Incidence Trends of Ischemic Stroke and Transient Ischemic Attacks in a Well-Defined French Population From 1985 Through 1994

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Background and Purpose—The changing incidence of ischemic stroke is of major concern in view of its public health impact, to define the population concerned, to identify risk factors, and to set up health-care systems. The aim of this study was to evaluate the time trends associated with the incidence of all the subtypes of ischemic stroke and transient ischemic attacks in a well-defined population for 10 years.

Methods—Since 1985, a population registry has recorded each patient living in Dijon (France) who suffered from a cerebrovascular disease (CVD) regardless of the type of management. This study involved all patients suffering from their first ischemic stroke and their first transient ischemic attacks (TIAs) during 1 calendar year between January 1, 1985 and December 31, 1994. The incidence changes according to age, sex, and type of cerebral ischemic event (cortico-subcortical infarct, lacunar infarct, and TIA) were studied on the basis of their annual variations.

Results—During the 10-year study period, 834 cortico-subcortical infarcts (52.1%), 296 lacunar infarcts (18.5%), 369 TIAs (23.1%), and 101 undetermined ischemic strokes (6.3%) were collected. The incidence of all ischemic events was relatively stable in both sexes over the 10-year period. However, the incidence rates differed according to age and type of ischemia. An increased incidence of cerebral cortico-subcortical infarct was observed in patients older than 75 years of age (+5.45% annual change [AC] in men, P<0.05; +5.09% AC in women, NS). In parallel, a higher proportion of emboligenic cardiac arrhythmias was observed in these patients (P<0.001). The incidence of lacunar infarcts tended to decrease, regardless of age but mainly in men under younger than 75 years of age (~12.74% AC in men, NS; +0.31% AC in women, NS). The incidence of TIAs was relatively stable in both sexes. Because our population consisted of a large number of elderly subjects, the increase in cardioembolic causes could partially explain the increased incidence of cerebral cortico-subcortical infarcts in patients older than 75 years of age.

Conclusions—These preliminary data emphasize the importance of stroke surveillance in considering the variations of the different mechanisms of ischemic cerebrovascular disease. Although the incidence of TIA is stable and the incidence of lacunes tends to decrease in men, mainly before 75 years of age, we emphasize the rise of the crude incidence of cortico-subcortical infarcts in men older than 75 years of age, induced by an increase in cardioembolic causes. (Stroke. 1999;30:371-377.)

Key-words: cerebral infarction • cerebral ischemia, transient • lacunar infarction • incidence

Epidemiological studies are essential in order to assess the extent of cerebrovascular disease (CVD), its natural course, major differences between countries, etiological and prognostic factors, and for planning therapeutic trials.1 The marked heterogeneity of CVD accounts for the various causes, various treatments, and diverse prognoses encountered in this disease. Analysis of incidence rates and their trends not only allows assessment of future needs but also provides data concerning changes in the various mechanisms responsible for CVD and possibly the influence of treatment on certain risk factors. These facts emphasize the importance of a stroke survey in monitoring the success of public health measures. Various hospital2,3 and well-defined population registries4–6 have been set up in several countries to evaluate these data, but secular trends are not homogeneous. It remains to be ascertained whether stroke incidence decreases in European countries.

With data from our population-based registry, in the present study we tried to assess changes in the incidence of ischemic CVD, according to their type, over a 10-year period in an urban French population (Dijon) to identify variations in
incidence and the role of cardioembolic disease, sex, and age in these observed variations.

Subjects and Methods

Stroke Registry and CVD Diagnostic Criteria

The Dijon Stroke Registry has recorded all first-ever strokes and first-ever transient ischemic attacks (TIAs) occurring since 1985 in the city of Dijon, with a population of 148,277 inhabitants in 1990. This registry is based on clinical data and CT findings, which confirmed the CVD and its mechanism. The collaboration of numerous investigators was required, from various departments of the University Hospital, 4 private hospitals, 3 private radiological centers, specialists (ie, neurologists, angiologists, neuroradiologists, and cardiologists), general practitioners, and town hall administrative authorities to consult death certificates. All information collected by the various correspondents was centralized in the Stroke Registry. To avoid duplicate entries, a file of patient names in alphabetical order was created and they were coded to allow anonymous data processing. All information concerning data collection and analysis has been previously published. Uniform criteria for diagnosis of CVD were used for the duration of the study. CVD was defined according to WHO recommendations, as sudden onset of a resolving neurological deficit lasting more than 24 hours, affecting motor, sensory, sensorial and speech functions, the brain, and cerebellum, and assumed to be of vascular origin, and in particular from an arterial origin in our registry. This very broad definition implies that all CVDs consist of a lesion (or at least a cerebral tissue dysfunction) responsible for a neurological deficit, associated with an underlying vascular lesion, which is the immediate cause of the stroke. It does not prejudge the hemorrhagic or ischemic nature of the lesion.

Imaging techniques combined with the WHO clinical criteria constitute an essential tool in the classification of CVD, allowing elimination of false-positives (eg, cerebral tumor, subdural hematoma, demyelinating plaques).

The diagnosis of cerebral infarction was confirmed by a normal first CT scan or the presence of low-density images confined to a vascular territory, evolving over several successive examinations. Since 1990, when the CT scan was unable to identify the mechanism, MRI was performed. The diagnosis of lacunar infarct was based on the presence of a clinical syndrome such as pure hemiplegia, pure hemianesthesia, clumsy-hand syndrome, or ataxic hemiplegia identified by a public or private neurologist. In all the cases, a CT scan was performed to observe a lacune mainly within the basal ganglia but also anywhere within the subcortical area (disease of small perforating arteries giving rise to small, deep-seated infarcts, 0.5 to 15 mm in diameter). TIA was diagnosed when the clinical symptoms disappeared within 24 hours without sequelae associated with a normal CT scan, because the presence of an ischemic picture usually points to cerebral infarction.

Ischemic CVD included 1) thrombotic cortico-subcortical infarcts due to cerebral artery atherosclerosis as detected by ultrasound examination and including a sudden or subacute cortical deficit (ie, hemiplegia, hemianesthesia, aphasia), related to a territorial infarction on CT scan and associated with either blood hypertension, diabetes, hypercholesterolemia, or tobacco abuse; 2) cardioembolic CVD evoked by clinical features (eg, sudden onset, troubles of consciousness at onset, headache, Wernicke aphasia, hemianopia), by CT scan features (polar localization of infarction, hemorrhagic transformation, or spontaneous sylvian artery at onset), and confirmed by the presence of cardiac arrhythmia on the ECG, associated with either heart failure, valve disease, cardiac ischemia on ECG, intra-cardiac thrombus, or spontaneous contrast on transthoracic or transoesophageal echocardiography; and 3) lacunar infarcts.

Undetermined ischemic strokes were those managed without any CT scan (elderly patients at home, early death) or those with a cerebral infarction whose cause remained unidentified despite complete cerebrovascular and cardiovascular investigations. Venous infarction was not studied in our work.

This methodology, with clinical and imaging criteria, have been consistently adopted throughout the study period with centralized coding of stroke subtypes.

Data Processing and Statistical Methods

For calculation of the incidence rates, the National Institute of Statistics provided census data for 1982 and 1990 concerning the population in Dijon in 1-year age groups and by sex. For each of the 10 years of the study, the population was then estimated year by year from these 2 censuses by a simple diagonal interpolation from 1982 to 1990, then by extrapolation after 1990. The crude incidence rate, the specific rate per age group, and the standardized rate in terms of the world population were calculated per year, per sex, and per mechanism.

The changing trends given in this study are those based on the annual crude incidence rates for the Dijon population, to avoid a loss of precision for the oldest patients. Incidence trends were also studied in various age groups (less than 55 years of age, between 55 and 74 years of age, and older than 75 years of age) and according to the mechanism. Our model was , where is the incidence rate and is the time in years. This model assumes that the percentage of the mean annual change of the incidence rate is constant during the 10-year observation period. Regression coefficients were estimated by the least squares method from incidence rates observed for each year. This calculation also estimated the standard deviation of the exponential coefficient (b), allowing comparison of this coefficient with zero by a Student’s t test. This method was therefore used to calculate the percentage of the mean annual change of the incidence and the 95% CI of this change.

No analyses were made in advance to appreciate the magnitude of change over time, because our study is a retrospective one on descriptive data from a population-based study. Statistical analysis was performed on an Alpha Server 1000 to 4/200 (DIGITAL) with BMDP software.

Results

During the 10-year study period (January 1, 1985, through December 31, 1994), 1231 first-ever ischemic strokes (834 cortico-subcortical infarcts, [52.1%], 296 lacunar infarcts, [18.5%] and 369 first-ever TIAs [23.1%]) and 101 undetermined ischemic strokes [6.3%] were registered. CT scan rate was stable with a mean of 90.9% during the 10-year period and varied between 90% in 1985 and 97% in 1997.

World Standardized Incidence

The incidence of ischemic events (cortico-subcortical infarcts, lacunar infarcts, TIAs) in the Dijon population varied slightly between 1985 and 1994, regardless of sex. The world standardized incidence for ischemic events occurring in the Dijon population varied between 59.3/100,000 inhabitants and 83.5/100,000 inhabitants in men and between 26.5/100,000 inhabitants and 48.2/100,000 inhabitants in women (Table 1a and 1b).

For each type of ischemic event, we observed the following results: Over the 10-year period, the proportion of cortico-subcortical infarcts remained relatively stable in both sexes. The standardized incidence for cortico-subcortical infarcts varied between 26.1/100,000 inhabitants and 51.8/100,000 inhabitants in men and between 14.5/100,000 inhabitants and 29.6/100,000 inhabitants in women (Table 1a and 1b). The incidence of lacunar infarcts varied between 9.2/100,000 inhabitants and 37.9/100,000 inhabitants in men and between 3.6/100,000 inhabitants and 10.6/100,000 inhabitants in women, with some annual variations from 1 year to another (Table 1a and 1b).
The incidence of undetermined strokes was stable throughout the 10 years and did not influence the trends of other types (Table 1). The incidence of TIA varied between 8.4/100 000 inhabitants and 29.2/100 000 inhabitants in men and between 3.9/100 000 inhabitants and 18.8/100 000 inhabitants in women but with marked annual variations during the 10-year period (Table 1a and 1b).

### Crude Incidence

Crude incidence rates for ischemic events occurring in the Dijon population varied between 89.6/100 000 inhabitants and 125.7/100 000 inhabitants in men and between 69.4/100 000 inhabitants and 117.0/100 000 inhabitants in women. The annual change was +3.1% ($P<0.05$) in men and +4.1% ($P<0.05$) in women (Table 2). The annual change of the

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**TABLE 1. Incidence of Cerebrovascular Disease (CVD) by Mechanism Between 1985 and 1994 per 100 000 Inhabitants per Year**

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<td>(49.1–82.5)</td>
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<td>8.4</td>
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<td>41.9</td>
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| **Women**          |      |      |      |      |      |      |      |      |      |      |
| Ischemic CVD       | 38.3 | 27.5 | 37.9 | 33.3 | 26.5 | 48.2 | 43.5 | 35.3 | 29.1 | 40.0 |
| CI                | (26.0–50.6) | (19.9–35.1) | (27.3–48.5) | (23.1–43.5) | (18.3–34.7) | (35.9–60.5) | (31.9–55.1) | (25.9–44.7) | (21.1–37.1) | (29.4–50.6) |
| n                 | 53   | 71   | 74   | 66   | 66   | 74   | 86   | 86   | 74   | 90   |
| Cortico-subcortical infarct incidence* | 14.5 | 17.4 | 29.6 | 17.0 | 15.5 | 23.4 | 16.9 | 15.6 | 19.1 | 25.6 |
| CI                | (7.2–21.8) | (11.1–23.7) | (20.2–39.0) | (9.9–24.1) | (9.2–21.8) | (14.6–32.2) | (9.8–24.0) | (9.7–21.5) | (13.0–25.2) | (17.6–33.6) |
| n                 | 25   | 44   | 56   | 36   | 40   | 44   | 34   | 44   | 51   | 62   |
| Lacunar infarct incidence* | 10.5 | 4.6 | 3.6 | 10.1 | 5.8 | 10.4 | 7.8 | 5.5 | 5.0 | 10.6 |
| CI                | (3.6–17.4) | (1.5–7.7) | (0.1–7.1) | (4.2–16.0) | (1.9–9.7) | (4.9–15.9) | (2.7–12.9) | (0.8–10.2) | (0.9–9.1) | (4.5–16.7) |
| n                 | 11   | 11   | 7    | 17   | 15   | 19   | 13   | 9    | 12   | 20   |
| Transient ischemic attack incidence* | 13.2 | 5.5 | 4.5 | 6.3 | 5.2 | 14.4 | 18.8 | 14.2 | 5.0 | 3.9 |
| CI                | (5.9–20.5) | (2.6–8.4) | (1.4–7.6) | (2.0–10.6) | (1.7–8.7) | (7.5–21.3) | (11.4–26.2) | (8.3–20.1) | (1.5–8.5) | (0.6–7.2) |
| n                 | 17   | 16   | 11   | 13   | 11   | 21   | 39   | 33   | 11   | 8    |
| UI stroke incidence* | 4.0 | 3.9 | 4.2 | 3.4 | 6.8 | 4.7 | 8.8 | 8.1 | 7.0 | 3.4 |
| CI                | (1.3–6.7) | (1.4–6.4) | (1.5–6.9) | (0.7–6.1) | (2.5–11.1) | (1.0–8.4) | (4.1–13.5) | (3.4–12.8) | (2.7–11.3) | (0.7–6.1) |
| n                 | 11   | 11   | 12   | 6    | 10   | 8    | 12   | 13   | 11   | 7    |

n indicates number of subjects; UI, undetermined ischemic.

*World standardization.
incidence of ischemic CVD was influenced by age and essentially concerned the age groups older than 75 years of age in men (4.45%; 95% CI: 0.74; 8.25%, P<0.05) and in women (5.35%; 95% CI: 2.10; 11.11%, NS).

Crude incidence rates for cortico-subcortical infarcts occurring in the Dijon population varied between 50.5/100 000 inhabitants and 82.4/100 000 inhabitants in men and between 32.7/100 000 inhabitants and 80.6/100 000 inhabitants in women (Figure 1). The annual change was 3.73% (NS) in men and 4.14% (NS) in women (Table 2). This progression was mainly seen in men older than 75 years of age (5.54%; 95% CI: 1.10; 9.83%, P<0.05) and in women, (5.11%; 95% CI: 2.11 to 12.31%, NS; Table 2, Figure 2). Similar trends were observed in the 55- to 74-year age group but less marked than in subjects older than 75 years of age.

Crude incidence rates for lacunar infarcts occurring in the Dijon population varied between 18.0/100 000 inhabitants and 43.9/100 000 inhabitants in men and between 7.9/100 000 inhabitants and 26.0/100 000 inhabitants in women (Figure 1). The annual change was −3.04% (NS) in men and +4.5% (NS) in women (Table 2). We observed a nonsignificant reduction in the incidence of lacunar infarcts in men younger than 75 years of age (Figure 2). The annual change showed negative trends in men between 55 and 75 years old (−12.7%; 95% CI: −29.4% to +3.9%, NS) and in men older than 75 years of age (−4.4%; 95% CI: −14.3% to +5.5%, NS), even if nonsignificant (Table 2). The small number of men younger than 55 years of age prevented the accurate calculation of time trends.

Crude incidence rates for undetermined strokes had no changes (Figures 1 and 2).

Crude incidence rates for TIA occurring in the Dijon population varied between 11.8/100 000 inhabitants and 47.8/100 000 inhabitants in men and between 10.4/100 000 inhabitants and 50.2/100 000 inhabitants in women (Figure 1). The annual change was 5.94% (NS) in men and 2.01% (NS) in women (Table 2). Many fluctuations in incidence rates were noticed from 1 year to the next. So large confidence intervals were found in the age-group analysis, and no conclusions could be drawn.

To try and explain this increased incidence in cortico-subcortical infarcts in the elderly, we identified the group with cardioembolic strokes. Patients older than 75 years of age had significantly more cardioembolic strokes (34%) than younger patients (11%, P<0.001). The annual change of the proportion of subjects older than 75 years of age, with a
cardioembolic stroke increased by +6.6%, over the 10 years of the study (95% CI: −2.0% to +15.2%, NS) in men and by +4.8% (95% CI: −3.4% to +12.6%, NS) in women. On the other hand, we tried to identify factors that could influence the incidence rates of lacunar infarcts. Analysis of the age-related frequency of hypertension in our patients did not reveal any significant difference over the 10-year period between men and women with lacunar infarcts and between patients younger than 75 years of age (63%) and those older than 75 years of age (65%). The annual change of the proportion of stroke patients who had a history of hypertension remained relatively stable for patients younger than 75 years, with a variation of +0.44% (95% CI: −4.7% to +0.5%, NS).

Discussion

The Dijon population has one of the lowest incidences of ischemic CVD in the world.6 Nevertheless, the number of ischemic stroke reported increased slightly in our population over the period 1985 through 1994. Our case survey method remained constant for 10 years and was based on a collaboration of numerous medical participants who are regularly informed about this data collection. The use of cerebral CT scan since 1985 and the rate of undetermined ischemic strokes remained stable over the 10-year period, eliminating any bias in the ascertainment of the cases. The low rate of undetermined ischemic strokes (6.3%) was the consequence of a high rate of performed CT scans and complete investigations, performed in all patients.
and repeated if necessary, to identify the mechanism and the cause of the stroke. Problematic cases were discussed in a medical staff meeting.

The increasing use of MRI since 1990 could have confirmed more lacunar infarcts, but the diagnosis was always made from a clinical event. Data quality control was regularly performed by 1 of the members of our team. It may be possible that some patients with minor CVD, probably among the oldest age groups, never had medical attention, but these cases most likely represent a very small proportion in view of the efficacy of the health-care structures in Dijon, and they would have very little influence on our overall results. All of these precautions therefore resulted in the collection of exhaustive, specific and reliable data.

The changing trends observed therefore cannot be attributed to changes of data recording procedures, and the increased incidence of ischemic stroke appears to be a disease-specific event.

To determine whether our results differ from those of other countries, indicating the need to investigate medical causes, it is essential to compare data obtained by teams working in various parts of the world, and this can only be achieved by standardization. It is also important to observe the crude incidence of this disease in all age groups and mainly in the oldest age groups to ensure inclusion of the populations at highest risk of this disease, with the use of the age distribution of Segi’s truncated world population.

Incidence trends differ according to region. Fluctuations have been in relation to time period. From selected publications, according to World-standardized results based on a long study period, and to similar methodology, we can perform the following comparisons. In Minnesota, the incidence of CVD in men and women tended to decrease, by 5% to 20% between 1980 and 1985, and then gradually increased from the second half of the 1980s onward. A similar trend was observed in East Germany from the 1970s to the 1980s; in Finland from 1983 through 1992; in two Japanese regions, during the period 1961 to 1976 and from 1965 to 1983; and in Hawaii in men between 45 and 65 years of age, from 1969 to 1988; and in Novosibirsk, Russia, from 1982 to 1992. In Auckland, New Zealand, during the period 1981 to 1991 and in Goteborg, Sweden, during the period 1971 to 1987, no overall change in stroke incidence was observed.

Sex-specific changes have also been reported. A slight decrease in the incidence in men older than 75 years of age was observed in Auckland, New Zealand, in China, and in Copenhagen, Denmark. In Söderhamn, Sweden, there was a marked increase of stroke incidence in women. In two studies, an increase of stroke in men was observed: in Frederiksborg, Denmark, an increased incidence was observed in elderly men between 1972 and 1990 and in Northern Sweden from 1985 through 1991.

These various incidence rates may be influenced by racial or dietary factors, or other risk factors but probably also by patient health care. However, overall incidence is not a good criterion to CVD trends, because the variations differ considerably as a function of age group and type of ischemic CVD.

In our study, the crude incidence rates of ischemic CVD increased significantly in men older than 75 years of age.

Our study is one of the few studies to evaluate changes in the crude incidence of ischemic stroke according to the type of ischemia (cortico-subcortical infarcts versus lacunar infarcts) and the patient’s age and therefore allows analysis of these different variations. The increased incidence in both sexes was mainly cases of cortico-subcortical infarcts, partially compensated for by a decreased trend of the incidence of lacunar infarcts.

No significant variation in the incidence of TIA was observed over the 10-year period, although a slight increase was observed after 1990. The incidence of TIA ranges from 0.3 to 1.1/1000 inhabitants in France and can be as high as 3/1000 inhabitants in other countries. Improvements in diagnostic sensitivity and the increasing use of CT scan and then MRI, allowing the detection of small infarcts, could account for the increased rates, according to some authors. In these situations, although the incidence of CVD increases, its severity differs, with a growing proportion of strokes with slight or transient neurological deficit, or decreasing quickly. However, our methods of evaluation were not modified over the last 10 years, and no increase in strokes with slight or transient neurological deficit was observed.

This increase can actually be partially explained by the age structure of our population, consisting of a growing number of patients at high risk of developing ischemic stroke (decreased mortality of ischemic heart disease, and of patients suffering from thromboembolic disorders in particular). Patients in whom the increased incidence was most marked and most significant (subjects older than 75 years of age suffering from a cortico-subcortical infarct) had a higher cardioembolic disease, regardless of sex. Their proportion appeared to increase progressively over the 10 last years. These data are consistent with Brown’s study, indicating that the improved survival of patients with ischemic heart disease was responsible for an increased incidence of ischemic strokes.

A decreased trend of the incidence of lacunar infarcts, in which hypertension is usually implicated as a risk factor, was observed in men. Lacunar infarcts were the only lesions for which the annual change was negative in subjects both younger and older than 75 years of age. The variation of the proportion of hypertensive subjects did not show any changes in these two age groups of men. Although no significant correlation was observed between lacunar infarcts and prevalence of hypertension in our population, the value of primary prevention including better control of hypertension, may explain the decreased incidence of CVD reported in other studies, as in Rochester between 1945 and 1949 and 1975 and 1979 (54% reduction).

This retrospective study, which deals with the trends of ischemic cerebrovascular disease according to subtype of ischemia in our population, is a preliminary one. Our population was followed for 10 years, which may seem to be a long period but actually constitutes a relatively brief period for observation of significant epidemiological changes. Our study was based on a relatively small community (about 150,000 inhabitants), and the number of cases reported was sometimes small, particularly for the
younger age groups for each type of ischemic CVD, thus accounting for major variations from year to year. These features could partially explain the absence of any significant variation and the low statistical power of most of our results. The statistical power will probably be improved with the increasing number of patients in forthcoming years. Nevertheless, we already tried to identify some trends for each subtype of CVD, which could be studied again in other countries with more patients, in larger populations, to compare and confirm or refute our data.

Thus, our study shows that various trends can be observed, regardless of type of ischemic CVD. The incidence of cortico-subcortical stroke increases in men older than 75 years of age essentially due to the rise of cardioembolic strokes. This fact could be the consequence of the best survival rates of patients with cardioembolic disease.

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References
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