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Atrial Fibrillation in Hypertrophic Cardiomyopathy: A Longitudinal Study

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The clinical outcome of 52 consecutive patients with hypertrophic cardiomyopathy who developed paroxysmal (<1 week) or established (≥1 week) atrial fibrillation between 1960 and 1985 was examined retrospectively and compared with that of a matched group of patients with hypertrophic cardiomyopathy and sinus rhythm. Follow-up study until death or the present ranged from 6 months to 24 years (median 11 years) from diagnosis and from 6 months to 22 years (median 7 years) from the onset of atrial fibrillation. Atrial fibrillation was present in 6 patients at the time of diagnosis, whereas it developed subsequently in 46. The acute onset of arrhythmia was associated with a change in symptoms in 41 (89%) of the 46. After initial treatment of acute atrial fibrillation, sinus rhythm was restored in 29 (63%) of the 46 patients; 43 (93%) of the 46 returned to their original symptom class. Stepwise logistic regression revealed that shorter duration of arrhythmia and amiodarone therapy were the most powerful predictors of return to sinus rhythm. Sinus rhythm was maintained during a median follow-up period of 5.5 years in 22 of the 29 patients in whom it was restored after initial therapy.

During follow-up study, 25 of the 52 patients were treated with conventional therapy alone and 7 with amiodarone alone. Amiodarone therapy was associated with maintenance of sinus rhythm, fewer alterations in drug therapy, fewer embolic episodes and fewer attempted direct current cardioversions (during a shorter follow-up period). The remaining 20 patients initially received conventional therapy but were not well controlled and were switched to amiodarone (median 200 mg/day), after which there were fewer alterations in drug therapy and fewer direct current cardioversions during a similar follow-up period.

There were 19 disease-related deaths. Estimated probability of surviving 5, 10, 15 and 20 years after the diagnosis of hypertrophic cardiomyopathy was 0.86, 0.71, 0.65 and 0.50 and was similar in a concurrent group of 122 patients with hypertrophic cardiomyopathy who remained in sinus rhythm (0.92, 0.82, 0.71 and 0.41), respectively.

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Atrial fibrillation develops in approximately 15% of patients with hypertrophic cardiomyopathy (1,2). It is associated with functional deterioration and embolic complications and is believed to herald a poor prognosis (3–6). To define the natural history of this complication, we retrospectively examined the presentation, treatment and outcome of 52 patients with hypertrophic cardiomyopathy who developed atrial fibrillation.

Methods

Study patients. Retrospective analysis of patients with hypertrophic cardiomyopathy who were seen at Hammersmith Hospital between 1957 and 1985 revealed 52 who had atrial fibrillation documented on physical examination and rest or ambulatory electrocardiography (ECG), or both. Atrial fibrillation was established (that is, duration ≥1 week) in 36 and paroxysmal (that is, duration >1 min and <1 week) in 16. Ambulatory ECG monitoring was available since 1978 and was performed at the time of diagnosis and at least annually thereafter. In five patients, all with paroxysmal episodes, atrial fibrillation was documented only during ambulatory ECG monitoring. Clinical details including symptoms, heart rate and rhythm, pharmacologic and electrical therapy and complications were examined before and after the acute onset of arrhythmia, after initial treatment once stable maintenance therapy was achieved and during

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Table 1. Clinical and Prognostic Features at Diagnosis in 52 Patients With Hypertrophic Cardiomyopathy and Atrial Fibrillation and 122 Patients With Hypertrophic Cardiomyopathy and Sinus Rhythm

	Atrial Fibrillation (n = 52)	Sinus Rhythm (n = 122)
Age at diagnosis (yr)		
<21	6 (12)	35 (29)
>21	46 (88)	87 (71)
Year of diagnosis		
1958–1969	15 (29)	34 (28)
1970–1979	32 (61)	66 (54)
1980–1985	5 (10)	22 (18)
Gender (male/female ratio)	1.26	1.25
Family history of HCM and sudden death	10 (19)	20 (16)
NYHA functional class at diagnosis		
I	17 (33)	53 (44)
II	22 (42)	59 (48)
III/IV	13 (25)	10 (8)
Syncope	7 (13)	32 (26)
Ventricular tachycardia on 48 h ECG		
Detected*	7 (13)	25 (20)
Unknown†	17 (33)	42 (34)
Not detected	28 (54)	55 (46)

*Twenty-three of 25 patients in sinus rhythm and all 7 in atrial fibrillation who had ventricular tachycardia detected received low dose amiodarone; †patients evaluated before 1978. Numbers in parentheses indicate percent. ECG = electrocardiogram; HCM = hypertrophic cardiomyopathy; NYHA = New York Heart Association.

long-term follow-up study. All surviving patients were reviewed between January and July 1986. Survival was compared with that in 122 patients with hypertrophic cardiomyopathy and sinus rhythm who were matched for age, duration and follow-up study from diagnosis and risk factors for sudden death and cardiac death (Table 1).

Clinical features. Of the 52 patients with atrial fibrillation, 29 were male and 23 female. They were aged 6 to 72 years (median 47) at the time of diagnosis of hypertrophic cardiomyopathy. Before the onset of atrial fibrillation, 22 (42%) had dyspnea (New York Heart Association functional class II, III or IV), 17 (33%) had exertional chest pain, 7 (14%) had experienced syncope and an additional 6 (12%) presyncope. Diagnosis was based on the demonstration of typical clinical and angiographic features (7) and, after 1980, the echocardiographic demonstration of unexplained left ventricular hypertrophy (8). Fifty of the 52 patients underwent left and right heart catheterization at diagnosis. Mean right atrial pressure was 4 to 14 mm Hg (mean 8). Pulmonary capillary wedge and left ventricular end-diastolic pressures were 7 to 35 mm Hg (mean 20) and 7 to 32 mm Hg (mean 21), respectively. A left ventricular outflow tract gradient of ≥30 mm Hg was recorded at rest in 25 patients (48%) and could be provoked in a further 8 patients. Twenty-seven (52%) of 50 patients had angiographic evidence of mitral regurgitation, which was graded as mild in 18, moderate in 7 and severe in 2 (9).

Twenty-six patients underwent conventional M-mode or two-dimensional echocardiographic examination, or both (10,11). In 10 patients studied 1 month to 4 years (median 7 months) before the onset of arrhythmia, M-mode echocardiography revealed left atrial dimensions of 30 to 50 mm (mean 43) and septal thickness of 15 to 40 mm (median 23). Left ventricular dimensions at end-systole and end-diastole were 20 to 40 mm (mean 31) and 32 to 50 mm (mean 41), respectively. In 16 who were examined 7 months to 22 years (median 4 years) after the appearance of atrial fibrillation, left atrial dimension was 35 to 69 mm (mean 49), maximal septal thickness was 15 to 35 mm (mean 20) and left ventricular dimensions were 22 to 40 mm (mean 33) and 32 to 52 mm (mean 44) at end-systole and end-diastole, respectively.

In 24 patients, technetium-99m equilibrium radionuclide cineangiography (12,13) was performed within 2 years before arrhythmia (n = 2) or during periods of sinus rhythm (range 1 month to 14 years, median 5 years after the onset of arrhythmia, n = 21). Mean ejection fraction was 71 ± 14%. Mean peak ejection rate and time to peak ejection were 3.2 ± 0.8 end-diastolic volume·s^{-1} and 182 ± 5 ms, respectively. Peak filling rate and time from R wave to peak filling were 3.1 ± 0.8 end-diastolic volume·s^{-1} and 506 ± 125 ms, respectively.

Treatment. Before 1980, atrial fibrillation was managed with conventional drugs, including digoxin, verapamil or a beta-adrenergic blocking agent combined with a class I antiarrhythmic agent (either quinidine or disopyramide) where necessary. After 1980, low dose amiodarone was used in 8 of 12 patients with recent onset atrial fibrillation and in those in whom chronic established or paroxysmal atrial fibrillation was refractory to conventional medical therapy (14,15). Selection criteria for initial therapy with amiodarone or conventional drugs reflected individual physician preferences; the two patient groups (amiodarone versus conventional treatment) were similar in age, gender, maximal left ventricular wall thickness and characteristics of atrial fibrillation. Patients received an oral loading dose of amiodarone (600 to 1,200 mg/day for 1 week), followed by a maintenance dose of 100 to 400 mg/day (median 200) adjusted to achieve control of arrhythmia with plasma amiodarone concentrations <1.5 mg/liter (14). All patients with either paroxysmal or established atrial fibrillation received coumarin anticoagulant therapy. The indications for the use of direct current cardioversion as an adjunct to pharmacologic treatment for acute and chronic atrial fibrillation differed according to physician preferences. All patients with established atrial fibrillation in whom pharmacologic cardioversion was unsuccessful underwent at least one attempt at direct current cardioversion.

Statistical analysis. Student's *t* test was used for comparison of mean values of normally distributed data. The Mann-Whitney test was used for unpaired ordinal data. Fisher's exact test was used for nominal data. The Wilcoxon rank sum test was used for comparison of paired ranked data. Multiple logistic regression analysis was used to determine significant differences in groups of variables, where appropriate. Survival in patients with atrial fibrillation was compared with that in a concurrent group of patients with hypertrophic cardiomyopathy and sinus rhythm using the log-rank test and two-tailed p values. The effect of other risk factors on the interpretation of these results was examined using the proportional hazards model. Kaplan-Meier estimates were calculated for the probability of surviving 5, 10, 15 and 20 years after diagnosis. Computer analyses were performed using the SAS statistical package.

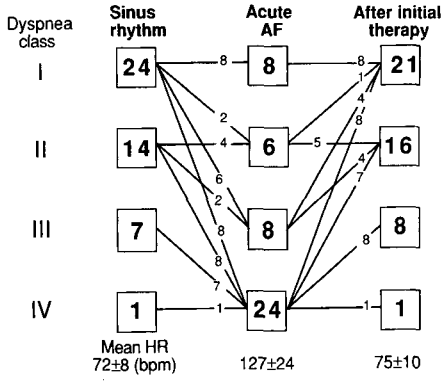

Figure 1. New York Heart Association functional class in patients in sinus rhythm before the development of atrial fibrillation (**left**), during acute atrial fibrillation (AF) (**center**) and after initial therapy (**right**). bpm = beats/min; HR = heart rate.

Results

Paroxysmal versus established atrial fibrillation. Established atrial fibrillation was present at diagnosis in 6 patients and developed in an additional 30 patients 1 month to 18 years (median 2 years) after diagnosis. Prior episodes of paroxysmal atrial fibrillation were recorded in 14 of the 30 patients, whereas in 16 patients established atrial fibrillation had not previously occurred. Ambulatory ECG monitoring was performed in a similar proportion of patients with and without documented paroxysmal episodes preceding the development of established atrial fibrillation. The remaining 16 patients who were followed up for 6 months to 13 years (median 4.3 years) after diagnosis had paroxysmal episodes without developing established atrial fibrillation. More of these latter patients received amiodarone ($p < 0.05$) and fewer were in functional class III or IV ($p < 0.05$), but they were similar with respect to age, left ventricular septal thickness, incidence and severity of left ventricular gradient and left ventricular end-diastolic pressure compared with the 14 patients with paroxysmal atrial fibrillation who developed established atrial fibrillation.

Initial Episode of Paroxysmal and Established Atrial Fibrillation

Symptoms. During the acute onset of atrial fibrillation, seven patients had new or more severe chest pain, five had presyncope and one had syncope. The clinical status of all patients in functional class III and of the majority in class I and II deteriorated by at least one functional class (Fig. 1). The 12 patients in class I or II whose status did not deteriorate were similar in age, left ventricular end-diastolic dimension, maximal wall thickness and ventricular response during atrial fibrillation to the 34 whose status did deteriorate, and a similar proportion were taking atrioventricular (AV) node blocking drugs (8 of 12 versus 18 of 34, respectively). Radionuclide measurements were available in 5 of the 12 patients who remained in the same symptom class after the acute onset of atrial fibrillation. They had a higher ejection fraction (84 ± 6.2% versus 64 ± 13%, $p < 0.02$), peak ejection rate (4.0 ± 0.6 versus 2.9 ± 0.4 end-diastolic volume·s^{-1}, $p < 0.02$) and peak filling rate (3.4 ± 0.7 versus 2.9 ± 0.8 end-diastolic volume·s^{-1}, $p < 0.08$) than the five patients whose status deteriorated after the acute onset of atrial fibrillation who were matched for age, gender and symptom class before atrial fibrillation.

After initial therapy for atrial fibrillation, sinus rhythm returned in 29 patients and persisted in 17. All patients with reversion to sinus rhythm and 14 of the 17 who remained in atrial fibrillation were restored to their original functional class.

Therapy. Details of initial therapy were available in the 46 patients who developed paroxysmal or established atrial fibrillation after diagnosis; 38 received conventional treatment, 7 received amiodarone and 1 had both treatments. Of those treated conventionally, 22 (58%) of 38 returned to sinus rhythm and 16 (42%) remained in atrial fibrillation, whereas 7 (87%) of 8 who received amiodarone returned to sinus rhythm. Initial treatment included attempted direct current cardioversion in 20 patients; 8 of 16 patients who received conventional therapy, 2 of 3 who took amiodarone and 1 patient who had both conventional therapy and amiodarone reverted to sinus rhythm. Of the 26 patients in whom cardioversion was not attempted, sinus rhythm returned in 14 of 22 on conventional therapy and 4 of 4 treated with amiodarone. Return to sinus rhythm was associated with less severe functional class during arrhythmia ($p < 0.01$), duration of arrhythmia <1 week (that is, paroxysmal fibrillation [$p < 0.01$]) and amiodarone therapy ($p < 0.05$). Stepwise logistic regression analysis revealed that duration of atrial fibrillation <1 week ($p < 0.005$) and amiodarone

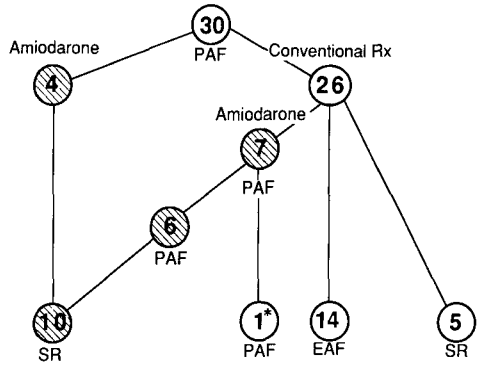

Figure 2. Outcome of 30 patients with paroxysmal atrial fibrillation (PAF) in relation to treatment (Rx). *Patient had exacerbation of paroxysmal atrial fibrillation/flutter on amiodarone and was returned to conventional therapy. Conventional therapy = **open circles**; amiodarone = **hatched circles**; EAF = established atrial fibrillation, SR = sinus rhythm.

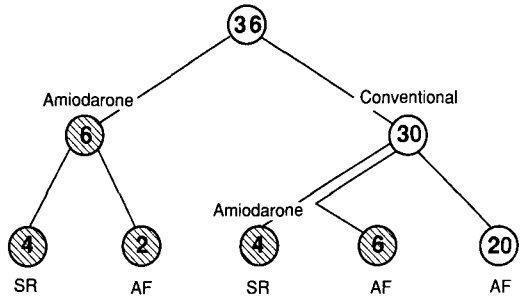

Figure 3. Outcome of 36 patients with established atrial fibrillation (AF) in relation to treatment. Fourteen of the 36 patients had experienced documented paroxysmal atrial fibrillation (see Fig. 2). Conventional therapy = **open circles**; amiodarone = **hatched circles**; abbreviations as in Figure 2.

therapy ($p < 0.03$) were the most powerful predictors of return to sinus rhythm.

Thromboembolism. The onset of atrial fibrillation was associated with thromboembolic episodes in two patients; one had multiple systemic emboli and the other had a pulmonary embolus. Two other patients had systemic thromboemboli 1 and 3 years, respectively, before the documented onset of atrial fibrillation.

Long-Term Follow-Up

Symptoms. During long-term follow-up study (median 7 years), 2 (13%) of 16 patients with paroxysmal and 5 (14%) of 36 with established atrial fibrillation showed a decline of one or more functional class.

Therapy. Of 30 patients with documented paroxysmal atrial fibrillation, 4 received amiodarone and 26 had conventional therapy (Fig. 2). All four patients who received amiodarone had remained in sinus rhythm. Of the 26 patients on conventional therapy, 14 developed established atrial fibrillation, 5 maintained sinus rhythm and 7 continued to have symptomatic episodes of paroxysmal atrial fibrillation. In the latter seven patients, treatment was changed to amiodarone and six remained asymptomatic in sinus rhythm.

Of 36 patients with established atrial fibrillation (including 14 with prior episodes of paroxysmal atrial fibrillation) 6 received amiodarone and 30 had conventional therapy (Fig. 3). Sinus rhythm was restored in four of the six on amiodarone therapy and atrial fibrillation persisted in two. Of those who received conventional therapy, all continued to have established atrial fibrillation, with a controlled ventricular response in 20 patients and poor control (mean heart rate at rest >90 beats/min) in 10. These 10 patients were switched from conventional therapy to amiodarone; 4 had reversion to sinus rhythm and 6 remained in atrial fibrillation with improved control of the ventricular response. Of these 36 patients with established atrial fibrillation, 3 required a demand pacemaker for conduction system disease associated with conventional therapy (n = 2) or amiodarone (n = 1).

In total, 45 of the 52 patients received conventional therapy either alone (n = 25) or followed by amiodarone (n = 20) (Fig. 4 and 5). The remaining seven patients received amiodarone alone; they had a shorter follow-up period (median 4 versus 8 years), fewer drug regimens (mean 1.1 per patient on amiodarone versus 2 per patient on conventional therapy, $p < 0.05$) and fewer embolic episodes (0 versus 9, respectively, $p < 0.01$). During a matched follow-up period of 3.5 years, sinus rhythm was maintained in 6 (87%) of 7 patients receiving amiodarone compared with 5 (11%) of 45 patients who received conventional treatment only ($p < 0.01$).

After a follow-up period of 6 months to 22 years (median 5.5 years), the 45 patients who received conventional therapy required a total of 98 drug regimens (mean 2.25 ± 1.8)

Figure 4. Treatment requirements, attempted direct current cardioversions and embolic complications in 25 patients receiving conventional therapy (**top**) and 7 who initially received amiodarone (**bottom**). The 20 patients who failed conventional therapy and who were switched to amiodarone are shown in the **center**. D.C. = direct current.

Treatment	Median follow-up (years)	D.C. shock per patient	Drug regimes per patient	Total embolic episodes
Conventional (n=25)	8.0	1.1	2.0	9
Conventional (n=20)	3.8	1.1	2.5	2
↓ Amiodarone	5.3	0.1	1.1	0
Amiodarone (n=7)	4.0	0.1	1.1	0

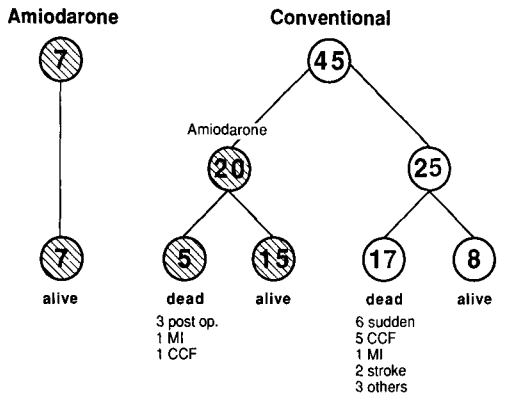

Figure 5. Cause of death in 52 patients with hypertrophic cardiomyopathy and atrial fibrillation in relation to treatment. See text for discussion. Conventional therapy = **open circles**; amiodarone = **hatched circles**; CCF = congestive heart failure; MI = myocardial infarction; post op. = after cardiac surgery.

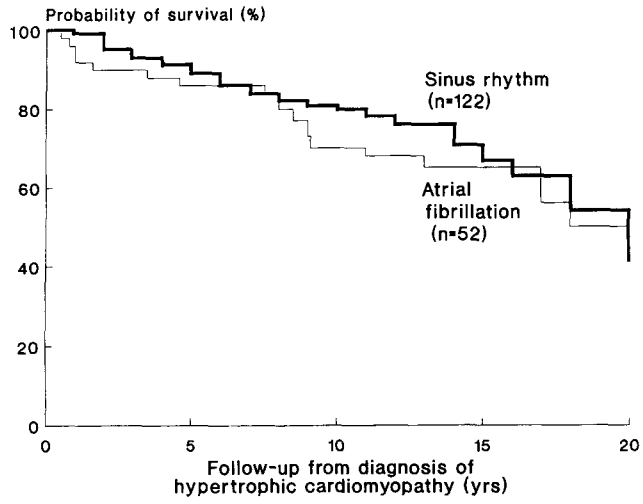

Figure 6. Probability of survival for 52 patients with hypertrophic cardiomyopathy and atrial fibrillation and 122 concurrent patients with hypertrophic cardiomyopathy who remained in sinus rhythm. The difference is not significant.

and 49 direct current cardioversion attempts (mean 1.1 ± 1.8) (Fig. 4). The 20 whose treatment was changed to amiodarone were analyzed separately; during a follow-up period of 3 months to 12 years (median 4 years) on conventional therapy, they had 50 drug regimens (mean 2.5) and 22 cardioversion attempts (mean 1.1). After the change to amiodarone, they had fewer alterations of therapy (20 versus 50 regimens, $p < 0.001$) and fewer cardioversion attempts (2 versus 20, $p < 0.006$) despite a longer follow-up period (2 months to 7.3 years, median 5.3 years).

Side effects. During conventional therapy (median 5.5 years), side effects that required alteration of treatment developed in 14 (31%) of 45 patients. During amiodarone therapy (median 4.9 years), unwanted side effects (photosensitivity, sleep disturbance, tremor, gastrointestinal) were seen in 16 (59%) of 27 patients; of these, 3 required alternative therapy.

Predictors of arrhythmia. The 17 patients with atrial fibrillation after initial therapy continued to have it during the long-term follow-up period of 1 to 22 years (median 8). Of 29 patients with sinus rhythm after initial therapy, 22 remained in sinus rhythm and 7 had recurrence of atrial fibrillation. Univariate analysis revealed that less severe functional impairment during initial arrhythmia ($p < 0.01$) and shorter follow-up from the development of paroxysmal or established atrial fibrillation (6 months to 13 years [median 5.5 years] versus 2.2 months to 17.8 years [median 9 years], $p < 0.05$) were associated with the maintenance of sinus rhythm. Stepwise logistic regression analysis indicated that shorter duration of follow-up was the most powerful predictor of maintenance of sinus rhythm ($p < 0.02$).

Thromboembolic events. During the follow-up period, embolism occurred in 10 male patients. Two patients had two separate embolic events and five had a single embolic episode 3 months to 8 years (median 1.5 years) after the onset of atrial fibrillation. In the remaining three patients, the development of atrial fibrillation and the embolic event preceded diagnosis. Systemic emboli lodged in the brain (n = 6), limbs (n = 2), gut (n = 1) and left coronary artery (n = 1); cerebral embolism was fatal in two of the six patients. All but 1 patient had established atrial fibrillation; 2 were in functional class I, 4 in class II, 3 in class III or IV, and 4 of the 10 were on anticoagulant therapy at the time embolism occurred.

Survival. There were 22 deaths: 6 sudden, 6 from cardiac failure, 2 after myocardial infarction, 3 perioperatively after cardiac myotomy/myectomy, 2 from a cerebrovascular accident and 3 from noncardiac causes (Fig. 5). Cumulative survival figures for all patients from the time of diagnosis of established or paroxysmal atrial fibrillation were 85%, 70% and 62% at 5, 10 and 15 years, respectively. At 5 years, the mortality rate for paroxysmal and established atrial fibrillation was similar (15% versus 10%, p = NS); the number of patients with paroxysmal atrial fibrillation and long-term follow-up were too few for comparison after 5 years.

The 52 patients with atrial fibrillation were compared with a concurrent group of 122 patients with hypertrophic cardiomyopathy and sinus rhythm to see if this arrhythmia affected survival. The presence of known risk factors (nonsustained ventricular tachycardia, syncope, functional class III or IV, family history of sudden death and diagnosis of hypertrophic cardiomyopathy at a young age) were taken into account in making the comparison. Table 1 compares the two groups for presence of risk factors, gender and calendar year of diagnosis. Estimated probability of survival was similar in patients with atrial fibrillation and sinus rhythm (Fig. 6, Table 2; log-rank test p = 0.5). None of 6 patients with atrial fibrillation aged ≤21 years at diagnosis died compared with

Table 2. Estimated Probability of Adults Surviving After Diagnosis of Hypertrophic Cardiomyopathy

	No. of Years			
	5	10	15	20
Patients with sinus rhythm (n = 122)	0.92 (0.03)* (n = 95)	0.82 (0.04)* (n = 59)	0.71 (0.06)* (n = 21)	0.41 (0.14)* (n = 4)
Patients with atrial fibrillation (n = 52)	0.86 (0.05)* (n = 44)	0.71 (0.07)* (n = 29)	0.65 (0.07)* (n = 18)	0.50 (0.09)* (n = 7)

*Standard error of probability of survival.

11 (31%) of 35 of similar age at diagnosis who did not develop atrial fibrillation. In those >21 years at diagnosis, 22 (48%) of 46 patients with atrial fibrillation died versus 17 (20%) of 87 patients with sinus rhythm ($p = 0.11$).

Discussion

Atrial fibrillation is common in hypertrophic cardiomyopathy. Data from referral centers (1,2,7,16) suggest that approximately 5% of patients have established atrial fibrillation at the time of diagnosis, and an additional 10% develop the arrhythmia during the next 5 years. Published reports on the outcome of patients with hypertrophic cardiomyopathy who develop atrial fibrillation are sparse. Invasive hemodynamic studies before and after direct current cardioversion and isolated reports (3,17) indicate that the acute onset of atrial fibrillation is poorly tolerated and potentially fatal. A poor prognosis has been assumed, though this is not confirmed by existing natural history studies (5,16).

Clinical effect of atrial fibrillation. In this study, the functional class in 34 (74%) of the 46 patients deteriorated after the onset of atrial fibrillation. In 12 patients (26%), however, the acute onset of atrial fibrillation was well tolerated; their mean heart rate was 120 beats/min, reflecting the prior administration of an AV node blocking drug; relative control of the ventricular response may have prevented serious deterioration. The finding of an increased ejection fraction and peak ejection and filling rate in patients whose status did not deteriorate also suggests that left ventricular function is potentially an important determinant of the symptomatic response to atrial fibrillation in hypertrophic cardiomyopathy. After initial therapy and either restoration of sinus rhythm or control of the ventricular response, 43 (93%) of 46 patients were returned to their original functional class, including 14 of the 17 who remained in atrial fibrillation. Thus, the loss of atrial systole was well tolerated and appeared to be less important than the hemodynamic consequences of a poorly controlled ventricular response.

After the initial documented episode of atrial fibrillation, 29 (63%) of 46 patients had a return to sinus rhythm with pharmacologic therapy alone (n = 18) or with additional cardioversion (n = 11). Return to sinus rhythm was best predicted by a shorter duration of arrhythmia and treatment with amiodarone. In patients with established atrial fibrillation, restoration and maintenance of sinus rhythm was less common; 28 of the 36 patients remained in atrial fibrillation over the long term (Fig. 3).

Clinical effect of amiodarone versus conventional therapy. During long-term follow-up study, patients who received amiodarone required fewer alterations in drug therapy, had fewer embolic episodes and significantly more (6 of 7 versus 5 of 45, $p < 0.001$) remained in sinus rhythm for >3 years after the initial episode of atrial fibrillation compared with those who received conventional therapy. In those with previously unsuccessful conventional therapy, amiodarone was associated with fewer cardioversion attempts during the follow-up study, fewer changes in drug therapy and a lower incidence of the development of established atrial fibrillation. Unwanted effects often limit the use of amiodarone, particularly when administered in daily doses of ≥400 mg (18–20). In this study, the median daily dose of amiodarone was 200 mg and no patient received more than 400 mg/day: 16 (59%) of 27 patients developed side effects, but in the majority, these were minor and only 3 patients (10%) required alternative therapy. On conventional therapy, side effects that required a change in treatment developed in 14 (31%) of 45 patients. These uncontrolled data suggest a beneficial effect of low dose amiodarone in the day-to-day management of atrial fibrillation, but this warrants confirmation in a controlled study.

Survival. The annual mortality rate in patients with hypertrophic cardiomyopathy is approximately 2% to 4%, and the majority die suddenly (16,21–23). The development of atrial fibrillation is thought to be a poor prognostic sign. In this study, the 5 year mortality rate was only 14%, and the majority of patients did not die suddenly. Nineteen of the 52 patients died from a disease-related cause, including 6 with cardiac failure, 3 perioperatively after myectomy, 2 from a cerebrovascular accident and 2 from myocardial infarction. These deaths were in patients >21 years of age; none of the six younger patients died. The 5 year survival rate was similar in patients with paroxysmal and established atrial fibrillation and in those who remained in sinus rhythm.

Limitations. A limitation of this retrospective study is the fact that clinical, ECG and Holter assessments were performed during routine clinical follow-up study over a 20 year period and not according to a fixed protocol. In particular, this may have influenced patient selection in relation to choice of therapy, and there is the potential for a sampling error in the assessment of paroxysmal atrial fibrillation in relation to the development of established atrial fibrillation. The decisions to use amiodarone and cardioversion were determined by physician preference and were not guided by a previously established protocol. The fact that clinical features were similar in the groups who received amiodarone and conventional treatment does not, however, suggest an important selection bias.

Conclusions. Atrial fibrillation does not represent an ominous development in the natural history of patients with hypertrophic cardiomyopathy. After the development of acute atrial fibrillation, symptoms are common and are related not only to control of the ventricular response, but also to impairment of left ventricular systolic and diastolic function. Most patients can not only be returned to their original functional class, but many are also restored to sinus rhythm. In the long term, amiodarone may be successful in preventing the progression of paroxysmal to established atrial fibrillation and may facilitate management in doses that are not associated with significant side effects. Long-term survival is common and, overall, patients who develop atrial fibrillation do not appear to have a worse prognosis than do those who remain in sinus rhythm.

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