Management of Arrhythmias in Hypertrophic Cardiomyopathy

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Summary. In the management of hypertrophic cardiomyopathy the goals should be the control of symptoms, and the identification and treatment of those at high risk. Arrhythmias, particularly atrial fibrillation and nonsustained ventricular tachycardia, are common in adult patients with hypertrophic cardiomyopathy. Atrial fibrillation has long been thought to herald an ominous prognosis, but this is probably not the case, and in the majority of patients atrial fibrillation can be controlled without accelerated symptomatic deterioration. Uncontrolled observations indicate that low-dose amiodarone may be the most useful drug in both paroxysmal and chronic atrial fibrillation.

The detection of nonsustained ventricular tachycardia on ambulatory ECG monitoring remains the single most useful indicator of the risk of sudden death in the adult patient, and the treatment of choice is again low-dose amiodarone. The mechanism of sudden death, and the mode of action of amiodarone in preventing it, are not known for certain in the majority of patients. The risk of sudden death is higher in children and adolescents, but arrhythmias are less common, and no useful predictive marker of increased risk has been found. The roles of invasive electrophysiological studies and the implantable cardioverter-defibrillator are still being evaluated.

Key Words. hypertrophic cardiomyopathy, arrhythmias, ventricular tachycardia, sudden death

The natural history of hypertrophic cardiomyopathy (HCM) has become progressively better defined in the 35 years since Teare's original description of the cardiac pathology [1]. Modern diagnostic methods, used in conjunction with family screening programs, have demonstrated large numbers of asymptomatic individuals. Most recently, the genetic basis of HCM has been identified in a number of families [2]. In adults, a marker of the risk of sudden cardiac death has been identified [3,4], and there is evidence that the risk can be modified by drug therapy [5]. In children and adolescents, sudden death may be the presenting feature of the disease, and the identification of those children who are at high risk of sudden death is particularly difficult [6,7]. In adults arrhythmias are common, and the influence of ventricular arrhythmias on prognosis has been established [3,4], but there is still debate about the prognostic importance of supraventricular arrhythmias.

Supraventricular Arrhythmias

Studies of cardiac rhythm in adults with HCM have shown that there is a 30–50% incidence of paroxysmal supraventricular tachycardia [3,8,9], the most common of which is atrial fibrillation. Approximately 5% of patients have established atrial fibrillation at the time of diagnosis, and an additional 10% will develop this arrhythmia during the subsequent 5 years [3,7,8]. A poor prognosis after its development has often been assumed, but a recent retrospective review of outcome in patients with HCM and atrial fibrillation suggests otherwise [10]. In this report, the outcome in 52 patients with atrial fibrillation was compared to that in a matched group of patients who remained in sinus rhythm [10]. In the majority (74%), the acute onset of atrial fibrillation was associated with a symptomatic deterioration of at least one NYHA functional class. There was no significant difference in heart rate during atrial fibrillation between those who deteriorated and those who did not, but left ventricular function was better in those patients who did not. After initial therapy 93% of those who had deteriorated were restored to their original symptom class. This included 14 of the 17 who remained in atrial fibrillation, in whom it appeared that the loss of atrial systole was less important than the hemodynamic consequences of a rapid ventricular rate.

Survival in the 52 patients with atrial fibrillation was compared to that of 122 well-matched patients, who remained in sinus rhythm during the same period. There were 22 deaths in the group with atrial fibrillation (14% 5-year mortality), 19 of which were disease related. Survival was similar in the patients
who remained in sinus rhythm during the study period. Ten of the 52 patients with atrial fibrillation had thromboembolic events during follow-up; ominously, four of them were anticoagulated at the time. There were no thromboembolic events in the patients who remained in sinus rhythm. Thus symptomatic deterioration associated with the acute onset of atrial fibrillation may be seen in patients who have impaired left ventricular function, but the majority of such patients can be restored to their previous functional class by treatment, even if they remain in atrial fibrillation. Furthermore, the development of atrial fibrillation did not have an adverse effect on survival.

**Accelerated AV Conduction and Accessory AV Pathways**

The incidence of accessory conduction in HCM is uncertain, and accurate diagnosis may be difficult when the surface electrocardiogram shows wide QRS complexes with a slurred upstroke and repolarization abnormalities. James first proposed that abnormal atrioventricular connections, seen in postmortem specimens from patients with HCM, could provide the potential substrate for rapid atrioventricular conduction [11], and there have been isolated case reports of patients with HCM and Wolff-Parkinson-White syndrome [12]. In one systematic electrophysiological study of HCM, Fananapazir et al. found evidence of accessory pathways in 7 (5%) of 155 patients, three of whom presented with palpitations and one with syncope [13]. They found dual AV nodal pathways in only three patients (1.9%), but did not comment on the presence of accelerated AV nodal conduction. By contrast, the incidence of accessory pathways in the general population is about 1 in 500 (0.2%), whereas dual AV nodal pathways are a commonly observed electrophysiological response, and are not necessarily associated with conduction abnormality or rhythm disturbance. The significance of Fananapazir et al.'s findings is uncertain.

**Conducting Tissue Disease**

The incidence of significant conduction tissue disease is also uncertain. Isolated examples of bradyarrhythmic syncope, and postmortem evidence of sinoatrial node fibrosis, suggest that conducting tissue abnormalities may complicate the disease, even in the young, but studies of Holter monitoring do not suggest an increased incidence of sinoatrial disease, or of atrioventricular nodal disease [3,8,9]. Abnormalities of sinus node function were, however, reported in 61 of 93 patients (66%) from the NIH [18]. In the same study abnormalities of atrioventricular nodal function were found in 9 of 146 (6%), and abnormal His-Purkinje conduction in 44 of 148 (30%) patients. The significance of these findings is uncertain because the prevalence of conduction tissue abnormalities was similar in asymptomatic patients and in those with cardiac arrest, syncope, or presyncope.

**Ventricular Tachycardia**

Sustained monomorphic ventricular tachycardia is rare in HCM [14,15]. In one study, 51 out of more than 200 patients had ventricular tachycardia detected by ambulatory monitoring, but sustained ventricular tachycardia (>30 beats at ≥120 beats/min) was seen in only two [15], both of whom had a left ventricular aneurysm. Inducible monomorphic ventricular tachycardia is also uncommon. In a series of seven consecutive patients investigated because of syncope, sustained monomorphic ventricular tachycardia was induced at electrophysiological study in three, but no cases of spontaneous ventricular tachycardia were documented [16].

In the NIH series programmed ventricular stimulation produced nonsustained ventricular tachycardia in 14% and sustained ventricular tachycardia in 43% [13]. The significance of these findings is uncertain because the stimulation protocol was very aggressive, and sustained monomorphic ventricular tachycardia was seen in only 16 of the 155 patients (10%). (Of the others in whom VT was induced, 48 patients had polymorphic VT and 2 had VF. These are usually considered nonspecific responses to programmed ventricular stimulation.) The combined European experience is in general agreement with the incidence of induced ventricular arrhythmias in relation to the aggressiveness of the stimulation protocols, but the patients with inducible polymorphic ventricular tachycardia in the European series have not experienced the adverse outcome predicted by this paper [17,18]. A subsequent paper from the NIH, however, described a high predictive value of inducible sustained VT for subsequent cardiac events (sudden death, cardiac arrest, or syncope) [19]. Further work in this controversial area is required.

Nonsustained ventricular tachycardia, on the other hand, is common in HCM, and can be detected in about 25% of adult patients [3,8]. This arrhythmia appears benign; it is invariably asymptomatic, and the rate is usually slow. Frequently it follows a period of relative bradycardia, and it is not associated with ST segment changes or alteration in the QT interval. Analysis of different episodes in the same patients has shown considerable variation in the QRS morphology, suggesting multiple sites of origin [9], which is in keeping with a diffuse disease process. The importance of nonsustained ventricular tachycardia is that it has been demonstrated, in simultaneous studies from two independent centers, that nonsustained ventricular tachycardia is the single best predictor of risk of sudden death in adult patients [3,4].