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Incidence of Atrial Fibrillation and Relationship With Cardiovascular Events, Heart Failure, and Mortality

A Community-Based Study From the Netherlands

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ABSTRACT

BACKGROUND Important improvements have been made in treatment of diseases associated with atrial fibrillation (AF), such as hypertension, myocardial infarction, and heart failure. Incidence rates and risk factors may have changed with the aging of the population and changing lifestyles. Currently, the risk for AF is only partially explained, possibly because of differences between older cohorts and contemporary populations.

OBJECTIVES This study investigated the incidence of AF in a contemporary cohort in the Netherlands, together with comorbidities associated with AF and associations of AF with cardiovascular outcomes.

METHODS Incident AF was ascertained for hospital and study electrocardiograms in 8,265 participants of the PREVEND (Prevention of Renal and Vascular End-Stage Disease) study in Groningen, the Netherlands.

RESULTS During 9.7 ± 2.3 years of follow-up, 265 participants developed AF, with a resulting overall AF incidence of 3.3 per 1,000 person-years. Advancing age, male sex, antihypertensive drug use, higher body mass index, previous myocardial infarction, and previous stroke were associated with AF. After multivariable adjustment, AF was associated with cardiovascular events (hazard ratio [HR]: 2.24; 95% confidence interval [CI]: 1.06 to 4.75; $p = 0.035$), heart failure with either reduced or preserved ejection fraction (HR: 4.52; 95% CI: 2.02 to 10.09; $p < 0.001$), and all-cause mortality (HR: 3.02; 95% CI: 1.73 to 5.27; $p < 0.001$).

CONCLUSIONS The incidence of AF in the present cohort was comparable to that shown in data of older studies. Obesity has become a major risk factor for incident AF. Although overall cardiovascular event rates were lower in the present study, the present study confirms the association of incident AF with such events. (J Am Coll Cardiol 2015;66:1000–7)

Atrial fibrillation (AF) affects millions of people worldwide, and numbers are expected to increase (1). AF has large impact on a person's life. It is accompanied by symptoms, impaired quality of life, increased risk of stroke, dementia, heart failure, mortality, and increasing health care expenses (2,3).

Multiple comorbidities have been associated with incident AF (4). However, current knowledge of AF

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incidence, prevalence, risk factors, and associated cardiovascular morbidity and mortality is derived from predominantly North American cohort studies that were initiated a long time ago or, more recently, from registries based on questionnaires or International Classification of Diseases (ICD) discharge codes (5-10). In recent years, important improvements were made in pharmacological and nonpharmacological treatment of associated diseases, such as hypertension, myocardial infarction, and heart failure (11-13). In addition, incidence rates and risk factors may have changed with the aging of the population and changing lifestyles. Currently, the risk for incident AF is only partially explained, possibly because of differences between older cohorts and more contemporary populations. We investigated the incidence of AF, comorbidities associated with AF, and the associations of AF with cardiovascular events, systolic and diastolic heart failure, and all-cause mortality in the Dutch community-based PREVEND (Prevention of Renal and Vascular End-Stage Disease) cohort study.

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METHODS

POPULATION. The PREVEND cohort study was founded in 1997 by inviting all inhabitants of the city of Groningen, the Netherlands, who were 28 to 75 years old (n = 85,421) (14). Of all invitees, 40,856 responded (47.8%). Persons with urinary albumin excretion >10 mg/l (n = 7,768) in their morning urine, as well as a randomly selected control group with urinary albumin excretion <10 mg/l (n = 3,394), were invited to the PREVEND outpatient clinic. After excluding patients with insulin-dependent diabetes mellitus, pregnant women, and persons unable or unwilling to participate, a final cohort of 8,592 patients was included and completed the baseline screening program. The baseline screening program consisted of 2 outpatient visits to assess demographic factors, anthropometric measurements, cardiovascular and metabolic risk factors, and health behavior and to collect blood samples and 2 24-h urine samples on 2 consecutive days. Participants were seen at 3-year intervals in the PREVEND outpatient clinic. For the present analysis, we excluded participants without an electrocardiogram (ECG) (n = 248), as well as participants with prevalent AF at the baseline screening (n = 79), thus leaving 8,265 participants. The PREVEND study was approved by the institutional medical ethics committee and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

ASSESSMENT OF AF. Incident AF was diagnosed if either atrial flutter or AF was present on a 12-lead ECG obtained at 1 of the 3 PREVEND follow-up visits or at an outpatient visit or hospital admission in the 2 hospitals in the city of Groningen (University Medical Center Groningen and Martini Hospital). A standard 12-lead ECG was performed at each PREVEND follow-up visit. All ECGs were digitally stored and electronically screened for the following criteria: PR interval absence, atrial flutter, or ectopic atrial rhythm. This method of electronic screening was validated with complete manual screening by 2 independent observers of all ECGs from the PREVEND baseline visit, and 100% sensitivity for the detection of AF or atrial flutter was reached. All ECGs determined by electronic screening to suggest suspected AF were manually reviewed by 2 independent observers. When an inconsistency was found or when both observers agreed on the diagnosis of AF or atrial flutter, the ECGs were validated by 2 independent cardiologists (Figure 1). Incident AF was diagnosed in 265 participants. For the date of incident AF, the date of the first ECG with a definite diagnosis of AF or atrial flutter was used.

COVARIATE DEFINITIONS. Systolic and diastolic blood pressures were calculated as the mean of the last 2 measurements of the 2 visits, by using an

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

BMI = body mass index

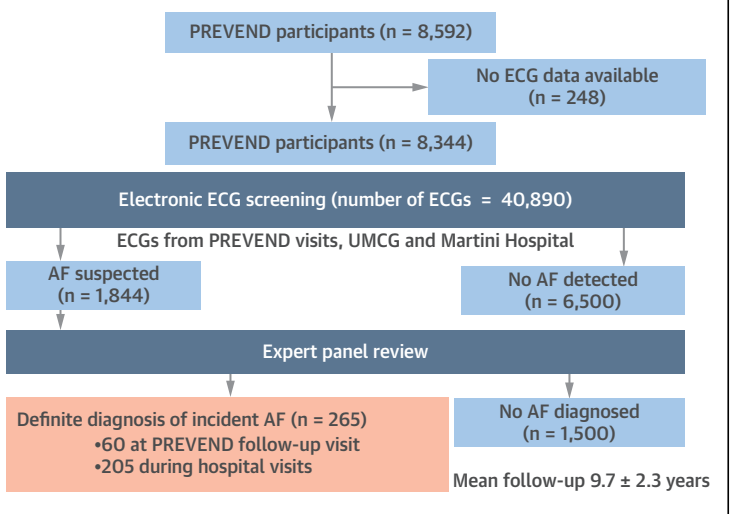
ECG = electrocardiogram

ICD = International Classification of Diseases

LVEF = left ventricular ejection fraction

NT-proBNP = N-terminal prohormone of brain natriuretic peptide

FIGURE 1 AF Ascertainment in the PREVEND Study



Flowchart of atrial fibrillation (AF) assessment in PREVEND (Prevention of Renal and Vascular End-Stage Disease) study participants, by using electrocardiograms (ECGs) made during PREVEND study visits and hospital visits. UMCG = University Medical Center Groningen.