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Diabetes mellitus as risk factor for atrial fibrillation hospitalization: Incidence and outcomes over nine years in a region of Northern Italy

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ABSTRACT

Aims: Diabetes mellitus (DM) and atrial fibrillation (AF) are worldwide public health challenges and major causes of death and cardiovascular events. The association between DM and AF is controversial in literature and data on outcomes of individuals with both diseases have not been evaluated in population studies. We tested the hypothesis that DM is independently associated to AF hospitalization and assessed the risk of stroke and mortality in people with both conditions.

Methods: We conducted a population-based cohort-study of DM patients and their corresponding controls identified in a administrative health database of the Lombardy Region. Both cohorts were followed for nine years. A multivariable Cox proportional-hazards-regression model was used to estimate the hazard ratio (HR) for first hospitalization for AF and for clinical outcomes.

Results: Out of 9,061,258 residents, 285,428 (3.14%) DM subjects were identified, mean age 65.8 ± 15 years, 49% were women. The cumulative incidence of AF in DM was 10.4% vs. 7.4% in non-DM. DM was a risk factor for AF (HR 1.32, 95% CI 1.30–1.34; $p < 0.0001$). Oral anticoagulants were prescribed in 34.8% of DM patients with AF. DM associated with AF, presented the highest HR for stroke: 2.63; 95% CI 2.47–2.80 and for total death, HR 2.41; 95% CI 2.36–2.47.

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Conclusions: In this population study, DM was an independent risk factor for AF hospitalization. DM patients with AF had the highest risk of stroke and total mortality. Early identification of AF and a structured plan to optimize the comprehensive management of DM and AF patients is mandatory.

1. Introduction

Diabetes mellitus (DM) is considered a pandemic disease and its prevalence is steadily rising worldwide. The number of adult Europeans with a diagnosis of DM in 2013 was 56.3 million (6.8%) [1,2] and currently in Italy more than three million (5.4%) people are affected [3].

Meanwhile the worldwide incidence and prevalence of atrial fibrillation (AF), the most common clinically relevant arrhythmia, is also rising progressively [4] involving more than 8.8 million of Europeans [5] and about 1.1 million Italian residents [6,7]. The prevalence and incidence of AF is expected to increase 2.5-fold by 2050 [8] reflecting the growing proportion of elderly people and the longer survival of patients with cardiovascular disease. American and European reports have shown a considerable increase in hospitalizations and mortality attributable to AF [9,10], highlighting that AF is a growing public health concern [4].

Both diabetes and AF are major causes of stroke, heart failure, cognitive impairment and mortality. Although micro and macro-vascular disorders are responsible for DM cardiovascular morbidity and mortality [11], there are few recent epidemiological studies regarding these issues in Europe [2].

AF is associated with a five times higher risk of stroke [12], double the risk of dementia, three times that of heart failure and 40–90% increases in mortality [13]. Cardioembolic stroke is the most severe type of ischemic stroke and AF is the most common cause, probably explaining why mortality rates are higher when the two events are combined [14,15].

The availability of a large representative population-based cohort in Northern Italy offered the opportunity to assess not only the association between DM and incident AF hospitalization, but also clinical outcomes in particular when the two conditions are combined.

2. Methods

2.1. Data source

This study used linkable administrative health databases of the Lombardy Region which include a population registry with the demographic data of all residents and detailed information on drug prescriptions and hospital admissions. Data were available for eleven consecutive years, from 2000 to 2010. With a population of more than ten million in 2010, Lombardy is the most heavily populated Italian region, comprising urban, industrial and rural areas. Health care in Italy is publicly funded for all residents, irrespective of social class or employment, and everyone is assigned a personal identification number kept in the National Civil Registration System. Residents are cared for by general practitioners (GPs) as part of the National Health System (NHS). The pharmacy prescription database contains the medication name and anatomic therapeutic chemical (ATC) classification code, quantity and dispensation date. The hospital discharge database gives the date of hospital admission, date of discharge or death, diagnoses, and procedures done. All persons with diabetes can obtain the necessary drugs, laboratory tests, visits and diabetes devices free of charge from the NHS, provided they have a certified diagnosis from a physician working in a public health institution. This certification is recorded in a specific database called the disease-specific exemption registry (ER).

All data used in this study were managed retrospectively and according to current Italian laws on privacy. Each person was identified by an anonymous and encrypted code. Approval from the Ethics Committee or specific written consent were not required to analyze encrypted administrative data.

2.2. Study cohort

People who in 2002 met at least one of the following criteria were defined as patients with diabetes: (1) prescription of at least an oral anti-diabetic drug (OAD) or insulin according to the ATC code A10*; (2) diagnostic code of DM (ICD9-CM code 250.xx) in at least one hospital admission; (3) DM diagnosis certification in the ER (013.250). Information on DM type (1, 2 or gestational) was not available. The comparison cohort consisted of two participants without DM matched for age ± 1 year, sex and GP, for each patient with DM. All participants were followed up until the first hospitalization for AF or death, emigration, admission to a nursing home or till December 31, 2010.

2.3. Incidence of atrial fibrillation, stroke and mortality

For the analyses of the incidence of AF we considered the first hospital admission for AF or atrial flutter (ICD 9 CM 427.31 and 427.32) starting from January 1st, 2002. Patients who had a hospital admission for AF or had been treated with oral anticoagulants (OAC, ATC code B01AA07, B01AA03) in the previous two years (2000–2001) were excluded from the cohort.

For the analyses of the incidence of stroke we considered the first hospital admission starting from January 1st, 2002 for subjects without AF hospitalization and from the date of discharge from the first hospital admission for AF for patients with AF. Patients admitted to a hospital for stroke in the two years before entering the study cohorts were excluded from