

The Cumulative Incidence of Stroke, Myocardial Infarction, Heart Failure and Sudden Cardiac Death in Patients with Atrial Fibrillation

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Abstract

Introduction: Atrial fibrillation is considered as a main cause of cardiovascular morbidity worldwide. A lot of progress was made to avoid the fatal complications of this type of cardiac arrhythmia. In Bosnia and Herzegovina there is no accurate published data on how much this arrhythmia is represented and how much is responsible for death and disability in our population.

Research Objectives: The objective of our study is to determine the cardiac and cerebrovascular events (myocardial infarction, heart failure, stroke, sudden cardiac death) and their cumulative incidence during 11 years follow up period.

Patients and methods: This study includes 2352 ambulant and hospitalized patients with atrial fibrillation (AF) who were enrolled during the follow up period. All patients underwent clinical evaluation in order to determine cardiac and cerebrovascular events (myocardial infarction, heart failure, stroke, sudden cardiac death) and their cumulative incidence.

Results: The results of cumulative incidence for sudden cardiac death were 1.71%, for stroke 2.56%, for myocardial infarction 1.20% and for heart failure was 5.73%. In our study the age-adjusted incidence and prevalence of AF was slightly lower in women. The study shows that the risk of death was higher in females than in males with AF.

Conclusion: Despite good progress in the management of patients with atrial fibrillation (AF), this arrhythmia remains one of the major causes of stroke, heart failure, sudden death. Effective treatment of patients with atrial fibrillation includes not only rate control, rhythm control, and prevention of stroke, but also management of cardiovascular risk factors and concomitant diseases.

Introduction

According to the recent data, in the world 20.9 million men and 12.6 million women are suffering from this type of cardiac arrhythmia, in the next 15 years the number of patients with atrial fibrillation will be significantly increased due to the aging of population in developed parts of the world. Atrial fibrillation is considered as a main cause of cardiovascular morbidity worldwide. A lot of progress was made to avoid the fatal complications of this type of cardiac arrhythmia. In Bosnia and Herzegovina there is no accurate published data on how much this arrhythmia is represented and how much is responsible for death and disability in our population [1,2,3].

Research Objectives

The first objective of our study is to determine the cardiac and cerebrovascular events (myocardial infarction, heart failure, stroke, sudden cardiac death) and their cumulative incidence during median follow up period 9.7 ± 1.8 years (September 2006-September 2016).

Patients and Methods

This study includes 2352 ambulant and hospitalized patients with atrial fibrillation (AF) who were enrolled during median 9.7 ± 1.8 follow up period (September 2006 until September 2016). A complete medical

history was taken and all patients underwent clinical evaluation which includes thorough assessment for concomitant conditions, establishing the AF pattern, estimation of stroke, myocardial infarction, heart failure and sudden death risk. The AF was documented by 12-lead ECG or ambulatory ECG Holter recording. All patients were subjected to echocardiography to assess left atrial diameter and volume. In this study the following types of AF were included: newly diagnosed, paroxysmal, persistent and permanent AF. During the follow up period, cardiac and cerebrovascular events were evaluated (myocardial infarction, heart failure, stroke, sudden death) and their cumulative incidence.

Statistical analysis was conducted using statistical package IBM Statistics SPSS V23.0 (Chicago, Illinois USA), Baseline characteristics were summarized by mean and SD or frequency percents and assessed for trends across the calendar years of AF diagnosis, considered as a continuous variable. Cumulative incidence is calculated by the number of new cases during a period divided by the number of subjects at risk in the population, or all registered cases with AF during the observed ten-year period (N=2352).

Results

During the follow up period, we analyzed and follow up 2352 patients with ECG documented different type of atrial fibrillation in order to

evaluate the cumulative incidence of sudden death, stroke, myocardial infarction and heart failure. The demographic data, risk factors, clinical and comorbidity characteristics for all patients are shown on Table 1. The cumulative incidence of sudden death, stroke, myocardial infarction and heart failure is shown on Figure 1. The cardiovascular drugs used for rhythm control are shown on Table 2.

In our study among 2352 patients, AF was reported to be first detected in 352, paroxysmal in 194, persistent in 728, and permanent in 1078 patients. Concomitant diseases were present in 84% of all patients. Oral anticoagulation with VKAs was prescribed in 35% and NOACs in 44% of patients, respectively. A rhythm control strategy was applied in 63% of currently symptomatic patients and in 47% of patients who never experienced symptoms according to the ESC guidelines.

In our study the age-adjusted incidence and prevalence of AF were slightly lower in women. The study shows that the risk of death was higher in females than that in males with AF, the risk of stroke was higher also in women with AF. The risk of myocardial infarction in our study was higher in men, the study shows that the risk of heart failure was almost same in both gender.

During median follow up period 9.7 ± 1.8 years, the cumulative incidence for sudden cardiac death was 1.71%, for stroke 2.56%, for myocardial infarction 1.20 and for heart failure was 5.73%. Our study shows that the majority of patients with atrial fibrillation have mild to moderate enlargement of left atrium; more than half of patients have mildly-moderately reduced LV EF.

Table1: Baseline demographics and clinical characteristics

Variable	Overall	Cox and sex adjusted P-value	Hazard Ratio (\pm 95 % CI)
No. of patients (n = 2352)			
Age, years	68 \pm 13	< 0.001	1.028 (1.021 - 1.035)
Male, n (%)	1223 (52)	0.3562	1.074 (0.902 - 1.253)
BMI, kg/m ²	26 \pm 7	0.0266	1.009 (1.004 - 1.014)
Normal BMI, n (%)	729 (31)	0.0031	0.764 (0.637 - 0.894)
Overweight, n (%)	1035 (44)	0.2253	0.847 (0.702 - 0.990)
Obesity, n (%)	588 (25)	0.0054	1.314 (1.071 - 1.561)
Sedentary lifestyle	1082 (46)	0.2184	1.503 (1.252 - 1.754)
Family history of AF	643 (27)	< 0.001	1.465 (1.287 - 1.682)
Family history of CAD	729 (31)	< 0.001	1.543 (1.359 - 1.746)
Current or past smoker, n (%)	1341 (57)	0.1464	1.240 (1.188 - 1.296)
Alcohol consumption acute/chronic, n (%)	635 (27)	0.1546	1.206 (1.094 - 1.319)
Hypertension, n (%)	1788 (76)	0.0027	1.352 (1.151 - 1.553)
Angina/CAD, n (%)	917 (39)	0.6842	0.916 (0.763 - 1.069)
Heart Failure	641 (27)	0.1603	1.425 (1.293 - 1.557)
Valvular heart disease, n (%)	258 (11)	< 0.001	1.280 (1.057 - 1.505)
Diabetes mellitus, n (%)	517 (22)	0.1761	1.170 (0.898 - 1.379)
Dyslipidemia, n (%)	1388 (59)	0.4892	1.082 (0.862 - 1.304)
Chronic obstructive pulmonary disease, n (%)	612 (26)	0.0468	1.194 (0.586 - 1.857)
Peripheral vascular disease, n (%)	376 (16)	0.6852	1.054 (0.792 - 1.312)
Thyroid disease, n (%)	78 (3)	0.1583	1.206 (0.995 - 1.417)
Open heart surgery, n (%)	282 (12)	0.5124	1.240 (1.045 - 1.435)
Chronic kidney disease, n (%)	240 (10)	0.4981	1.165 (0.917 - 1.410)
Obstructive sleep apnea, n (%)	47 (2)	0.1573	1.521 (0.861 - 2.181)

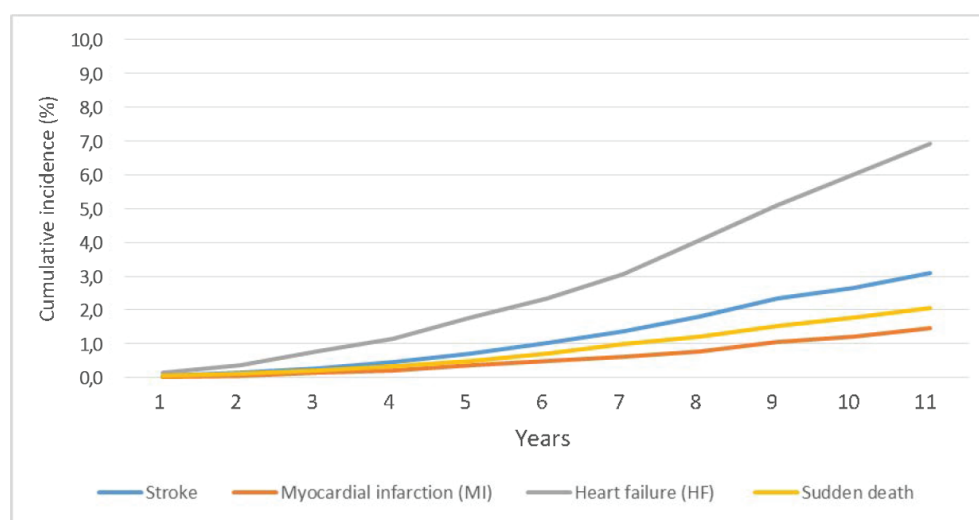


Figure 1: The cumulative incidence of stroke, MI, HF and SD during the follow up period

Table 2: Pharmacological therapy n (%)

Amiodarone	1324 (56)
Beta blockers	631 (27)
Calcium channel blockers	511 (22)
Digoxin	725 (31)
ACE-I/ARB	1084 (46)
Diuretics	1284 (55)
Alpha blockers	420 (18)
Nitrates	752 (32)
Statins	1657 (70)
Antiplatelet agents (Aspirin/Clopidogrel)	514 (22)
Anticoagulants (VKAs)	588 (25)
NOACs	447 (19)
Antidiabetics- oral	346 (15)
Insulin	171 (7)
Number of cardiovascular drugs (mean)	2,62 ± 1,84

Discussion

Atrial fibrillation is the most common arrhythmia in the general population, with a prevalence of 1.5-2%, which increases with age. In addition, it occurs more frequently in males, with a male to female ratio of 1.2:1. In 2010, the estimated numbers of men and women with AF worldwide were 20.9 million and 12.6 million, respectively, with higher incidence and prevalence rates in developed countries. One in four middle-aged adults in Europe and the US will develop AF. By 2030, 14-17 million AF patients are anticipated in the European Union, with 120 000-215 000 newly diagnosed patients per year. Given that AF is associated with significant morbidity and mortality, this increasing number of individuals with AF will have major public health implications [1,2,4-8].

In our study, the mean age of the patients was 68 ± 13 years; the males represent 52% of patients with AF. The published studies also have reported a predominance of males (generally around 60%), the mean age of the patients in most reports is between 65 and 70 years, which is comparable to the mean age of our population [9,10].

In our study, family history of CAD was present in 31% of patients with AF, [HR 1.543 (CI 1.359-1.746)], also CAD was found in 39% of patients [HR 0.916 (CI 0.763-1.069)], which is in consistent with the results of published studies. Viola F et al. In their investigation they searched MEDLINE via PubMed and Cochrane database between 1965 and 2015. All observational clinical studies and interventional trials reporting 1-year incidence of MI in AF were included. The main conclusion was that AF patients had a significant residual risk of MI despite anticoagulant treatment [11].

Echocardiography provides vital information about cardiac chambers and function, complications, and prognosis in patients with AF. This information may be helpful in determining the conditions associated with AF, the risk for recurrent AF following cardioversion, and the hemodynamic benefit of maintaining sinus rhythm, also identification of patients at increased risk for thromboembolic complications of AF before cardioversion and in patients with chronic AF [3,12-15].

In the reviewed literature, the prescription of oral anticoagulation on hospital discharge was also lower in patients with paroxysmal vs. permanent AF (51 vs. 80%, 55 vs. 74%, 78 vs. 91%). In a Swiss registry of outpatients with AF seen by cardiologists, prescription of anticoagulants reached 88% in patients with a CHADS2 score ≥ 1 . However, 57% of the patients with a score of zero also received anticoagulants [16-27].

During median follow up period 9.7 ± 1.8 years, the cumulative incidence for sudden cardiac death was 1.71%, for stroke 2.56%, for

myocardial infarction 1.20 and for heart failure was 5.73%. The cumulative incidences of stroke, myocardial infarction, heart failure and sudden cardiac death are similar to those in published studies and meta-analysis [28,29]. The published studies shows the following cumulative incidence for stroke 5-7.5%, MI 0.4 - 2.5%, heart failure 6 - 35% [1,2,4,5,8,9,11,24,30].

In our study, the most prescribed and used drugs for rhythm control were Amiodarone 56%, followed by digitalis 31% and beta-blockers 27%. The same drugs were used in other published studies. Lafuente-Lafuente C et al. They performed a systematic review to determine the effect of long-term treatment with those drugs on death, embolisms, adverse effects, and atrial fibrillation recurrence. Forty-four trials were included, with a total of 11 322 patients. They conclude that Class IA, IC, and III drugs are effective in maintaining sinus rhythm but increase adverse effects, and class IA drugs may increase mortality [31].

Krijthe BP et al. they calculate projections on the number of individuals with AF in the European Union from 2010 to 2060 using the information collected in the community-based prospective cohort study: The Rotterdam Study. They estimate that the number of adults 55 years old and over with AF in the European Union will be more than double. As AF is associated with significant morbidities and mortality, this increasing number of individuals with AF may have major public health implications [32-36]. In other systematic review by Wolowacz S.E. et al. for the economic burden of AF, hospitalizations consistently represented the major cost driver. In the USA, AF hospitalizations alone cost \$6.65 billion in 2005. Costs and hospitalizations attributable to AF have increased markedly over recent decades and are expected to increase in future due to ageing populations [37].

Conclusion

Despite good progress in the management of patients with atrial fibrillation (AF), this arrhythmia remains one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world. AF is associated with a 4-fold increase in the risk of stroke, 3-fold increase in the risk of heart failure, and 1.5-1.9 increased risk of death. AF is known to have a significant impact on healthcare costs, with the major cost drivers being hospitalizations, stroke, and loss of productivity. Atrial fibrillation should be considered as a manifestation of hypertensive heart disease. Effective treatment of patients with atrial fibrillation includes not only rate control, rhythm control, and prevention of stroke, but also management of cardiovascular risk factors and concomitant diseases.

Study limitations

1. We didn't have IBR approval or patient's consents; the data was collected from outpatient's medical records and regular visits to the cardiologist and from hospital discharge reports and hospitals data base.
2. Unfortunately, in the last 2 decades despite several attempts to establish the laboratory for electrophysiological studies (EPS) and AF ablation, until now we don't have such one. So, we are not able to perform AF ablation. In the last 2 years, several medical centers have cooperation with experts in EPS from Norway and neighbor countries for education and training of young cardiologists for EPS and we hope that we will have soon our lab for EPS.
3. During this study we didn't have subgroup analysis to compare all the outcomes in rate control vs rhythm control due to the reason mentioned above, also we don't have data about difference in outcomes between VKA and NOCA drugs. The NOCA drug Rivaroxaban was registered in Bosnia and Herzegovina before several years.

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