	Women (n = 137) cases (%)	Men (n = 148) cases (%)	*P**	< 75 (n = 104) cases (%)	≥ 75 (n = 181) cases (%)	*P**
Paralysis	57 (41.6)	58 (39.2)	NS	31 (29.8)	84 (46.4)	< .01
Paresis	62 (45.3)	91 (61.5)	< .01	58 (55.8)	95 (52.5)	NS
Paresthesia	47 (34.3)	59 (39.9)	NS	45 (43.3)	61 (33.7)	NS
Consciousness disorders	68 (49.6)	55 (37.2)	< .05	37 (35.6)	86 (47.5)	< .05
Speech disorders	99 (72.3)	94 (63.5)	NS	66 (63.4)	127 (70.2)	NS
Sudden loss of sight	9 (6.6)	12 (8.1)	NS	9 (8.6)	12 (6.6)	NS
Incontinence	34 (24.8)	33 (22.3)	NS	12 (11.5)	55 (30.4)	< .01
Other	25 (18.2)	26 (17.6)	NS	17 (16.3)	34 (18.8)	NS

Abbreviation: NS, not significant.
*Chi squared test.

Nearly 60% (59.4%) of episodes were attended initially by the general practitioner, 34.9% went to the hospital emergency department, and 5.7% were attended by the emergency ambulatory services. There were no differences in the frequency of this variable among age groups. There was a lower proportion of women (36.7% *v* 44.1% of male patients) using the emergency departments and emergency services. This was not statistically significant.

At 24 hours after the stroke, 74.6% of patients were in the hospital, 13.4% at home, and 12.0% had died. The fatality rate at 24 hours was 16.1% for women and 8.1% for men ($P < .05$).

Discussion

The Spanish health sentinel networks have been in operation since 1989 and use homogeneous standard methods that allow the development of multicenter studies and the comparison of the results.[12,14] The sentinel networks participating in this study have an experience of 19 years in CYL, 17 in CVA, and 10 in EXT. Each of the 3 networks involved in this study carry out representative estimates in their territory. There is not any trend in cases diagnosed through the year and no differences among regions, which indicates a stable ascertainment and no changes in diagnosis criteria over time.

For the study of stroke, the data from primary care appear to be the most adequate as they include patients who do not go to a hospital, or who go to the emergency department but are not admitted and consequently do not generate an entry. These cases represented 35.4% of the episodes studied, and included the deaths that occurred outside the hospital.

Completeness of cases is assured because patients' relatives always contact the physician for death certificate or get receipts from public health services. Doctors in

Table 5. *Risk factors in acute episodes of stroke by sex and age group*

Risk factor	Sex			Age group, y		
	Women (n = 137) cases (%)	Men (n = 148) cases (%)	*P**	< 75 (n = 104) cases (%)	≥ 75 (n = 181) cases (%)	*P**
Hypertension	87 (63.5)	79 (53.4)	= .08	60 (57.7)	106 (58.6)	NS
Dyslipidemia	44 (32.1)	41 (27.7)	NS	38 (36.5)	47 (26.0)	= .06
Diabetes	33 (24.1)	41 (27.7)	NS	35 (33.6)	39 (21.5)	< .05
Obesity	39 (28.5)	31 (20.9)	NS	17 (16.3)	53 (29.3)	< .05
Physical inactivity	72 (52.5)	51 (34.5)	< .01	33 (31.7)	90 (49.7)	< .01
Smoking	3 (2.2)	38 (25.7)	< .01†	29 (27.9)	12 (6.6)	< .01
Alcohol consumption	3 (2.2)	28 (18.9)	< .01†	20 (19.2)	11 (6.1)	< .01
Heart disease	43 (31.4)	42 (28.4)	NS	28 (26.9)	57 (31.5)	NS
Peripheral arterial disease	19 (13.9)	13 (8.8)	NS	8 (7.7)	24 (13.3)	NS
Surgery	5 (3.6)	5 (3.4)	NS	4 (3.8)	6 (3.3)	NS
Anticoagulation	46 (33.5)	41 (27.7)	NS	21 (20.2)	66 (36.5)	< .05

Abbreviation: NS, not significant.
*Chi squared test.
†Fisher test.

primary care do not have access to hospital records, but a complete discharge form is sent to the physician with diagnosis and clinical information assuring the continuity of treatment, and including the death certificate or circumstances of death in the case. In addition, although the information generated at this level of care is more limited from the diagnostic point of view, it is more complete as far as the risk factors, clinical prodrome, and the public health determinants and consequences are concerned.[15] This study is one of the few that have been carried out on the incidence of strokes counting on population representation.

This type of approach limits the clinical, diagnostic, and therapeutic information as complete data regarding the hospital care that the great majority of these patients receive are not available. On the other hand, better knowledge of the situation before the episode and the personal and medical characteristics of the population available to the primary care professionals means that the epidemiologic information, and that which is of more importance in public health, is greater and of better quality.

The importance of stroke is not only in the morbidity and mortality, but also in the social and health costs. Although there are not many long-term monitoring studies, 47% of patients with stroke who survive have a moderate to severe physical disability and psychologic dysfunctions that require the presence of a caregiver to look after them.[14]

An economic study with US data[16] sets the average cost per capita as a result of a stroke at between $15,000 and $25,000. This includes ambulance services, hospitalization, rehabilitation, health care in the home, medical consultations, treatments, costs of informal caregivers, and potential loss of earnings.

The incidence of stroke in the population under study (141/100,000) was relatively low if compared with estimates in Nordic populations where it triples in women and almost quadruples in men.[17] Estimates carried out using the Framingham cohort set the average annual incidence at 530 cases per 100,000 inhabitants between 1990 and 2004.[18] A calculation made using hospital admissions in the United States estimates an incidence of 269 cases per 100,000 inhabitants in 1996.[19] In Spain, the information is limited. The incidence calculated in a study into a cohort in the city of Manresa was 183 cases per 100,000 inhabitants, with 64% occurring after the age of 60 years.[10] Estimates from hospital databases are lower, particularly in women: 127 cases per 100,000 inhabitants.[20] In a population-based study in the province of Segovia, the crude incidence was estimated in 80 cases per 100,000 inhabitants.[21]

The incidence of stroke in the areas studied in Spain was not homogeneous. The areas with a more elderly population, such as CYL, showed very high crude rates, but on adjustment by age the real variations in risk were shown. The greater incidence in CVA compared with CYL and the lower incidence in EXT should be studied in greater detail to evaluate the possible associated, and to-date unknown, risk factors, mainly in the age group younger than 65 years. The patients younger than 65 years were mainly men (71.2% over the whole study), which appears to indicate a high and uncontrolled risk in this group of the population. The prevalence of the classic cardiovascular risk factors estimated in the national health survey[22] appears to show a lesser global risk in CYL (lower rate of smokers, hypertension, excess weight, and obesity), but does not justify the difference between EXT and CVA.

Certain symptoms or signs tend to show up depending on sex and age, which in some cases can be explained by the patient's different subjective perception. However, paraesthesia and sudden loss of vision are noticeable, which were higher in patients younger than 75 years.

As far as the risk of predisposing factors and those relating to smoking, alcohol, physical inactivity, and anticoagulation are concerned, they seem to be distributed by age and sex in a logical and comprehensible way. However, the higher percentage of dyslipidemia in patients younger than 75 years compared with older patients is noticeable, which could directly imply this risk factor in the incidence of the younger groups, as has already been mentioned by some authors.[23] In light of these data, an in-depth study into the risk factors that are marking the difference in the population groups with a high incidence seems necessary.

Although in this study only fatalities that occurred within 24 hours were evaluated, the figures are consistent with the results found in the Swedish study, in which the rate is around 10% (although it should be pointed out that the figures correspond to the period 1989-1998). This study did not show differences according to sex, whereas our data estimate double the fatality rate among women as opposed to men, independent of the age group. This observation, together with that of a higher rate of hospitalization in men could be associated with different medical attention in the first instance, which in turn could be related to a bias in care according to sex. This would be worth studying in more depth.

The information on stroke generated in primary care has been proved valid and accurate for estimating incidence and describing patients' clinical epidemiologic patterns. The inclusion of the episodes treated in outpatients, or which result in fatality outside the hospital, allows a better approximation of the true incidence of the disease (only the paucisymptomatic episodes that are not attended by a doctor are excluded). It also permits the completion of the information on risk factors and other epidemiologic characteristics of the 30% of patients who usually do not appear in hospital registers.

Stroke, as a public health problem, goes further than an acute episode, and the economic consequences for the

family and society cannot be evaluated with these particular studies. For this reason, our group has monitored these patients to evaluate the fatality rate and the state of health and disability 12 months after the episode, which will give continuity to these initial results.

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