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Differences of disease progression in congestive heart failure due to alcoholic as compared to idiopathic dilated cardiomyopathy

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In patients with alcoholic cardiomyopathy there is evidence that mild heart failure is reversible if patients abstain from alcohol, but there is no consensus whether the disease is progressive once structural myocardial dilatation has evolved. The aim of the present study was to compare the long-term course of congestive heart failure due to alcoholic and idiopathic dilated cardiomyopathy.

Of 75 patients with overt congestive heart failure, 23 had alcoholic cardiomyopathy and were compared to 52 patients with idiopathic cardiomyopathy. The mean age was 48 ± 12 years. Despite medical therapy, heart failure class New York Heart Association III–IV was present in 52% of patients with alcoholic and 47% of patients with idiopathic cardiomyopathy (not significant). Their mean left ventricular ejection fraction was 30 ± 12% vs 28 ± 12% and left ventricular end-diastolic volumes were 264 ± 125 ml and 254 ± 100 ml respectively (not significant). Overall survival at 1, 5 and 10 years was 100%, 81% and 81% for the group with alcoholic dilated cardiomyopathy and 89%, 48% and 30% for the group with idiopathic cardiomyopathy, respectively ($P=0.041$), and the difference was even greater for transplant-free survival ($P=0.005$). Clinical and invasive signs of left and right heart failure as well as left ventricular dimensions were predictive of a fatal outcome; however, symptom duration and left ventricular volumes were only predictive in patients with idiopathic cardiomyopathy, suggesting that in the two patient groups different mechanisms may lead to death.

Mortality in patients with severe congestive heart failure and left ventricular dilatation due to alcoholic cardiomyopathy is significantly lower than that in patients with idiopathic cardiomyopathy and similar degrees of heart failure. Thus, despite structural changes inherent in marked left ventricular dilatation, disease progression in alcoholic dilated cardiomyopathy is different from that in idiopathic cardiomyopathy and thus may have implications for the choice of therapy.
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Key Words: Alcoholic cardiomyopathy, left ventricular dilatation, congestive heart failure, survival prognosis.

Introduction

The natural history of idiopathic cardiomyopathy has been described by several authors, with 5-year survival rates ranging between 65% and 25%[1–6]. It has recently been recognized that referral bias affects the apparent natural history of idiopathic dilated cardiomyopathy and that survival in referral patients with this disease is significantly better than previously described[7]. Heart transplantation, a therapeutic option for end-stage congestive heart failure, is usually withheld in patients whose cardiomyopathy has an alcoholic aetiology. Instead the treatment of choice is abstinence from alcoholic beverages as well as medical therapy with diuretics, ACE inhibitors and digitalis. Alcohol withdrawal may have remarkable short-term effects, especially in milder forms of the disease[8–10], but this may not be the case in patients with left ventricular dilatation due to structural changes[11]. In addition, it is well recognized that many patients will not remain abstinent even after their first left heart decompensation[12]. Despite a relatively large number of such patients in Europe, there is almost no long-term data available describing the natural history and outcome of their disease.

The aim of the present study was, therefore, to investigate the long-term outcome of patients with signs and symptoms of overt heart failure due to alcoholic

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dilated cardiomyopathy and to compare it to that of patients with similar degrees of congestive heart failure due to idiopathic cardiomyopathy.

Methods

Patients

In a retrospective analysis, all patients referred to our hospital for invasive evaluation of overt congestive heart failure between 1981 and 1992 were screened. Patients were excluded from this analysis if they had a left ventricular ejection fraction >50% or if a cause other than alcohol abuse could be identified as being responsible for their disease (i.e. coronary artery disease, hypertensive heart disease or history of hypertension, valvular or congenital heart disease, thyrotoxic heart disease, diabetes mellitus). The remaining 75 patients fulfilled the inclusion criteria and formed the study population for the present analysis. In 23 of them (31%) an alcoholic aetiology of their heart disease could be identified based on their history, clinical examination and laboratory findings. All of these patients had been drinking at least 80 g of ethanol per day over a period of at least 5 years. In the remaining 52 patients (69%) no specific aetiology could be found and they were considered to suffer from idiopathic cardiomyopathy.

Clinical evaluation

All patients were clinically examined and followed by experienced cardiologists. The initial evaluation included a 12-lead electrocardiogram, chest X-ray and left heart catheterization by the Judkins technique in all patients. For most of them, additional data from other investigations such as right heart catheterization (n=46) and echocardiography (n=50) were available for analysis. Patients were regularly followed in our outpatient clinic or by their private cardiologists. Final follow-up information was obtained from the patients directly or from their private physicians. Deaths were verified through hospital records, autopsy reports and death certificates where necessary. All-cause mortality was used as sole end-point. In order to account for a survival benefit due to heart transplantation in patients with end-stage heart failure, transplant-free survival was also assessed.

Statistics

All values are presented as mean ± one standard deviation. Comparison between groups were done using the two-tailed Student's t-test for unpaired samples and the Chi-square test for proportions. Actuarial life table analysis was calculated based on the method described by Kaplan-Meier[13]. Survival was calculated as overall survival and transplant free survival. A P-value of <0·05 was considered to indicate a significant difference.

Table 1 Clinical findings at the time of diagnosis

	IDCM	ADCM
Age (years)	49 ± 15	47 ± 8
Duration of symptoms (months)	19 ± 29	20 ± 22
Dyspnoea		
NYHA class I–II (%)	53	48
NYHA class III–IV (%)	47	52
Syncope (%)	23	17
Chest pain (%)	55	61
Atrial fibrillation (%)	21	22
Third heart sound (%)	45	52
Positive hepato-jugular reflux (%)	18	22
Heart size (cm)	17·7 ± 2·2	16·9 ± 2·0
Cardiothoracic ratio	0·55 ± 0·06	0·51 ± 0·05

ADCM=alcoholic dilated cardiomyopathy; mean values ± one standard deviation are given; IDCM=idiopathic dilated cardiomyopathy; NYHA class=New York Heart Association functional classes: I — asymptomatic, II — symptoms during strong exercise, III — symptoms during mild exercise, IV — symptoms at rest. There were no statistically significant differences.

Results

Clinical parameters

Patient characteristics are described in Table 1. All patients were referred for management of congestive heart failure and presented with symptoms lasting for an average of 21 to 24 months before inclusion in the study. Symptoms were shortness of breath (47–52% in New York Heart Association class III–IV despite medical therapy), atypical chest pain and syncope. In 49% of the patients the resting heart rate was elevated to above 90 beats per minute and a third heart sound was present in 47% of the patients. Atrial fibrillation was documented in 21% and 22% respectively. Standard chest X-ray documented a heart size ≥15·5 cm in 83% of patients. Sixty-eight percent of patients were on diuretics and 45% on digoxin; ACE inhibitors were only available in the latter part of the study, where it became standard treatment. As indicated in Table 1, there were no significant differences in any of these parameters between patients with alcoholic and idiopathic cardiomyopathy, respectively.

Haemodynamic and laboratory measurements

Haemodynamic and laboratory data are given in Tables 2 and 3. The stroke volume index was 31 ± 13 ml . m^{-2} in patients with idiopathic cardiomyopathy and 28 ± 11 ml . m^{-2} in patients with alcoholic dilated cardiomyopathy, respectively (P not significant). Left ventricular ejection fraction and left as well as right sided filling pressures and volumes were markedly increased (end-diastolic volumes: 254 ± 100 ml for idiopathic cardiomyopathy and 264 ± 124 ml for alcoholic dilated

Table 2 Haemodynamic data at the time of diagnosis

	IDCM	ADCM
Heart rate (beats . min^{-1})	89 ± 16	95 ± 16
Systolic blood pressure (mmHg)	121 ± 16	125 ± 18
Diastolic blood pressure (mmHg)	80 ± 10	81 ± 10
Stroke volume index (ml . m^{-2})	31 ± 13	28 ± 11
PAP mean (mmHg)	28 ± 10	23 ± 10
CVP (mmHg)	9 ± 5	8 ± 3
PCW (mmHg)	21 ± 8	17 ± 8
LVEF (%)	28 ± 12	30 ± 12
LVEDV (ml)	254 ± 100	264 ± 125
LVEDP (mmHg)	20 ± 9	20 ± 9

CVP=central venous pressure; LVEDP=left ventricular end-diastolic pressure; LVEDV=left ventricular end-diastolic volume; LVEF=left ventricular ejection fraction; PAP=pulmonary artery pressure; PCW=pulmonary capillary wedge pressure There were no statistically significant differences.

Table 3 Laboratory data at the time of diagnosis

	IDCM	ADCM	*P*-value
Haemoglobin (g . dl^{-1})	14·9 ± 1·6	15·5 ± 1·5	ns
Leucocytes (10^9 . l^{-1})	8·1 ± 3·0	8·9 ± 2·0	ns
Platelet count (10^9 . l^{-1})	235 ± 69	214 ± 47	ns
γGT (<60 U . l^{-1})	73 ± 137	181 ± 186	<0·05
SGOT (6–25 U . l^{-1})	20 ± 11	31 ± 18	<0·05
SGPT (3–36 U . l^{-1})	27 ± 20	57 ± 55	<0·01
Creatinine (71–120 μmol . l^{-1})	100 ± 45	87 ± 18	ns

SGOT=aspartate aminotransferase; SGPT=alanine aminotransferase; γGT=gamma glutamyl transferase. Normal values are referenced in parenthesis.

cardiomyopathy patients; *P* not significant). Hence, there were no relevant differences in haemodynamic measurements between the two study groups at baseline. This was confirmed by echocardiographic measurements in 50 patients; however, Doppler ultrasound demonstrated the presence of mitral regurgitation in 69% of idiopathic vs only 22% ($P<0·05$) in alcoholic patients. There were no significant differences in laboratory parameters, except for measurements of gamma glutamyl transferase, aspartate aminotransferase and alanine aminotransferase, which were significantly higher in patients with alcoholic compared to patients with idiopathic cardiomyopathy (at least $P<0·05$), confirming hepatic disease due to chronic alcohol intoxication.

Survival and predictors of death

Figure 1 shows the overall and transplant-free survival for the whole study population over a 10-year period. Overall mortality for the group as a whole was 7% at one year and 43% at 5 years. A total of eight patients with idiopathic cardiomyopathy but none with alcoholic dilated cardiomyopathy underwent heart transplantation during the follow-up period (two at 2, two at 6 months and one at 8, 11, 51 and 57 months of follow-up, respectively).

The probability of survival was 81% at 10 years in the group with alcoholic dilated cardiomyopathy compared to 30% in the group with idiopathic cardiomyopathy ($P<0·05$; Fig. 2). If transplant-free survival was compared (Fig. 3) the difference between the two groups was even greater, with transplant free survival after 10 years of only 20% for idiopathic cardiomyopathy as compared to 81% for alcoholic dilated cardiomyopathy patients ($P<0·01$). Overall survival after one year was 100% and 89% for the groups with alcoholic dilated cardiomyopathy and idiopathic cardiomyopathy, respectively; this decreased to 81% and 68% after 2 years and to 81% and 48% after 5 years, respectively.

Dyspnoea New York Heart Association class III–IV, presence of a positive hepato-jugular reflux and neck vein congestion as signs of biventricular heart failure were the most important clinical predictors of

Table 4 Univariate positive predictors of fatal outcome in patients with idiopathic (IDCM) and alcoholic dilated cardiomyopathy (ADCM)

	IDCM			ADCM		
	Alive (n=25)	Dead (n=27)	*P*	Alive (n=20)	Dead (n=3)	*P*
Age (years)	51 ± 10	48 ± 15	ns	46 ± 8	47 ± 6	ns
Symptom duration (months)	12 ± 13	35 ± 35	<0·01	22 ± 23	7 ± 5	ns
Dyspnoea NYHA III–IV (%)	16	52	<0·01	20	100	<0·01
Neck vein congestion (%)	8	46	<0·01	25	67	ns
Hepato-jugular reflux (%)	0	35	<0 01	15	67	<0·05
Diuretics (%)	64	93	<0·05	30	100	<0·05
Digoxin (%)	36	70	<0·05	20	67	ns
LVEF (%)	34 ± 9	23 ± 11	<0·01	32 ± 12	15 ± 6	ns
LVEDV (ml)	208 ± 50	300 ± 116	<0·01	265 ± 130	250	—
LVESV (ml)	131 ± 35	246 ± 120	<0·01	185 ± 113	203	—
LVEDP (mmHg)	16 ± 7	24 ± 9	<0·01	19 ± 9	21 ± 9	ns

Abbreviations as in Table 2. LVESV=left ventricular end-systolic volume.

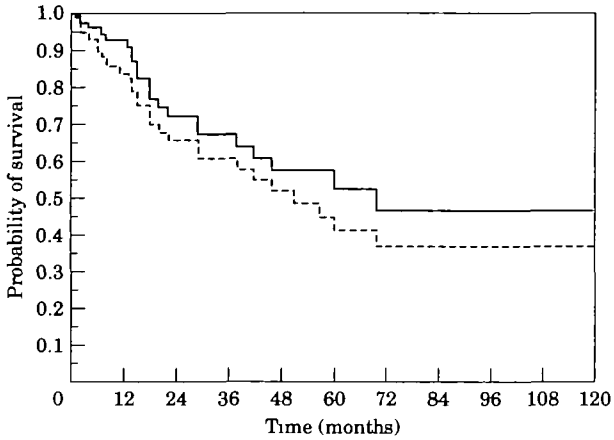

Figure 1 **Overall survival (solid line) and transplant-free survival (dotted line) in the study population. The survival curves are shown for the whole study group comprising 23 patients with alcoholic and 52 patients with dilated cardiomyopathy.**

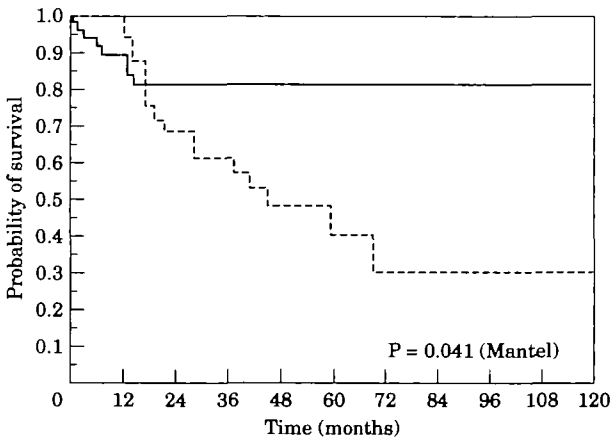

Figure 2 **Overall survival comparing patients with idiopathic cardiomyopathy (dotted line) and alcoholic dilated cardiomyopathy (solid line).**

death, whereas atrial fibrillation was not. These clinical findings were substantiated by invasive measurements: left ventricular ejection fraction and volumes as well as left ventricular filling pressures were predictive of a fatal outcome by univariate analysis; however, these results were only significant in patients with idiopathic cardiomyopathy and not in patients with alcoholic dilated cardiomyopathy due to the low death rate in this latter group. Age was not a predictor of death in these patients and symptom duration was only predictive in idiopathic cardiomyopathy patients.

Discussion

All patients in this study presented with clinical signs of heart failure, which had lasted for an average of almost 2 years at the time they were included. Severely

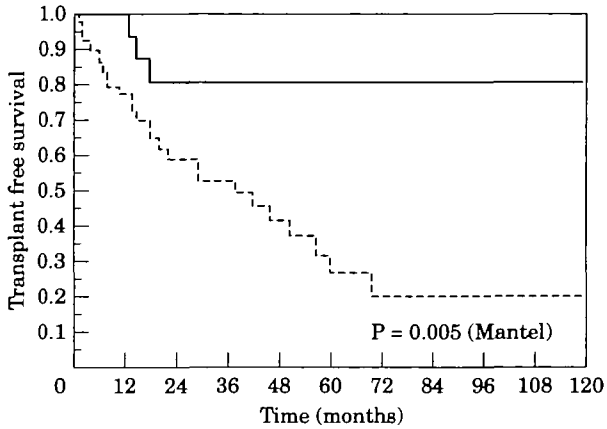

Figure 3 **Transplant-free survival comparing patients with idiopathic cardiomyopathy (dotted line) and alcoholic dilated cardiomyopathy (solid line). Note, eight patients with idiopathic cardiomyopathic underwent heart transplantation during the 10-year follow-up, compared to none of the patients with alcoholic dilated cardiomyopathy.**

depressed left ventricular ejection fraction and markedly increased left ventricular volumes were indicative of dilatative cardiomyopathy and documented invasively in all patients. All patients required aggressive medical treatment and eight with idiopathic cardiomyopathy underwent heart transplantation. In contrast none of the patients with alcoholic cardiomyopathy was transplanted. Overall survival over 10 years was significantly better for patients with alcoholic dilated cardiomyopathy than for those with idiopathic cardiomyopathy and this difference was even greater for transplant-free survival.

Patient selection

The characteristics of our patient population were similar to those of previously published reports on patients with congestive heart failure due to idiopathic cardiomyopathy. The mean age of 48 years was relatively low in the present study [8,14–16], but the duration of symptoms at the time of presentation, the prevalence of heart block and atrial fibrillation were comparable to findings of others[8,14,15,17–20]. In contrast to other reports, all of our patients underwent angiography combined with left ventriculography, providing the advantage that patients with silent coronary artery disease were excluded from this study and an accurate measurement of left ventricular function was obtained at the same time.

Alcoholic cardiomyopathy

The diagnosis of alcoholic cardiomyopathy was based on the diagnosis of idiopathic cardiomyopathy in patients admitting regular consumption of large

amounts of alcohol. The amount of daily alcohol intake necessary to induce alcoholic cardiomyopathy varies widely in individuals and there are also large variations reported in the literature[6,11,12,21,22]. In our patients the admitted amount of alcohol intake was also very variable, but all of them consumed at least 80 g alcohol per day on a regular basis. In our series, myocardial biopsies were performed in only four patients, resulting uniformly in non-specific findings; this is in accordance with findings from other studies which found no specific histopathological markers for idiopathic or alcoholic cardiomyopathy[23]. For the development of alcoholic dilated cardiomyopathy, the level of liver and cardiac enzyme activity appears to be of great importance, a hypothesis which is confirmed by experiments with rats in which this disease developed only when there was simultaneous alcohol administration and inhibition of catalase activity[24]. In our study, alanine aminotransferase, aspartate aminotransferase and gamma glutamyl transferase enzyme levels were markedly increased in patients with alcoholic dilated cardiomyopathy as compared to patients with idiopathic cardiomyopathy. Richardson and co-workers noted that myocardial and liver enzymes are increased in patients with alcoholic dilated cardiomyopathy and correlate with the amount of alcohol intake[25]. Since alcoholic dilated cardiomyopathy and liver disease are usually not associated, these authors argued that their findings support the concept of alcoholic heart muscle disease as a distinct entity.

There is evidence from experimental[26] and human[9,10] studies that alcohol withdrawal may normalize left ventricular dysfunction, at least in acute or early stages of the disease. Whether this is true in patients presenting with congestive heart failure and left and right heart dilation with corresponding structural changes[10,26] is not known. In fact, two studies[8,27] reported improved survival in some patients abstaining from alcohol, whereas another study showed no survival benefit from alcohol abstinence in such patients[28]. Even in the study with improved survival after alcohol abstention[8], the clinical cardiac status did not improve in most patients.

Survival of patients with alcoholic cardiomyopathy

In view of the difficulties in differentiating cardiac non-sudden death due to heart failure from sudden death in such patient groups[16,18], and considering the low prevalence of sudden death due to alcoholism in young and middle-aged persons[29], total mortality only is reported in this study. Since it was intended to describe the natural history of the disease, both overall and transplant-free survival were analysed in order to correct for the bias incurred by the survival benefit from heart transplantation in the group with idiopathic cardiomyopathy. The observed long-term survival of patients with congestive heart failure due to idiopathic cardiomyopathy was similar to that previously published[6]. Survival of patients with alcoholic dilated cardiomyopathy, however, was significantly better, particularly if transplant-free survival was compared. This contrasts with another similarly large series reported it the literature[6] where no difference in mortality was found. The reasons remain speculative, but this difference could partly be explained by more aggressive medical treatment, firm advice to refrain from alcohol and the enrollment of patients in supervised alcohol withdrawal programmes whenever feasible; however, the effect of this strategy, and particularly whether or not patients remained abstinent, was not controlled in this retrospective study and remains subject to a prospective trial. The comparatively low mortality rate observed in patients with alcoholic dilated cardiomyopathy, severe congestive heart failure and marked left ventricular dilatation indicates that these patients may have an unexpectedly good long-term course on medical treatment and may, therefore, not qualify for heart transplantation.

Predictors of death

Previous studies have identified shortness of breath, age, underlying coronary artery disease, systolic blood pressure and heart size as predictors of death in patients with congestive heart failure due to idiopathic cardiomyopathy[2,5,17,30–33]. In contrast, there are controversial reports about the prognostic impact of left ventricular ejection fraction[15,16,20,30,31], atrial fibrillation[1,14,16,20] and ventricular dilatation[3,34–36] in these patients. The present study did not intend to define such prognostic predictors; however, our observations in patients with idiopathic cardiomyopathy identified clinical findings of overt biventricular heart failure, such as severe physical limitation (dyspnoea New York Heart Association class III–IV), congested neck veins and a positive hepatojugular reflux as predictors of a fatal outcome, which is in accordance with previous studies. These clinical findings were substantiated by invasive measurements of left ventricular dysfunction and dilatation. However, these latter parameters were only predictive in patients with idiopathic but not in those with alcoholic dilated cardiomyopathy. Although this difference may be due to the smaller number of alcoholic dilated cardiomyopathy patients, the low event rate in this group suggests a different disease progression and thereby supports the hypothesis that left ventricular dilatation has a different prognostic importance in patients with alcoholic as compared to idiopathic congestive cardiomyopathy. Similarly, a longer duration of symptoms before diagnosis was predictive of death in patients with idiopathic cardiomyopathy but not alcoholic dilated cardiomyopathy, indicating that mechanisms other than long-standing congestive heart failure might lead to death in patients with alcoholic cardiomyopathy.

Limitations of the study

The present study is a retrospective analysis based on a population referred for work-up and management of overt congestive heart failure. Since it was performed retrospectively, the effect of medical therapy and documented alcohol abstinence on long-term survival and disease progression could not be properly evaluated. One very recent report on a very small subgroup of seven patients suggested that alcohol abstinence may lead to improved function even in the presence of markedly depressed left ventricular ejection fraction[36]. However, the strength of the study is the homogeneity of the well investigated patient population, in which all patients presented with overt congestive heart failure in the documented absence of coronary artery disease or any other form of secondary cardiomyopathy as well as a complete follow-up over a period of 10 years. There is only one previous study[6] which compared the long-term follow-up of such patients, and those authors focused their attention mainly on patients with idiopathic cardiomyopathy.

Clinical implications

Despite the above limitations, the present study indicates that the long-term outcome of patients presenting with severe congestive heart failure and left ventricular dilatation due to alcoholic cardiomyopathy is more favourable than that of patients with idiopathic cardiomyopathy and similar degrees of heart failure and left ventricular dilatation. This suggests that despite structural changes inherent in marked left ventricular dilation, disease progression is different in alcoholic compared to idiopathic congestive cardiomyopathy. Medical therapy and strong encouragement to avoid alcohol are the treatment of choice for these patients, and even in cases of documented alcohol abstinence the indication for heart transplantation should be made restrictively.

Addendum

After submission of the manuscript, a similar study focusing on Indium-labelled monoclonal antimyosin antibody imaging in patients with idiopathic and alcoholic cardiomyopathy was published[37]. In patients with similar baseline values (ejection fraction of 29% in both groups) to those of the present report, survival after 23 ± 16 months was better in 29 patients with alcoholic as compared to 88 with idiopathic cardiomyopathy: 72% vs 52% ($P<0.05$). Thus, our observations confirm these results and extend them with our much longer follow-up. The intensity of antibody uptake in the study by Obrador *et al.*[37] was found to be helpful for risk stratification of patients with dilated cardiomyopathy. In addition, these authors demonstrated parallel improvements in antibody uptake and left ventricular ejection fraction in a small subgroup of patients who became abstinent.

References

[1] Segal JP, Stapleton JF, McClellan JR, Waller BF, Harvey WP. Idiopathic cardiomyopathy: clinical features, prognosis and therapy. Curr Probl Cardiol 1978; 3: 9–49.

[2] Kuhn G, Breithardt G, Knieriem HJ *et al.* Prognosis and possible presymptomatic manifestations of congestive cardiomyopathy. Postgrad Med J 1978, 54: 451–9.

[3] Fuster V, Gerch BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. The natural history of dilated cardiomyopathy. Am J Cardiol 1981; 47: 525–31.

[4] Smith DI. Relationship between morbidity and mortality due to alcoholic cardiomyopathy and alcohol consumption in Australia. Adv Alcohol Subst Abuse 1990; 8: 57–65.

[5] Keogh AM, Baron DW, Hickie JB. Prognostic guides in patients with idiopathic or ischemic dilated cardiomyopathy assessed for cardiac transplantation. Am J Cardiol 1990; 65: 903–8.

[6] Ikram H, Williamson HG, Won M, Grozier IG, Wells EJ. The course of idiopathic dilated cardiomyopathy in New Zealand. Br Heart J 1987; 57: 521–7.

[7] Redfield MM, Gersh BJ, Bailey KR, Ballard DJ, Rodeheffer RJ. Natural history of idiopathic dilated cardiomyopathy: effect of referral bias and secular trend. J Am Coll Cardiol 1993; 22: 1921–6.

[8] Demakis JG, Proskey A, Rahimtoola SH *et al.* The natural course of alcoholic cardiomyopathy. Ann Intern Med 1974; 80: 293–7.

[9] Pavan D, Nicolosi GL, Lestuzzi C, Burelli C, Zardo F, Zauntti D. Normalization of variables of left ventricular function in patients with alcoholic cardiomyopathy after cessation of excessive alcohol intake: an echocardiographic study. Eur Heart J 1987; 8: 535–40.

[10] Milani L, Bagolin E, Sanson A. Improvement of left ventricular function in chronic alcoholics following abstinence from ethanol. Cardiology 1989; 76: 299–304.

[11] Knochel JP. Cardiovascular effects of alchohol. Ann Intern Med 1983; 98: 849–54.

[12] Regan TJ. Alcoholic cardiomyopathy. Progr Cardiovasc Dis 1984; 27: 141–52.

[13] Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53: 457–81.

[14] Lengyel M, Kokeny M. Follow-up study in congestive cardiomyopathy Cardiologica 1981; 36: 35–48.

[15] Likoff MJ, Chandler SL, Kay HR. Clinical determinants of mortality in chronic congestive heart failure secondary to idiopathic dilated or to ischemic cardiomyopathy. Am J Cardiol 1987; 59: 634–8.

[16] Kelly TL, Cremo R, Neilsen C, Shabetai R. Prediction of outcome in late-stage cardiomyopathy. Am Heart J 1990; 119: 1111–21.

[17] Hatle L. Orjavic O, Storstein O. Chronic myoardial disease. I. Clinical picture related to long-term prognosis. Acta Med Scand 1976; 199: 399–405.

[18] Unverferth DV, Magorien RD. Moeschberg ML, Baker PB, Fetters JK, Leier CV. Factors influencing one-year mortality of dilated cardiomyopathy. Am J Cardiol 1984; 54: 147–52.

[19] Shugoll GI, Bowen PJ, Moore JP, Lenkin ML. Follow-up observations and prognosis in primary myocardial disease. Arch Intern Med 1972; 129: 67–72.

[20] Convert G, Delaye J, Beaune J, Biroin A, Gonin A. Etude prognostique des myocardiopathies primitives non obstructives. Arch Mal Cûr 1980; 72: 227–37.

[21] Alexander CS. Idiopathic heart disease 1. Analysis of 100 cases with special reference to chronic alcoholism. Am J Med 1966; 41: 213–28.

[22] Brigden WW, Robinson JF Alcoholic heart disease. Br Med J 1964; ii: 1283–9.
[23] Schwarz F, Mall G, Zebe H *et al.* Determinants of survival in patients with congestive cardiomyopathy; quantitative morphologic findings and left ventricular hemodynamics. Circulation 1984; 70: 923–8.
[24] Tsiplenkova VG, Vikhert AM, Cherpachenko NM. Ultrastructural and histochemical observations in human and experimental alcoholic cardiomyopathy. J Am Coll Cardiol 1986: 8 (Suppl A): 22A–32A
[25] Richardson PJ, Wodak AD, Atkinson L, Saunders JB, Jevitt DE. Relation between alcohol intake, myocardial enzme activity and myocardial function in dilated cardiomyopathy. Br Heart J 1986; 56: 165–70.
[26] Segel LD, Rending SV, Mason DT. Alcohol-induced cardiac hemodynamic and Ca-flux and dysfunctions are reversible. J Moll Cell Cardiol 1981; 13: 443–55.
[27] Koide T, Kato A, Takabatake Y *et al.* Variable prognosis in congestive cardiomyopathy: role of left ventricular function, alcoholism and pulmonary thrombosis. Jap Heart J 1980; 21. 451–60.
[28] Shugoll GI, Bowen PJ, Floore JP, Lenain ML. Follow-up observations and prognosis in primary myocardial diseases. Arch Intern Med 1972; 129: 67–72.
[29] Sarkioja T, Hirvonen J. Causes of sudden unexpected death in young and middle-aged persons. Forensic Sci Int 1984; 24: 247–54.
[30] Wilson JR, Schwartz JS, Sutton MS *et al.* Prognosis in severe heart failure· relation to hemodynamic measurements and ventricular ectopic activity. J Am Coll Cardiol 1983; 2: 403–10.
[31] Cleland JGf, Dargie HJ, Ford I. Mortality in heart failure: clinical variables of prognostic value. Br Heart J 1987; 58: 572–82.
[32] Gradman A, Deedwania P, Cody R *et al.* Predictors of total mortalty an sudden death in mild to moderate heart failure. J Am Coll Cardiol 1989; 14: 564–9.
[33] Cohn JN. Prognostic factors in heart failure: poverty amidst a wealth of variables. J Am Coll Cardiol 1989; 14: 571–2.
[34] Meinertz T, Hofmann T, Kasper W *et al* Significance of ventricular arrhythmias in idiopathic dilated cardiomopathy. Am J Cardiol 1984; 53: 902–7.
[35] Diaz RA, Obasohan A, Oakley CM. Prediction of outcome in dilated cardiomyopathy. Br Heart J 1987; 58: 393–9.
[36] Gavazzi A, De Maria R, Renosto G *et al.* on behalf of the SPIC (Italian Multicenter Cardiomyopathy Study) Group. The spectrum of left ventricular size in dilated cardiomyopathy: clinical correlates and prognostic implications. Am Heart J 1993; 125· 410–22.
[37] Obrador D, Ballester M, Carrio I *et al* Presence, evolving changes and prognostic implications of myocardial damage detected in idiopahtic and alcoholic dilated cardiomyopathy by ^{111}In monoclonal antimyosin antibodies. Circulation 1994; 89· 2054–61.