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Background and Purpose—There are no community-based studies on the incidence of transient ischemic attacks (TIAs) in Portugal. This study was designed to determine TIA incidence and the risk of stroke occurrence in rural and urban populations in northern Portugal.

Methods—All suspected first-ever TIAs occurring between October 1998 and September 2000 in 18 677 residents in a rural municipality and 86 023 living in the city of Porto were entered into a population-based registry. Standard definitions and comprehensive sources of information were used for identification of patients who were followed up at 3 and 12 months after the TIA.

Results—During a 24-month period, 141 patients with a first-ever TIA were registered, 36 in rural and 104 in urban areas. The vascular territory was carotid in 66.7% of the patients, vertebrobasilar in 29.1%, and undetermined in 4.3%. The overall crude annual incidence rate per 1000 was 0.67 (95% CI, 0.45 to 1.04), 0.61 (95% CI, 0.38 to 1.01) for rural, and 0.96 (95% CI, 0.43 to 2.33) for urban populations. The risk of stroke within the first 7 days of the index event was 12.8% (95% CI, 7.3 to 18.3), reaching 21.4% (95% CI, 14.6 to 28.1) at 1 year. Three factors were associated with stroke occurrence within 120 days after TIA: patients' age ≥65 years and an episode in the carotid distribution lasting ≥3 hours.

Conclusions—The incidence of TIA in northern Portugal, particularly in rural populations, ranks among the highest reported in community-based studies, following closely the stroke incidence trend (ACINrpc). Early recognition of TIA by patients and physicians is crucial for effective stroke prevention. **(*Stroke*. 2006;37:50-55.)**

Key Words: epidemiology ■ incidence ■ prognosis ■ transient ischemic attack

Despite the increasing number of scientific reports depicting a significant short-term risk of stroke in patients with a transient ischemic attack (TIA),[1,2] community-based studies of the incidence of TIA are scarce in general and nonexistent in Portugal. Previous results of a community prospective study in urban and rural populations from northern Portugal[3] have shown a high incidence of stroke, particularly in rural areas. Effective stroke prevention must be based on adequate knowledge of the extension of disease in the community and subsequent study of patients at a higher risk.[4] Therefore, this study was designed to assess TIA incidence and short-term prognosis in these populations to understand regional variations on stroke incidence and help delineating strategies for its prevention.

Subjects and Methods

The project Neurological Attacks prospective community register (ACINrpc), is a 2-year community-based study (1998 to 2000) planned to assess the incidence and prognosis of first-ever-in-a-lifetime stroke and transient focal neurological symptoms and signs resulting from a dysfunction of the central nervous system (TFNS) in northern Portugal.

Within the Portuguese National Health Service, free medical care is provided through a network of health centers (HCs) and hospitals, where citizens are registered and assigned a unique identification number. The study population[3] thus comprised all persons registered on September 30, 1999 (midstudy period), at 3 HCs in the city of Porto, covering 10 of the 15 parishes within the city, and at 2 HCs from the rural municipalities of Vila Pouca de Aguiar (VPAguiar) and Mirandela.

For the registration of patients, a "hot pursuit" of cases was established using direct information from routine appointments of general practitioners (GPs; 100) and emergency at VPAguiar HC, emergency and admission medical services provided by the 3 hospitals covering the study population, and visits to nursing homes in the study area. Furthermore, a "cold pursuit" allowed identification of patients through daily checking of emergency admission lists and review of inpatient discharge records, death certificates, and lists of imaging services. Private practice neurologists were contacted to obtain information on patients under their care. The study was

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conducted under approval of Hospital Geral de Santo António ethics committee, and all registered patients, or the next of kin when appropriate, gave informed consent.

A study neurologist examined all suspected patients and a computed tomography (CT) scan was performed soon after the event. The hospital or GP records were reviewed to check details on any previous stroke or TIA events and risk factors. The principal investigator reviewed the information collected for each patient for establishing a definite diagnosis, avoiding possible differential bias. Study neurologists examined all patients at 3 and 12 months after the index event for nonfatal events and for assessment of handicap and disability.

TIA was defined as a clinical syndrome characterized by acute loss of focal cerebral or monocular (amaurosis fugax) function lasting <24 hours and thought to be attributable to inadequate cerebral or ocular blood supply as a result of arterial thrombosis or embolism associated with arterial, cardiac, or hematological disease.[5] We classified attacks of unilateral motor or sensory symptoms, dysphasia, or transient monocular blindness as carotid-distributed TIAs. Attacks of vertigo, diplopia, bilateral motor or sensory symptoms, loss of vision in 1 homonymous field (in isolation) or in both homonymous fields, loss of balance (unsteadiness/ataxia), dysphagia, and dysarthria as vertebrobasilar-distributed TIAs. Vertigo, dysphagia, dysarthria, and diplopia were not considered TIAs if they occurred in isolation. Only first-ever-in-a-lifetime TIAs occurring within the study period were included. All patients who had a stroke before the index event were excluded.

To improve reliability of TIA diagnosis,[6] all GPs and neurologists involved in the study attended workshops to discuss clinical features and diagnosis criteria adopted. To avoid loss or undertreatment of stroke and TIA patients by diagnosis difficulties, GPs were encouraged to report any patient presumed to have experienced a stroke or TFNS.

Incidence is reported as crude rates and age-standardized rates to the Portuguese[7] and standard European populations.[8] The 95% CIs for incidence were calculated using the Poisson distribution. The Kaplan–Meier product limit method was used to estimate cumulative survival free of stroke occurrence after the index event. For comparison of survival curves, the log-rank test was used, and for controlling of possible confounding factors, the Mantel–Haenszel χ^2 test was used.

Results

After the 3-month pilot study, it became evident an under-reporting of TFNS cases by Mirandela GPs (21 of 18 412) compared with VPAguiar (199 of 18 677), which led us to restrict the study population to Porto and VPAguiar, keeping the Mirandela GPs blinded to this decision to avoid possible under-reporting of stroke patients. Thus, the population comprised all individuals registered at the 4 HCs on September 30, 1999, 86 023 in the city of Porto (male/female 0.76), and 18 677 in the rural municipality of VPAguiar (male/female 0.96). The proportion of those ≥65 years of age was 20.7% in urban and 19.6% in rural populations. The resident population based on the 2001 census was 95 506 in Porto (male/female 0.82), with a proportion of those ≥65 years of age of 20.4%; in VPAguiar, it was 14 998 (male/female 0.96), with 20.7% aged ≥65 years.

During the registration period, 1229 patients were enrolled for a suspected TFNS. After clinical assessment, 130 patients from this group (25 of them formerly not recognized as TIAs) and 11 from the 802 reported as having had stroke were diagnosed with a first-ever-in-a-lifetime TIA. A total of 141 patients were included, 4 of them identified retrospectively after occurrence of a stroke shortly afterward. Overall, 80.1% of the patients were identified by "hot pursuit" (Table 1); the emergency services at VPAguiar (83.3%) and Porto (62.9%) were the most common sources. The patient's average age was 69.9 years, and 56.7% were females. The time interval between onset of TIA symptoms and neurological examination was <48 hours for 48.2% of the cases and 61.7% were observed within 7 days after the TIA. A brain CT scan was performed in 85.8% of the patients, and in 62.8% of them, within the first 48 hours after onset of symptoms. Based on the definition adopted, 66.7% of the attacks were in the carotid and 29.1% in the vertebrobasilar territories. More than

TABLE 1. Assessment of Patients Included in Rural and Urban Areas

	Rural		Urban	
	n=36	%	n=105	%
Source of information				
"Hot pursuit"	33	91.7	80	76.2
Emergency service				
Hospital	2	5.6	66	62.9
HC	30	83.3	0	...
HC/hospital clinic	1	2.8	11	10.5
Domiciliary/nursing home visit	0	...	3	2.9
"Cold pursuit"	3	8.3	25	23.8
Emergency service	3	8.3	21	20.0
Others	0	...	4	3.8
Patient characteristics				
Women	21	58.3	59	56.2
Mean age, y (SD)				
All	70.6	(10.1)	69.7	(11.9)
Men	72.3	(6.8)	67.8	(11.9)
Women	69.3	(11.9)	71.2	(11.9)
Delay between onset and assessment				
0–24 h	19	52.8	33	31.4
25–48 h	5	13.9	11	10.5
3–7 d	3	8.3	16	15.2
>7 d	9	25.0	45	42.9
CT scanning	31	86.1	90	85.7
Delay between onset and CT				
0–24 h	13	41.9	49	55.1
25–48 h	4	12.9	10	11.2
3–7 d	3	9.7	8	9.0
>7 d	11	35.5	22	24.4
Vascular territory distribution				
Carotid	24	66.7	70	66.7
Amaurosis fugax	0	...	2	1.9
Vertebrobasilar	10	27.8	31	29.5
Undetermined	2	5.6	4	3.8
Time to resolution of deficit (min)				
<30	14	38.9	42	40.0
30–59	7	19.4	13	12.4
60–179	5	13.9	25	23.8
180–359	2	5.6	8	7.6
≥360	8	22.2	17	16.2

TABLE 2. Age–Sex-Specific Annual Incidence per 1000 Population for TIA in Rural and Urban Areas, Northern Portugal (1999 to 2000)

	Rural			Urban			Both		
Sex/Age	n/n at risk	Rate	95% CI	n/n at risk	Rate	95% CI	n/n at risk	Rate	95% CI
Men									
0–44	0/5661	0.00	...	0/21 454	0.00	...	0/27 115	0.00	...
45–54	0/1022	0.00	...	6/5168	0.58	0.21–1.26	6/6190	0.48	0.18–1.05
55–64	2/905	1.10	0.06–3.99	12/4202	1.43	0.74–2.49	14/5107	1.37	0.75–2.30
65–74	7/977	3.58	1.44–7.38	13/3916	1.66	0.88–2.84	20/4893	2.04	1.25–3.16
75–84	5/496	5.04	1.63–11.76	12/1991	3.01	1.56–5.26	17/2487	3.42	1.99–5.47
≥85	1/122	4.10	0.12–22.83	3/519	2.89	0.60–8.45	4/641	3.12	0.85–7.99
Total	15/9183	0.82	0.25–3.12	46/37 250	0.62	0.30–1.35	61/46 433	0.66	0.36–1.20
ASRP								0.50	0.45–0.55
ASRE		0.56	0.38–0.89		0.47	0.29–0.80		0.50	0.31–0.84
Women									
0–44	0/5382	0.00	...	1/25 302	0.02	0.00–0.11	1/30 684	0.02	0.00–0.11
45–54	4/1023	1.96	0.53–5.00	6/6582	0.46	0.17–0.99	10/7605	0.66	0.32–1.21
55–64	3/1024	1.46	0.30–4.28	6/5590	0.54	0.20–1.17	9/6614	0.68	0.31–1.29
65–74	5/1097	2.28	0.74–5.32	18/5856	1.54	0.91–2.43	23/6953	1.65	1.05–2.48
75–84	8/716	5.59	2.41–11.01	23/3915	2.94	1.86–4.41	31/4631	3.35	2.27–4.75
≥85	1/252	1.98	0.06–11.05	5/1528	1.64	0.53–3.82	6/1780	1.69	0.62–3.67
Total	21/9494	1.11	0.36–3.52	59/48 773	0.60	0.32–1.20	80/58 267	0.69	0.40–1.23
ASRP								0.50	0.47–0.53
ASRE		0.79	0.55–1.17		0.35	0.19–0.63		0.41	0.24–0.70
All									
0–44	0/11 043	0.00	...	1/46 756	0.01	0.00–0.06	1/57 799	0.01	0.00–0.05
45–54	4/2045	0.98	0.27–2.50	12/11 750	0.51	0.26–0.89	16/13 795	0.58	0.33–0.94
55–64	5/1929	1.30	0.42–3.02	18/9792	0.92	0.54–1.45	23/11 721	0.96	0.62–1.47
65–74	12/2074	2.69	1.49–5.05	31/9772	1.59	1.08–2.25	43/11 846	1.81	1.31–2.44
75–84	13/1212	5.36	2.85–9.17	35/5906	2.96	2.06–4.12	48/7118	3.37	2.49–4.47
≥85	2/374	2.67	0.32–9.65	8/2047	1.95	0.84–3.85	10/2421	2.07	0.99–3.80
Total	36/18 677	0.96	0.43–2.33	105/86 023	0.61	0.38–1.01	141/104 700	0.67	0.45–1.04
ASRP								0.49	0.47–0.51
ASRE		0.67	0.45–1.04		0.40	0.23–0.69		0.44	0.26–0.73

ASRP indicates age-standardized rate, northern Portuguese population, 1999; ASRE, age-standardized rate, European population.

half of TIA symptoms resolved within 1 hour (53.9%) and 17.7% remained for ≥6 hours.

The crude overall annual incidence of TIA per 1000 population was 0.67 (95% CI, 0.45 to 1.04), slightly higher in the rural at 0.96 (95% CI, 0.43 to 2.33) than in the urban area at 0.61 (95% CI, 0.38 to 1.01; Table 2). The largest difference in TIA incidence between the rural and urban areas was observed for those 75 to 84 years of age. The incidence rate for rural and urban areas standardized to the European standard population was 0.67 of 1000 (95% CI, 0.45 to 1.04) and 0.40 of 1000 (95% CI, 0.23 to 0.69), respectively.

As shown in Table 3, the risk of stroke during the 1-year

TABLE 3. Kaplan–Meier Estimates of Risk of Stroke Occurrence Within Defined Time Periods After TIA in Rural and Urban Areas, Northern Portugal (1999 to 2000)

Time	Urban			Rural			Both		
Period, d	No.	Risk, %	95% CI	No.	Risk, %	95% CI	No.	Risk, %	95% CI
2	10	9.5	3.9–15.1	4	11.1	8.4–21.4	14	9.9	5.0–14.8
7	11	10.5	4.6–16.3	7	19.4	6.5–32.4	18	12.8	7.3–18.3
30	15	14.3	7.6–21.0	10	27.8	13.1–42.4	25	17.7	11.4–24.0
120	19	18.2	10.8–25.5	10	27.8	13.1–42.4	29	20.6	13.9–27.3
300	20	19.2	11.6–26.8	10	27.8	13.1–42.4	30	21.4	14.6–28.1

follow-up was 21.4% (95% CI, 14.6 to 28.1). The occurrence of stroke is higher in the first days, a 2-day risk of 9.9% (95% CI, 5.0 to 14.8) and a 7-day risk of 12.8% (95% CI, 7.3 to 18.3), reaching 17.7% (95% CI, 11.4 to 24.0) at 30 days (Table 3). The highest difference in stroke risk between urban and rural areas was reached by the end of the first month, at 14.3% (95% CI, 7.6 to 21.0) versus 27.8% (95% CI, 13.1 to 42.4). Sixteen patients died, a death risk of 11.4% (95% CI, 6.9 to 18.2); in half of them, death occurred after the stroke and was a consequence of it in 5 of them (3.5%).

The risk of stroke in the first 4 months after TIA by patient's age, vascular territory, and time to resolution of TIA deficit is shown in Figure 1. Patients ≥65 years of age have the highest risk of stroke (χ^2=5.8; df=1; P<0.02). After adjustment for age, patients with a carotid-distributed TIA were at higher risk than the remainder (χ^2=5.4; df=1; P<0.02) as well as those for which the TIA lasted for ≥3 hours (χ^2=3.9; df=1; P<0.05). Residential area and gender were not risk factors for stroke (χ^2=1.6; df=1; P>0.1 and χ^2=0.1; df=1; P>0.8, respectively). A score based on the 3 risk factors identified was calculated (1 for ≥65 years of age, 1 for carotid territory, 1 for time of resolution of ≥3 hours, and 0 for the other categories). As shown in Figure 2, there was an increase in the risk of stroke occurrence with the number of risk factors present (χ^2=16.6; df=3; P<0.001).

Discussion

The ACINrpc-project is the first community-based TIA incidence study in Portugal and the only one comparing rural and urban populations. The study design fulfilled the standard recommended criteria for community-based studies,[9] a large representative population of which structure is known, a comprehensive method for ascertainment of cases, and an early detailed neurological assessment, including CT scan examination.

Considering the study population involved, the list of individuals registered at the HCs is a reliable source for calculation of population denominators, although not equivalent to the Census numbers because it may also include those who work in the neighboring villages and those who keep attendance while emigrated temporarily outside the country. This may explain the differences observed between the population registered at the study HCs and the resident population in the same administrative divisions in the 2001 Census. Nonetheless, all patients were contacted and re-evaluated throughout the follow-up period, indicating a fairly stable population with an age–sex structure similar to that of the Census.

Because the study scope was comprehensive and liberal criteria were used for the ascertainment of cases, the number reported was high, but we preferred not to risk losing patients by misdiagnosis/underreporting of TIAs. Moreover, given the diagnosis difficulty of TIA and frequent disagreement between doctors[10] and experienced neurologists,[6] the information network established was crucial, allowing neurologists to readily examine patients. The principal investigator monitored the identification process in Porto and VPAguiar, visiting the HCs every fortnight and more often if necessary. In Mirandela, by lack of human resources, this procedure

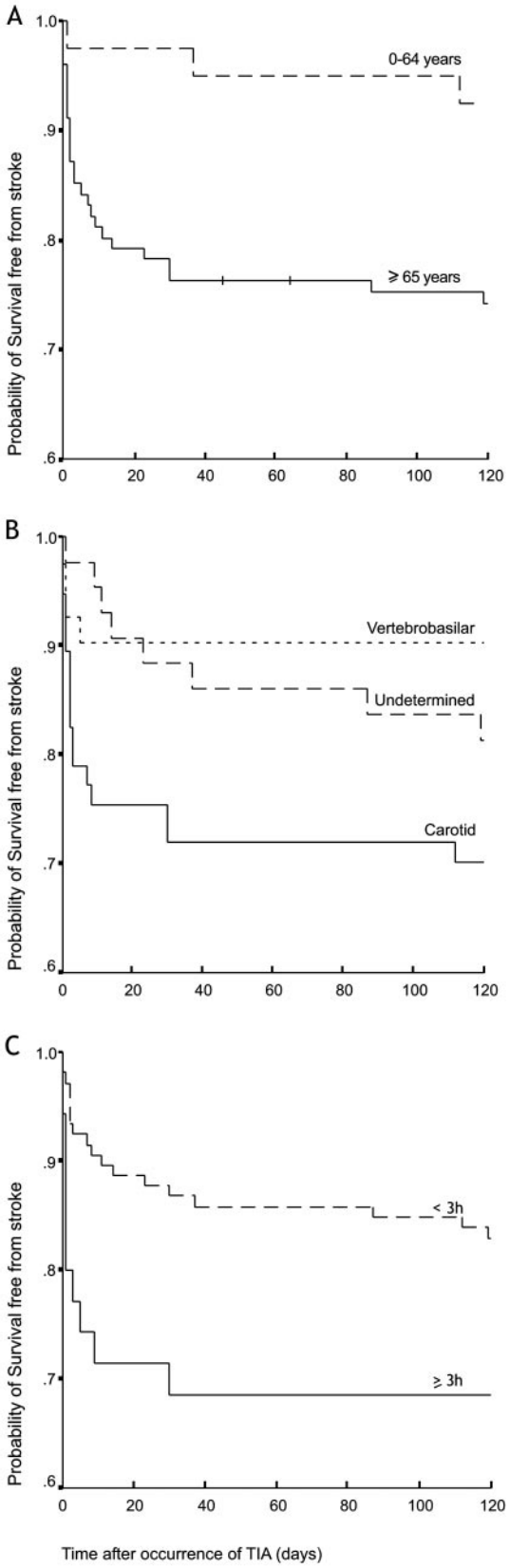

Figure 1. Kaplan–Meier survival curve showing the probability of a patient with a TIA will remain free of stroke occurrence stratified by Age (A), vascular territory (B), and time to resolution of TIA deficit (C).

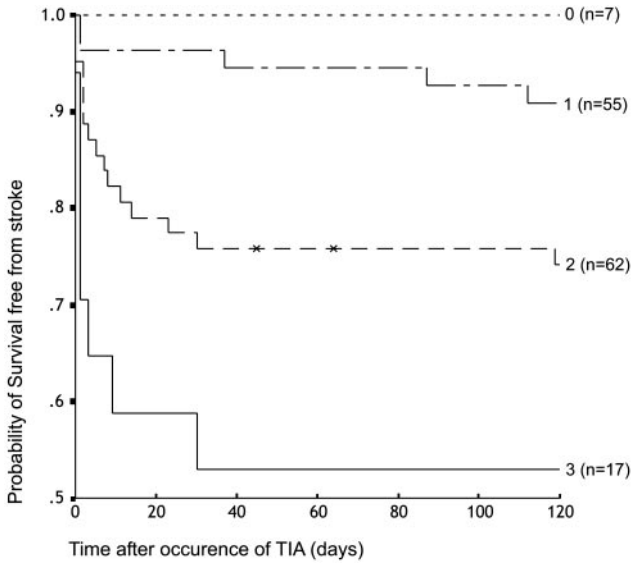

Figure 2. Kaplan–Meier survival curve showing the probability of a patient with a TIA will remain free of stroke occurrence, stratified by number of risk factors (0 to 3).

could not be adopted, possibly contributing to the underreporting by local GPs, and its subsequent exclusion from the study.

For most of the patients enrolled, the emergency services were the main source of information identifying 69.5% of the patients. The frequency of CT scan was 85.7% higher than in the studies of Umbria[11] (61.7%) and Belluno[12] (56%) and lower than in Dijon[13] (97%) and Segovia[14] (100%).

The crude annual incidence rate per 1000 for the first TIA in northern Portugal is 0.67 (0.61 in the urban compared with 0.96 in the rural area), this being the highest reported in community-based studies, even when standardized to the European population (Table 4). In Porto, the incidence almost doubles that reported in Segovia,[14] a study following the same definition criteria than ours. In the remaining studies, symptoms such as dysphagia and dysarthria appearing in isolation were also considered, which might explain their higher incidence rates. But even using a more restrictive criteria, the incidence in VPAguiar is higher than in Rochester,[16] the highest ever reported. The pattern of variation with age is similar to that reported in these studies; an increasing trend until 84 years of age followed by a slight decrease afterward.

The proportion of carotid-distribution TIAs (66.7%) is the lowest described; other studies reported values ranging from 72% in Belluno[12] to 80% in Oxfordshire.[15] The different vascular distribution found in our study may result from the proportion of amaurosis fugax (1.4%), a clear carotid-distributed TIA, much lower than Oxford[15] (17%) and Rochester[16] (18.3%) and close to Segovia[14] (1%). The most common symptoms occurring in our carotid-distributed TIAs were contralateral weakness or sensory disturbance, which, in the absence of cortical dysfunction (as observed in this study), may be attributed to small-vessel disease. This may suggest that small-vessel disease could be a relevant etiologic mechanism of TIA in Portugal. Alternatively, the lower frequency of Amourosis Fugax may be attributable to a higher proportion of cardioembolic TIAs in our group than in other studies.[17] Studying the etiology of TIAs and the subtypes of cerebral infarcts registered in the ACIN-project could help understand these differences.

The risk of stroke was higher in the very first days after TIA, 9.9% at 2 days, 12.8% at 7 days, and 17.7% within 30 days, exceeding the values reported in the recent reanalysis of the Oxfordshire study,[18] 8.6% risk of stroke at 7 days, and 12.0% at 12 months, as well as those of the Oxford Vascular Study (OXVASC),[1] Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS),[19] and Ontario[2] studies. The 12-month risk of death after a first TIA was 11.4%, higher than reported in Alberta,[20] and 3.5% of the patients died after occurrence of the first stroke after the TIA. Three risk factors for stroke occurrence within 120 days after TIA were patients age ≥65 years of age, carotid vascular territory and duration of symptoms of ≥3 hours, 2 of them mentioned in previous studies.[4,20] Based on a recent review,[21] in community-based studies, one might expect higher odds of stroke in carotid-distributed versus vertebrobasilar TIAs and an opposite trend in hospital-based studies. Although community based, this study does not confirm such trend, mainly because it shares

TABLE 4. Annual Age-Specific Incidence of TIA per 1000 Population; Studies Are Ordered by Increasing Incidence

		Age, y						
Study	Study Period	0–44	45–54	55–64	65–74	75–84	≥85	ASRE
Dijon[13]	1990–1994	0.001	0.013	0.054	0.122	0.248	0.280	0.027
Segovia[14]	1992–1994	0.03§		0.48	1.07	1.68	1.35	0.21
Novosibirsk[22]	1996–1997	0.01	0.56†		1.34	1.85‡		0.31
Porto	1998–2000	0.01	0.51	0.92	1.59	2.96	1.95	0.40
Umbria[11]	1986–1989	0.09§		1.03	1.8	2.69	2.62	0.42
OCSP[15]	1981–1986	0.01	0.25	0.92	1.61	2.57	2.32	0.54
Belluno[12]	1992–1993	0.03§		1.06	2.24	6.39	10.06	0.58
Rochester[16]	1985–1989	0.03	0.56	1.11	2.96	5.84	4.74	0.65
VPAguiar	1998–2000	0.00	0.98	1.30	2.69	5.36	2.67	0.67

§Age group 0–54 years; †age group 45–64 years; ‡age group ≥75 years.
ASRE indicates age-standardized rate, European population.

some features of hospital-based studies such as confirmation of diagnosis by neurologists and definition criteria. The combined effect of the identified risk factors in most patients may explain in part the high risk of stroke occurrence after the first TIA because patients with ≥2 of them had a higher risk. The case mix of urban and rural patients, although residence was not a risk factor, may be worsening the overall short-term prognosis of these patients compared with other studies.[1,2,18,19] Overall, our more stringent definition criteria and diagnosis confirmation methods might be decreasing the overall incidence of TIA and worsening its short-term prognosis. On the other hand, isolated dysphagia and dysarthria,[15,16] if included, would be classified as undetermined territory TIAs, a group with milder prognosis, thus increasing the risk difference between carotid-distributed and the remaining TIAs. Although the reported incidence of TIA in northern Portugal is in accordance with the previously observed incidence of stroke,[3] following an identical age trend and with mounting evidence toward populations living in rural areas being at higher risk, the high incidence of a first stroke in rural areas may in part have its origin in the occurrence of a first TIA, proving that TIA is not a benign condition, carrying with it a high early risk of stroke and death.

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