Original article

The association between relevant co-morbidities and prevalent as well as incident heart failure in patients with atrial fibrillation

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A R T I C L E   I N F O

A B S T R A C T

Background: Congestive heart failure (CHF) is a serious complication in patients with atrial fibrillation (AF).
Objective: To study associations between relevant co-morbidities and CHF in patients with AF.
Methods: Study population included all adults (n = 12,283) ≥45 years diagnosed with AF at 75 primary care centers in Sweden 2001–2007. Logistic regression was used to calculate odds ratios with 95% confidence intervals (CIs) for the associations between co-morbidities, and prevalent CHF. In a subsample (n = 9424), (excluding patients with earlier CHF), Cox regression was used to estimate hazard ratios with 95% CIs for the association between co-morbidities, and a first hospital diagnosis of CHF, after adjustment for age and socio-economic factors.
Results: During 5.4 years' follow-up (standard deviation 2.5), 2259 patients (24.0%; 1135 men, 21.8%, and 1124 women, 26.7%) were diagnosed with CHF. Patients with hypertension were less likely to have CHF, while a diagnosis of coronary heart disease, valvular heart disease, diabetes, or chronic obstructive pulmonary disease (COPD), was consistently associated with CHF among men and women. CHF was more common among women with depression. The relative fully adjusted risk of incident CHF was increased for the following diseases in men with AF: valvular heart disease, cardiomyopathy, and diabetes; and for the following diseases in women: valvular heart disease, diabetes, obesity, and COPD. The corresponding risk was decreased among women for hypertension.
Conclusions: In this clinical setting we found hypertension to be associated with a decreased risk of CHF among women; valvular heart disease and diabetes to be associated with an increased risk of CHF in both sexes; and cardiomyopathy to be associated with an increased risk of CHF among men.

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia in the population, with a prevalence of 2% in Sweden, defined as a recorded diagnoses in the nationwide patient register [1]. Even if ischemic stroke is the most important complication among patients with AF [2], i.e. with a five times higher risk compared to individuals without AF [3], there are also other risks with AF. Congestive heart failure (CHF) and AF are interrelated [4,5], with CHF being three times more common among AF patients compared to non-AF individuals [6]. Among elderly, CHF is the most common cardiovascular disease (CVD) [7], and, according to a recent study in the USA, the development of CHF after a diagnosis of AF has not declined over time [8]. Furthermore, CHF in AF patients is also associated with an increased mortality [6], with one study finding

a doubled mortality compared to AF patients without CHF [8]. CHF is also the most common cause of death among AF patients, corresponding to 30% of deaths [9].

AF is also associated with other CVDs. Coronary heart disease (CHD) is a common comorbidity in AF [10], as well as an important risk factor for both CHF [11], and mortality [12] among AF patients. In a Japanese study, the existence of structural heart disease, i.e. myocardial infarction, valvular heart disease, and cardiomyopathy, was found to be the only predictive factor for development of CHF among AF patients [13]. In a study of women with AF in the USA, modifiable risk factors such as obesity, hypertension, smoking, and diabetes accounted for the majority of the female population's risk of incident CHF [14]. In addition, hypertension is common in AF and also regarded as a risk factor for future CHF [15]. Additionally, some respiratory diseases are associated with AF, i.e. chronic obstructive pulmonary disease (COPD) [16,17], and obstructive sleep apnea [18], and with CHF [19,20]. Furthermore, the rate of CHF among AF patients varies in different countries, and other than clinical factors seems to be of importance for the development of CHF [9].

Thus, it is important to study risk factors for the development of CHF in patients with AF. Actually, one study in the USA found a 2-fold higher rate of CHF than those of stroke or transient ischemic attack (TIA) [8], suggesting why it is possible that prevention of CHF needs to be prioritized in AF treatment as much as the prevention of ischemic stroke.

There are also gender differences as regards to AF, with AF being more common among men [1], and being diagnosed on average five years earlier among men than among women [21]. On the other hand, women with AF exhibit both a higher risk of stroke as well as of mortality than men with AF [22]. Thus, it is important to analyze men and women separately.

CHF could be prevented in AF, provided that the relevant risk factors are known, and under the hypothesis that cardiovascular co-morbidities and sociodemographic factors are important for the development of CHF. The aims herein were therefore to study the association between relevant co-morbidities and CHF among men and women with AF in Swedish primary care, and to study factors associated with a first hospital diagnosis of CHF among patients with AF who still had not developed CHF. We hypothesized that both co-morbid CVD conditions, such as hypertension, CHD, valvular heart disease, cardiomyopathy, and cerebrovascular diseases, as well as other important diseases, including diabetes, depression and anxiety, and socio-demographic factors, could affect the risk of incident CHF in AF patients.

Methods

Design

The study used individual-level patient data from 75 primary health care centers (PHCCs), 48 of which were located in Stockholm County. Individuals attending any of the participating PHCCs between 2001 and 2008 were included in the study. We used *Extractor* software (http://www.slso.sll.se/SLPOtemplates/SLPOPage1____10400.aspx; accessed September 19, 2010) to extract individual electronic patient records (EPRs). National identification numbers were replaced with new unique serial numbers to ensure anonymity. The files were linked to a dataset including data from the Total Population Register, the National Patient Register (NPR), and the Swedish Cause of Death Register, which contains individual-level data on age, sex, education, cause of death, and hospital diagnosis for all residents registered in Sweden. Thus, a new research dataset containing clinical data and information on socioeconomic status on the individuals ($n = 1,098,420$) registered at the 75 PHCCs was created. Data from the Cause of Death Register were used for the follow-up.

The investigation conforms with the principles outlined in the Declaration of Helsinki. Ethical approvals were obtained from regional boards at Karolinska Institutet and the University of Lund.

Study population

The study included all patients with diagnosed AF, identified by the presence of the ICD-10 code (10th version of the World Health Organization's International Classification of Diseases) for atrial fibrillation (I48) in patients' medical records at the PHCCs. The following cardiovascular-related disorders were used as covariates: hypertension, CHD, cerebrovascular diseases (CVD), and diabetes mellitus (for specific codes, see below). Patients with CHF during the study period were identified in two ways, either through a diagnosis in the EPR in the PHCC or through a hospital diagnosis. In total, 12,283 individuals (6646 men and 5637 women), aged 45 years or older at the time of AF diagnosis and who visited any of the 75 participating PHCCs from January 1, 2001, until December 31, 2007, with data on neighborhood socioeconomic status available, were included in the study. In the subset studying first hospital CHF diagnosis, patients with an earlier CHF were excluded ($n = 2859$), yielding 9424 patients (5211 men and 4213 women) in the analysis.

Outcome variable

For logistic regression: prevalent CHF. For Cox and Laplace regression: time from first AF diagnosis to first hospital diagnosis of CHF (until December 31, 2010).

Demographic and socio-economic variables

Sex was stratified into men and women.

Individuals were divided into the following *age groups* 45–54, 55–64, 65–74, 75–84, and ≥85 years. Individuals younger than 45 years were excluded.

Educational level was categorized as ≤9 years (partial or complete compulsory schooling), 10–12 years (partial or complete secondary schooling), and >12 years (college and/or university studies).

Marital status was classified as married, unmarried, divorced, or widowed.

Neighborhood socioeconomic status (SES) was categorized into three groups according to the neighborhood index: more than one standard deviation (SD) below the mean (high SES or low deprivation), more than one SD above the mean (low SES or high deprivation), and within one SD of the mean (middle SES or deprivation). The neighborhood index was based derived from the following four variables: low educational status (<10 years of formal education), low income (<50% of the median individual income from all sources), unemployment, and receipt of social welfare. The neighborhood deprivation index was categorized into three groups: more than one standard deviation (SD) below the mean (high SES or low deprivation level), more than one SD above the mean (low SES or high deprivation level), and within one SD of the mean (moderate SES or moderate deprivation level).

Co-morbidities

We identified the following cardiovascular co-morbidities from the EPRs among the individuals in the study population: hypertension (I10–15); CHD (I20–25), also including registered hospitalizations for myocardial infarction from the NPR; CHF (I50 or I110), also including hospitalizations for CHF from the NPR; non-rheumatic valvular diseases (I34–38); cardiomyopathy (I42); CVD (I60-69), also including registered hospitalizations for