The Epidemiology of Atrial Fibrillation and Stroke

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KEYWORDS

• Epidemiology • Atrial fibrillation • Stroke • Cardioembolic stroke • Cryptogenic stroke

KEY POINTS

- The incidence of atrial fibrillation and stroke are expected to increase worldwide in the next decades as a result of the progressive aging of the population and the growing diffusion of unhealthy cardiovascular habits.
- The contribution of atrial fibrillation to the incidence and outcome of ischemic stroke is huge, as shown by the fivefold increased risk of stroke in patients with the arrhythmia.
- Atrial fibrillation is commonly responsible for cardioembolic stroke, which is particularly severe in terms of mortality and residual disability.
- Atrial fibrillation may be underdiagnosed in some cases and be responsible for a high proportion of cryptogenic strokes.

INTRODUCTION

Atrial fibrillation (AF) is one of the major cardiac rhythm disturbances, responsible for a high rate of cardiovascular and cerebrovascular morbidity and mortality, resulting in a high health care cost and public health burden. It is defined as a supraventricular tachyarrhythmia with uncoordinated atrial activation and consequently ineffective atrial contraction.[1] It is commonly classified according to the duration of single episodes.[1] Specifically, an episode that terminates spontaneously or with intervention within 7 days from onset is classified as paroxysmal AF, whereas a more sustained disease, lasting more than 7 days or more than 12 months, is defined as persistent AF or longstanding persistent AF, respectively. Moreover, paroxysmal episodes may recur with a variable frequency along the life span and both paroxysmal and persistent episodes may coexist in the same individual. On the other hand, the term permanent AF implies a condition of irreversibility, which is mainly deduced by clinical findings and refers to patients in whom a consensus to stop further attempts to restore and/or maintain sinus rhythm has been reached.[1] Finally, depending on the underlying pathophysiology, the AF may be classified as valvular or nonvalvular, the latter denoting a form characterized by the absence of rheumatic mitral stenosis, mechanical or bioprosthetic heart valve, or mitral valve repair. AF may be asymptomatic or present with a wide spectrum of symptoms, including fatigue, palpitations, dyspnea, hypotension, and syncope.[1,2] It may coexist with many other comorbidities, such as hypertension, hyperlipidemia, ischemic heart disease, heart failure, anemia, diabetes mellitus, arthritis, and chronic obstructive pulmonary disease. Finally, it is a

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well-known risk factor for ischemic stroke, which, in some cases, may represent the first manifestation of the arrhythmia, and for myocardial infarction, and heart failure.[3]

EPIDEMIOLOGY OF ATRIAL FIBRILLATION

The frequency of AF in the general population is progressively increasing as a result of greater life expectancy, increased prevalence of risk factors for AF, and improved survival after myocardial infarction. The worldwide age-adjusted prevalence of AF, as estimated in the 2010 Global Burden of Disease Study, is 5.96 per 1000 in men and 3.73 per 1000 in women, accounting for approximately 33 million people.[4] In the United States, AF affects about 3 to 5 million individuals and it is expected to affect greater than 8 million people by 2050.[5] In Europe, AF affects about 8 million people and it is expected to rise dramatically to 18 million by 2060.[6] The prevalence of AF in the general population is about 3%. Prevalence may vary across different countries: the highest prevalence rates have been found in United Kingdom (7.2%), followed by Spain (6.1%), Netherlands (5.5%), and Australia (4%). The lowest rates have been reported in Iran (2.8%), Portugal (2.5%), Brazil (2.4%), Germany (2.2%), Sweden (2%), France (1.6%), United States (1.1%), Switzerland (0.9%), China (0.9%), Kenia (0.7%), Thailand (0.4%), and India (0.1%).[7–21] Discrepancies in prevalence rates across different countries can be attributed to differences in study design, and to genetics and environmental factors. Moreover, the prevalence of AF is significantly higher in white individuals (8.0%) compared with black (3.8%), Hispanic (3.6%), and Asian (3.9%) ethnic groups.[22,23] Prevalence progressively increases with the advancing age, reaching almost 6% to 8% in patients aged 75 years and 10% in the oldest old.[24,25] In this respect, the Screening for Atrial Fibrillation in the Elderly (SAFE) study recently reported a prevalence of 7.2% in patients aged 65 years and older and a prevalence of 10.3% in those age 75 years and older.[26] The age distribution also shows some geographic variations as highlighted by the Randomized Evaluation of Long-term anticoagulant therapY (RE-LY) Atrial Fibrillation Registry showing that patients with AF in Africa, India, and the Middle East are on average 10 to 12 years younger than patients from other regions of the world.[25] The prevalence is higher in men than in women across all the age groups and in all countries with the exception of China.[27] Moreover, paroxysmal AF is more common than persistent AF in young patients and in women.[28]

Recent evidences suggest that AF is often underdiagnosed and its real prevalence may be higher than that reported.[29,30] The reason for missed diagnoses is that spot electrocardiograms (ECGs), compared with continuous ECG monitoring are at risk of underestimating the incidence of paroxysmal silent AF. In this respect, a recent study in a Swedish 75 to 76-year-old population found that a stepwise screening program for AF, based on the combination of a 12-lead ECG recording, followed by a 2-weeks continuous ECG recording, significantly improved the recognition of silent AF especially in subjects with vascular risk factors.[29] Specifically, after including the share of patients who underwent a 2-week continuous ECG recording, the baseline prevalence of AF increased from 9.6% to 14%, thus confirming that isolated ECG recordings may fail to capture paroxysmal AF and that AF screening programs may have useful implications for stroke prevention.[29] Similarly, systematic screening programs based on intermittent ECG recordings showed that mass screening for AF in an elderly population is able to identify a significant proportion of participants with untreated AF.[30] Finally, other studies and meta-analyses evaluated whether screening programs are really cost-effective in the framework of stroke prevention.[31,32] These studies suggested that opportunistic rather than systematic screening, based on pulse taking, followed by invitation for ECG in the presence of an irregular pulse, may be the most cost-effective method for AF screening.[31,32] In the light of these evidences, both the American Heart Association and the American Stroke Association Primary Prevention of Stroke Guidelines, and the 2012 Focused Update of AF Guidelines from the European Society of Cardiology, recommended this opportunistic screening in the primary care setting of patients 65 years and older.[33,34] However, further research is needed to ascertain which screening method is most suitable to detect new cases of AF compared with routine practice and which patients may benefit from prophylactic anticoagulation following the detection of a silent AF.

Risk factors associated with the development of AF include obesity, smoking, hypertension, diabetes, and the presence of cardiac diseases such as coronary artery disease, heart failure, rheumatic heart disease, and valvular heart disease. Hypertension and diabetes are the most common medical conditions associated with AF worldwide, being present in greater than 70% and in greater than 19% of the patients with AF, respectively.[35,36] A close link between an elevated body mass index (BMI) and the development of AF has also been reported, suggesting that the risk of