Impact of the Ageing Population on the Burden of Stroke: The Dijon Stroke Registry

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Keywords

Registry · Epidemiology · Elderly · Incidence · Population-based study · Case-fatality · Stroke · Recurrent stroke

Abstract

Background: We aimed to evaluate the impact of the ageing population on temporal trends in burden of stroke and to provide projections for the coming years. **Methods:** Stroke cases (ischemic strokes, spontaneous intracerebral hemorrhages, or undetermined strokes) were prospectively identified between 1987 and 2015 in Dijon, France, using a population-based registry. Age-standardized incidence rates of first-ever and recurrent stroke were calculated, and their temporal trends were assessed using age- and sex-adjusted annual incidence rate ratios (RR). **Results:** The population of Dijon increased by 3.8% over time, with an increase by 28% in the number of residents aged ≥ 75 years. We recorded 5,899 strokes including 5,101 patients with a first-ever event. Incidence of first-ever stroke was stable both in people < 75 and ≥ 75 years old, but an increase in standardized incidence rates of total strokes was noted due to a rise in the incidence of recurrent stroke (from 4.7/100,000/year in 1987–1994 to 12.3/100,000/year in 2009–2015 in people < 75 years old, RR

1.036; $p < 0.001$; from 74/100,000/year in 1987–1994 to 200/100,000/year in 2009–2015 in people ≥ 75 years, RR 1.040; $p < 0.001$). The absolute number of first-ever strokes increased by 43%, and that of total stroke events rose by 58% over time, with a more pronounced increase in people ≥ 75 years old (+47 and +65% respectively). The annual number of patients who survived > 90 days after a first-ever stroke increased by 90%. According to demographic projections, the total number of strokes will increase by 55% (+65% patients ≥ 75 years, and +25% patients < 75 years) by 2,030 in Dijon. **Conclusions:** Ageing and growth of the population led to a rise in the absolute number of strokes, especially in the elderly, that is expected to increase dramatically in the coming years. Improved stroke care was accompanied with an increase in stroke survivors that contributed to a rise in recurrent events. Urgent action is needed to meet this epidemiological challenge.

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Introduction

The incidence of stroke declined over the last 2 decades in high-income countries, thanks to improvement in vascular primary prevention [1]. According to the

Global Burden of Disease (GBD) study, age-standardized incidence decreased by 12% between 1990 and 2010, and mortality rates were reduced by 37% over this period [2]. Although encouraging, these results should be interpreted with caution when framing policies with regard to stroke care organization. Indeed, since the incidence of stroke is greatly influenced by age, with rates doubling with each decades after the age of 50 years [3], the ageing population in western countries will have a dramatic impact on stroke epidemiology, with an expected increase in the number of elderly patients affected by a stroke in turn. In addition, because of a better acute management of stroke patients, the number of stroke survivors is on the rise, with a current and future major impact on the need for post-stroke facilities and the risk of stroke recurrence.

In this context of rapid demographic changes, the aim of this study was to evaluate temporal trends in the burden of stroke in Dijon, France, with a focus on elderly patients, and to provide estimations of number of events for coming years.

Methods

Study Population and Case-Ascertainment Procedures

This study was based on data from the Dijon Stroke Registry [4, 5], an on-going population-based study that complies with the defined criteria for conducting “ideal” incidence stroke studies [6], and the guidelines for the reporting of incidence and prevalence studies in neuroepidemiology according to Standards of Reporting of Neurological Disorders [7]. Case-collection as well as adjudication procedures have been described extensively elsewhere [4, 5]. To ensure the exhaustiveness of case-collection, multiple overlapping sources of information are used. Both cases of stroke and transient ischemic attack that occur among residents of the city of Dijon, France are registered using several procedures including a review of medical records of all patients referred to the Dijon University Hospital where the only stroke unit is located, as well as a review of computerized hospital diagnostic codes using the International Classification of Diseases, tenth revision (I61, I62, I63, I64, G45, G46, and G81); A review of medical records from private hospitals of the city; A collaboration with the general practitioners and private neurologists of the city to identify stroke patients from home or nursing homes, and Dijon residents who had their stroke when outside the city; A review of the medical records of patients identified from a computer-generated list of all requests for imaging to radiology centers of the city; and regular checking of the death certificates to identify fatal strokes outside hospital. For this study, only stroke patients including ischemic stroke, spontaneous intracerebral hemorrhage, and stroke of undetermined origin were considered. Stroke was defined according to the WHO diagnostic criteria (i.e., “rapidly developing clinical signs of focal, at time global, disturbance of cerebral function, lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin”) [8]. Of note, patients who were treated with IV thrombolysis or mechanical thrombectomy were registered as having

ischemic stroke even though a total recovery was observed within the first 24 h. Each suspected cases of stroke were adjudicated by stroke-trained neurologists of the study team. For the present study, patients who were registered between January 1, 1987 and December 31, 2015 were included.

Definition of Epidemiological Data and Statistical Analysis

Annual incidence rates were calculated and were defined as incidence rates of first-ever stroke (first stroke occurring in a patient's life), and incidence rates of total strokes (including both first-ever and recurrent strokes). Denominators concerning the population of Dijon according to age groups and sex were based on data provided by the National Institute of Statistics. Age-standardized rates were evaluated by the direct method with the 2013 European population as the standard [9]. Five-year age bands were used for standardization. CIs for rate estimates were calculated using the Poisson distribution. Results were presented according to 4 study periods: 1987–1994, 1995–2001, 2002–2008, and 2009–2015. To assess temporal trends in incidence rates, annual rate ratios (RRs) adjusted to age (5-year bands) and sex were calculated using a Poisson regression. *p* values <0.05 were considered statistically significant. Based on 90-day case-fatality rates, we also evaluated the annual mean number of stroke survivors. Finally, using projections of the French population provided by National Institute of Statistics we estimated annual total number of strokes by 2,030 when considering similar trends in incidence rates. The statistical analysis was performed with STATA@13 software (Stata-Corp LP, College Station, TX, USA).

Results

Demographic Changes in the Study Area

Over the study period, a slight population growth was observed in Dijon. Mean annual population increased by 3.8%, from 146,848 inhabitants during the first study period to 152,368 inhabitants during the last study period. This growth was accompanied with an aging population as illustrated in Figure 1. An increase by 28% in the number of residents aged ≥ 75 years was observed between the first and last study periods, with consistent results in men (+30%) and women (+27%). As a result, the proportion of people ≥ 75 years old increased from 7.4% during the period 1987–1994 to 9.2% during period 2009–2015. In addition, the number of men ≥ 85 years old rose by 85% and that of women ≥ 85 years old increased by 71%.

Temporal Trends in Incidence Rates of First-Ever, Recurrent, and Total Strokes

A total of 5,899 stroke cases were recorded, including 5,101 patients with a first-ever event, and 798 recurrent strokes. The median age of patients with first-ever stroke increased with time from 77.8 (interquartile range 68.4–

Fig. 1. Mean annual population of Dijon, France, by age groups, gender, and study periods.

84.0) years old during period 1987–1994 to 79.1 (interquartile range 65.0–86.6) years old during period 2009–2015. Over the whole study period, 3,565 patients (69.9%) were ≥ 75 years old. Incidence of first-ever stroke was stable over time both in people < 75 and in those ≥ 75 years old (Table 1), with consistent results observed in men and women (Fig. 2 and Table 2). In contrast, an increase in incidence rates of total strokes was noted in both age groups over time due to a rise in incidence rates of recurrent events (Fig. 1 and Table 2). Hence, the age-standardized incidence of recurrent stroke increased from 4.7/100,000/year in 1987–1994 to 12.3/100,000/year in 2009–2015 in people < 75 years old (RR 1.036; 95% CI 1.021–1.052, $p < 0.001$). A similar trend was observed in people ≥ 75 years (age-standardized incidence: 74/100,000/year in 1987–1994 and 200/100,000/year in 2009–2015, RR 1.040; 95% CI 1.029–1.052, $p < 0.001$).

Changes in the Absolute Number of Strokes and Stroke Survivors Over Time

The annual mean number of recorded first-ever strokes increased by 43% between 1987–1994 and 2009–2015 (Fig. 3). Trends were similar in men (+44%) and women (+42%). The increase in the number of first-ever strokes was more pronounced in people ≥ 75 years old (+47%; men: +45%, women: +48%) than in those < 75 years old (+37%; men: +43%, women: +29%). In the very old (≥ 85 years old), the increase was by 100% (+104% in men and +98% in women).

The number of total stroke events increased by 58% in both men and women due to a rise in the number of recurrent events (+209% in men and +273% in women). In

people ≥ 75 years old, there was an increase by 65% in the total number of stroke events (+66% in men and +65% in women) related to a rise in that of recurrent events (+267% in both sexes). Of note, the total number of stroke events increased by 128% in both men and women ≥ 85 years old. In people < 75 years old, we observed an increase by 47% in the total number of stroke events (+52% in men and +39% in women) due to a rise in that of recurrent events (+186%; +153% in men and +300% in women).

The annual number of patients who survived > 90 days after a first-ever stroke increased by 90% between 1987–1994 and 2009–2015 (Fig. 4). Corresponding numbers were +123% in patients < 75 years old and +59% in patients ≥ 75 years old. The number of stroke survivors ≥ 85 years old rose by 116%.

Projected Trends for Stroke Numbers

Projections of annual total stroke events by 2030 in Dijon are shown in Figure 5. According to expected demographic changes, the total number of strokes recorded each year will increase by approximately 55%, with an increase by 65% in people ≥ 75 years old, and by 25% in those < 75 years old.

Discussion

This long-term population-based study demonstrated that the incidence of first-ever stroke was stable but that of recurrent events increased over time. Despite a slight population growth in Dijon, the absolute number of

strokes dramatically increased. These trends were particularly pronounced in the elderly, thus mirroring the ageing population. Finally, a rise in the number of stroke survivors was also observed.

A significant reduction in age-standardized rates of first-ever stroke has been observed in high-income countries. Indeed, in a meta-analysis of data from population-based registries, a decrease by 42% in incidence rates was noted between 1970 and 2008, with similar trends between people <75 and those ≥75 years old [1]. Contrasting with these findings, we observed stable incidence rates of first-ever stroke over 29 years. Another interesting result of the present study is the increase in the incidence of total strokes due to a rise in that of recurrent events. Few data about incidence rates of recurrent stroke are available in the literature because most epidemiological studies reported first-ever events only. Based on the proportion of first-ever stroke provided by studies evaluating both first-ever and recurrent strokes, the GBD study reported a decrease by 12% in the incidence of overall strokes between 1990 and 2010 [2]. However, the decrease was in fact observed between 1990 and 2005, and numbers were approximately stable between 2005 and 2010.

Several explanations could account for our results. In a previous study, we showed that incidence rates were lower in Dijon than in other European population-based studies during the 80s and 90s [10]. However, differences vanished over time, thus suggesting that primary prevention in France could have been more effective than that in other populations 3 decades ago but have not sufficiently improved or reached a plateau since. Although no specific information is available for the population of Dijon, several data from nationwide surveys argue for this hypothesis. Hence, a recent French cross-sectional study conducted in 2014–2016 found a prevalence rate of hypertension of 30.6% in adults aged 18–74 years [11]. The authors concluded to the absence of any decrease in the prevalence of hypertension in France since 2006. Moreover, no improvement in the detection and management of the disease was observed. Similarly, no reduction in tobacco consumption has been noted in France [12], and prevalence of diabetes is on the rise [13]. Finally, the prevalence of atrial fibrillation (AF), a major contributor of stroke especially in the elderly, has been increasing worldwide [14]. Despite this trend, we reported a decrease in the incidence of ischemic stroke due to AF in Dijon between 1985 and 2006, which was attributed to changes in clinical practice traduced by improvements in the use of antithrombotic agents that took place in the 90s, after the demonstration of the efficacy of adjusted-dose warfarin

Table 1. Temporal trends in standardized incidence rates of stroke

	1987–1994			1995–2001			2002–2008			2009–2015			RR	95% CI	p value
	pop.	n	INC	95% CI	pop.	n	INC	95% CI	pop.	n	INC	95% CI			
First-ever stroke															
Age <75 years	135,964	501	64.8	59.1–70.5	137,725	471	68.7	62.4–74.9	138,046	505	70.6	64.3–76.8	1.004	0.998–1.009	0.166
Age ≥75 years	10,884	698	806	746–866	11,886	652	771	711–830	13,107	775	840	781–899	1.003	0.999–1.008	0.114
Recurrent stroke															
Age <75 years	135,964	36	4.7	3.2–6.3	137,725	57	8.5	6.3–10.7	138,046	72	10.4	8–12.8	1.036	1.021–1.052	<0.001
Age ≥75 years	10,884	64	73.7	55.6–91.7	11,886	116	139	114–165	13,107	157	170	143–197	1.040	1.029–1.052	<0.001
Total strokes															
Age <75 years	135,964	537	69.5	63.6–75.4	137,725	528	77.1	70.5–83.8	138,046	577	81	74.3–87.7	1.007	1.002–1.012	0.005
Age ≥75 years	10,884	762	880	817–942	11,886	768	910	845–974	13,107	932	1,010	945–1,075	1.009	1.005–1.013	<0.001
Pop., annual mean population; n, number of cases; INC, Standardized incidence to 2013 European population (expressed as n/100,000/year); RR, age- and sex-adjusted annual incidence rate ratio.

Fig. 2. Incidence rates of first-ever and total strokes standardized to the 2013 European population by study periods and gender.

Fig. 3. Annual mean number of first-ever and total strokes by study periods and age groups.

Table 2. Temporal trends in standardized incidence rates of stroke stratified by age and gender. RR indicates annual incidence rate ratios adjusted to age

	Age <75 years				Age ≥75 years			
	women		men		women		men	
	RR	<i>p</i> value	RR	<i>p</i> value	RR	<i>p</i> value	RR	<i>p</i> value
First-ever stroke	1.004	0.29	1.004	0.26	1.004	0.15	1.003	0.48
Recurrent stroke	1.042	0.002	1.034	<0.001	1.037	<0.001	1.045	<0.001
Total strokes	1.008	0.049	1.007	0.024	1.008	0.001	1.009	0.005

Fig. 4. Annual mean number of patients who survived >90 days after a first-ever stroke by study periods and age groups.

Fig. 5. Projections of the number of stroke events by 2,030 in Dijon, France.

in reducing the risk of stroke in AF patients [15]. However, during a more recent period (2002–2012), no decrease in the incidence of AF-related ischemic stroke was observed in the OXVASC study because of a persistent underuse of oral anticoagulants in AF patients [16]. These results indicate that it could be assumed that the ageing population, together with the increase in the prevalence of AF, will be associated with a future increase in the incidence of AF-related stroke if no progress in the management of elderly patients with AF is made. Therefore, it

will be interesting to assess whether the availability of new direct oral anticoagulants may have an impact on future overall rates of anticoagulation in older age groups, and its consequences in terms of changing AF-related stroke epidemiology in the elderly.

To explain our results about recurrent stroke, the decrease in case-fatality rates in Dijon [4, 17], as observed in other regions [1], led to a rise in stroke survivors who are individuals at high risk of recurrence. In addition, a greater use of antithrombotic agents in the elderly may increase

the incidence of intracerebral hemorrhage [18]. Whatever the underlying reasons, our findings indicate that a greater attention should be paid to secondary stroke prevention, especially in a context of the ageing population.

Beyond incidence rates, we presented the overall stroke burden in terms of absolute number of people affected by this condition. As a result, we showed a rise in the annual total number of recorded cases. The increase was particularly dramatic in the elderly, and even more pronounced in the very old (≥ 85 years). These findings are consistent with the GBD study in which although incidence rates decreased, the absolute number of strokes increased by 25% between 1990 and 2010 in high-income countries, with a corresponding rise by 34% in people ≥ 75 years [19]. Together with the increase in the number of stroke survivors, such a trend has major implications in terms of clinical practice and stroke care organization. Clinicians must address the issue of more and more elderly patients admitted for stroke, and there is an urgent need for developing adequate resources for acute stroke management, and post-stroke dedicated services. This call for an urgent action is reinforced by our projections of the future number of stroke events that indicate that this phenomenon will magnify in coming years. In the European Union, the total number of stroke events is expected to increase by 34% by 2035 [20].

The major strength of our study is the continuous case collection over a very long period of time using the same definition of stroke (classical epidemiological WHO definition) to avoid a potential bias related to a change in the definition of transient ischemic attack, which would have led to a shift from this diagnosis toward that of ischemic stroke. Despite constant procedures, we cannot exclude that a better identification of stroke patients occurred with time due to several reasons including a better aware-

ness of stroke in the population leading to more patients seeking medical attention, especially those with minor symptoms, which may have been better diagnosed thanks to the increasing use of brain magnetic resonance imaging in routine practice. Another limitation of our study is that we were not able to investigate trends in stroke incidence according to ethnicity because the French legislation does not allow collecting such data, and the population of Dijon has only a limited diversity.

To conclude, this study highlights that ageing and growth of the population led to a rise in the absolute number of strokes, especially in the elderly, that will magnify in the coming years. Improved stroke care was accompanied with an increase in stroke survivors that contributed to a rise in recurrent events. Urgent action is needed to meet this epidemiological challenge.

Ethics Statement

The Dijon Stroke Registry was approved by the Comité d'Evaluation des Registres (French National Committee of Registers) and Santé Publique France (French Institute for Public Health Surveillance).

Disclosure Statement

Y.B. received honoraria for lectures or consulting fees from AstraZeneca, Daiichi-Sankyo, BMS, Pfizer, Medtronic, MSD France, Amgen, and Boehringer-Ingelheim. Other authors declare that they have no conflicts of interest to disclose.

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