



Gender-related differences in risk of cardiovascular morbidity and all-cause mortality in patients hospitalized with incident atrial fibrillation without concomitant diseases: A nationwide cohort study of 9519 patients [☆]



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ABSTRACT

Background: Previous studies of patients with “lone” and “idiopathic” atrial fibrillation (AF) have provided conflicting evidence concerning the development, management and prognosis of this condition.

Methods: In this nation-wide, retrospective, cohort study, we studied patients diagnosed with incidental AF recorded in national Swedish registries between 1995 and 2008. Controls were matched for age, sex and calendar year of the diagnosis of AF in patients. All subjects were free of any in-hospital diagnosis from 1987 and until patients were diagnosed with AF and also free of any diagnosis within one year from the time of inclusion. Follow-up continued until 2009. We identified 9519 patients (31% women) and 12,468 matched controls.

Results: Relative risks (RR) versus controls for stroke or transient ischemic attack (TIA) in women were 19.6, 4.4, 3.4 and 2.5 in the age categories <55, 55–64, 65–74 and 75–85, years respectively. Corresponding figures for men were 3.4, 2.5, 1.7 and 1.9. RR for heart failure were 6.6, 6.6, 6.3 and 3.8 in women and 7.8, 4.6, 4.9 and 2.9 in men. All RR were statistically significant with $p < 0.01$. RR for myocardial infarction and all-cause mortality were statistically significantly increased only in the two oldest age categories in women and 65–74 years in men.

Conclusions: Patients with AF and no co-morbidities at inclusion had at least a doubled risk of stroke or TIA and a tripled risk of heart failure, through all age categories, as compared to controls. Women were at higher RR of stroke or TIA than men.

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1. Introduction

Atrial fibrillation (AF) has been reported to be an independent risk factor of death and morbidity [1]. The mortality risk increases in the presence of co-morbidities, while AF in patients without co-morbidities has been considered relatively harmless, possibly because this arrhythmia is often found in younger individuals [1,2]. The number of patients with AF without co-morbidities is dependent on the definition of the study populations, but there is as yet no study on the

long-term course of a very large cohort of patients and controls with this condition.

Patients below 60 years of age have been considered to have lone AF if they have no evidence of cardiopulmonary disease, while idiopathic AF requires the absence of any other disease, irrespective of age [1,3]. However, the definitions of lone and idiopathic are heterogeneous, the age criterion has been questioned and the studied populations have been small or have lacked controls free from AF [4–12].

A statistically significant increase in all-cause mortality has only been found in one study of patients with lone or idiopathic AF (Table 1) [5,6,8,11,12]. Previous studies of heart failure in the general population have shown an increased prevalence in men compared to women and that patients with AF have an increased risk of heart failure [1,2,11,13–15]. However, studies with 41 to 76 patients with lone or idiopathic AF have not shown any statistically significantly increased

[☆] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1
Studies of lone or idiopathic atrial fibrillation with controls.

First author	N	Controls	Age-mean (years)	Follow-up (years)	Stroke/TIA	Heart failure	Myocardial infarction	All-cause mortality	Combined endpoint
Brand et al [4]	43	Age–sex matched	70.6 (men) 68.1 (women)	30	0.9% vs 0.2% ^a (<i>p</i> < 0.01)	ns	ns (coronary heart disease)	–	
Jouven et al [5]	25	Age–sex matched	47.6	23	–	–	–	RR 1.95 (<i>p</i> = 0.02)	
Jangahir et al [6]	76	Age–sex specified incidence rates	44.2	30	0.9% vs 0.5% ^a (<i>p</i> = 0.004)	ns	–	ns	
Weijls et al [7]	41	Age–sex matched	58	5.5 (mean)	ns	ns	ns	ns	8.9% vs 3.6% ^{a,b} (<i>p</i> = 0.006)
Kopecky et al [8]	97	Life-table analysis and difference between isolated, recurrent and chronic AF	44.0	14.8 (mean)	Low ^c	–	Low ^c	ns	
Stewart et al [11]	15	Age–sex matched	^d	20	–	–	–	ns	ns ^e
Kopecky et al [12]	55	Age–sex matched	74	9.6 (median)	2.0% vs 0.2% ^a (<i>p</i> < 0.01)	–	2.6% vs 1.1% ^a (<i>p</i> = 0.02)	ns	5.0% vs 1.3% ^{a,f} (<i>p</i> < 0.01)

Abbreviations: N, numbers of patients; TIA, transient ischemic attack; ns, not statistically significant; RR, relative risk; vs, versus; y, years.

^a Annual rates in percentage.

^b Cardiovascular death, myocardial infarction, cerebrovascular accident, heart failure, coronary artery disease and new onset hypertension.

^c Confirmed low incidence.

^d Age not specified in subgroup of patients with lone atrial fibrillation.

^e Cardiovascular hospitalization and death.

^f Stroke, transient ischemic attack, myocardial infarction, valvular heart disease, coronary heart disease and cardiac surgery.

risk of heart failure while reports diverge on the risk of coronary heart disease in these patients [4,6,7,12]. Cohorts of 43 to 76 patients with lone or idiopathic AF had an increased risk of stroke with annual rates between 0.9% and 2.0%, and equal rates between in men and women have been found [4,6,12].

National health registries in Sweden record the discharge diagnoses of all hospitalized patients and provide high quality information [16,17]. Personal identification numbers allow comprehensive coverage of all non-emigrated patients throughout life. Due to the all-inclusive nature

of the information recorded in the registries, it is possible to obtain a national estimate of long-term cardiovascular risks. The registries are well established and allow researchers to make retrospective analyses in large patient cohorts, and they permit the performance of prospective nationwide randomized trials [2,18–20].

Our purpose was to estimate the risk of stroke or transient ischemic attack, heart failure, myocardial infarction and all-cause mortality in all patients hospitalized with incident AF as the only diagnosis and in matched controls in a comprehensive nation-wide study.

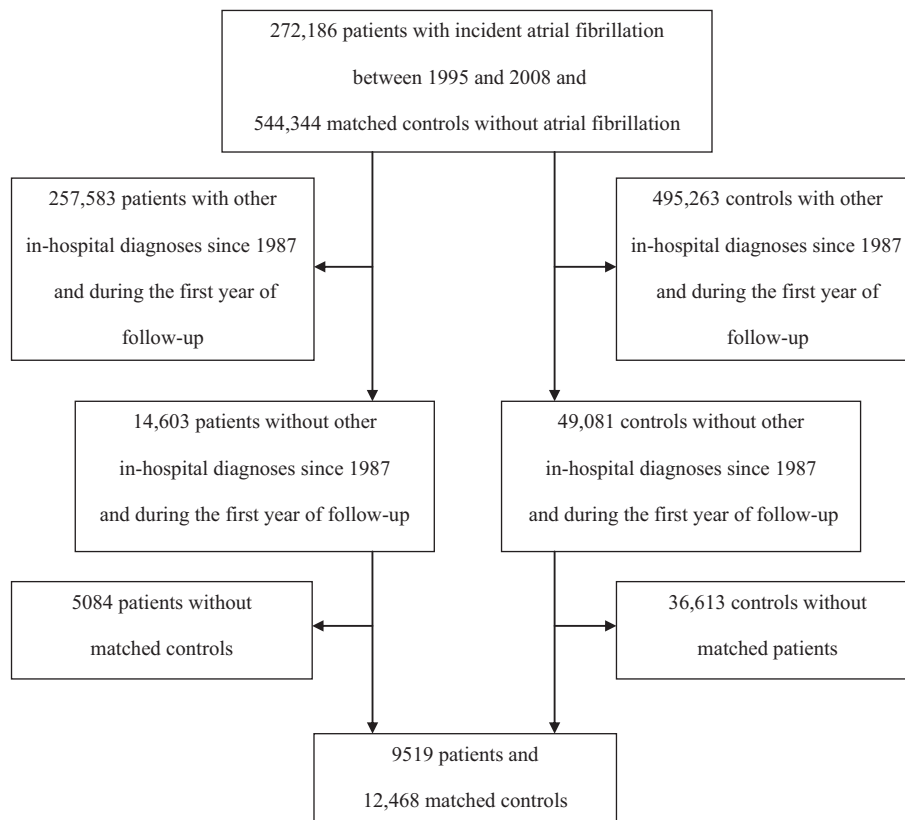


Fig. 1. Flowchart of patients with incident atrial fibrillation and matched controls without other diagnoses.

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