Long-Term Mortality of Nonvalvular Atrial Fibrillation

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ABSTRACT

Introduction: This study sought to determine long-term all-cause mortality and cardiovascular mortality in patients with nonvalvular atrial fibrillation (AF).

Patients and Methods: The study included 352 patients (153 males, 199 females; mean age 62 years; range 34 to 82 years) who presented to our clinic between 1995 and 2010 and were diagnosed with nonvalvular AF. The follow-up ranged from 72 to 176 months (mean 110 months).

Results: The causes or associated conditions of AF were hypertension (51.1%), coronary heart disease (29.9%), heart failure (48.8%), diabetes mellitus (11.9%), and pulmonary hypertension (9.9%). Seventy-two patients (21%) died during the follow-up period. Cardiovascular death was noted in 30 patients (41.7%). Sudden death was seen in six patients (8.3%). Death from stroke occurred in 20 patients (27.8%), and 16 patients (22.2%) died of other causes (malignancies, accidents, infectious causes, etc.).

Conclusion: The major cause of death was of cardiovascular origin in patients with nonvalvular AF.

Key Words: Nonvalvular atrial fibrillation; mortality

Kapak Dışı Atriyal Fibrilasyonda Uzun Dönem Mortalite

ÖZET

Giriş: Kapak dışı atriyal fibrilasyonu (AF) olan hastalarda uzun dönemde gerçekleşen tüm sebeplere bağlı ve kardiyovasküler nedenlere bağlı mortaliteyi belirlemeyi amaçladık.

Hastalar ve Yöntem: 1995 ile 2010 yılları arasında kliniğimize başvuran ve kapak dışı AF tanısı konan 352 hasta (153 erkek, 199 kadın; ort. yaş 62; dağılım 34-82) geriye dönük olarak incelendi. Takip süresi 72-176 ay arasında değişmekteydi (ort. 110 ay).

Bulgular: Atriyal fibrilasyon etkeni veya ilişkili durumu olarak hipertansiyon (%51.1), koroner kalp hastalığı (%29.9), kalp yetersizliği (%48.8), diabetes mellitus (%11.9), pulmoner hipertansiyon (%9.9) saptandı. İzlem sırasında 72 hastanın (%21) öldüğü belirlendi. Ölümler 30 hastada (%41.7) kardiyovasküler nedenli, 20 hastada (%27.8) inme kaynaklı, altı hastada (%8.3) ani ölüm idi; 16 hastada (%22.2) ölümler diğer nedenlere (malignite, kaza, infeksiyon vb.) bağlandı.

Sonuç: Kapak dışı AF'li hastalarda uzun dönemde ana ölüm nedeninin kardiyovasküler kaynaklı olduğu görüldü.

Anahtar Kelimeler: Kapak dışı atriyal fibrilasyon; mortalite

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1-2% of the general population. With an aging population, its prevalence is estimated to increase two-fold in the next 50 years[(1)]. The prevalence of AF increases remarkably with age, being 0.5% at 40-50 years of age and 5-15% at 80 years of age. Men are more often affected than women[(1-3)].

Atrial fibrillation is associated with increased rates of death, stroke and other thromboembolic events, heart failure, hospitalization, poorer quality of life, decreased exercise capacity, and left ventricular (LV) dysfunction. As an independent cause of mortality, AF is associated with doubled rates of death[(4)].

Atrial fibrillation is associated with a 5-fold risk of stroke, with one in five strokes being attributed to this arrhythmia. Ischemic strokes, in particular, are often fatal in AF patients, and those who survive become more disabled and are more likely to develop a recurrence than

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patients with stroke of other causes. Consequently, AF-related stroke doubles the risk for death and increases the cost of care by 1.5-fold[4].

The aim of this study was to examine all-cause mortality and cardiovascular mortality in patients with nonvalvular AF in the long-term.

PATIENTS and METHODS

This retrospective study included patients with nonvalvular AF who presented to the arrhythmia section of İstanbul University Cardiology Institute during the period from 1995 to 2010. The total number of the patients who presented during this period was 1.170. Of these, 352 patients (mean age 62 years; range 34 to 82 years) were found to be eligible for the study, including 153 males (43%) and 199 females (57%). The follow-up ranged from 72 to 176 months (mean 110 months).

Patients with acute causes of AF like acute coronary syndrome and cardiac surgery, valvulopathy, advanced left ventricular systolic dysfunction (LVEF ≤ 25%), pre-excitation, known malignancy or any advanced chronic disease and patients with a poorly-documented history were not included. The cause of death was obtained from medical records (hospital records, death certificate, or autopsy report). The diagnosis of stroke was made by a neurologist. Records from neurology wards of local hospitals or neurology clinics were also obtained to document central embolism. Systemic embolism was diagnosed by a vascular surgeon.

RESULTS

Baseline characteristics of the patients are shown in Table 1. The causes and associated conditions of AF were hypertension in 51.1%, coronary heart disease in 29.9%, heart failure in 48.8%, diabetes in 11.9%, and pulmonary hypertension in 9.9% of the patients. Of these, hypertension and heart failure were the most common.

The vast majority of the patients with chronic AF (91%) were under the therapeutic strategy for rate control. The most widely used medication was beta-blockers (57%). Eighty percent of these patients were receiving anticoagulation therapy (warfarin). Medications used by the patients are shown in (Table 2).

During the study period, 72 patients (21%) died. Cardiovascular death was noted in 30 patients (41.7%). Sudden death occurred in six patients (8.3%). Death from stroke was seen in 20 patients (27.8%). Other causes of death in 16 patients (22.2%) were malignancies, accidents, infectious causes, etc. (Table 3).

DISCUSSION

Atrial fibrillation is independently associated with a 50% to 90% increased risk for death. Increased mortality is seen in both men and women. It is associated with excess mortality, which persists even after adjustment for coexisting cardiovascular conditions[5].

Table 1. Baseline characteristics of patients

Characteristics		
Age (years)	34-87	mean 62
Gender (M/F)	153 (43.4%)	199 (56.6%)
Hypertension	180 (51.1%)	
CHD	105 (29.9%)	
Previous MI	52 (14.8%)	
History of CHF	170 (48.8%)	
Diabetes mellitus	42 (11.9%)	
Smoking	95 (27.0%)	
COPD/PHT	35 (9.9%)	

CHD: Coronary heart disease; CHF: Congestive heart failure; MI: Myocardial infarction; COPD: Chronic obstructive pulmonary disease; PHT: Pulmonary hypertension.

Table 2. Medications received by patients

Medication	n	%
Antiarrhythmic	320	91
Beta blocker	200	57
Calcium channel blocker	127	36
Digitalis	102	29
Propafenone	56	16
Amiodoarone	18	5
Anticoagulant (warfarin)	274	78
ASA	113	32
Clopidogrel	18	5
Statine	88	25
ACE-I/ARB	186	53
Sprinolactone	60	17
Other diuretics	28	8

ASA: Acetylsalicylic acid; ACE-I: Angiotensin converting enzyme inhibitor; ARB:Angiotensin receptor blocker.

Table 3. Mortality distribution of the patients

	n	% (n/352)	% (n/72)
Cardiovascular death	30	8.5	41.7
Stroke	20	5.7	27.8
Sudden death	6	1.7	8.3
Others*	16	4.5	22.2
Total mortality	72	21.0	100.0

* Malignancies, accidents, infectious causess etc.

Death rates are doubled by AF, independently of other known predictors of mortality[4]. The AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) Study compared survival in AF patients at high risk for stroke

or death treated with rate-control versus rhythm-control. A total of 4.060 patients were randomized over a four-year period. The mean duration of follow-up was 3.5 years, with a maximum of six years. Overall mortality was 26.3%, being 25.9% in the rate-control group, and the rhythm-control strategy offered no survival advantage over the rate-control strategy[6]. The rate of overall mortality was higher than that found in our study (21%). This is possibly due to the selection of patients with higher risks in the AFFIRM study. Our study included only nonvalvular AF patients.

The Atrial Fibrillation and Congestive Heart Failure Trial compared the benefits of rhythm control and rate control in a randomized, multicenter trial of 1.376 patients with AF and congestive heart failure[7]. After a mean follow-up of 37 months, no difference was found between the rhythm-control and rate-control groups in the primary endpoint of death from cardiovascular causes. Mortality occurred in 182 patients (27%) in the rhythm-control group, compared with 175 patients (25%) in the rate-control group. Secondary outcomes which included death from any cause, worsening heart failure, and stroke were also similar in the two groups.

While rheumatic heart disease, mitral stenosis and hyperthyroidism are well-documented causes of AF, some diseases or risk factors are highly associated with AF without having a direct causative role. For example, advanced age is closely related to AF, but it is not a disease. Atrial fibrillation usually develops in elderly patients (in our group, the average age was 62 years) with multiple comorbid diseases like hypertension, coronary heart disease (CHD), and congestive heart failure (CHF). It may be difficult to identify what the real cause of AF is for an individual case. In our study, the causes and associated conditions of AF were hypertension (51.1%), CHD (29.9%), heart failure (48.8%), and diabetes (11.9%).

In the ALFA (Etude en Activite Liberale sur la Fibrillation Auriculaire) study, an underlying heart disease was present in 534 patients (70.6%), while 29.4% of the patients (referred to as lone AF) did not have an underlying heart disease. The most common underlying condition was hypertension (39.4%), and 21.4% of the study patients had hypertensive heart disease[8]. In our study, 51.1% of the patients were hypertensive. Of interest, the incidence of coronary artery disease was lower (16.6%) compared to that found in our study (29.9%).

Another longitudinal observational study included 1.100 patients with nonvalvular AF. Mortality occurred in 85 patients (7.7%), the most common forms being sudden death (31.7%), death from CHF (21.2%) and stroke (16.5%). Cardiovascular causes accounted for 62 deaths (72.9%)[9].

It is not surprising that AF and CHF usually accompany each other, because they arise from the similar or same risk factors, and more importantly development of one means a direct predisposition to the other[10,11]. About 30% of AF patients have symptomatic heart failure (New York Heart Association classes II–IV) and 30-40% of heart failure patients have AF[12,13]. Atrial fibrillation may lead to heart failure as in tachycardiomyopathy or decompensation in acute onset AF and conversely, heart failure may cause arrhythmia resulting from increased atrial pressure and volume overload, secondary valvular dysfunction, or chronic neurohumoral stimulation. In our study, 48.8% of AF patients had heart failure.

Coronary artery disease is seen in ≥ 20% of AF patients[12,13]. It has yet to be established whether uncomplicated coronary artery disease alone (atrial ischaemia) predisposes to AF and how AF affects coronary perfusion[14]. Coronary heart disease was seen in 29.9% of our study group.

Another accompanying condition of AF is diabetes mellitus requiring medical treatment. It may contribute to atrial damage and about 20% of AF patients have diabetes[15]. In our patient group, this rate was 11.9%.

Patients with AF may also have chronic obstructive pulmonary disease. Its prevalence is 10-15% among AF patients. Its role as a marker for AF is possibly less than that for cardiovascular disease[15].

Nonvalvular AF is an important independent risk factor for stroke. With a five-fold increase in its risk, stroke in AF is often severe, resulting in long-term disability or death[4]. The risk for stroke can be reduced by only two-thirds with anticoagulation, and by one-fifth with antiplatelet therapy[16,17]. The use of anticoagulats was 78% in our study.

Among stroke patients with AF, the reported rates of early case-fatality vary from 18% to 38% [18-21]. Stroke-related mortality occurred in 20 patients and accounted for 27.8% of all-cause mortality.

Limitations

The main limitation to this study is its retrospective and nonrandomized nature; thus, a cause-and-effect relationship of various factors with the risk of death could not be demonstrated. Documentation of drug use with precise start and stop times was not satisfactory. There must have been many potential changes that were left unmeasured over the course of the study period, such as changes in clinical factors and drug therapies.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Consept/Desing: CB, ZY
Analysis/Interpretation: OA, CK, AY
Data acquisition: ZY, MS, UC
Writing: CB
Critical revision: UC, ZY, OA, AY, CK, MS
Final approval: All of authors

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