Sex Differences in Stroke Attack, Incidence, and Mortality Rates in Northern France

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Background: Age and sex have a major impact on stroke onset. *Aims:* We aimed to compare the attack, incidence, and 28-day mortality rate for stroke as well as risk factors in men and women aged 35 and over. *Methods:* Data were obtained between 2008 and 2015 from the stroke population-based registry covering the city of Lille (northern France). *Results:* A total of 2426 strokes (1917 incident strokes) were recorded. The number of strokes was lower in women than in men when considering individuals under the age of 75 but was twice as high when considering individuals aged 75 or over. Overall, there were 25% more strokes in women than in men. The age-adjusted attack ($P = .017$) and incident ($P = .027$) rates of stroke were ~30% lower in women than in men (a ~30% lower risk of ischemic stroke ($P = .02$) and a ~40% lower risk of intracerebral hemorrhage (ICH) ($P = .004$)). The age-adjusted mortality rate after ICH was ~35% lower in women than in men ($P = .014$). With regard to cardiovascular risk factors, women with stroke were older, smoked less, and were more likely to have a history of migraine or atrial fibrillation than the men. *Conclusion:* The risk of stroke is lower in women than in men under the age of 75 but is similar when comparing women and men after that age. Nevertheless, the age structure of the population (with more elderly women than elderly men) translates into a higher absolute number of strokes in women than in men. **Key Words:** Stroke—incidence—mortality—registry—risk factors.

Introduction

Sex differences in stroke have attracted increasing interest but have yielded inconsistent results; the prevalence, symptoms, clinical features, treatments, outcomes and risk factors are likely to vary as a function of the data collection period and the source population. Although stroke is primarily considered to be a disease affecting men, it is now recognized as a major public health problem in women as well.[1] Worldwide, there are more female stroke cases than male stroke cases, and more women than men die of stroke.[2]

Most stroke patients have several vascular risk factors. The presence, severity, and time course of these risk factors are important determinants of stroke. It is essential to consider sex- and age-specific risk factors when seeking to understanding the epidemiology and etiology of stroke. An accumulation of stroke risk factors with age may be

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more likely in women because they have a longer life expectancy and are older at stroke onset than men (for a review, see Reference 3).

Aims

There are few population-based data on sex differences in stroke incidence and mortality and in clinical risk factors as a function of age groups and stroke subtypes. Hence, we sought to evaluate these features in a French population-based registry with a permanent and exhaustive registration during 8 years, in order to provide robust, up-to-date information on the characteristics and epidemiology of stroke and its main subtypes.

Methods

The Lille Stroke Registry

The Lille Stroke Registry was created in 2008 and has been accredited by the French Institute for Public Health Surveillance and the French National Institute of Health and Medical Research (INSERM). The registry constitutes an ongoing, population-based study of adults aged 35 or over living in the city of Lille and the adjoining towns of Lomme and Hellemmes. According to French national census data for 2013, the area contains 231,491 individuals, of whom 92,343 are aged 35 or over. Cases of stroke were identified using several overlapping sources of case ascertainment in all public- and private-sector hospitals, nursing homes, emergency departments, and neurology departments. The sources were cross-checked to ensure exhaustiveness (with a review of discharge letters, radiography department records, computerized lists covering the diagnosis upon discharge from hospital, emergency department case lists, death certificates, etc.). All incident (first-ever) and recurrent strokes were taken into account, regardless of whether or not the patient was hospitalized.

Cases of stroke were defined (according to the World Health Organization guidelines and the international classification) as "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin."[4] The cases were assessed on the basis of the patient's medical history (symptoms for more than 24 hours), clinical examinations, and radiological data. The patients' medical records and the registry database were screened for previous strokes. Patients having experienced a transient ischemic attack (i.e., an attack in which cognitive and neurological symptoms disappeared within 24 hours), brain tumors, multiple sclerosis, epilepsy, intracerebral hemorrhage (ICH), or subdural hematoma related to traumatic brain injury (TBI) were not included in the registry.

The stroke subtype was diagnosed on the basis of clinical signs and cerebral imaging. Radiographic data were used to define the stroke as an ischemic stroke (IS), a spontaneous ICH, or a subarachnoid hemorrhage. Patients with the latter condition were excluded from the present study, because it is rare and is usually related to anatomic malformations. Stroke of undetermined origin corresponds to stroke for which the mechanism cannot be reliably identified (as a result of either death at home, incomplete assessment, or the absence of cerebral imaging data). Survival was evaluated at 28 days post stroke. All deaths were checked (1) with the patient's general practitioner, (2) in the local registry office, and (3) in the death certificate database.

The presence or absence of the following risk factors for stroke was recorded from 2008 onward: current high blood pressure, diabetes, hypercholesterolemia, and a history of stroke, transient ischemic attack, myocardial infarction, ischemic coronary artery disease, atrial fibrillation, migraine, TBI, sleep apnea syndrome, or lower limb arteriopathy. Smoking was also noted from 2011 onward, and a history of dementia or cognitive disorders was noted from 2013 onward.

All events registered between January 1, 2008 and December 31, 2015 were included in the present study.

Statistical Analyses

Statistical analyses were performed with SAS software (version 9.1, SAS Institute Inc., Cary, NC).

All participants were divided into six 10-year age groups (i.e., 35-44, 45-54, 55-64, 65-74, 75-84, and ≥85 years of age).

The incidence, attack, and 28-day mortality rates were calculated with (1) the number of de novo strokes, the number of de novo and recurrent strokes, and the number of de novo and recurrent stroke patients who died within 28 days as the respective numerators, and (2) the person-years at risk in the same age group and of the same sex in the area covered by the registry over the same period (provided by the French National Institute of Statistics and Economic Studies, INSEE) as the denominator.

Age-adjusted incidence rate ratios for women versus men (with men as the reference) were estimated using Poisson regression models.

Standardized rates were calculated directly and expressed per 100,000 inhabitants with regard to populations of the same age in France (obtained from the 2011 national census data computed by the French National Institute of Statistics and Economics), Europe (1967),[5] and the world (1966).[6]

Clinical risk factors were compared in women versus men by using logistic regression models adjusted for age and the year of recruitment. Sex × stroke subtype interactions were tested by including the corresponding interaction term in the regression model.