Arrhythmias in dilated cardiomyopathy

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Summary: Sixty-five patients with dilated cardiomyopathy underwent 24 hour electrocardiographic monitoring: 62 (95.4%) showed ventricular arrhythmias and 52 (80%) complex ventricular arrhythmias (multiform ventricular extrasystoles, paired ventricular extrasystoles and ventricular tachycardia).

Complex ventricular arrhythmias correlated significantly with some haemodynamic indices of ventricular dysfunction: patients with multiform and paired ventricular extrasystoles and with ventricular tachycardia had lower values of ejection fraction ($31.9 \pm 11.8\%$, $P = 0.002$) and of cardiac index (2.9 ± 0.7 litres/min/m², $P = 0.029$) than the others ($41.1 \pm 11.1\%$ and 3.5 ± 0.9 litres/min/m² respectively).

Patients were followed for a period of 30 ± 18 months (20 days to 64 months). During follow-up 19 died and mortality was higher among patients with multiform and paired ventricular extrasystoles and/or ventricular tachycardia.

Complex ventricular arrhythmias are frequent in dilated cardiomyopathy: ventricular tachycardia and multiform and paired ventricular extrasystoles seem to be related to a more depressed ventricular function and to a poor prognosis. The importance of antiarrhythmic treatment in these patients has still to be evaluated.

Introduction

Studies on dilated cardiomyopathy have focused primarily on congestive heart failure. Relatively little attention has been given, on the contrary, to arrhythmias, despite considerable evidence that ventricular arrhythmias and sudden death are important and challenging problems in this disease (Johnson & Palacios, 1982; Huang *et al.*, 1983; von Olshausen, 1984; Meinertz *et al.*, 1984).

A prospective study was therefore undertaken in 1979 to examine the prevalence of arrhythmias, their characteristics and the correlation between arrhythmias and clinical and haemodynamic findings.

Methods

Sixty-five patients with dilated cardiomyopathy (52 males and 13 females, mean age 52 ± 13 years, range 15 to 70 years), were admitted into the study.

All patients underwent right and left heart catheterization, coronary angiography, M-mode and 2D echocardiography and 52 right and/or left endomyocardial biopsy. Criteria for diagnosis were: (1) reduced left ventricular ejection fraction ($< 55\%$); (2) absence of critical obstruction ($> 50\%$) in any of the major coronary arteries or of their branches; (3) exclusion of active myocarditis, primary valvular heart disease, cor pulmonale, specific muscle disease,

systemic or heredofamilial disorders.

Fifty-one patients (78.5%) were taking digoxin, 53 (81.5%) diuretics and 21 (32.3%) vasodilator drugs. Seven patients did not receive therapy.

Ambulatory electrocardiographic monitoring

All patients underwent ambulatory electrocardiographic monitoring for at least 24 hours with a two-channel recorder Avionics 445B. All records were analysed with an Avionics 660B until January 1981, and with an Avionics Trendsetter thereafter. The number of episodes of ventricular tachycardia in 24 hours, the number of beats per episode, the mean ventricular tachycardia rate, the prematurity index of the first beat (R-R'/QT) and the heart rate before the initiating beat of the ventricular tachycardia were analysed.

The total number of ventricular extrasystoles in 24 hours and mean frequency of extrasystoles per hour were calculated. A modified Lown grading system, as described by Ryan *et al.* (1975), for ventricular arrhythmias was used: grade 0, no ventricular extrasystoles in 24 hours; grade 1, occasional ventricular extrasystoles but no more than 30 in any hour of monitoring; grade 2, more than 30 ventricular extrasystoles in any hour of monitoring; grade 3, multiform ventricular extrasystoles; grade 4a, (two consecutive ventricular extrasystoles); grade 4b, multiform ventricular extrasystoles and paired ventricular

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extrasystoles; grade 5, ventricular tachycardia (three or more ventricular extrasystoles in succession).

Sustained ventricular tachycardia was defined as an episode of tachycardia lasting more than 30 seconds and not self-terminating.

All patients underwent ambulatory monitoring in the absence of antiarrhythmic therapy.

Follow-up The following-up lasted 30 ± 18 months (from 20 days to 64 months). No patient was lost at follow-up. During the observation period 45 patients received antiarrhythmic treatment: 41 were treated with amiodarone; 1 each with propafenone, mexiletine, disopyramide and verapamil; 20 patients did not receive antiarrhythmic therapy.

A total of 14 pace-makers were implanted: for sick sinus syndrome in 2 cases; second, advanced and third degree atrio-ventricular block in 11 cases; recurrent ventricular tachycardia in one.

Deaths which occurred within one hour from the onset of symptoms were considered sudden and unexpected; those of patients in a state of chronic, disabling, refractory heart failure were considered to be due to heart failure.

Fourteen of the 19 patients who died were submitted to post-mortem examination.

Statistical methods

Data are expressed as the mean $\pm$ standard deviation. The *t* test for unpaired data, the Yates corrected chi-square correlation test and the Fisher's exact test were used, where appropriate, to assess statistical significance. With the two tail test a probability value <0.05 was considered to be significant. Correlation between continuous data was calculated using the linear regression method. Actuarial analysis of survival was performed by life-table methods.

Results

Symptoms at entry into the study and the most relevant non-invasive and invasive data are summarized in Table I.

Sinus rhythm was present in 54 cases (83.1%) and chronic atrial fibrillation in 11 (16.9%). Atrial extrasystoles were detected in 31 patients (47.7%) and paroxysmal supraventricular tachycardia in 5 (7.7%). In 6 patients (9.2%) paroxysmal atrial fibrillation was also recorded. Sixty-two patients (95.4%) had ventricular extrasystoles with complex forms in 52 (80%) (Table II).

Among these patients, 43.1% had more than 1000 extrasystoles/24 hours, and in the group with ventricular tachycardia 15 cases (51.7%) had more than one episode in 24 hours.

In 29 patients with ventricular tachycardia a total of 152 episodes was recorded: 14 patients (42%) had 1 episode, 10 (34%) between 2 and 10, 3 (10%) between 11 and 20 and 2 (7%) more than 20 episodes.

All episodes but one were not sustained and usually not noticed by the patient. The ventricular rate ranged from 110 to 240 beats/min (mean 162 ± 35.45); in some patients relevant changes of heart rate in different episodes were noted. The mean heart rate just before ventricular tachycardia was 82 ± 15 beats/min (range 46–136). No correlation was found with the rate of the subsequent tachycardia episode. The R-R interval preceding the beginning of the tachycardia ranged from 441 to 731 ms. The prematurity index (R-R'/QT of the first beat of ventricular tachycardia) ranged from 0.8 to 2.6 (mean 1.61 ± 0.38) and was more than 1.0 in all but one patient. The prematurity index differed by more than 0.5 in 3 of the patients who experienced multiple episodes of ventricular tachycardia.

No significant correlations were found between ventricular arrhythmia grading and NYHA functional class, echocardiographic end-diastolic diameter, end-diastolic pressure and end-diastolic volume.

Patients with ventricular arrhythmia grade 4b and 5 had significantly lower values of ejection fraction ($31.9 \pm 11\%$ vs $41.1 \pm 11.1\%$, $P = 0.002$) and cardiac index (2.90 ± 0.7 vs 3.5 ± 0.9 litres/min/m², $P = 0.029$) than other patients.

During follow-up 19 patients died (29.2%) one of non-cardiac causes and 14 died of congestive heart failure, 11 of whom had ventricular tachycardia and 1 multiform and paired ventricular extrasystoles on the ambulatory monitoring.

Of the 4 patients who died suddenly only one presented with ventricular tachycardia on the ambulatory monitoring; 2 other patients had multiform ventricular extrasystoles and uniform and paired ventricular extrasystoles; the fourth patient, an 18 year old man, had only frequent ventricular extrasystoles.

Twelve of the 18 deaths due to cardiac cause occurred in the group of patients who had ventricular tachycardia; in contrast, only 6 of the patients with lower grades of ventricular arrhythmias died ($P < 0.025$).

Discussion

These data are in agreement with those previously published, indicating that in patients with dilated cardiomyopathy ventricular extrasystoles, complex ventricular arrhythmias and ventricular tachycardia are frequent findings (Huang *et al.*, 1983; von Olshausen *et al.*, 1984; Fonda *et al.*, 1980).

Runs of ventricular tachycardia were initiated, in

Table I Clinical, ECG, echocardiographic and cardiac catheter findings in 65 patients with dilated cardiomyopathy

		No. of cases	(%)
Presenting symptoms	Heart failure	49	75
	Palpitation	19	19
	Chest pain	8	12
	Systemic emboli	3	5
	Ventricular fibrillation	3	5
	Syncope	4	6
	NYHA class I	8	12
	II	17	26
	III	34	52
	IV	6	9
Surface ECG:	Sinus rhythm	54	83
	Atrial fibrillation	11	17
	1st degree A-V block	17	26
	2nd degree A-V block	1	2
	3rd degree A-V block	8	12
	Left ventricular hypertrophy	8	12
	Right ventricular hypertrophy	1	2
	Left anterior hemiblock (LAH)	9	14
	Left bundle branch block (LBBB)	11	17
	LBBB with left axis deviation	19	29
	Right bundle branch block (RBBB)	4	6
	RBBB + LAH	3	5
	Non-specific ST-T changes	9	14
		Mean	Range
Echocardiography: end-diastolic dimension		7.05 ± 0.99	5–8.9
Cardiac catheterization:	LVEDP (mmHg)	14.55 ± 6.89	4–30
	CI (ml/min/m ²)	3.18 ± 0.84	1.37–5.18
	LVEDV (ml/m ³)	123.7 ± 38.3	53–210
	EF (%)	35.68 ± 12.2	12–55

LVEDP(V) = left ventricular end diastolic pressure (volume); CI = cardiac index; EF = ejection fraction.

Table II Ventricular arrhythmia grade in dilated cardiomyopathy

	Ventricular arrhythmia grade**						
	0	1	2	3	4a	4b	5
Maximum grade							
No. (%) of patients	3 (4.6)	5 (7.7)	5 (7.7)	6 (9.2)	7 (10.8)	10 (15.4)	29 (44.6)
Cumulative grade*	3 (4.6)	20 (30.7)	42 (64.5)	45 (72.6)	36 (55.4)	25 (38.5)	29 (44.6)

*Grades 0–2 and grades 3–5 are not mutually exclusive, e.g. a patient may have > 30 ventricular extrasystoles in one hour (grade 2) which are multiform and paired (grade 4b). **Ryan *et al.*, 1975.

the great majority of cases, by late coupled ventricular extrasystoles with a prematurity index which ranged from 0.8 to 2.6 (mean 1.61 ± 0.38).

In these patients the prematurity index did not seem to be an important predictor of subsequent ventricular tachycardia. Similar observations were made for ventricular tachycardias detected with ambulatory monitoring, after acute myocardial infarction (Anderson *et al.*, 1978).

Frequent ventricular extrasystoles and complex ventricular arrhythmias have been observed also in hypertrophic cardiomyopathy (McKenna *et al.*, 1981) and in ischaemic heart disease after myocardial infarction (Anderson *et al.*, 1978), although they seem to be less frequent in these diseases.

Recent studies showed that functional class, presence of atrial fibrillation, cardiac volume (Segal *et al.*, 1978), age, cardiothoracic ratio, left ventricular conduction delays, capillary wedge pressure, mean right atrial pressure and ejection fraction (Unverferth *et al.*, 1984; Fuster *et al.*, 1981) are important and useful prognostic indicators in dilated cardiomyopathy. However, the relationship between ventricular function and arrhythmias remains uncertain.

Some authors (Huang *et al.*, 1983; Meinertz *et al.*, 1984) have found no relationship between the severity of ventricular arrhythmias (particularly paired ventricular extrasystoles and ventricular tachycardia) and clinical findings, cardiomegaly on X-ray, electrocardiographic abnormalities and ejection fraction; on the other hand, von Olshausen *et al.* (1984) found a significant difference ($P < 0.01$) in NYHA functional class, cardiac index, end-diastolic pressure and ejection fraction between patients with and without ventricular tachycardia.

Also, in our experience, ejection fraction and cardiac index differed significantly ($P = 0.002$ and $P = 0.029$ respectively) between patients with the highest ventricular arrhythmia grades (multiform and paired ventricular extrasystoles and ventricular tachycardia) and the others. On the contrary, like other authors (von Olshausen *et al.*, 1984), we found no difference in clinical and haemodynamic parameters between patients with frequent (> 1000) or infrequent (< 1000) extrasystoles/24 hours.

Finally, no relationship seems to be present between number and characteristics of extrasystoles and end-diastolic volume.

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Because of antiarrhythmic treatment, we cannot identify with certainty the prognostic value of ventricular arrhythmias and their relations with the cause of death.

We observed, however, that patients with multiform and paired ventricular extrasystoles and/or ventricular tachycardia episodes have a higher mortality rate than patients with lower grades of ventricular arrhythmia. These data are in agreement with those of other authors (Unverferth *et al.*, 1984) who found in dilated cardiomyopathy a relationship between the severity of ventricular arrhythmia and mortality.

We found no relation between arrhythmia grading and incidence of sudden death. Also other authors (Huang *et al.*, 1983; von Olshausen *et al.*, 1984), probably because of the inadequate follow-up, could not identify by ambulatory monitoring the patients at risk of sudden death.

On the other hand, Meinertz *et al.* (1984) found that patients who died suddenly had a significantly higher average number of arrhythmic events (particularly paired ventricular extrasystoles and ventricular tachycardia, in association with a low ejection fraction) than survivors and than patients who died of congestive heart failure. The patients studied by these authors, had not been treated with antiarrhythmic drugs.

The low incidence of sudden death among our patients, during the relatively long follow-up (average 30 months) may be related to the antiarrhythmic treatment.

Conclusion

Ventricular arrhythmias and particularly complex ventricular arrhythmias are frequent in dilated cardiomyopathy. Patients with ventricular tachycardia and/or multiform and paired extrasystoles showed more depressed indices of ventricular function and had a higher mortality.

The effects of an antiarrhythmic treatment in dilated cardiomyopathy are still unknown. However, in our preliminary studies (Fonda *et al.*, 1980; Mestroni *et al.*, 1983) with amiodarone, it was possible to observe a significant reduction in the incidence of ventricular arrhythmias.

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