Presence, Evolving Changes, and Prognostic Implications of Myocardial Damage Detected in Idiopathic and Alcoholic Dilated Cardiomyopathy by $^{111}$In Monoclonal Antimyosin Antibodies

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Background The clinical relevance of myocardial cell damage in dilated cardiomyopathy is uncertain. Myocardial uptake of $^{111}$In monoclonal antimyosin antibodies (MAA) was used to study myocardial damage in patients with idiopathic (IDC) and alcoholic (ADC) dilated cardiomyopathy and to assess its prognostic implications.

Methods and Results MAA and echocardiographic studies were performed in 117 patients. Intensity of antibody uptake was measured by heart-to-lung ratio (HLR) (normal <1.55). Studies were repeated in survivors and patients who did not receive a cardiac transplant. Follow-up extended up to 62 months (mean, 23±16 months). Eighty-eight patients with IDC showed a 77% prevalence of abnormal MAA. After acute-onset IDC, reduction of HLR (1.81±0.2 to 1.56±0.1) (P=.007) with improvement in ejection fraction (EF) (35±10% to 46±14%) (P=.018) was observed. No changes in HLR or EF were detected in patients with chronic stable IDC. Twenty-nine patients with ADC showed a lower prevalence (48%) of abnormal MAA studies than those with IDC (P=.003). HLR was higher in 13 active (1.78±0.3) than in 16 past consumers (1.49±0.2) (P=.019); in the former, HLR decreased to 1.44±0.2 (P=.012), and EF improved (35±14% to 53±18%) (P=.05) after abstinence. Intensities of uptake HLR of >1.87 were associated with increased risk of death or transplantation.

Conclusions In patients with IDC, variations of MAA uptake are detected in patients who present acutely but not in those with chronic stable disease. In patients with ADC, MAA uptake mainly depends on alcohol consumption. In both situations, reduction of uptake correlates with improvement of ventricular function. Higher intensities of MAA uptake are associated with a worse outcome. The intensity of antibody uptake, along with other clinical and functional variables, may be helpful in risk stratification of patients with dilated cardiomyopathy. (Circulation. 1994;89:2054-2061.)

Key Words • alcohol • cardiomyopathy • antibodies • echocardiography • nuclear medicine

The clinical relevance of active myocardial cell damage in the context of dilated cardiomyopathy is uncertain. Detection of the presence of such damage by endomyocardial biopsy, using uniform histopathological criteria, has been limited by the low sensitivity of the method. $^{1}$-$^{4}$ Myocardial uptake of $^{111}$In-labeled monoclonal antimyosin antibodies (MAA) provides another tool to detect myocardial cell damage. Antibody uptake occurs when the sarcolemma is disrupted and myocytes become irreversibly damaged. $^{5}$-$^{7}$ This technique has been used in the diagnosis of acute myocardial infarction. $^{8}$-$^{9}$ and to detect acute myocarditis. $^{10}$-$^{11}$ anthracycline toxicity. $^{12}$-$^{13}$ and rejection after heart transplantation. $^{14}$-$^{18}$

We recently reported that a high prevalence of antimyosin uptake is detected in patients with chronic stable idiopathic dilated cardiomyopathy, suggesting the presence of ongoing active myocardial damage in this condition. $^{19}$ In the present study, we sought to assess the presence and intensity of MAA uptake related to the time of clinical onset and the pattern of alcohol intake. In addition, changes in the degree of antibody uptake over time were correlated with variations of left ventricular size and function and long-term outcome.

Methods From October 1986 to July 1991, 198 patients with dilated cardiomyopathy were referred for evaluation for heart transplantation. In 134 patients (67%), $^{111}$In MAA uptake studies could be performed. Seventeen patients were excluded for the following reasons: 1 had predominantly right ventricular dilated cardiomyopathy, 2 were treated with immunosuppression, 2 had hypertension, 1 had diabetes, and 11 were excluded because no adequate estimate of alcohol intake could be obtained, leaving 117 patients with dilated cardiomyopathy to be included.

Significant coronary artery disease was ruled out in 87 patients (74%) in whom coronary angiography was performed;
in the remaining 30, 28 of whom were less than 50 years old with no risk factors for coronary disease and no chest pain, angiography was not undertaken. Endomyocardial biopsy was performed in all 87 catheterized patients, with a Cordis biotome20 used to take a mean of four samples with a wet weight of 1 to 3 mm. In only 2 patients (2.2%) was myocarditis detected, as defined by the Dallas criteria.21

Patients were treated with diuretics (89%), nitrates (16%), hydralazine (45%) (at a dose of 75 to 400 mg/d [mean, 250±75 mg/d]), captopril (30%) (at a dose of 36 to 150 mg/d [mean, 76±24 mg/d]), or digitalis (54%). Intravenous dobutamine was used in 2.3% of patients; in these cases, antimyosin imaging was delayed several weeks after withdrawal of intravenous drugs. Every patient received anticoagulant therapy.

Because of the potential effects of alcohol on the myocardium, identification of cases of cardiomyopathy of possible alcoholic origin was considered advisable. Therefore, quantitative estimation of alcohol intake was assessed by questioning both patients and their close relatives and included grams of alcohol intake per day and number of years of alcohol consumption. On the basis of these data, cumulative alcohol intake was calculated for each patient. Twenty-nine of the 117 patients (25%) had drank ≥100 g alcohol/d for more than 10 years or consumed >70 g/d and had a cumulative alcohol intake of >360 kg (equal to ≥100 g/d for ≥10 years). These patients were considered to have cardiomyopathy of possible alcoholic origin.22 None of these patients had been referred from a psychiatric unit because we considered this population to be unsuitable for heart transplantation. The remaining 88 patients (75%) were diagnosed as idiopathic.

**Patient Subsets**

Patients with idiopathic dilated cardiomyopathy were allocated to subsets according to the interval between the time of clinical onset and the antimyosin study. These intervals were acute (0 to 3 months), subacute (4 to 12 months), chronic stable (patients with dilated cardiomyopathy for <12 months who had been evaluated in the outpatient clinic), or chronic unstable (patients with dilated cardiomyopathy for >12 months who had been readmitted to hospital for heart failure).

Patients with alcoholic dilated cardiomyopathy who admitted alcohol intake up to the time of antimyosin study or within the previous 3 months were classified as active consumers, and the remaining were considered past consumers.

**Echocardiography**

Left ventricular function was assessed with echocardiography by an independent observer who was unaware of the clinical data and scanning results. Measurement of diameters was made with two-dimensional guided M-mode, and left ventricular ejection fraction was calculated using Simpson's method.23

**Isotopic Preparation and Imaging**

A dose of 0.5 mg of R11D10-Fab-diethylenetriamine pentaacetic MAA (Centocon) was labeled with 2.0 mCi of 111In chloride and administered intravenously. No adverse reactions were noted. Imaging was undertaken at 48 hours in the anterior projection using a conventional large-field-of-view camera with a high-resolution medium-energy collimator and 209 window centered on 247- and 173-keV peaks. A minimum of 500 000 counts between 5 to 10 minutes was collected. Analog and digital images collected in a 128×128 matrix were stored for subsequent analysis.

Interpretation of the antibody studies was performed by an expert independent observer by calculation of the heart-to-lung ratio, as previously reported.11 This method provides a semiquantitative estimation of the relative cardiac antimyosin uptake with very low intraobserver and interobserver variability; a cutoff of a heart-to-lung ratio of 1.55 was established to differentiate normal from abnormal antimyosin studies.11

**Table 1. Clinical, Echocardiographic, and Isotopic Features of Patients With Idiopathic and Alcoholic Dilated Cardiomyopathy**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Idiopathic (n=88)</th>
<th>Alcoholic (n=29)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>43±13</td>
<td>44±10</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>63/25</td>
<td>29/0</td>
<td>.001</td>
</tr>
<tr>
<td>Onset of heart disease, mo (%)</td>
<td>40±47</td>
<td>50±54</td>
<td>NS</td>
</tr>
<tr>
<td>Acute, n (%)</td>
<td>17 (19.3)</td>
<td>3 (10.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Subacute, n (%)</td>
<td>16 (18.1)</td>
<td>6 (20.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic stable, n (%)</td>
<td>39 (44.3)</td>
<td>15 (51.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic unstable, n (%)</td>
<td>16 (18.1)</td>
<td>5 (17.2)</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA, I or II/III or IV</td>
<td>47/41</td>
<td>15/14</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol, g/d</td>
<td>19±28</td>
<td>120±73</td>
<td>.0001</td>
</tr>
<tr>
<td>Consumption, y</td>
<td>6.2±9.5</td>
<td>20.4±7.8</td>
<td>.0001</td>
</tr>
<tr>
<td>Cumulative alcohol intake, kg</td>
<td>100±158</td>
<td>844±451</td>
<td>.0001</td>
</tr>
<tr>
<td>LV diastolic diameter, mm</td>
<td>71.9±12</td>
<td>72±10</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>29.3±9.9</td>
<td>29.9±13</td>
<td>NS</td>
</tr>
<tr>
<td>Prevalence AM uptake at follow-up study, %</td>
<td>77</td>
<td>48</td>
<td>.003</td>
</tr>
<tr>
<td>Heart-to-lung ratio</td>
<td>1.74±0.27</td>
<td>1.62±0.31</td>
<td>.04</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence AM uptake at initial study, %</td>
<td>70</td>
<td>35</td>
<td>.01</td>
</tr>
<tr>
<td>Heart-to-lung ratio</td>
<td>1.63±0.19</td>
<td>1.46±0.17</td>
<td>.003</td>
</tr>
<tr>
<td>Transplantation, n (%)</td>
<td>28 (31)</td>
<td>4 (13)</td>
<td>.05</td>
</tr>
<tr>
<td>Death CHF, n (%)</td>
<td>11 (12)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Sudden death, n (%)</td>
<td>3 (3.4)</td>
<td>1 (3.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Survivors, n (%)</td>
<td>46 (52)</td>
<td>21 (72)</td>
<td>.05</td>
</tr>
</tbody>
</table>

NYHA indicates New York Heart Association; LV, left ventricular; AM, monoclonal antimyosin antibodies; and CHF, congestive heart failure.

**Follow-up Echocardiographic and Antimyosin Studies**

Echocardiographic and antimyosin studies were repeated in patients who survived or did not receive a transplant.

**Statistical Analysis**

Differences between the alcoholic and idiopathic dilated cardiomyopathy groups were assessed by Student's t test for continuous variables. In the latter, the differences between clinical groups were tested by ANOVA and Duncan's procedure for multiple comparisons. In patients who had repeat studies, a paired t test was used to compare changes in antimyosin uptake and left ventricular dilatation and ejection fraction. To test the relation between categorical variables for independent groups, χ² analysis was used; for paired data, McNemar's test was used. Correlation analysis was performed to assess the relation between pairs of continuous variables.

Survival curves were estimated with the Kaplan-Meier method: end points were death or heart transplantation. Differences between curves for different levels of a specific categorical variable were evaluated with Mantel-Cox's log-rank test.
Table 2. Clinical Features of Subsets of Patients With Idiopathic Dilated Cardiomyopathy

<table>
<thead>
<tr>
<th></th>
<th>Acute (n=17)</th>
<th>Subacute (n=16)</th>
<th>Chronic Stable (n=39)</th>
<th>Chronic Unstable (n=18)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>37±17</td>
<td>38±11</td>
<td>45±10</td>
<td>47±11</td>
<td>.04*</td>
</tr>
<tr>
<td>Onset of heart disease, mo</td>
<td>1.9±1.9</td>
<td>5.3±1.6</td>
<td>64±51</td>
<td>60±40</td>
<td>.0001†</td>
</tr>
<tr>
<td>NYHA, I or II/III or IV</td>
<td>9/8</td>
<td>9/7</td>
<td>25/14</td>
<td>4/12</td>
<td>.03‡</td>
</tr>
<tr>
<td>LV diastolic diameter, mm</td>
<td>65±12</td>
<td>71±8</td>
<td>70±11</td>
<td>83±12</td>
<td>.01§</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>35±10</td>
<td>28±9</td>
<td>29±9</td>
<td>24±7</td>
<td>.009</td>
</tr>
<tr>
<td>Prevalence of antimyosin uptake, %</td>
<td>82</td>
<td>69</td>
<td>82</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>Heart-to-lung ratio of uptake</td>
<td>1.75±0.3</td>
<td>1.69±0.3</td>
<td>1.69±0.17</td>
<td>1.90±0.38</td>
<td>.05§</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart transplantation, n</td>
<td>1</td>
<td>6</td>
<td>9</td>
<td>12</td>
<td>.001**</td>
</tr>
<tr>
<td>Death CHF, n</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sudden death, n</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

NYHA indicates New York Heart Association; LV, left ventricular; and CHF, congestive heart failure.

Differences between groups (A indicates acute; SA, subacute; C, chronic stable; and U, chronic unstable): *A-(C,U); †A-(C,U), SA-(C,U); §U-(A,C); ¶U-(A,SA,C); ||A-(C,U); ¶C-U; **U-(A,SA,C).

In the multivariate analysis, continuous variables were categorized. To optimize the cutoff level that would discriminate two risk groups for these variables, the formula for threshold computation devised by Robert et al.24 was used. This procedure, which assumes a normal distribution of the original variable, is a probabilistic approach based on Bayes' rules that maximizes the chances of a correct classification by solving a second-degree polynomial. This non–a priori approach also provides impartiality. All the variables included in the logistic model except age were categorized.

Relative risks for end points were estimated with unconditional logistical regression,25 because the proportionality of the hazards26 corresponding to the levels of a variable over time did not meet the requirements of the Cox model.27

BMDP and spss statistical packages were used for tables and bivariate contrasts, and EGRET (Statistics and Epidemiology Research Corp, Seattle, Wash) was used for Cox and logistic regression modeling.

Results

The age of the 117 patients studied ranged from 13 to 73 years (mean, 43±12 years), the duration of disease was 1 to 256 months (mean, 43±49 months), and follow-up extended from 1 to 62 months (mean, 23±16 months).

Idiopathic Dilated Cardiomyopathy Group

This group comprised 88 patients, (63 men and 25 women; age range, 13 to 71 years; mean age, 43±13 years) (Table 1, left). Of these, 68 (77%) showed abnormal cardiac antimyosin uptake, with a heart-to-lung ratio of 1.74±0.27 (range, 1.20 to 2.80). No correlation was detected between the heart-to-lung ratio of antimyosin binding and New York Heart Association (NYHA) class or left ventricular end-diastolic diameter or ejection fraction.

Analysis of clinical features according to time from onset (Table 2) showed that patients with acute (n=17) or subacute (n=16) disease were younger than those with chronic stable (n=39) or chronic unstable (n=18) disease. Patients in the acute or subacute subset had a smaller left ventricular chamber size and a higher left ventricular ejection fraction than patients with chronic unstable disease. Although prevalence of MAA uptake was similar in all subsets, higher heart-to-lung ratios of antimyosin uptake were detected in chronic unstable patients compared with the chronic stable group (Table 2).

Follow-up and Repeated Studies

Heart transplantation was performed in 28 patients, with significant differences noted between the chronic unstable and the remaining groups (P<.001). Death due to heart failure involved 11 patients, and sudden unexpected death occurred in 3 chronic stable patients; Table 2 shows the distribution of mortality and need for transplantation in these patient subsets.

Echocardiographic and antimyosin antibody studies were repeated in 43 patients who survived or did not receive a cardiac transplant. In 4 patients (3 chronic stable and 1 chronic unstable), studies could not be repeated.

In the acute subset, a second study was performed in 15 patients (mean, 7.7±7.4 months) after the initial evaluation. The heart-to-lung ratio of antibody uptake decreased from 1.81±0.2 to 1.56±0.19 (P<.007), the left ventricular diastolic diameter remained unchanged (65±3 mm to 62±11 mm), and the ejection fraction increased from 35±10% to 46±14% (P<.01).

In the subacute subset, studies were repeated in 9 patients (mean, 10±6.7 months) after the initial study. The heart-to-lung ratio of antimyosin uptake decreased from 1.72±0.14 to 1.60±0.03 (P<.04), but changes in left ventricular size or ejection fraction (70±5.8 mm to 66±10 mm and 29±10% to 37±15%, respectively) were not significant.

Grouping of data from acute and subacute patients, which showed changes in the same direction, resulted in increased statistical power (Fig 1). At the time of repeat studies, the prevalence of abnormal antimyosin scans for both groups was 62%.

In the 18 patients with chronic stable disease who had been restudied, no significant changes were noted in antimyosin uptake (heart-to-lung ratio, 1.71±0.15 to 1.66±0.16), left ventricular size (70±10 mm to 71±13 mm), or ejection fraction (29±8.9% to 29±12%) 16±9 months after the initial study (Fig 1, right). Only 1 of the 16 patients in the chronic unstable subset was restudied, and no significant changes were noted.
Alcoholic Dilated Cardiomyopathy Group

All 29 patients in this group were male (age range, 25 to 73 years; mean age, 44±10 years). Table 1 (right) shows their clinical, echocardiographic, and scintigraphic features.

The interval between onset of symptoms and antimonyosin study ranged from 1 to 256 months (50±54 months). The heart-to-lung ratio of antimonyosin uptake for the whole group ranged from 1.20 to 2.50 (mean, 1.62±0.31). Comparison between active and past alcohol consumers (Table 3 and Fig 2) showed that age, NYHA, left ventricular diastolic diameter, and left ventricular ejection fraction were similar. The only significant differences were the prevalence and intensity of antimonyosin uptake. The heart-to-lung ratio in 13 active consumers was 1.78±0.31 compared with 1.49±0.24 in 16 past alcohol consumers (P=.009); positive scans involved 10 of 13 active consumers but only 4 of 16 past consumers (P=.005). There was a significant inverse correlation between the interval from cessation of alcohol consumption to antimonyosin study and the intensity of antimonyosin antibody uptake (r = -0.41, P=.02). However, the calculated cumulative alcohol intake did not correlate with the degree of left ventricular dilatation or ejection fraction or the presence or intensity of antimonyosin uptake.

Follow-up and Repeated Studies

Patients were followed a mean of 29±18 months (1 to 54 months). In 7 of the 13 active alcohol consumers, a second antimonyosin study could be performed after cessation of alcohol intake 15 months after the initial study.
TABLE 3. Clinical, Echocardiographic, and Isotopic Features of Patients With Alcoholic Dilated Cardiomyopathy According to the Activity of Alcoholism at the Time of Antimyosin Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Active (n=13)</th>
<th>Past (n=16)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>45±11</td>
<td>43±10</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA, 1 or II/III or IV</td>
<td>7/6</td>
<td>8/8</td>
<td>NS</td>
</tr>
<tr>
<td>LV diastolic diameter, mm</td>
<td>71±12</td>
<td>72±12</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>27±13</td>
<td>31±12</td>
<td>NS</td>
</tr>
<tr>
<td>Prevalence AM uptake</td>
<td>10/13</td>
<td>4/16</td>
<td>.005</td>
</tr>
<tr>
<td>Heart-to-lung ratio</td>
<td>1.78±0.31</td>
<td>1.49±0.24</td>
<td>.009</td>
</tr>
</tbody>
</table>

NYHA indicates New York Heart Association; LV, left ventricular; and AM, monoclonal antimyosin antibodies.

The remaining 6 patients could not be restudied because they underwent cardiac transplantation (4 patients) or died of congestive heart failure (2 patients).

In these 7 patients, the presence of abnormal antibody uptake was reduced after abstinence from 6 to 2 patients (difference not significant), the intensity of uptake decreased (1.72±0.17 to 1.44±0.2) (P=.012), and ejection fraction improved (35%±14 to 53%±18) (P=.05). No significant changes were detected in left ventricular diastolic diameters (70±13 to 64±13 mm).

Eight of the 16 patients considered past consumers were also restudied, but no changes were detected in the heart-to-lung ratio (1.47±0.43 to 1.43±0.12), left ventricular size (67±8 mm to 65±11 mm), or left ventricular ejection fraction (37±14% to 43±14%).

Differences Between Idiopathic and Alcoholic Dilated Cardiomyopathy

Aside from the amount and length of alcohol consumption, which constituted the criteria for group allocation, differences between groups were sex distribution, prevalence and degree of antimyosin uptake, and need for transplantation (Table 1). At the time of repeat studies, the differences remained in the prevalence and the intensity of antimyosin uptake.

Estimation of Prognosis and Risk Factors in Dilated Cardiomyopathy

The cutoff points for left ventricular diastolic diameter, left ventricular ejection fraction, and heart-to-lung ratio of antimyosin uptake that better discriminated groups of alive patients from those dead or transplanted were 74 mm, 29%, and 1.87, respectively.

Variables that showed significant differences in the bivariate analysis (survivors versus death or transplantation) were NYHA, clinical presentation (acute or chronic), etiology of dilated cardiomyopathy (alcoholic or idiopathic), diastolic diameter, ejection fraction, and heart-to-lung ratio of antimyosin uptake. When included in the logistic regression model, together with age and sex (Table 4), results showed that age, NYHA, chronic presentation, idiopathic dilated cardiomyopathy, and left ventricular size were independent risk factors for death or need for heart transplantation. Despite showing an excess risk of 50% and 100%, respectively, both heart-to-lung ratio and ejection fraction did not reach statistical significance as independent risk factors.

The overall 1- and 3-year probabilities of survival or transplantation were 73% and 57%. Survival curves for the variables included in the logistic regression model are shown in Fig 3.

Discussion

The present series provides the first report of the spontaneous evolution of myocardial cell damage detected by 11In MAA in patients with idiopathic or alcoholic dilated cardiomyopathy.

Idiopathic Dilated Cardiomyopathy

This study confirms the high prevalence of myocardial cell damage in idiopathic dilated cardiomyopathy,19,28,29 Use of a semiquantitative method to assess the presence and degree of antibody uptake shows that in patients...
presenting with acute or subacute disease, a decrease in uptake is associated with improvement in ejection fraction, as described by Dec et al.\textsuperscript{28} These changes occur spontaneously, as none of these patients were receiving immunosuppressive drugs. The fact that after the acute episode uptake persists in a large proportion of patients (62%) and that in chronic stable patients the prevalence of uptake is high indicate the presence of ongoing myocardial disease, as we previously suggested rather than a burned-out cardiomyopathy.\textsuperscript{19} The present study also shows that in acute and subacute idiopathic disease, the decrease in the degree of myocardial cell damage is associated with functional improvement, whereas no changes occur in chronic stable patients.

**Alcoholic Dilated Cardiomyopathy**

In idiopathic dilated cardiomyopathy and dilated cardiomyopathy of alcoholic origin, the left ventricle is similar,\textsuperscript{30-32} and its differentiation is based on clinical grounds.\textsuperscript{33,34} However, acceptance of alcoholic heart
muscle disease as a distinct entity is not universal. Whether ethanol abuse causes myocardial damage is central to the existence of alcoholic heart muscle disease. Although several important clinical reports\(^5\) provide firm evidence of the deleterious effect of alcohol on the myocardium, such evidence is indirect. In fact, no study in humans has been able to establish this causal relation because no adequate noninvasive method of detecting myocardial damage has been available. MAA studies provide such a method.

In the present study, patients with alcoholic dilated cardiomyopathy showed significantly lower prevalence and less intense antibody uptake than those in the idiopathic cardiomyopathy group. In addition, patients in the former group who actively consumed alcohol at the time of the antimyosin study had a prevalence and intensity of antibody uptake significantly higher than those who had been past consumers, and a reduction of antibody uptake was observed after alcohol abstention accompanied by an increase in ejection fraction. Therefore, the present report provides direct evidence of the deleterious effect of chronic alcohol consumption on the myocardium and links improvement of left ventricular function after cessation of alcohol consumption to reduction or disappearance of alcohol-induced myocardial damage.

**Mechanisms of Myocardial Injury in Dilated Cardiomyopathy**

Alcohol consumption appears as the main mechanism of myocardial damage in patients presumed to have alcoholic dilated cardiomyopathy. The low (35%) prevalence of antimyosin uptake in past consumers or in active consumers after alcohol withdrawal favors this assertion. Although the relation between heavy alcohol consumption and myocardial injury is suggested, the present report does not address the capability of alcohol to induce such injury in the general population. Because not all alcoholic patients develop heart muscle disease, the possibility that patients with alcoholic dilated cardiomyopathy might represent individuals susceptible to the effects of alcohol should be taken into account.

In idiopathic dilated cardiomyopathy, the nature and changes of myocardial cell damage are uncertain. Active myocarditis—in its histological meaning—is unlikely to be a relevant cause of antimyosin uptake, as few patients with dilated cardiomyopathy and positive antimyosin scans show this histological pattern in cardiac explants.\(^5\) Persistent enterovirus disease without inflammatory disease could provide an explanation to the ongoing myocardial damage. Virus persistence has been associated with a poor outcome.\(^4\) Whether positive antimyosin uptake might reflect persistent viral infection is uncertain, and at present it is being evaluated.

The possibility that heart failure per se could produce myocardial damage due to a combination of subendocardial ischemia through increased wall stress and low perfusion pressure in patients with dilated cardiomyopathy has been suggested.\(^41\) However, several facts suggest that the myocardial injury seen in these patients might not be due to the effects of heart failure. First, patients with severe left ventricular dilatation and important reduction of ejection fraction due to causes other than dilated cardiomyopathy (e.g., severe end-stage coronary heart disease without angina) who are referred for transplantation do not show antimyosin uptake.\(^19\) Second, in the present study, functional class classification, left ventricular size, and ejection fraction in idiopathic and alcoholic dilated cardiomyopathy were similar despite important differences in the prevalence and degree of antimyosin uptake (Table 1). In addition, in active and past alcohol consumers with dilated cardiomyopathy, a similar degree of functional impairment was noted despite significant differences in antimyosin uptake (Table 3). Third, no correlation was detected in the present series between the degree of functional disability, left ventricular size or ejection fraction, and the degree of antimyosin uptake. These observations suggest that the presence of antimyosin uptake in dilated cardiomyopathy reflects the presence of myocardial injury not necessarily related to the effects of heart failure.

**Risk Factors for Mortality and Need of Cardiac Transplantation**

The present series confirm that NYHA, diastolic diameter, and ejection fraction are variables associated with increased mortality or the decision to transplant. However, several previously unpublished data stem from the present series. First, patients with acute or subacute dilated cardiomyopathy have better survival than those with chronic disease. Functional improvement after the initial episode in the acute or subacute group could explain these differences, and this should be an important consideration when selecting patients for transplantation. Second, alcoholic patients fared better than those with idiopathic disease; this could be ascribed to beneficial long-term effects of alcohol withdrawal on ventricular function. Finally, no reports are available on the impact of myocardial cell damage on long-term survival. In the present series, intense antibody uptake (heart-to-lung ratio > 1.87) was associated with increased mortality or need for heart transplantation compared with less intense uptake. This suggests a certain relation between the degree of myocardial damage and prognosis and indicates that the degree of antibody uptake, with other clinical and functional variables, may be helpful in risk stratification of patients with dilated cardiomyopathy.

**Study Limitations**

The population included possible heart transplantation candidates: they were relatively young, and none had diabetes or primary hepatic, pulmonary, or renal disease. These considerations caution against the application of results to a less-selected population with dilated cardiomyopathy. On the other hand, allocation of patients to idiopathic and alcoholic groups was clinical and probably imperfect, as questioning of alcohol habits may not provide a realistic estimation of alcohol consumption.

In conclusion, variations of degree of myocardial damage can be detected using MAA in dilated cardiomyopathy. In alcoholic patients, uptake depends on the activity of alcohol consumption; in idiopathic dilated cardiomyopathy, variations of uptake are seen in the acute and subacute cases. Such reduction correlates with improvement in ventricular function. The intensity of uptake may be useful for risk stratification and selection for transplantation.
Acknowledgments

This work was supported in part by Fondo de Investigaciones Sanitarias de la Seguridad Social (FISS) grants 950/87 and 0724/89 and Premio Fundación Arcees 1988. We are grateful to Carme Casanova for her secretarial work and to Dr. Gaitè Peramany Miralda and Professor Leonard C. Archard for invaluable critical comments.

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Circulation. 1994;89:2054-2061
doi: 10.1161/01.CIR.89.5.2054

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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