

# Atrial Fibrillation: A Negative Prognostic Factor for Patients with Dilated Cardiomyopathy

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## Abstract

The dilated cardiomyopathy (DCM) is a myocardial disease characterized by a dilated left ventricle (LV) and an impaired systolic function of the left ventricle. Most common secondary DCM is ischemic, but severe uncorrected valvulopathies also can lead to the enlargement of LV due to volume or pressure overload. In almost half of DCM patients, the etiology remains unknown. The dilated cardiomyopathy will lead to a progressive, irreversible heart failure, despite the big progressions made in both medical treatment and heart assisting devices. Atrial fibrillation (AF) is a commonly seen arrhythmia in patients with dilated cardiomyopathy, due to the structural modifications of left atrial myocytes.

The objective of this study is to observe the impact of the association between dilated cardiomyopathy and atrial fibrillation on the severity of heart failure. For this purpose, 139 patients were taken into observation, from the moment of their emergency hospitalization for heart failure, and were followed for a year. At baseline, 64 patients (46.04%) had permanent atrial fibrillation, and the rest of 75 (53.96%) were in sinus rhythm. From all patients, 70.5% (98) were men, the incidence of DCM being greater in men than women. Patients with AF were older, required prolonged hospitalization, had Lower Left Ventricle Ejection Fraction (LVEF), greater New York Heart Association (NYHA) class and more frequently associated right ventricle disfunction (RV).

**Keywords:** Dilated Cardiomyopathy • Atrial Fibrillation • Heart Failure • Prognosis

## Introduction

The dilated cardiomyopathy is one of the most common causes of heart failure in adult patients, and it is known to be main indication for heart transplant in adults and children [1]. Depending on its etiology, there are two types of dilated cardiomyopathy: primary, that involves a large panel of genetic mutations in myocardial cells, and secondary, caused by infiltrative and inflammatory systemic diseases, neuromuscular diseases, cardiotoxic medication, endocrine diseases, valvulopathies and ischemic heart diseases [2]. Sixty percent of DCM is caused by ischemic heart disease in all of its forms [3]. Secondary dilated cardiomyopathies are the result of cardiac muscle remodeling, due to hypoxia, volume or pressure overload, which leads to systolic function impairment and left ventricle dilatation [4]. One of the controversial causes of left ventricle impairment is septic shock, the complete mechanism is still to be studied [5]. The left ventricle remodeling process leads to the damage of the ultrastructure of left atrial myocytes and therefore, to its progressive enlargement. This results in the development of multiple re-entry circuits that eventually takes to the apparition of atrial fibrillation [6]. Because of the impact that DCM has on the patient quality of life, and the reserved prognosis of chronic heart failure (HF), a series of negative predictive factors for mortality were observed, such as: older age, Pulmonary Arterial Hypertension (PAH), NYHA class III and IV, decreased dp/dt on mitral regurgitation, prolong

QT interval, unsustainable ventricular tachycardia, very low left ventricle ejection fraction, and the onset of atrial fibrillation. AF is associated with the progression of chronic heart failure and increased mortality in all types of cardiomyopathies [7].

Atrial fibrillation is the most frequent encountered arrhythmia, and its prevalence increases with age. Multiple population-based studies have shown that patients with permanent atrial fibrillation have an increased mortality risk [8], mostly because of the cardio-embolic complications.

Chronic heart failure is a major public health problem, with a difficult evolution and a reserved prognosis, despite the development of new treatment regimens. Permanent atrial fibrillation is a common complication of dilated cardiomyopathy that leads to a decreased cardiac output because of the deficient filling of the ventricles in atrial systole. The result of this mechanism is worsening symptoms of heart failure, up to rest dyspnea and pulmonary edema. Earlier studies have shown that patients with permanent atrial fibrillation have significantly reduced myocardial perfusion reserve and increased coronary resistance in nonischemic DCM [9]. The use of beta-blockers in patients with heart failure appears to be effective in the prevention of atrial fibrillation [10]. A meta-analysis that followed the preventive role of Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARB), showed a lower prevalence of atrial fibrillation in patients receiving either of this drugs, but the effect appears to be limited to patients with systolic left ventricular dysfunction or LV hypertrophy [11].

Through this observational study, it was evaluated the hemodynamic impact of atrial fibrillation in patients with dilated cardiomyopathy and observe to what extent the patient's symptoms are affected due to the occurrence of this supraventricular arrhythmia. Our objective is to establish a negative correlation between DCM and AF, and atrial fibrillation as an individual risk factor for patients with dilated cardiomyopathy.

## Materials and Methods

For the purpose of this study, 139 patients diagnosed with dilated

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cardiomyopathy in different chronic heart failure stage have been taken into consideration, divided in two groups, depending on the presence or absence of AF at presentation. 64 (46.04%) of the patients had permanent atrial fibrillation at enrolment. In the AF group, 46 (71.87%) of patients were male and 18 (28.13%) were female, of 60 ± 15 age. DCM diagnosis was based on the echocardiographic 2D assessment of left ventricular ejection fraction, volume and dimensions. Atrial fibrillation was objectified on 12-leads electrocardiogram. Patient's symptoms were quantify using the New York Hearth Association (NYHA) classification. Patients with other types of arrhythmias besides permanent atrial fibrillation have not been included in the present study. All the patients received standard heart failure treatment (beta-blockers, ACEI or ARB, diuretics). It was observed, through this study, the decline of left ventricular ejection fraction and increase NYHA functional class under the influence of atrial fibrillation in patients with dilated cardiomyopathy.

**Statistical analysis**

Numerical values of variables were expressed as mean ± standard deviation (SD). Were used frequency tables; tests: Chi square, Fisher (for 2 qualitative variables) tests: Student, Mann-Whitney, ANOVA (for a qualitative variable and one quantitative). Univariate statistical analysis, multiple logistic regressions was performed using the program STATISTICA 8.0. All parameters studied were included in multiple logistic regressions. Results were considered statistically significant if p <0.05.

**Results**

The clinical evaluation of the patients allowed the assessment of the severity of symptoms, with the help of NYHA functional class. At baseline, 64 patients (46.04%) had permanent fibrillation and had ongoing anticoagulation treatment. In our patient lot, the predictive factors for atrial fibrillation were observed to be the presence of moderate to severe mitral regurgitation, the presence of pulmonary atrial hypertension, dilated left atrium and age. Compared to sinus rhythm patients, AF patients did not differ in LV dimensions, but the left atrium and right ventricle were significantly larger.

It was observed that the number of patients with dyspnea at rest (NYHA class IV) has been double in the permanent atrial fibrillation group. In addition, it was also observed that in one third of DCM patients without arrhythmias, dyspnea appears after sustaining a mild effort (NYHA II). Patients distribution according NYHA class revealed significant differences between groups (p=0.02) (Figure 1).

The left ventricular ejection fraction was measured thought echocardiography in M mode, using the Teicholtz method, and in 2D mode, using Simpson method. It can be observed that there is a significant increase in the number of patients with severe dysfunction of the left ventricle (LVEF ≤ 20%) among the patients with permanent atrial fibrillation (21.88%). The percentage of patients with mild left ventricular dysfunction increases (37.34%) in patients who did not develop this rhythm disorder (p=0.04) (Figure 2). Furthermore, patients with atrial fibrillation associated with dilated cardiomyopathy, require a prolonged hospitalization in order to treat acute decompensation and develop more frequently a moderate/severe pulmonary hypertension.

The adverse prognostic factors for patients with dilated cardiomyopathy were: older age, NYHA class III or IV, the presence of pulmonary stasis, pulmonary hypertension, increased uric acid and NT-proBNP, significant left ventricle dilation and a low ejection fraction. It was observed that these parameters are more frequent in patients with atrial fibrillation (Figure 3).

**Discussion**

Idiopathic dilated cardiomyopathy is a rare heart disease that affects the myocardium and it is mostly diagnosed between the age 20 and 50 [12]. However, secondary DCM appears in older patients, due to long time evolution of other heart conditions. If in idiopathic DCM the first manifestation is hearth failure, in secondary etiology, patients experience the symptoms of the baseline heart disease, and heart failure as the final stage.

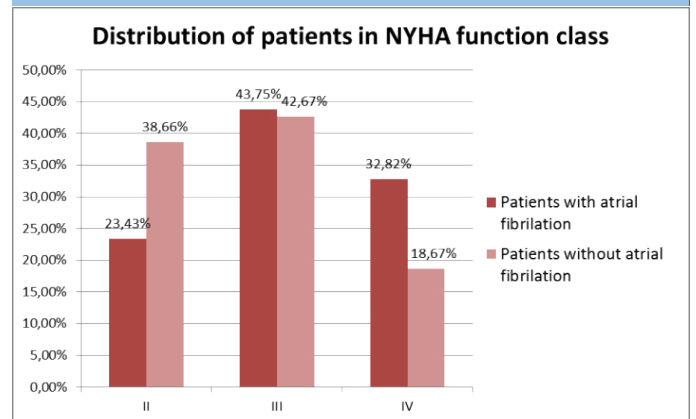
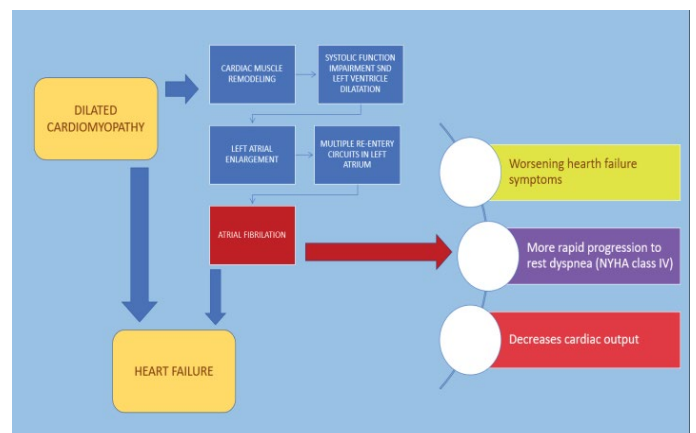


Figure 1. Distribution of patients in NYHA function class.

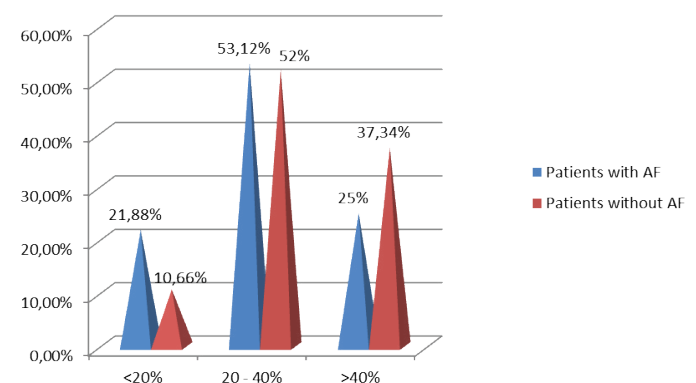


Figure 2. Distribution of patients considering left ventricular ejection fraction.

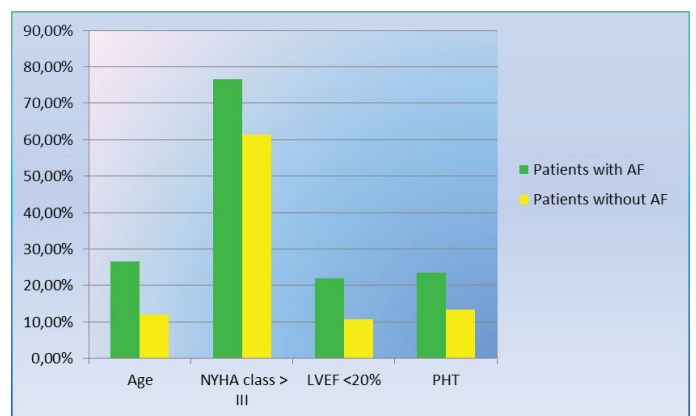


Figure 3. Negative prognostic factors.

Atrial fibrillation is the most common sustained arrhythmia, and it is expected that its prevalence will increase rapidly, because longer survival

heart disease, and the important development of medical therapies and heart sustaining devices. The Framingham study claims that 5% of patients that reach the age of 70 have atrial fibrillation, and it is doubled with every decade [13]. Atrial fibrillation, through its disabling thromboembolic complications, such as stroke, has a very important economic and social impact, which is why it is important to study the risk factors that lead to its occurrence and find methods to prevent it or post-pone it. A meta-analysis from 2009 is supporting the protective role of statins in atrial fibrillation development [14].

It was observed that new-onset atrial fibrillation complicating an acute decompensation of heart failure was associated with the highest risk for adverse complications, such as stroke [15]. Individual risk factors for developing AF are: old age and male gender, as well as high body mass index, high blood pressure, and previous cardiovascular disease [16].

Every time the human body is changing its position from supine to orthostatic position, an amount of blood volume is displaced. The inotropic and chronotropic functions of the heart muscle make this phenomenon unnoticeable. The cardiovascular system adjusts to the changing of body position with the help of baroreceptor reflexes and the activation of cardiac mechanoreceptors. In an ischemic myocardium, the mechanoreceptors are dysfunctional, leading to a delayed adjustment to postural change. Autonomic nervous system dysfunction is often seen in heart failure patients [17]. This leads to an increased sympathetic nervous system stimulation, and a reduction of vagal activity. The reduction of the left ventricle ejection fraction in dilated cardiomyopathy leads to an increased end-diastolic volume, and the increase of all inotropic hormones. This process translates into an increase of sympathetic nervous system tonus and therefore, to the worsening of the adjustment to volume displacement. The dysfunction of the myocardial response to the stimulation of cardiac mechanoreceptors occurs due to the maladaptive remodeling from all dilated cardiomyopathies, and inhibits the adjustment to volume displacement.

In our group of patients, who suffered of DCM and heart failure, nearly half (46.04%) had permanent atrial fibrillation. This data is consistent with the finding of other earlier study, which claimed that atrial fibrillation is a common complication of DCM, and that its rapid treatment and conversion to sinus rhythm is essential [18-20].

A German study published in 2003 in *Circulation* [21] claims that atrial fibrillation is most likely to develop in patients with lower LVEF that are not treated with beta-blockers. In the observed patient sample, we found that the number of patients with AF is double in the subgroup with LVEF lower than 20%. One of the most important negative prognostic factor is the progression of heart failure to NYHA class III or IV, and AF induces a more rapidly progression to severe heart failure. Our study supports this information, more than two thirds of the patients with AF had NYHA III and IV heart failure [22].

The appearance of atrial fibrillation in a dilated, insufficient heart is associated with a low survival rate at 5 years [23]. In the present observational study, the incidence of negative vital prognostic factors (older age, NYHA > III, FEV5 < 20%, PHT) were more frequently found in the group with AF. The same patients had worse stage heart failure, were hospitalized more often and more prolonged.

A sub-group from the COMMET trial, that was observing the prognostic impact of AF in heart failure patients who were treated optimal medical HF treatment (ACE/ARB, beta-blockers, diuretics) found that the presence of AF at baseline was associated with more severe symptoms, longer duration of heart failure, and a 28% increased risk of death. However, the presence of AF did not independently predict all-cause mortality [24].

The CHARM trial showed that the presence of atrial fibrillation at baseline is associated with an increased risk of morbidity and mortality in patients with symptomatic heart failure regardless of baseline ejection fraction of left ventricle. For patients with preserved left ventricle ejection fraction, AF seem to have a greater negative impact, absolute risk levels being as high as those for patients with CHF and low EF who are in SR [25].

## Conclusion

In our cohort, the prevalence of atrial fibrillation was 46.04%, and all patients received standard heart failure treatment. After one year follow-up, we observed that systolic left ventricle dysfunction was aggravated in patients with permanent atrial fibrillation and NYHA class progresses further after the appearance of this supraventricular tachyarrhythmia. When conversion to sinus rhythm is attempted and succeeded, HF symptoms are improved; therefore, conversion should always be in question. We can conclude that atrial fibrillation is an individual factor for negative prognostic in dilated cardiomyopathy.

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