Hypertrophic Cardiomyopathy and Atrial Fibrillation: A Change Of Perspective*

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Hypertrophic cardiomyopathy was first recognized from pathologic studies in 1958 (1) and subsequently analyzed in detail from hemodynamic (2), echocardiographic (3) and electrophysiologic standpoints (4). It is characterized by a hypertrophied heart with a nondilated left ventricular chamber in the absence of any illness that induces an increased myocardial mass. It is frequently associated with dynamic left ventricular outflow obstruction, mitral regurgitation and left ventricular diastolic dysfunction due to impaired relaxation processes and reduced compliance (5). It is also associated with a relatively high prevalence of supraventricular (11% to 54%) and ventricular (19% to 88%) arrhythmias (6), a significant annual mortality rate (3% to 4%) and an alarming incidence rate of sudden cardiac death (2% annually, accounting for over half of all cardiac deaths in this disease) (7). Interestingly, the major risk factors for mortality in patients with hypertrophic cardiomyopathy are clinically and arrhythmia related and are unrelated to hemodynamic variables. These include younger age at diagnosis (<20 years), family history of hypertrophic cardiomyopathy and sudden death, history of syncope, history of severe exertional dyspnea and occurrence of complex ventricular ectopic rhythm and nonsustained ventricular tachycardia, or both (8).

Impact of atrial fibrillation. The occurrence of atrial fibrillation in patients with hypertrophic cardiomyopathy has been associated with such marked clinical and hemodynamic deterioration (including acute pulmonary edema, angina, syncope, hypotension and systolic embolization [5]) that it engenders a poor prognosis in these patients. Sporadic reports with small numbers of cases seem to confirm this impression (9). Indeed, this assumption has prompted some investigators experienced in hypertrophic cardiomyopathy to recommend any and all therapeutic interventions to suppress atrial fibrillation, including septal myotomy or myectomy. Unfortunately, previous reports (9) suggest that, although conversion to sinus rhythm is common, its maintenance, particularly in patients with an enlarged left atrium, is unusual. Also, pathophysiologic considerations have suggested that merely controlling the ventricular rate of the atrial fibrillation is not sufficient to prevent clinical deterioration and that its persistence often leads to exertional symptoms and the development of congestive heart failure (9). Thus, the occurrence of atrial fibrillation in hypertrophic cardiomyopathy has been called “an ominous milestone” in its clinical course (9).

Present study. In this issue of the Journal, Robinson et al. (10) reexamine the impact of atrial fibrillation on the natural history of hypertrophic cardiomyopathy in an important way that changes our perspective on the influence of this arrhythmia. Their study utilized a much larger patient group with a longer duration of follow-up than previous studies and generated a comparison of mortality statistics with a large group of concurrent control subjects who were well matched for mortality risk factors. The key new observations in this study are the following: 1) the onset of atrial fibrillation in hypertrophic cardiomyopathy is not uniformly associated with severe clinical and hemodynamic deterioration (26% of the study group showed no change in functional status with the onset of atrial fibrillation); 2) failure to maintain sinus rhythm and to restore atrial systole does not imply a worsening functional status (82% of patients remaining in atrial fibrillation returned to their baseline functional status); 3) maintenance of sinus rhythm after pharmacologic or electrical cardioversion, or both, can be achieved in a higher percent of patients (63%) than previously thought; 4) long-term survival in patients with hypertrophic cardiomyopathy and atrial fibrillation is much better than previously suspected and not significantly less than that in patients remaining in sinus rhythm; and 5) amiodarone may have a particularly beneficial effect in controlling atrial fibrillation and reducing the associated incidence of embolic complications.

Previous studies. These findings are in distinct contrast to those of a previous report (9) that noted much higher mortality rates with the development of atrial fibrillation, more frequent recurrence of the arrhythmia after initial conversion and consistent worsening of clinical status with its persistence. These discrepancies are due in part to the smaller number of patients and the shorter duration of follow-up in the previous study (9) and in part to patient selection. The patients in the present study are more representative of the currently recognized diversity in hemodynamic subgroups of hypertrophic cardiomyopathy: only half

*Editorials published in Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

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0735-1097/90/$3.50
of them had obstruction at rest (the remainder had latent or no obstruction) and only 35% had moderate to severe mitral regurgitation. The previous study (9) comprised patients with obstruction at rest only and a 63% prevalence of significant mitral regurgitation. Because obstruction at rest and mitral regurgitation generally correlate with more extensive ventricular hypertrophy (5) and because this in turn is associated with an increased degree of diastolic dysfunction (11), progressive clinical deterioration and the occurrence of complex ventricular arrhythmias (6), the patients in the previous study would have a built-in higher mortality rate. Atrial fibrillation would also be expected to develop in these patients because of worsening diastolic dysfunction, left atrial and ventricular dilation and the onset of congestive heart failure rather than as a primary electrical phenomenon. This is supported by the observation that the time of appearance of atrial fibrillation after a diagnosis of hypertrophic cardiomyopathy averaged 18 years in the previous study (9) compared with only 2 years in the present study (10). Furthermore, the development of atrial fibrillation in such a patient group would also be expected to have more dire hemodynamic consequences when superimposed on the preexisting severe diastolic dysfunction and left ventricular outflow obstruction than in the patient group from the present study.

Role of amiodarone in reducing mortality. An additional explanation for the improved mortality rate observed in the present study (10) compared with that in previous studies may be related to newer therapies for atrial fibrillation, particularly amiodarone. Amiodarone has recently been shown to reduce the overall mortality rate in patients with hypertrophic cardiomyopathy, mainly by reducing the rate of sudden cardiac death (12). Because amiodarone was not readily available before 1980, this difference could account for the lower mortality rate in the present study. Furthermore, amiodarone’s documented suppression of nonsustained ventricular tachycardia and associated reduction of the rate of sudden death would be expected to have a greater impact on mortality rates in the age group with the highest prevalence of sudden death, that is, patients aged <20 years. It is intriguing that the improvement in mortality rates demonstrated in the present study is concentrated in this younger age group, where the mortality rate for patients with atrial fibrillation (0 of 6 patients) was not statistically different from that for patients remaining in sinus rhythm (11 of 35 patients). In contrast, in the older age group (>20 years), the mortality rate was significantly greater in patients with atrial fibrillation (22 of 46 patients) than in those remaining in sinus rhythm (17 of 87 patients). This documented age-dependent difference in the improvement of mortality rates for patients with hypertrophic cardiomyopathy and atrial fibrillation compared with the rates in patients without atrial fibrillation strongly supports a causative role for amiodarone in reducing mortality in this group of patients. The liberal use of amiodarone, particularly in the younger patients (perhaps related to the higher percentage of younger compared with older patients diagnosed after 1980) may also explain the otherwise unexpectedly low mortality rate for the younger patients in the present study (0 of 6 patients). However, the small size of this group may have skewed the mortality results, and further investigations will be necessary to confirm the apparently remarkable efficacy of amiodarone in reducing mortality.

In summary, Robinson et al. (10), by analyzing a larger and more representative group of patients with hypertrophic cardiomyopathy and atrial fibrillation and by following them up by obtaining detailed clinical echocardiographic and hemodynamic data over a long period of time, have altered our perspective on the impact of atrial fibrillation on the natural history of hypertrophic cardiomyopathy. They have also suggested the possibility of a very important role for amiodarone in the treatment of atrial fibrillation in patients with hypertrophic cardiomyopathy.

References