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# Atrial Fibrillation and Heart Failure — Cause or Effect?

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There are emerging epidemics of atrial fibrillation (AF) and heart failure in most developed countries, with a significant health burden. Due to many shared pathophysiological mechanisms, which facilitate the maintenance of each condition, AF and heart failure co-exist in up to 30% of patients. In the circumstance where known structural causes of heart failure (such as myocardial infarction) are absent, patients presenting with both conditions present a unique challenge, particularly as the temporal relationship of each condition can often remain elusive from the clinical history. The question of whether the AF is driving, or significantly contributing to the left ventricular (LV) dysfunction, rather than merely a consequence of heart failure, has become ever more pertinent, especially as catheter ablation now offers a significant advancement over existing rhythm control strategies. This paper will review the inter-related physiological drivers of AF and heart failure before considering the implications from the outcomes of recent clinical trials in patients with AF and heart failure.

**Keywords** 

Atrial fibrillation • Heart failure • Cardiomyopathy • Myocardial fibrosis • Catheter ablation • Pathophysiology

### Introduction

There are rising epidemics of atrial fibrillation (AF) and heart failure in developed countries around the world, and Australia is no exception [1]. The prevalence of AF in Australia in those older than 55 years is 5.4%, projecting to 6.4% by 2034, equating to more than 600,000 Australians. Similarly, the health burden from heart failure continues to increase. It affects roughly 2% of the population, with a three-fold higher incidence in the elderly [2]. Atrial fibrillation and heart failure frequently coexist, given there are physiological mechanisms common to both. In the Framingham Heart Study, over 38 years of follow-up, heart failure was the strongest predictor of incident AF, conferring a six- to eight-fold increase in the incidence of AF, with an attribut-able risk of 10–12% [3]. Atrial fibrillation was present in 21% of a "real world" population of 3,513 heart failure patients.

Age, the presence of NHYA class greater than II and a nonischaemic aetiology of heart failure were strong predictors for co-existence of AF [4]. Importantly, the co-existence of both conditions confers increased mortality and morbidity [5].

### **Physiological Interrelationship of AF and Heart Failure**

Atrial fibrillation and heart failure are each associated with physiological conditions that contribute to the initiation and maintenance of the other. Atrial fibrillation precipitates left ventricular (LV) dysfunction via (1) the loss of atrial contraction, (2) the precipitating irregular ventricular rhythm and, (3) rapid ventricular rates. Conversely, heart failure precipitates AF by contributing to atrial remodelling due to (1)

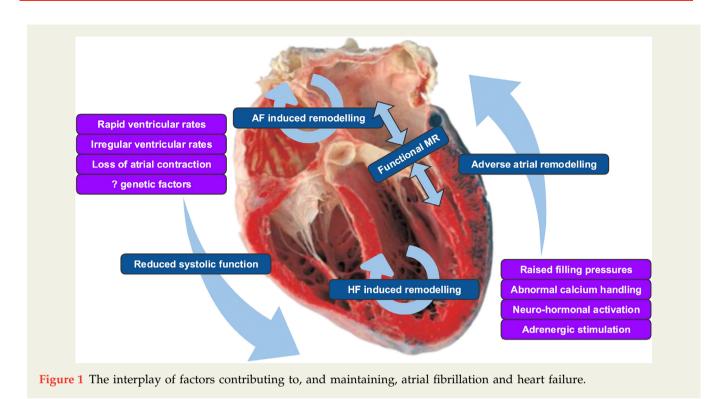
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increased filling pressures, (2) alterations in calcium handling and (3) alterations to the electrical properties of the atrial tissue. As such, a circuitous 'cause and effect' or chicken and egg relationship underpins the complex interaction between these two conditions. Figure 1 shows the interplay of factors contributing to and maintaining AF and heart failure.

### **AF-induced Heart Failure**

The mechanisms behind heart failure precipitated by AF have been explored in both animal models and extrapolated from clinical experience.

#### Tachycardia

Rapid ventricular rates have a well-described deleterious impact upon LV systolic function in canine rapid-pacing models [6,7]. The physiological mechanisms implicated in precipitating LV impairment include haemodynamic stress, activation of neurohormonal systems, myocardial and cardiac exoskeleton remodelling and, if tachycardia continues, eventual induction of apoptosis, cell death and replacement fibrosis [8]. Clinically, incessant or high burden rapid regular tachycardias such as those seen in focal atrial tachycardia (FAT) are often accompanied by LV systolic dysfunction which is reversed following the restoration of sinus rhythm by catheter ablation [9]. Medi et al. demonstrated that LV dysfunction was largely confined to those with incessant atrial tachycardia with slower ventricular rates, speculating that symptoms may be more subtle, as such patients present later with heart failure rather than earlier with palpitations [9]. This highlights that rapid rates alone do not explain the entirety of LV dysfunction precipitated by arrhythmia. Indeed, 60 patients (20%) with normal LV function had incessant or high burden tachycardia, at a higher average rate than those with reduced LV function [9]. As such, the term arrhythmia-mediated cardiomyopathy is more appropriate than tachycardia-mediated cardiomyopathy.

#### Heart Rate Irregularity

Apart from rapid ventricular rates, the irregularity of ventricular rate itself can have adverse haemodynamic effects resulting in LV dysfunction. Naito et al. explored the impact of various pacing strategies upon cardiac output in a canine model with iatrogenic atrioventricular (AV) block. They found that, in both AV sequential pacing and in underlying AF, irregular ventricular rhythm with the same average ventricular cycle length of 400 ms, resulted in a significant 7–9% reduction in cardiac output [10]. Similarly, Clark et al. examined the haemodynamic impact of regular and irregular ventricular pacing following atrioventricular node (AVN) ablation in 16 patients with high burden or chronic AF undergoing AVN ablation. At equivalent average ventricular cycle lengths (587 ms), cardiac output was notably diminished in patients paced irregularly compared with regular ventricular pacing (4.4 versus 5.2 L/min, p < 0.01). Rightand left-sided filling pressures, as determined by right atrial pressure and pulmonary capillary wedge pressure, were also significantly elevated during irregular pacing [11].

#### Loss of Atrial Systolic Function

Pacing studies have utilised iatrogenic A-V dysynchrony to quantify the contribution of atrial systolic function to cardiac

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