International Journal of Cardiology 167 (2013) 733–738

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Trends in stroke incidence after hospitalization for atrial fibrillation in Sweden 1987 to 2006

Lars G. Olsson [a,b,*], Karl Swedberg [b], Georg Lappas [b], Simon Stewart [c], Annika Rosengren [b]

[a] Department of Medicine, Mora Hospital, Mora, Sweden
[b] Department of Emergency and Cardiovascular Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden
[c] Baker IDI Heart and Diabetes Institute, Melbourne, Australia

ARTICLE INFO

Article history:
Received 25 November 2011
Received in revised form 24 January 2012
Accepted 3 March 2012
Available online 30 March 2012

Keywords:
Atrial fibrillation
Acute stroke
Epidemiology
Prevention

ABSTRACT

Background: To investigate recent trends in incidence of hemorrhagic and non-hemorrhagic strokes in patients with atrial fibrillation (AF).
Methods: The Swedish Hospital Discharge and Cause of Death Registries were linked to provide outcome data.
Results: 321,276 patients 35 to 84 years (56.5% male, mean age 71.5 years) free of prior stroke with a first AF diagnosis during 1987–2006 were included. Over 3 year follow-up 24,733 patients (7.7%) were diagnosed with ischemic stroke and 2292 (0.7%) with hemorrhagic stroke. The 3-year incidence of ischemic stroke decreased from 8.7% for patients diagnosed in 1987–1991 to 6.6% for those diagnosed in 2002 to 2006. The corresponding incidence of hemorrhagic stroke increased from 0.38% for patients diagnosed in 1987–1991 to 0.57% for those diagnosed in 2002 to 2006. Covariable-adjusted risk of ischemic stroke was significantly reduced (HR 0.65; 0.63–0.68) while risk of hemorrhagic stroke was significantly increased (HR 1.19; 1.05–1.36). Compared to the general population, total stroke risk decreased more among AF patients.
Conclusion: We found a considerable decrease in risk of ischemic stroke in Sweden in patients without prior stroke and with a first hospital diagnosis of AF. There was an increased risk of hemorrhagic stroke, but because hemorrhagic stroke represented only a small proportion of all strokes, the overall risk of stroke declined.

1. Introduction

Patients with atrial fibrillation (AF) have an increased risk of stroke. Up to 25% of all patients with acute stroke have AF on their admission ECG. Moreover, AF-related strokes tend to be more severe with more lasting disabilities and increased long- and short-term mortality [1–4]. Cost-effective evidence-based strategies for stroke prevention in AF patients, such as monitored anticoagulation therapy, have been available for several decades [5], but underutilization persists [6–9]. Given that several epidemiological studies show that the incidence and prevalence of AF have increased and will continue to increase in the foreseeable future the temporal trends of stroke in these patients is of particular interest [10,11]. Analyses from North American studies show considerable declines in stroke incidence over time in AF patients [12,13]. Equivalent results from European studies are more ambiguous [14,15]. However, because the overall population incidence of stroke varies considerably over time, the AF specific component for the observed change against a background of a potential broader change in stroke incidence in the population is uncertain. Also, the temporal trends on incidence of hemorrhagic strokes in this patient category have not been widely studied [13,15].

We wanted to examine trends in the incidence of ischemic and hemorrhagic stroke up to three years after an index admission for AF at the whole population level, during the period 1987–2006, by linking the Swedish hospital discharge registry to the national Swedish death registry. We then compared AF-specific trends over this 20-year period with those observed within the general population.

2. Methods

2.1. Patient population

Sweden has a universal health care system that provides low-cost health care (including hospital care) to the Swedish population (population ranging from 8.4 to 9.1 million people during the period 1987 to 2006). Registration in the hospital discharge register is mandatory for all hospitalized patients. Diagnosis at discharge is coded with the International Classification of Diseases (ICD) system (ICD 8th revision until 1986, ICD 9th revision until 1996, ICD 10th revision thereafter). Each patient is given a principal diagnosis and up to five secondary diagnoses. For the purpose of the present study, data from the national hospital discharge and cause-specific death registers were linked through the personal identification number (PIN), which is unique for all Swedish citizens. The hospital discharge register has been in existence since the 1960s and operating on a nationwide basis, with near-complete coverage, since 1987.

* Corresponding author at: Department of Medicine, Sahlgrenska University Hospital/Östra, SE-416 85 Göteborg, Sweden. Tel.: +46 31 3434086; fax: +46 31 258933.
E-mail address: larsgustavo@hotmail.com (L.G. Olsson).

0167-5273/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.ijcard.2012.03.057

2.2. Index hospitalization for AF

We identified all first hospital admissions with a principal or secondary discharge diagnosis of AF in men and women aged 35 to 84 years during the period 1987 to 2006. In order to ascertain freedom from earlier hospitalizations and to ensure that patients from all years had the same chance to be identified as new cases, we censored for hospitalizations with a diagnosis of AF up to 7 years before the index hospitalization. Patients with prior ischemic or hemorrhagic stroke within 7 years were excluded in the same manner. The reason for this was to minimize the risk for ambiguity on timing of first AF hospital diagnosis and to minimize the inclusion of recurrent strokes, a common problem. The specific diagnose codes used to identify incident atrial fibrillation cases were: 427.92 (ICD-8) (only used for exclusion of patients with AF before 1987), 427D (ICD-9), and I48 (ICD-10). The discharge codes used to identify stroke cases were: Ischemic stroke: (432–434 (ICD-8 and ICD-9) and I63 (ICD-10) and hemorrhagic stroke (430, 431 (ICD-8 and ICD-9), I60–I62 (ICD-10).

2.3. Comorbidity

Significant comorbidities during the preceding 7 years and index hospitalization were recorded. The specific discharge codes used were: ischemic heart disease: 410–414 (ICD-8 and ICD-9), I20-I25 (ICD-10); chronic heart failure 427.00 (ICD-8), 428A, 428B, 428X (ICD-9) and I50 (ICD-10); diabetes: 250 (ICD-8 and ICD-9), E10, E11, E14 (ICD-10); hypertension: 401–405 (ICD-8 and 9), I10–I15 (ICD-10); valvular disease: 393–398, 424 (ICD-8 and ICD-9), I05–I09, I34–I35 (ICD-10); hyperthyroidism: 242 (ICD-8 and ICD-9), E05 (ICD-10); cancer: 140–207 (ICD-8 and ICD-9), C00–C97 (ICD-10); chronic obstructive pulmonary disease 490–492 (ICD8 and ICD-9), J40–44 (ICD-10); asthma 493 (ICD-8 and ICD-9), J45 (ICD-10).

2.4. Follow-up

We examined age- and sex-specific incidence of fatal and non-fatal ischemic and hemorrhagic stroke (as classified above) from 1 day up to 1095 days (3 years) after the index hospitalization by 5-year periods (1987–1991, 1992–1996, 1997–2001 and 2002–2006). We attempted to identify predictors of occurrence of ischemic strokes among baseline variables and time period of AF occurrence. We also examined the age- and gender-adjusted stroke occurrence in this cohort and compared it to that of the whole Swedish population.

2.5. Validity of the registers

In the period from 1987 to 1996, a primary discharge diagnosis was lacking in 0.8% of all admissions to Swedish departments of internal medicine (including admissions for cardiovascular reasons) [16]. In a random sample of 100 randomly selected patients with a hospital diagnosis of AF enrolled in the Malmö Diet and Cancer Study, 95 were verified by ECG while 2 probably had AF (ECG missing) [17]. In a validation study of all first-ever strokes in the city of Örebro February 1999–January 2000, 333/377 of the diagnoses in the hospital discharge and cause of death registries were identified in the community-based registry, giving a sensitivity of 88% and specificity of 92% [4]. In an earlier study based on the Swedish MONICA material 3492/3562 of stroke cases in patients 25–74 years old 1985–1989 were identified by the hospital discharge registry, yielding a 98% sensitivity, due to a 32% rate of false positives there was a positive predictive value of 68,5% [18].

2.6. Statistical analysis

All analyses were carried out using the Statistical Analysis System (SAS), version 9.2, and the R statistical computing system, version 2.9.0. Means and proportions for continuous and categorical variables were calculated. Estimates of the cumulative incidence of ischemic stroke with death or hemorrhagic stroke as competing risk, within 3 years were calculated, and are presented for each period of AF hospitalization, gender and age group. The estimates for hemorrhagic stroke were calculated in a similar manner. Additionally, the cumulative incidence function for stroke with death as a competing risk is illustrated graphically for the whole population within a 3-year interval from admission, for each period of AF hospitalization, and for men and women separately. When comparing men and women, age adjustment was done implicitly through comparison of age-matched subsets. The hazard ratios between the first period, 1987–1991, and all other periods of AF admission for total, ischemic and hemorrhagic stroke were estimated through Cox regression independently of age, gender and comorbidity. To estimate the excess risk, when compared with a normal population, of stroke after AF hospitalization we used the age and sex standardized morbidity ratio (SMR), as calculated from the number of people with a first-time stroke (within 7 years) for each age-, sex- and year-specific cell.

3. Results

3.1. Baseline

A total of 321,276 patients with a first hospitalization for AF and no recorded history of stroke within 7 years were discharged from Swedish hospitals 1987–2006. Patient characteristics at hospital discharge are summarized in Table 1. Overall, 56.5% were male and mean age was 71.5 years. Men were on average 4 years younger than women. Slightly less than a third had concurrent ischemic heart disease, with more men than women affected. A similar proportion of men and women (28.2 and 28.9%, respectively) had chronic heart failure. Valvular disease was diagnosed in 7.1% of cases and hyperthyroidism in only 0.4% of cases.

Table 1
Baseline characteristics.

		Men	Women	Total
Number of patients		181,496	139,780	321,276
Age at discharge	Mean	69.7 ± 10.6	73.9 ± 8.6	71.5 ± 10.0
Ischemic heart disease	*n* (%)	54871 (30.2)	34360 (24.6)	89231 (27.8)
Chronic heart failure	*n* (%)	51216 (28.2)	40450 (28.9)	91666 (28.5)
Diabetes mellitus	*n* (%)	20664 (11.4)	16037 (11.5)	36701 (11.4)
Hypertension	*n* (%)	33073 (18.2)	29855 (21.4)	62928 (19.6)
Valvular heart disease	*n* (%)	12315 (6.8)	10445 (7.5)	22760 (7.1)
Cancer	*n* (%)	22116 (12.2)	17567 (12.6)	39683 (12.4)
Hyperthyreosis	*n* (%)	804 (0.4)	2360 (1.8)	3164 (1.0)
Pulmonary disease*	n (%)	12867 (7.1)	9939 (7.1)	22806 (7.1)

*Includes asthma and chronic obstructive pulmonary disease

3.2. Time trends in 3-year stroke incidence

Between 1987 and 2006, 24,733 (7.7%) of this cohort were diagnosed with a fatal or non-fatal ischemic stroke and 2292 (0.7%) with a fatal or non-fatal hemorrhagic stroke within 3 years from the index hospitalization. There was a 27% relative reduction in the 3 year total stroke incidence (hazard ratio (HR) 0.73; 95% confidence interval (CI) 0.71 to 0.76) between 1987–1991 and 2002–2006, corresponding to an absolute decline from 9.1% to 7.2%. This was mainly driven by a 29% relative decrease in ischemic stroke incidence (HR 0.71; 0.68 to 0.73), in absolute percentages from 8.7% to 6.6% (Fig. 1), while there was a 32% relative increase in 3-year hemorrhagic stroke incidence (HR 1.32; 1.13-1.56) corresponding to an absolute change from 0.38% to 0.57% (Fig. 2). Between 1987–1991 and 1992–1996 there was a non-significant increase in incidence of total stroke; reflecting an increase in both ischemic and hemorrhagic strokes. Total stroke and ischemic stroke then decreased, while hemorrhagic strokes rose markedly between 1997–2001 and 2002–2006. With the exception of hemorrhagic strokes during 2002–2006, incidence rose evenly during the 3-year follow-up. Women had a higher 3-year stroke incidence (10.5% during 1987–1991 versus 7.7% during 2002–2006 than did men (7.2% versus 4.2%). This translated to a 26%

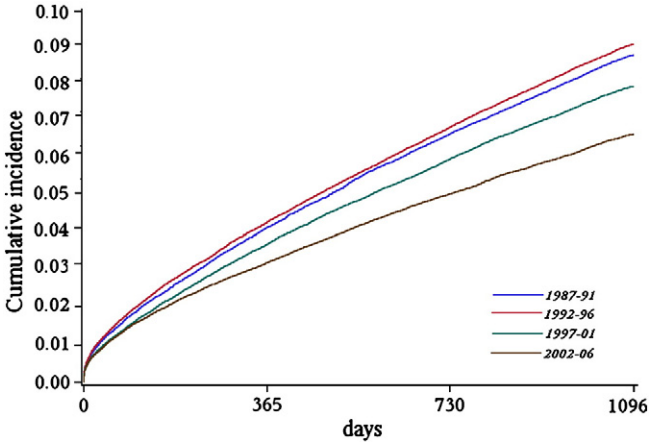

Fig. 1. Secular trends of ischemic stroke incidence after first hospitalization for atrial fibrillation in Sweden 1987–2006.