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REVIEW

Atrial Fibrillation in Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is an inherited cardiac disorder with a spectrum of clinical manifestations. Patients with HCM are predisposed to developing atrial fibrillation (AF) due primarily to advanced diastolic dysfunction and left atrial (LA) dilatation and remodelling. Atrial fibrillation causes a progressive symptomatic and functional decline, as well as increased thromboembolic risk and mortality, particularly in the setting of rapid ventricular rates and left ventricular outflow tract (LVOT) obstruction. The mainstay of management of AF in HCM is a combination of non-pharmacological lifestyle and risk factor modification, long-term anticoagulation, and rhythm control with antiarrhythmic medications. There is a growing body of evidence indicating that an early and aggressive rhythm control strategy may result in more favourable outcomes.

Introduction

Hypertrophic cardiomyopathy (HCM) is clinically defined as the presence of left ventricular (LV) hypertrophy, usually asymmetric and involving the interventricular septum, in the absence of abnormal loading conditions. It is most often caused by autosomal dominant mutations in one of several sarcomere genes which code for components of the contractile apparatus [1–7]. Hypertrophic cardiomyopathy is a heterogeneous disease with a wide spectrum of clinical manifestations, including an asymptomatic state, symptomatic heart failure, arrhythmias, and sudden cardiac death. Atrial fibrillation (AF) is the most common sustained arrhythmia in patients with HCM, and is known to be associated with adverse clinical outcomes and a worse prognosis [2–6,8,9]. Although prevention of sudden death and management of LV outflow tract (LVOT) obstruction have traditionally been the key priorities of HCM management, AF is more common than both sudden death and medically refractory obstruction [3]. This review article covers a range of issues concerning AF in patients with HCM, with a focus on pathophysiology, predisposing factors and management.

Prevalence and Incidence

Hypertrophic cardiomyopathy is the most common inherited cardiac condition, with a population prevalence of up to 1 in 200 [3–6,10]. It is an important cause of heart failure, and is a common cause of unexplained sudden death in the young [11]. Atrial fibrillation is the most common sustained arrhythmia in both the general and HCM population, with rates of AF four- to six-fold higher in patients with HCM than the similarly aged general population [3]. Previous studies, including a meta-analysis of 7,381 patients, have estimated an annual incidence of 2–3%, and a lifetime prevalence of approximately 20–30% in HCM patients, with rates as high as 40% in those older than 70 years [3–6,12]. In a retrospective study of 4,248 patients, all of whom were in sinus rhythm at baseline, 740 (17.4%) developed AF within 10 years [2]. Atrial fibrillation tends to be paroxysmal in two-thirds of HCM patients and persistent/permanent in the remaining one-third [13,14].

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Pathophysiology

The development of AF in HCM patients is likely a multifactorial process, including genetic factors, structural abnormalities, and electrophysiological abnormalities causing impaired atrial conduction.

Mutations in sarcomeric proteins account for approximately 60% of HCM cases, and of the genes known to be associated with HCM, the three most predominant are β-myosin heavy chain (MYH7), cardiac troponin T, and myosin-binding protein C [7]. The mis-sense mutation Arg663His in the MYH7 gene has been associated with an increased risk of AF (47% prevalence over a seven-year follow-up period) [15], and polymorphisms in the angiotensin receptor gene (AGTR1) have also been linked to the development of AF in patients with HCM [6].

The diagnosis of HCM has been shown to precede the onset of AF in the majority of cases, suggesting that structural and electrophysiological abnormalities play the main role in pathogenesis [5,13] (Figure 1). In HCM, a hypertrophied LV with reduced compliance results in impaired diastolic filling of blood from the left atrium (LA). Therefore, an elevated LV end-diastolic pressure (LVEDP) due to diastolic dysfunction causes an increase in LA afterload, and the LA undergoes progressive dilatation causing a secondary left atrial myopathy. This process of atrial stretch and remodelling is exacerbated by the presence of a LVOT obstruction as well as associated systolic anterior motion of the mitral valve causing mitral regurgitation, both of which are common phenotypic features of HCM [4,6]. Left atrial dilatation and remodelling shortens the effective atrial refractory period, which, in turn, increases the dispersion of repolarisation, thus potentiating the ability of ectopic triggers to maintain AF [9,16].

Furthermore, patients with HCM have a higher prevalence of atrial fibrosis [6,17] and atrial myofibril disarray, which can serve as an arrhythmogenic substrate for AF by impairing conduction of sinus impulses and causing intra-atrial reentry [6,8,9]. Finally, other proposed mechanisms for precipitating AF in HCM include abnormal calcium handling causing triggered activity from delayed after-depolarisations, hypertrophy of the muscle sleeves responsible for conducting pulmonary vein triggers to the LA, and coronary microvascular dysfunction which results in atrial ischaemia/infarction and provides a substrate for development of AF [8,9,18].

In patients with HCM, the presence of AF with a rapid ventricular response reduces LV diastolic filling time and causes loss of organised atrial depolarisation and contraction during diastole. These factors, compounded by reduced LV compliance in a hypertrophied LV, can result in reduction in cardiac output and subsequent clinical deterioration [4,6]. Atrial fibrillation is, therefore, often poorly tolerated by patients with HCM, with common symptoms being palpitations, dyspnoea, and chest pain. Patients with concomitant LVOT obstruction are also predisposed to hypotension, presyncope, and syncope. In a study of 52 HCM patients [14], the acute onset of AF caused worsening symptoms in 89% of patients, with 93% returning to their original symptom class with reversion to sinus rhythm or ventricular rate control.

Risk Factors for Development of AF in HCM

The strongest independent predictors of AF in HCM patients described in the literature are LA diameter and volume, age,

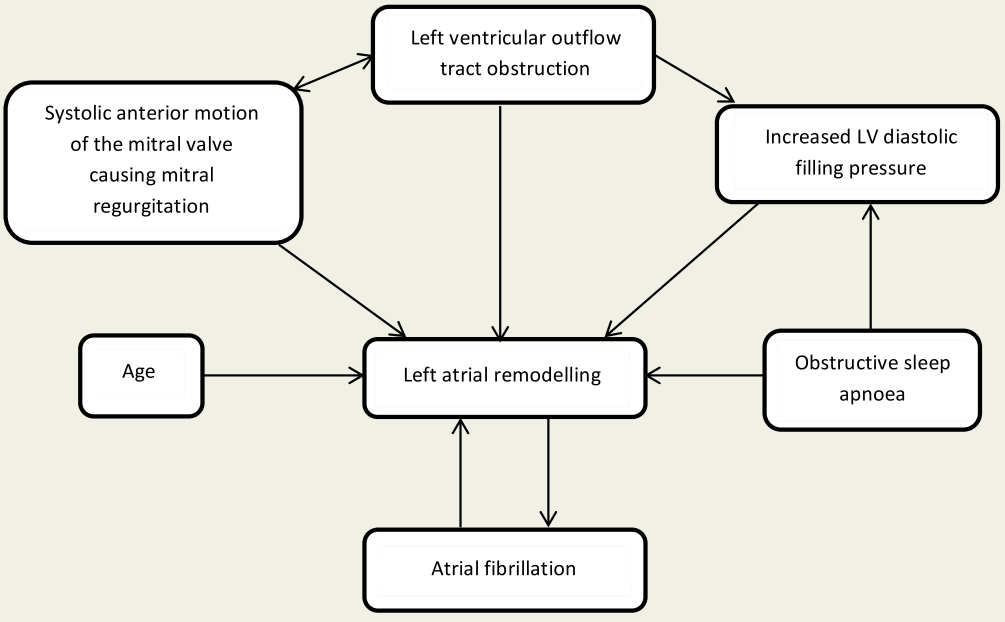

Figure 1 Pathophysiology of AF in HCM.

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