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Incidence, risk factors and short-term mortality of stroke in Vittoria, southern Italy

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Abstract We determined the incidence, risk factors, and short-term mortality of stroke in a well-defined area of southern Italy, i.e. the city of Vittoria, Sicily (58 833 inhabitants). The medical records of the local hospitals and the outpatient files of the local neurologist referring to the calendar year 1991 were retrospectively investigated. Stroke was defined according to standard criteria and classified as first-ever (FE) and recurrent (R). Risk factors for stroke were diagnosed from medical history, laboratory and instrumental findings, and in the presence of specific treatments. Short-term mortality was assessed as 30-day case-fatality rate. The sample included 120 cases (61 men) aged 34–94 years, 89 of whom (48 men) had a FE stroke. The overall annual crude incidence rate of FE stroke was 165.3 per 100 000 (men, 178.4; women 152.2); for FE and R stroke together it was 222.9 (men,

226.8; women 219.1). The standardized rates were 245.3 (FE stroke) and 321.9 (FE and R stroke). The age-specific rates for FE stroke were 9.4 (<55 years), 262.2 (55–64 years), 645.2 (65–74 years), 2019.7 (75–84 years), and 3246.8 (≥85 years). The corresponding values for FE and R stroke were 11.7, 412.0, 887.1, 2565.5, and 4220.8. In patients with FE stroke, cerebral infarction was the main type. Hypertension, diabetes and cardiac disorders were the commonest risk factors, with similar distribution among FE and R stroke. The 30-day case-fatality rate was 28% for FE and R stroke and 38% for FE stroke. Compared to other reports, the incidence of stroke in Vittoria was lower in the youngest but higher in the oldest age groups. Although the small sample size and possibility of misdiagnoses may partly explain our findings, the roles of different dietary, social, and genetic factors in the local population warrant investigation.

Key words Stroke • Occurrence • Risk factors • Mortality

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Introduction

In western countries, crude incidence rates for stroke vary between 117 and 272 per 100 000 persons [1]. Most of the variability still depends on accuracy in case ascertainment and different diagnostic definitions. However, even with these limitations, the rates can significantly vary according to age and, to a lesser extent, sex and race [2]. Several factors have been implicated in the occurrence of stroke, including genetic susceptibility, dietary habits, physical activity, stress, alcohol consumption and smoking [2].

Based on published reports [3–7], in Italy the overall, sex- and age-specific incidence rates of stroke tend to be similar to those of other European and non-European industrialized countries. However, the populations studied were mostly from northern and central Italy, and the only report from southern Italy [7] was based on a mixed case-finding design, in which subjects experiencing a minor stroke not diagnosed

before death could have been missed. In southern Italy, the population is of Mediterranean ancestry and has certain specific dietary, occupational and sociocultural habits. This might explain differences in susceptibility to stroke.

For this reason, we undertook this epidemiological survey of stroke in a well-defined area of southern Italy, with the following aims: (1) to provide overall, age- and sex-specific incidence rates of stroke; (2) to identify the commonest risk factors; and (3) to assess short-term mortality.

Subjects and methods

Vittoria is a town located in southeastern Sicily, with 58 833 inhabitants (1991 census). Agriculture (50%), is the leading professional activity, followed by trading and clerical work (about 20% each). Mean annual income per resident is € 20 000. Recent migratory trends are limited in this population. The structure of the population of Vittoria is compared to that of the Italian population in Fig. 1. In Italy, medical assistance (comprising office and home consultations and hospitalizations) is largely free of charge. Patients with acute clinical conditions are generally seen at the emergency room of the local hospitals and admitted when symptoms persist at the time of the hospital visits. This is also true for neurological conditions, like stroke, which may require hospital admission even for the very elderly.

All the residents of the town of Vittoria having neurological conditions requiring consultation were generally seen by the only practicing neurologist (FI) who at the time of the study was consul-

tant for two local hospitals (Vittoria and Comiso) and did outpatient visits in private practice. The occurrence of stroke was evaluated by two of us for the year 1991 after examining several source documents, including the medical records of the Internal Medicine and Intensive Care Units of the two hospitals (the only two departments known to admit stroke patients), and the outpatient neurological records of the individuals seen privately.

According to the World Health Organization criteria [8], stroke was defined as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin”. Stroke was further classified as first-ever, i.e. occurring for the first time during the patient’s lifetime, or recurrent. Stroke subtypes were classified based on the results of computed tomography (CT). Cerebral infarction was diagnosed when CT showed no signs of cerebral hemorrhage. Patients in whom the clinical diagnosis was not supported by CT were classified as having undefined stroke. Transient ischemic attacks and subarachnoid hemorrhage were not included. Hypertension, diabetes and cardiac disorders were diagnosed when indicated as such in the medical history, when suggested by sustained laboratory and instrumental abnormalities, when reported in the discharge diagnosis, or in the presence of specific treatments at admission or during hospital stay. For each eligible patient, relevant demographic, clinical, biochemical and neuroradiological findings were collected on a semistructured questionnaire, specifically inquiring about stroke subtype, risk factors, clinical severity and outcome.

Data on the incidence, risk factors and mortality were provided for the entire stroke population (first-ever and recurrent) and for first-ever stroke separately. Overall, age- and sex-specific inci-

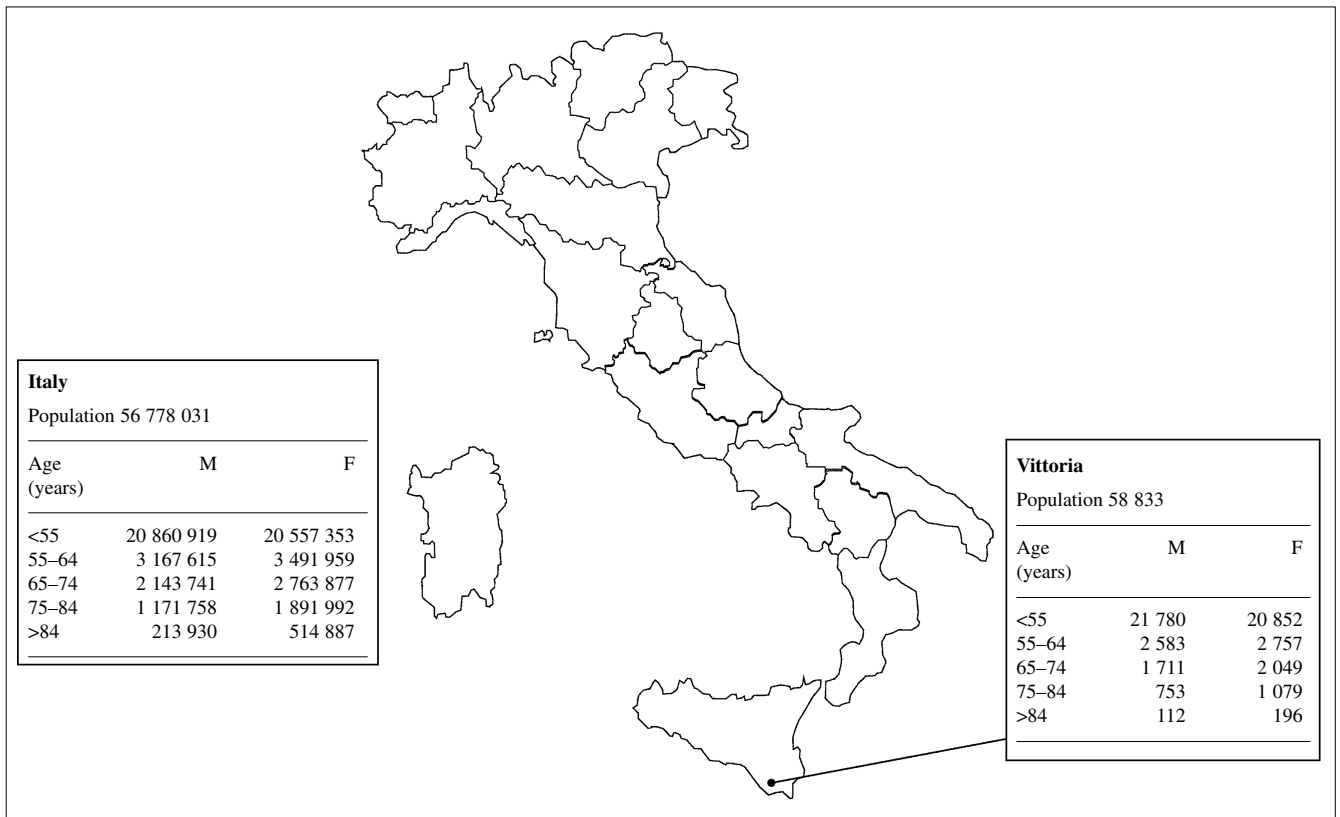


Fig. 1 Main demographic characteristics of the population in Vittoria, compared to the Italian population. Data are from the 1991 census

dence rates were calculated with 95% confidence intervals (95% CI) [9]. Age- and sex-adjusted rates were also provided with reference to the 1991 Italian population (Fig. 1). We calculated 24-h and 30-day case-fatality rates to assess immediate and short-term mortality. One of us examined the death certificates of the residents of Vittoria who died during the index year, in whom stroke (or an equivalent term) was reported as the underlying, intermediate or immediate cause of death, to assess short-term mortality and to see how many patients had died of stroke before reaching hospital.

Results

During the study period, 120 subjects with stroke were traced from the hospital records (Table 1). None of the individuals seen as outpatients in private consultation and not

Table 1 Characteristics of the 120 subjects with stroke (first-ever or recurrent) and of the 89 cases of first-ever stroke

Variable	Stroke n (%)	First-ever stroke n (%)
Sex		
M	61 (51)	48 (54)
F	59 (49)	41 (46)
Age (years)		
<55	5 (4)	4 (4)
55–64	22 (18)	14 (16)
65–74	33 (28)	24 (27)
75–84	47 (39)	37 (42)
85+	13 (11)	10 (11)
Risk factors		
Hypertension	72 (60)	56 (63)
Diabetes	28 (23)	22 (25)
Heart disease	26 (22)	19 (21)
Hyperlipidemia	4 (3)	3 (3)

hospitalized satisfied the diagnostic criteria. The sample included 61 men and 59 women aged 34–94 years (mean, 72 years). Of these, 89 (74%) had a first-ever stroke. The age and sex distributions of the whole sample compared to patients with first-ever stroke were similar (Table 1). In both groups, hypertension was the commonest risk factor, followed by diabetes, cardiac disease, and hyperlipidemia. Forty-nine patients (41%) had only one risk factor, 21 (17%) had two, and three (2%) had three. Cerebral infarction was present in 53 cases (first-ever stroke, 33 cases) and cerebral hemorrhage in 14 (first-ever, 13). Lesion type was undefined in 53 cases (first-ever, 43) for whom a CT scan was unavailable.

The overall annual crude incidence rate of first-ever stroke was 165.3 per 100 000 (men, 178.4; women, 152.2), and 222.9 for first-ever and recurrent stroke (men, 226.8; women, 219.1) (Table 2). The standardized rates were 245.3 (first-ever stroke) and 321.9 (first-ever and recurrent stroke). Age- and sex-specific incidence rates for the two study populations are reported in Table 2. In both sexes the age-specific rates for first-ever stroke were 9.4 (<55 years), 262.2 (55–64 years), 645.2 (65–74 years), 2019.7 (75–84 years), and 3246.8 (≥85 years). The corresponding values for first-ever and recurrent stroke were 11.7, 412.0, 887.1, 2565.5, and 4220.8. The rates were higher in men for all the age classes, except for patients under age 55.

Compared to other reports, including the Italian studies, the incidence of first-ever stroke in Vittoria was lowest in patients aged less than 55 years and highest in the 75–84 years group and, with few exceptions, in the oldest age group (85+ years) (Table 3) [3–7, 10–21].

Immediate mortality after stroke was 9%. The mean hospital stay was 8 days (range, 1–22). By the time of discharge, 61 patients with first-ever stroke (69%) were improved, nine (10%) were stable, ten (11%) were worsened, two (2%) had a relapse, and seven (8%) died (one just after discharge). The 30-day mortality rate was 28% in the entire study population and 38% in patients with first-ever stroke.

Table 2 Age- and sex-specific incidence rates per 100 000 persons for first-ever stroke or first-ever and recurrent stroke in Vittoria, southern Italy

Age (years)	First-ever stroke						First-ever and recurrent stroke					
	Men			Women			Men			Women		
	n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI
<55	1	4.6	0.1–25.6	3	14.4	3.0–42.0	2	9.2	1.1–33.2	3	14.4	3.0–42.0
55–64	8	309.7	133.5–610.1	6	217.6	80.0–474.4	12	464.6	240.2–813.0	10	362.7	174.1–667.4
65–74	16	1017.4	582.0–1648.2	8	439.2	189.3–865.2	18	1077.2	638.8–1702.0	15	732.1	410.0–1208.0
75–84	18	2390.4	1417.5–3776.8	19	1760.9	1060.1–2747.0	22	2921.6	1831.8–4411.6	25	2317.0	1499.1–3429.2
≥85	5	4464.3	1446.4–10401.8	5	2551.0	826.5–5943.8	7	6250.0	2506.2–12875.0	6	3061.2	1123.5–6673.4
Total	48	178.4	131.5–237.3	41	152.2	109.3–207.0	61	226.8	173.5–290.3	59	219.1	166.7–282.6

Table 3 Age-specific incidence rates (per 100 000 person) of first-ever stroke in different study populations

Reference	Age, years							All ages	Cases, n
	<35	35–44	45–54	55–64	65–74	75–84	≥85		
Oxfordshire, UK [10]	NG ^a	23	57	291	690	1434	1987	160	675
Sicily, Italy [7]	NG ^b	NG ^b	NG ^b	300	740	1820	2110	190	138
Rochester, USA [11]	3	33	63	273	668	1371	2351	145 ^c	496
Dijon, France [12]	15	69	111	165	531	926	1369	145	179
Umbria, Italy [3]	NG	28	0	194	506	1227	2378	136 ^c	108
Valle d'Aosta, Italy [4]	NG	23	0	234	729	1642	3236	215 ^c	254
Malmo, Sweden [13]	NG ^d	NG ^d	74	183	546	1100	1719	225	524
Frederiksberg, Denmark [14]	NG	21	0	306	702	1310	1600	306	262
Shiga, Japan [15]	NG	24	102	233	477	803	1081	212 ^c	401
Warsaw, Poland [16]	3 ^e	31	83	221	413	731 ^f	1137 ^g	127	462
Belluno, Italy [5]	NG	46	114	242	720	1317	3413	170 ^c	474
Jyvaskyla, Finland [17]	5 ^h	35	83	251	602	1219	2174	227 ^c	190
L'Aquila, Italy [6]	NG ⁱ	34	94	228	816	1587	2875	275	819
Innherred, Norway [18]	NG ^j	NG ^j	40	217	741	1820	3039	221 ^c	235
Arcadia, Greece [19]	7	25	82	218	568	1220	2661	344	555
Erlangen, Germany [20]	4	21	105	196	508	1226	2117	134	354
Melbourne, Australia [21]	NG ^a	44	111	299	747	1928	3976	133	285
Present study	NG ^k	NG ^k	NG ^k	262	645	2020	3247	245 ^c	89

^a 0–14 years, 3; 15–24 years, 6; 25–34 years, 8

^b 0–54 years, 10

^c Standardized rate

^d 0–44, 10 years

^e <30 years

^f 75–79 years

^g >80 years

^h 25–34 years

ⁱ 0–14 years, 0; 15–24 years, 2; 25–34 years, 5

^j 15–44 years, 12

^k 0–54 years, 9

NG, not given

Discussion

The incidence of stroke in the population of Vittoria was comparable to other industrialized countries [10–21] but for the younger age classes the rate was lower and for the older age classes it was higher than others, including the Italian studies [3–7]. One possible explanation, particularly for the younger individuals, is a chance finding reflecting the small sample size. The wide 95% confidence intervals are in accordance with this assumption. In fact, hospital-based stroke registries are biased toward younger patients with more severe strokes. A second possible interpretation is overdiagnosis of stroke by the caring physician in the elderly, and not disproved by the reviewing investigator.

Although the information in the medical records was considered adequate to make a clinical diagnosis of stroke in all eligible cases, and cerebral infarction or hemorrhage was

documented by CT in 56% of the entire sample, it was impossible to verify the diagnosis in all patients. Among 821 patients admitted to an acute stroke unit, the initial diagnosis of stroke proved incorrect in 108 (13%); the diagnostic accuracy varied with clinical skill and ranged from 38% to 89% [22]. Diagnostic accuracy would have not been expected to improve by increasing the number of cases undergoing CT. Norris and Hachinski [22] also showed that the frequency of incorrect diagnoses was similar in patients investigated with or without CT.

As our study was hospital-based, under-ascertainment of stroke patients who were not hospitalized should be considered. The community studies conducted in Belluno and in L'Aquila, Italy [5, 6], which screened several sources of cases, found that 7% of patients were traced outside the hospital, i.e. treated at home (6%) or deceased before admission (1%). Similarly, 8% of first-ever strokes in Umbria were never admitted to hospital during the acute phase [3]. In

Aosta, up to 18% of patients were cared for at home [4]. The percentage of patients with stroke not admitted to the hospital varies across countries (from 5% to 40% of incident cases) [23]. These may include several older individuals with less severe strokes. Although a post-hoc interview of a sample of general practitioners failed to detect non-hospitalized cases and no additional patients were found in the local neurologist's outpatient files, a proportion of stroke patients similar to that of other studies may have escaped hospital admission. By contrast, loss of stroke patients possibly admitted to other hospitals is unlikely because there are no hospitals with neurology departments within a 100 km radius and the residents of the city of Vittoria are invariably referred to the local hospital for any acute or subacute clinical condition.

Seventy patients were traced with a diagnosis of stroke in their death certificate during the index year 1991. However, the presence of stroke as cause of death in these cases could not be verified. In addition, in many of these cases stroke may have been diagnosed before the index year. The reliability of the diagnosis reported in death certificates has been repeatedly confirmed to be poor [24, 25]. In 35%–61% of cases from other Sicilian communities with a diagnosis of stroke in the death certificate, this diagnosis could not be confirmed at further investigation [7, 26]. Some of the cases found in the death certificates might have been also missed as having stroke while being treated in departments other than those screened. Had we not missed these patients, our incidence rate would have been even higher, particularly in older individuals who were most commonly represented in the death certificates.

Comparable incidence rates for stroke in the Mediterranean countries and in developing countries, where different genetic, dietary and social factors may play a role, are scanty. The incidence of stroke (including recurrent stroke) was reported to be 63 per 100 000 in Libya [27] and 26 per 100 000 in Nigeria [28]. Although case under-ascertainment in these countries may be even greater, differences in the ethnic background, age distribution and prevalence of the commonest risk factors may also be an explanation. A study using a similar case finding strategy, done in San Giovanni Rotondo, southern Italy, where the environmental, dietary and sociocultural factors are similar to those of our population, provided an age-standardized incidence rate of 210 per 100 000 [29].

Where comparable, the distribution of the principal risk factors in our stroke population was fairly similar to that of other Italian samples [4, 5] and to that expected in many industrialized countries [30]. These findings suggest that, except for age, most risk factors for stroke do not explain the higher incidence of stroke in our very elderly population. However, major differences in incidence rates across studies may reflect dissimilarities in the age structure of the populations [5, 16, 27].

The higher incidence of stroke reported here in men is at variance with the pooled rates from several other studies [6, 15–17, 19]. Although chance is a likely explanation, given the small sample size, this finding may also reflect the different genetic background and the higher prevalence of selected risk factors in men [30].

Patients with subarachnoid hemorrhage were excluded in this study. Exclusion of subarachnoid hemorrhage hampers comparison with several epidemiological studies. However, given the low incidence of subarachnoid hemorrhage in the general population [31], our rates are not likely to be grossly underestimated.

The 30-day case-fatality ratio in our study (28% in the whole sample and 38% for first-ever stroke) was higher than in some Italian reports and other countries (12%–26%) [6, 10, 12, 32] but comparable to some other Italian studies (31%–33%) [4, 5]. Again, chance is the most likely explanation of the differences, given the small sample. Alternative interpretations are selection bias (patients with less severe disease varieties might not have been hospitalized) and less-than-optimal quality of care for stroke in the study area. Changes in the acute treatment of stroke and a better control of vascular risk factors might have an important role in explaining the low fatality rates reported in some countries. In the present study stroke patients were admitted in departments of general medicine as neurology or stroke units were not available. Compared to general wards, treatment of patients in stroke units has been followed by fewer deaths from complications of stroke and reduced need for institutional care in the community and in selected stroke populations [33–35].

Sommario Lo studio si pone l'obiettivo di fornire il tasso di incidenza per stroke in un'area ben definita della Sicilia. Si tratta di uno studio retrospettivo riferito alla popolazione residente nella città di Vittoria (58 833 abitanti) nell'anno 1991. I residenti di Vittoria con problemi neurologici acuti confluiscono generalmente in due nosocomi (Vittoria e Comiso). Due neurologi consulenti nei suddetti ospedali selezionarono i casi di stroke registrati durante l'anno 1991 mediante la consultazione di varie fonti (cartelle cliniche dei reparti di medicina interna e di terapia intensiva, archivi dei medici di base, certificati di morte). Gli stroke ed i relativi sottotipi furono definiti in base a criteri standard e classificati in eventi primari e recidive. L'ipertensione arteriosa, il diabete mellito e i problemi cardiologici, i fattori di rischio più frequenti, furono identificati attraverso l'anamnesi, gli esami di laboratorio e gli accertamenti strumentali. Durante il periodo in studio furono individuati 120 pazienti (61 M, 59 F) di età compresa fra i 34 e 94 anni (età media, 72 anni); di questi 89 (48 M, 41 F) presentavano un evento primario e 31 una recidiva. Il tasso annuale di incidenza per gli eventi primari fu di 165,3/100 000 e per la totalità

dei casi 222,9/100 000. Il tasso standardizzato fu rispettivamente di 245,3 (primo stroke) e 321,9 (tutti i casi). Tra i pazienti con primo stroke il 72% ebbe un infarto ischemico cerebrale. I fattori di rischio avevano una distribuzione simile fra gli stroke primari e le recidive. La mortalità, analizzata come case-fatality ratio a 30 giorni, fu del 28% per tutti i casi e del 38% per i soli eventi primari. Rispetto ai dati della letteratura, l'incidenza di stroke a Vittoria nel 1991 è risultata inferiore nella popolazione più giovane e più elevata nella popolazione più anziana. Per quanto le differenze possano essere giustificate dagli errori diagnostici e dai piccoli numeri, il ruolo di fattori dietetici, sociali e generici va considerato per studi futuri.

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