# Atrial Fibrillation in the Structural Heart Disease Population

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Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. Patients with structural heart disease (SHD) are at an increased risk of developing this arrhythmia and are particularly susceptible to the deleterious hemodynamic effects it carries. Catheter ablation (CA) has emerged as a valuable strategy for rhythm control and is currently part of the standard care for symptomatic relief in patients with AF.

Keywords: atrial fibrillation ; structural heart disease ; patients

# 1. Introduction

Atrial fibrillation (AF) is the most prevalent arrhythmia in clinical practice <sup>[1]</sup> and it is even more frequent in patients with structural heart disease (SHD) <sup>[2]</sup>.

SHD encompasses a heterogeneous group of patients that share some important features, whatever the underlying disease. First, they are characterized by reduced hemodynamic tolerance to elevated heart rates and/or to the loss of atrial contribution to left ventricle (LV) filling, which are associated with atrial fibrillation (AF); second, in this population, the choice of anti-arrhythmic drugs (AADs) is limited, owing to possible side-effects; and third, the probability of rhythm control success on AADs is lower than in non-SHD patients <sup>[3]</sup>. Additionally, structural heart disease (SHD) patients are less represented in large clinical trials on AF catheter ablation (CA); therefore, except for a suggested higher recurrence rate <sup>[4]</sup>, little evidence is available concerning interventional management of these patients.

The purpose of this research is to briefly review the clinical knowledge on interventional treatment of AF in this population.

#### **Structural Heart Disease Definition**

"Structural heart disease" (SHD) is an over-reaching term first introduced by Martin Leon at the 1999 Transcatheter Cardiovascular Therapeutics Meeting to encompass all cardiac disease processes <sup>[5]</sup>.

The European Society of Cardiology (ESC) guidelines identify AF as secondary to SHD when a left ventricle (LV) systolic or diastolic dysfunction is demonstrated or LV hypertrophy, valvular disease, and/or other SHDs are documented <sup>[6]</sup>. Subsequent literature evolved the nomenclature so that, currently, SHD includes: (a) heart failure with reduced ejection fraction (HFrEF, previously severe or moderate LV systolic dysfunction); (b) heart failure with preserved ejection fraction (HFpEF, previously LV diastolic dysfunction); (c) valvular heart disease (VHD), ranging from prosthetic valves to rheumatic ones; and (d) specific cardiomyopathies, such as hypertrophic cardiomyopathy (HCM) <sup>[Z]</sup>.

According to the ESC Guidelines definition, criteria to identify SHD patients are based on non-specific parameters [I]. Thus, the SHD impact on AF prevalence and patient's prognosis could be different according to the underlying pathology and the severity of the disease.

In studies dealing with AF, specific biomarkers to assess hemodynamic status (e.g., natriuretic peptides) are rarely available and seldom reported and the degree of atrial remodeling is not uniformly defined because of the use of different parameters and imaging techniques (e.g., echocardiography or magnetic resonance).

# 2. Impact of Structural Heart Disease on Atrial Fibrillation

Independently of the underlying disease, a common final pathway is supposed to lead to AF: elevated left atrial pressure, causing "atrial myopathy" <sup>[8]</sup>. Indeed, atrial hypertension is associated with chamber dilation, extracellular matrix

remodeling, autonomic imbalance, and calcium handling defects, which have a well demonstrated proarrhythmic effect and are involved in the induction and maintenance of AF [9][10].

The actual incidence and prevalence of AF in the overall SHD population have not been assessed, but data are available for specific subgroups.

# 2.1. Heart Failure with Reduced Ejection Fraction

In 2003, Maisel estimated that the AF prevalence ranges from <10% in New York Heart Association (NYHA) functional class I patients to nearly 50% in NYHA IV patients. Overall, HF patients have a sixfold increased risk of AF in the long term <sup>[11]</sup>.

Both AF and HF have a higher prevalence in the elderly, and this might partially explain the correlation between the degree of functional impairment and the occurrence of AF. Nevertheless, there are several pathophysiological reasons for why they are supposed to favor each other, leading to the concept that "AF begets HF and vice versa" <sup>[12]</sup>.

In particular, myocardial inflammation and fibrosis, leading to atrial interstitial fibrosis, are present in both AF and HF. Thus, during exertion, AF itself could be less tolerated in HF patients and, thereby, may trigger clinical recognition of this condition.

In a sample from the Framingham cohort including data between 1980 and 2012, it was found that a greater proportion of individuals have AF without HF, and AF more commonly precedes HF than in cohorts studied in previous years <sup>[12]</sup>. However, different strategies to detect AF have been implemented over time, making these results hardly comparable. Regarding the temporal relationship between AF and HF onset, it has been noted that patients who develop HF first and AF later have a worse clinical progression compared with the opposite <sup>[13]</sup>.

# 2.2. Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction (HFpEF) often coexists with other cardiac diseases; thus, it might be difficult to isolate its specific effect. Diastolic dysfunction should be graded according to American Society of Echocardiography recommendations and the evaluation should be based on parameters that are not affected by the presence of AF <sup>[14]</sup>.

In a population study by Chen et al., one-third of patients with isolated diastolic dysfunction and HF-related symptoms show AF in the ECG presentation <sup>[15]</sup>.

In a longitudinal study by Tsang and colleagues, abnormal LV diastolic function is associated with new onset of AF in almost 10% of cases within 4 years. In particular, the presence of grade 2 or 3 diastolic dysfunction was associated with a 2.5-fold increase in AF recurrence risk when compared with grade 1 dysfunction or normal diastolic function <sup>[16]</sup>.

## 2.3. Valvular Heart Disease (VHD)

The presence of rheumatic mitral stenosis, repaired mitral valve or prosthetic valve are three different conditions. The presence of just one of the three is sufficient to distinguish valvular and non-valvular AF  $^{[17]}$ .

In 1990, data from surgical series were published by Wipf et al., who reported an AF prevalence close to 75% in rheumatic heart disease (RHD) at the time of surgical treatment <sup>[18]</sup>. In addition, in early studies on patients treated with AAD, AF frequently complicated RHD, with more than 30% of patients with AF episodes over long-term follow-up <sup>[19]</sup>.

Even if a decline in RHD prevalence was recorded in Western countries, the presence of a valvular heart disease is still associated with a 1.8-3.4-fold increased risk for AF <sup>[20]</sup>, and mitral stenosis and mechanical prosthetic valves are associated with a further increase in thromboembolic risk <sup>[21]</sup>.

## 2.4. Cardiomyopathies

Hypertrophic cardiomyopathy (HCM) is the most common hereditary cardiomyopathy <sup>[22]</sup>, and thus the best investigated. The estimated prevalence of AF in HCM is 22.5% and the annual incidence is 3.1% <sup>[23]</sup>.

The maintenance of sinus rhythm could be of a particular importance in HCM patients, as this is associated with a significant improvement in the New York Heart Association functional (NYHA) class and quality-of-life score <sup>[24]</sup>. These benefits seem to depend on heart rate control and atrial active contraction, which increase the LV filling, reducing outflow obstruction.

Furthermore, dyspnea and other heart failure symptoms are frequently associated with AF, which is a major cause of hemodynamic deterioration and an ominous prognostic indicator <sup>[24]</sup>.

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