Predictors of treatment failure in recurrent atrial fibrillation

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ABSTRACT

Introduction: Atrial fibrillation (AF) is the most frequent cardiac arrhythmia. Yet, it is questionable whether long-term maintenance of sinus rhythm (SR) is really possible.

Objectives: The present study investigates the independent predictors of treatment outcome in patients who had recurrent AF during last 1 to 30 years.

Material and Methods: In a group of 43 pts (mean age 58.1 ± 10.6 years, 32 males), with recurrent episodes of AF, we analysed potential independent predictors of treatment efficacy after follow up of 1 to 9 years, mean 3.6 ± 2.2 years. Analysis was performed using multiple regression statistical method.

Results: At the end of study 35/43 pts (81.4%) were in permanent AF because of either unsuccessful cardioversion (18 pts) or development of chronic AF refractory to treatment (17 pts), while only 8/43 pts (18.6%) retained sinus rhythm with or without repeated conversions (11.6% and 7% respectively). Multiple logistic regression model with dependent variable "outcome of treatment" and independent variables age, gender, AF duration (48 hours to 108 months, mean 8.5 months), lone AF (16 pts), cardiac diseases (26 pts), noncardiac diseases (9 pts), any disease at all (27 pts) and echocardiographically documented left atrial enlargement (left atrial diameter >40 mm, 27 pts) identified presence of any disease (relative risk 51) and AF duration over 48 hours before cardioversion (relative risk 88), with 95% CI, as independent predictors of permanent atrial fibrillation.

Discussion: It appeared that only 19% of pts may be successfully treated by maintenance of SR during period longer of several years. Underlying disease and arrhythmia duration exert powerful impact on long term outcome of these pts.

Conclusions: Since presence of any disease and arrhythmia duration independently predicts the risk of permanent AF in patients with recurrent arrhythmia, these patients should be treated by the most effective antiarrhythmics (i.e. amiodarone) or frequency control strategy should be employed.

INTRODUCTION

During the last few decades it became clear that treatment of atrial fibrillation is mandatory, since the risk of thromboembolic events, left ventricular dilatation and/or heart failure is significantly increased in patients with this arrhythmia. The exercise tolerance and overall quality of life are significantly decreased in these patients. Moreover, atrial fibrillation may independently increase mortality up to 2 times [1,2]. Restoration and maintenance of sinus rhythm (i.e. rhythm control) have been considered, for a long time, as therapy of choice for patients with atrial fibrillation, while ventricular frequency control in permanent atrial fibrillation has been recognized as treatment failure. However, recent studies, such as AFFIRM, RACE and PIAF, showed that rhythm control has no advantage in comparison to ventricular frequency control. Indeed, complications were more frequent in the rhythm control study groups [3,4]. Although these surprising results were criticized shortly after publishing, the fact is that rhythm control has already lost some of its previous superiority and the question who are the suitable patients for rhythm control strategy remains open. Obviously, if the failure of treatment with rhythm control could be anticipated with reasonable probability, such patients would be assigned to frequency control therapy from the very beginning.

OBJECTIVES

Present study investigates the possible independent clinical and echocardiographic predictors of treatment outcome in patients who had recurrent atrial fibrillation during last 1 to 30 years and who were assigned to rhythm control therapeutic approach.

MATERIAL AND METHODS

In a group of 43 patients with recurrent paroxysmal and/or persistent atrial fibrillation, documented by electrocardiography and/or by 24-hour Holter monitoring of cardiac rhythm, we analyzed the presence of
potential baseline independent clinical and echocardiographic predictors of treatment efficacy. Successful treatment was defined as maintenance of sinus rhythm for at least 1 year, with repeated cardioversion if needed. Relevant clinical features (age, gender, the duration of atrial fibrillation at the beginning of the study, the total time from first episode of atrial fibrillation in a lifetime, the presence of cardiac and/or noncardiac diseases) and routine transthoracic echocardiographic parameters (left atrial anteroposterior diameter and left ventricular ejection fraction calculated by Teicholz formula) were registered at the beginning of follow up, which lasted 1 to 9 years, mean 3.6±2.2 years. Left atrium was classified as dilated if anteroposterior diameter was greater than 40 mm, and left ventricular ejection fraction was considered to be normal if greater than 54%. All patients have already had at least one episode of atrial fibrillation before enrollment.

Patients with recognizable acute causes of atrial fibrillation (i.e. hyperthyreosis, acute myocardial infarction, acute myocarditis and/or pericarditis, acute heart failure, recent heart or other thoracic surgery) as well as patients with permanent pace makers, heart conduction system disorders, significant valvular heart disease or Syndrome Wolff-Parkinson-White were not included in the study. After detailed clinical and echocardiographic assessment at the beginning of the study, each patient was assigned to appropriate antiarrhythmic agent for rhythm control, according to current ESC/AHA/ACC Guidelines for diagnosis and management of atrial fibrillation [5]. Patients with normal left ventricular systolic function received class IC (propafenone, flecainide) or class III (sotalol) agents, while amiodarone was administered to patients with significant left ventricular systolic dysfunction and to patients with frequent recidivant atrial fibrillation. Class IA (dysopiramide and quinidine) agents were used rarely, for a small number of patients with evidence of vagotonic atrial fibrillation. During the follow up each patient underwent regular detailed clinical examination once in 2 to 3 months and control echocardiographic examination was performed at least once per year.

Database was recorded in Microsoft Excel 97 programme and analysis were performed using SPSS (Statistical Package for Social Sciences). The statistical significance of difference between continuous variables was assessed by Student’s t-test, while noncontinuous variables were compared by Chi-square test. Independent predictors of treatment outcome were identified by multiple regression statistical method, within 95% Confidence Interval.

RESULTS
Mean age of study group was 58.5±10.6 (21 to 75) years. There were 11 females (25.6%) and 32 males (74.4%). Atrial fibrillation, at the beginning of the study, lasted 48 hours to 108 months (mean 8.5 months). The total time from the first episode of atrial fibrillation was 12 to 360 months (mean 125.9±88.3 months). Lone atrial fibrillation was present in 16 patients (37.2%), cardiac diseases in 26 patients (60.5%), noncardiac diseases in 9 patients (20.9%) and any disease at all were noted in 27 patients (62.8%).

cho cardiographically documented left atrial enlargement was present in 27 patients (62.8%), while left ventricular ejection fraction was normal in 29 patients (67.4%).

At the end of the study, after the follow up of 1 to 9 years (mean 3.6±2.2 years), permanent atrial fibrillation was evident in 35 patients (81.4%) either because of unsuccessful cardioversion (18 patients), or because of development of chronic atrial fibrillation refractory to treatment (17 patients). Only 8 patients (18.6%) retained sinus rhythm, with or without repeated cardioversions (11.6% and 7%, respectively).

Multiple logistic regression model with dependent variable “outcome of treatment” (i.e. permanent atrial fibrillation at the end of the study) and independent variables age, gender, duration of atrial fibrillation, the total time from the first episode of atrial fibrillation, lone atrial fibrillation, cardiac disease, noncardiac disease, any disease, left atrial diameter and left ventricular ejection fraction identified presence of any disease (Relative risk 51, lower 3.0, higher 60.4, p=0.029), atrial fibrillation lasting more than 48 hours before cardioversion (Relative risk 88, lower 2.0, higher 90.3, p=0.019) and the total time from first atrial fibrillation (Relative risk 1.1, lower 0.97, higher 1.50, p=0.050).

DISCUSSION
Earlier epidemiological studies have documented that after successful cardioversion of atrial fibrillation only approximately one-quarter of patients will retain sinus rhythm at one year if no additional therapy is used [6]. On the other side, there are plenty of studies that have assessed and compared the efficacy of various antiarrhythmic agents in maintenance of sinus rhythm after conversion of atrial fibrillation. Nowadays it is well known that amiodarone is the most successful agent, with efficacy reported to be as high as 90%, while other antiarrhythmic drugs exert efficacy between 40% and 60% [7]. But, most of these studies deserve serious criticism. Since the main end point of these studies usually was the evaluation and proofing of drug efficacy, patients selection was carefully adjusted to end point. Furthermore, the usual follow up lasted 6 to 12 months, rarely longer than few years. The question how long sinus rhythm may be maintained using therapy...
As appeared in our study, only 19% of patients with atrial fibrillation may be successfully treated by maintenance of sinus rhythm during period longer than several years, even when the various antiarrhythmic drugs and serial cardioversions are implemented. The majority of patients, as much as 81%, will finally experience the development of permanent atrial fibrillation after approximately 10 to 20 years of fighting with recurrent arrhythmia. But, for patients in their third or forth decade of life this period may be the most productive part of their lives, making it worthwhile to attempt to restore and to maintain sinus rhythm as long as possible.

According to our results, presence of any disease and arrhythmia duration longer than 48 hours prior to cardioversion exert powerful impact on long-term outcome of patients with atrial fibrillation, meaning that otherwise healthy persons have the best chances to maintain sinus rhythm for a long time if treatment is started shortly after beginning of atrial fibrillation. These findings are concordant to results of other authors. It is well known that various cardiovascular diseases, such as arterial hypertension, coronary heart disease, dilated cardiomyopathies with left ventricular systolic dysfunction and heart failure and valvular heart disease, may predispose to atrial fibrillation and may influence the success rate of rhythm control therapeutic approach. Some noncardiac disorders, such as diabetes mellitus, hiatus hernia, obesity etc. may have significant influence, as well [8].

The duration of atrial fibrillation before cardioversion has been most consistently proofed to independently predict the risk of recurrence of atrial fibrillation. A cut-off of one year duration of atrial fibrillation has been widely accepted as indicator of low probability of long-term success in maintenance of sinus rhythm [6,9]. However, atrial fibrillation in current era rarely lasts that long before the treatment is introduced. The usual duration of arrhythmia, as reported in majority of studies, varies from several weeks to few months. According to our results, the treatment should begin even earlier, within the first 48 hours of arrhythmia.

Finally, our results showed that total time from the very first episode of atrial fibrillation also independently predicts the long-term outcome of treatment. In other words, if the patient already have had atrial fibrillation in the past, independently of whether arrhythmia have been treated or not, the probability of development of permanent atrial fibrillation is higher. The longer the total time, the higher the risk of permanent atrial fibrillation. We could not find comparable data when we reviewed the published literature. This finding may be explained by left atrial electrical and mechanical remodeling as a consequence of atrial fibrillation.

The assessment of risk for development of permanent atrial fibrillation in patients with recurrent paroxysmal and/or persistent arrhythmia is very important, since the treatment by rhythm control includes the out-of-hospital, long-term use of various antiarrhythmic drugs with possible serious side effects. The proarhythmic effect of these drugs may be unpredictable and may cause a sudden cardiac death [10].

CONCLUSIONS
Since presence of any disease, the duration of atrial fibrillation prior to cardioversion, as well as the total time from the very first episode of atrial fibrillation independently predicts the risk of permanent atrial fibrillation in patients with recurrent arrhythmia, these patients should treated by the most effective antiarrhythmic agents (i.e. amiodarone) or frequency control strategy should be employed.

BIBLIOGRAPHY

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