Low-dose dobutamine responsiveness in idiopathic dilated cardiomyopathy: relation to exercise capacity and clinical outcome

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Aims To evaluate myocardial contractile reserve using low-dose dobutamine echocardiography in patients with chronic heart failure secondary to idiopathic dilated cardiomyopathy stratified by peak exercise oxygen consumption (VO₂).

Methods and Results Sixty clinically stable patients (56 ± 11 years; 45 males) with idiopathic cardiomyopathy and NYHA class I to III symptoms of heart failure were studied and followed-up for 13 ± 3 months. All patients underwent cardiopulmonary exercise testing and low-dose dobutamine. The dobutamine infusion protocol consisted of an initial dose of 2·5 μg.kg⁻¹ per 3 min, increasing by 2·5 μg.kg⁻¹ per min every 3 min; the maximal dose was 10 μg.kg⁻¹ per min. The end-systolic volume index, left ventricular ejection fraction and cardiac output were measured at baseline and peak dobutamine dose and their change calculated as ((peak dose value-baseline value)/baseline value] x 100. Ten normal subjects with normal left ventricular function and no coronary artery lesions served as a control group to compare low-dose dobutamine results. All analysed echocardiographic variables either at baseline or following dobutamine infusion were significantly lower in patients with chronic heart failure as a whole compared to the control group. When the patients were grouped according to Weber’s classification, a statistically significant decrease in percentange changes in end-systolic volume index (β=0·77; P<0·0001), left ventricular ejection fraction (β=−0·72; P<0·0001) and cardiac output (β=−0·82; P<0·0001) from class A to class C was observed. The mean percentage decrease in end-systolic volume index following the dobutamine infusion was 28·7 ± 9% in class A (peak VO₂ > 20 ml.kg⁻¹.min⁻¹), 18·6 ± 8% in class B (peak VO₂ between 16 and 20 ml.kg⁻¹.min⁻¹), and only 6·4 ± 6% in class C (peak VO₂ between 10 and 16 ml.kg⁻¹.min⁻¹) patient groups. At multivariate analysis, only the percentage change in end-systolic volume index was significantly associated with a peak VO₂ <15 ml.kg⁻¹.min⁻¹ (P=0·006). During the follow-up, 17 patients had events (15 readmissions for worsening heart failure and two deaths). At multivariate analysis, only the percentage change in end-systolic volume index was significantly associated with the occurrence of events (P=0·003). The area under the receiver operating characteristic curve for percentage change in end-systolic volume index was not significantly different from that for peak VO₂ (0·86 ± 0·04 vs 0·80 ± 0·06; P:ns).

Conclusion This study indicates that in patients with chronic heart failure secondary to idiopathic cardiomyopathy, the cardiac response to low-dose dobutamine, as assessed by echocardiography, is correlated with peak VO₂, an objective and accurate measure of the severity of the disease and clinical outcome.

Key Words: Low-dose dobutamine; idiopathic dilated cardiomyopathy; peak VO₂.

Introduction

Dobutamine is a direct-acting beta-agonist that has been used to evaluate myocardial contractile reserve non-invasively in chronic heart failure. Beta-adrenergic contractile reserve, as assessed by dobutamine echocardiography, may be related to severity of chronic heart failure. In a study of 35 patients with ischaemic dilated cardiomyopathy, dobutamine echocardiography was found to be correlated with the New York Heart Association (NYHA) functional classes. However, NYHA classification is subjective and non-parametric and hence may not accurately reflect the severity of
chronic heart failure. Peak exercise oxygen consumption (VO₂) determination permits evaluation of chronic heart failure severity in a more reliable, objective and parametric manner than NYHA classification\(^2\). In addition, peak VO₂ is a most powerful predictor of prognosis\(^6\). The aim of this study was to evaluate myocardial contractile reserve by low-dose dobutamine echocardiography in patients with chronic heart failure secondary to idiopathic dilated cardiomyopathy stratified by peak VO₂. The value of low-dose dobutamine in predicting clinical progression of the disease was also assessed.

**Methods**

**Study group**

Sixty clinically stable patients with idiopathic cardiomyopathy and NYHA class I to III symptoms of chronic heart failure were included in the study. All patients had a left ventricular ejection fraction of 40% or less and angiographically proven absence of coronary artery lesions. The criterion of >80% endocardial definition at echocardiography had to be met for inclusion. Five patients (5/65, 7.7%) who did not satisfy this criterion were excluded from the study. Patients with general systemic disease, specific heart muscle disease or atrial fibrillation were excluded from the study. Those patients judged to be poorly motivated or presenting any non-cardiac conditions potentially limiting the ability to exercise, such as chronic obstructive pulmonary disease, anaemia, musculo-skeletal disorders, and obesity were also excluded.

In patients, low-dose dobutamine and cardiopulmonary exercise testing were performed after optimizing treatment with diuretics and/or angiotensin-converting enzyme inhibitors, if needed. Treatment with digitalis was discontinued for at least 1 week before performing the tests. No patient was being treated with beta-blockers prior to the tests. Ten normal subjects who had undergone coronary angiography for evaluation of chest pain served as a control group to compare the low-dose dobutamine results. All of these subjects had a normal left ventricular function and no coronary artery lesions. Written informed consent was obtained from all patients and subjects.

**Dobutamine echocardiography**

A complete Doppler and two-dimensional examination was performed in all patients and subjects with a Hewlett Packard Sonos 2500 ultrasound system (Andover, Massachusetts U.S.A.) connected to a 2.5 MHz probe. The dobutamine infusion protocol consisted of an initial dose of 2.5 μg.kg\(^{-1}\).min\(^{-1}\) for 3 min, increasing by 2.5 μg.kg\(^{-1}\).min\(^{-1}\) every 3 min; the maximal dose was 10 μg.kg\(^{-1}\).min\(^{-1}\). The patients and subjects were monitored continuously by a 12-lead electrocardiogram. Parasternal long- and short-axis, as well as apical two-, four- and long axis chamber views were obtained at baseline and at peak dobutamine dose and digitized in a quad screen format. The following variables were measured: end-systolic volume index\(^1\), left ventricular ejection fraction and cardiac output (CO). End-systolic volume and left ventricular ejection fraction were calculated using a biplane formula (modified Simpson’s formula)\(^4\). Cardiac output was calculated using the following method\(^5\), the left ventricular outflow diameter was measured in systole from the parasternal long axis view just below the insertion of the aortic cusps, and the area was then calculated according to the formula π r\(^2\). Five measurements were averaged. The velocity of aortic flow was measured by pulsed-wave Doppler from the apical-chamber view. The sample volume was positioned in the middle of the outflow tract immediately below the aortic cusps and the time velocity integrals, recorded over five consecutive cycles, were digitized using the leading edge convention. Cardiac output was then calculated according to the formula: time velocity integral × left ventricular outflow tract cross-sectional area × heart rate.

**Reproducibility**

To evaluate the reproducibility of the two-dimensional echocardiographic measurements of end-diastolic and end-systolic volumes, the echocardiograms of the first 20 patients were evaluated three times by the cardiologist who performed all the echocardiographic measurements in the study. These echocardiograms were re-examined without knowledge of the previous evaluation results. Variance of the three repeated measurements was calculated for each patient. Intra-observer variance was estimated as the average of the values obtained for the 20 patients\(^5\). Reproducibility, expressed as standard deviation (square root of intra-observer variance), was 3.5 ml for the end-diastolic volume and 3.3 ml for the end-systolic volume (mean value 180 ml for the end-diastolic volume, 134 ml for the end-systolic volume).

**Cardiopulmonary exercise testing**

Treadmill exercise testing with expiratory gas analysis was performed using the modified Bruce protocol\(^6\). Patients were encouraged to continue exercising until dyspnoea or fatigue forced them to stop. Those patients who were not familiar with exercise testing underwent a preliminary test. Oxygen uptake and carbon dioxide output were measured breath-by-breath using an automated system (Sensor Medics system 2900, Anaheim, California). Measurements were taken at rest and every 20 s throughout exercise and recovery. Raw ventilatory and gas exchange parameters were stored on floppy
disks. The anaerobic threshold was defined as the point at which the respiratory exchange ratio (\( \text{VCO}_2/\text{VO}_2 \)) was 1.00 or, subordinately, as the point at which the ventilatory equivalent for \( O_2 \) (\( \text{VE}/\text{VO}_2 \)) was minimal, followed by a progressive increase or by the V-slope method\[^{[17,18]}\]. All patients achieved the anaerobic threshold. Peak oxygen uptake was defined as the \( \text{VO}_2 \) measured at the end of exercise. According to their attained peak \( \text{VO}_2 \), the patients were classified as being in Weber’s class A (peak \( \text{VO}_2 \geq 20 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)), B (peak \( \text{VO}_2 \) between 16 and 20 ml \( \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)), or C (peak \( \text{VO}_2 \) between 10 and 16 ml \( \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)). The only two patients who achieved a peak \( \text{VO}_2 \leq 10 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \) were included in class C.

**Follow-up**

The mean follow-up was 13 ± 3 months (range: 4 to 18 months). No patient was lost to follow-up. Clinical progression was defined as death or hospital re-admission for worsening heart failure, which was ascertained by interviewing each of the surviving patients. Data on re-admissions were based on the primary diagnosis at discharge. The patient’s chart of those readmitted outside our Institute was reviewed by the study physician in order to confirm the diagnosis.

**Statistical analysis**

Data are reported as mean and standard deviation. Percentage change in left ventricular ejection fraction (%LVEF), end-systolic volume index (%ESVI) and cardiac output (%CO) following the dobutamine infusion was calculated as \([\text{peak dose value}−\text{baseline value}] / \text{baseline value}) \times 100\). Comparisons between the control group and chronic heart failure patients was performed by the t-test for independent samples. Spearman’s \( \rho \) was computed to analyse the correlation between echo variables and Weber’ s classification. Logistic regression was performed to identify univariate and multivariate predictors of a reduced peak \( \text{VO}_2 \) (<15 ml \( \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \)) and predictors of the occurrence of events during follow-up. A forward-stepwise approach was used to identify variables entering the final model in the multivariate analysis. The accuracy of peak \( \text{VO}_2 \) and %ESVI to predict events was measured by computing the area under the receiver operating characteristic curve\[^{[19,20]}\]; for each area under the curve the standard error of mean (SEM) was also computed. Receiver operating characteristic curves were obtained by plotting the sensitivity vs the true negative rate (1-specificity) obtained for different cut-off values of the variables. The two area under the curves were compared by \( Z \) statistics\[^{[21]}\]. A \( P \) value <0.05 was considered statistically significant.

**Results**

The baseline characteristics of the study population are reported in Table 1. All analysed echocardiographic variables were significantly lower in patients with chronic heart failure as a whole compared to the control group (Table 2).

When the patients were grouped according to Weber’s classification, there was a statistically significant decrease in %LVEF (\( \rho = −0.72; P<0.0001 \)), %ESVI (\( \rho = −0.77; P<0.0001 \)), and %CO (\( \rho = −0.82; P<0.0001 \)) from class A to class C (Fig. 1). Eighteen patients had a peak \( \text{VO}_2 \leq 15 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \). No significant differences in age (62 ± 9 vs 54 ± 11), sex distribution (male 67 % vs 79%), left ventricular ejection fraction (23 ± 5 % vs 28 ± 6 %), end-systolic volume index at peak dobutamine dose; %ESVI was computed to analyse the correlation between echo variables and Weber’ s classification.

**Table 1 Clinical characteristics of study population**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=60)</td>
<td>(n=10)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.5 ± 11</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>45/15</td>
</tr>
<tr>
<td>Duration of heart failure (years)</td>
<td>2.9 ± 2.9</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>19 (31.7%)</td>
</tr>
<tr>
<td>II</td>
<td>17 (28.3%)</td>
</tr>
<tr>
<td>III</td>
<td>24 (40%)</td>
</tr>
<tr>
<td>LVEF at baseline (%)</td>
<td>26.5 ± 5</td>
</tr>
<tr>
<td>ESVI at baseline (ml.m⁻³)</td>
<td>75.05 ± 28</td>
</tr>
<tr>
<td>EDVI at baseline (ml.m⁻³)</td>
<td>100.5 ± 33</td>
</tr>
<tr>
<td>Peak VO₂ (ml·kg⁻¹·min⁻¹)</td>
<td>18.8 ± 5</td>
</tr>
<tr>
<td>Respiratory exchange ratio</td>
<td>1.109 ± 0.09</td>
</tr>
</tbody>
</table>

Weber Class

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>28</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>A (%)</td>
<td>46.7%</td>
<td>21.7%</td>
<td>31.6%</td>
</tr>
<tr>
<td>Therapy*</td>
<td>Diuretics</td>
<td>61.8%</td>
<td>46%</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>56 (93%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>31 (52%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Eventual treatment with digitalis was discontinued at least 1 week before the test. No patient was treated with beta-blockers before the test.

**Table 2 Comparison between study population and control group**

<table>
<thead>
<tr>
<th></th>
<th>CHF patients</th>
<th>Controls</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF bs (%)</td>
<td>26.5 ± 6</td>
<td>52.3 ± 2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EF dob (%)</td>
<td>34.54 ± 11</td>
<td>70.60 ± 4</td>
<td>0&lt;01</td>
</tr>
<tr>
<td>%EF</td>
<td>+29.2 ± 26</td>
<td>+35.8 ± 8</td>
<td>ns</td>
</tr>
<tr>
<td>ESVI bs (ml.m⁻³)</td>
<td>75.05 ± 28</td>
<td>29.87 ± 8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESVI dob (ml.m⁻³)</td>
<td>62.41 ± 29</td>
<td>94.19 ± 5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>%ESVI</td>
<td>−19.4 ± 12</td>
<td>−30.4 ± 14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CO bs (l.m⁻³)</td>
<td>3.55 ± 1.0</td>
<td>4.48 ± 0.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CO dob (l.m⁻³)</td>
<td>5.11 ± 1</td>
<td>8.23 ± 0.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>%CO</td>
<td>+43.6 ± 30</td>
<td>+84.5 ± 25</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

EF=ejection fraction; ESVI=end systolic volume index; CO=cardiac output; %EF=percentage change of ejection fraction at peak dobutamine dose; %CO=percentage change of cardiac output at peak dobutamine dose; %ESVI=percentage change of end systolic volume index at peak dobutamine dose; bs=baseline, dob=dobutamine infusion.
We also classified the patients into two groups according to their change in end-systolic volume index following the dobutamine infusion. The peak VO\textsubscript{2} achieved by the group showing a decrease in end-systolic volume index of less than 15% was significantly lower than that achieved by the group exhibiting a decrease in end-systolic volume index of 15% or more (Fig. 3).

During the 13-month follow-up, 17 patients had events (15 re-admissions for worsening heart failure and two deaths). Univariate and multivariate association of study variables with the occurrence of events during follow-up are reported in Table 4. At multivariate analysis only the percentage change in end-systolic volume index following the dobutamine infusion was significantly associated with the occurrence of events ($P=0.003$). A <15% decrease in end-systolic volume index had 82% sensitivity, 74% specificity, 56% positive predictive power, and 91% negative predictive value. The event-free survival curves for the group of patients showing a decrease in end-systolic volume index <15% or >15% are shown in Fig. 4. The area under the curve for peak VO\textsubscript{2} was 0.80 (SEM=0.06), while the area under the curve for %ESVI was 0.86 (SEM=0.04); the difference between the two areas was not statistically significant (Fig. 5).

**Discussion**

Dobutamine has prominent inotropic effects and increases cardiac contractility primarily via direct beta receptor activation with only a minimal increase in heart rate\textsuperscript{[22]}. When given to patients with chronic heart failure, dobutamine also reduces systemic resistance as cardiac output rises, so that arterial pressure remains relatively constant\textsuperscript{[22]}. In chronic heart failure, the sympathetic nervous system activity is chronically increased, leading to a variety of maladaptive changes in the regulation of cardiovascular function\textsuperscript{[23]}. Beta-adrenergic receptor pathway desensitization, a fundamental abnormality in chronic heart failure resulting from chronic activation of the sympathetic nervous system\textsuperscript{[24]}, is the main determinant of the attenuated cardiac response to dobutamine\textsuperscript{[25–27]}. It depends on the degree of myocardial failure as well as on on the nature

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**Table 3** Univariate and multivariate predictors of a peak VO\textsubscript{2} <15 ml . kg\textsuperscript{-1} . min\textsuperscript{-1}

<table>
<thead>
<tr>
<th>Univariate P</th>
<th>Multivariate P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.03</td>
</tr>
<tr>
<td>EF bs</td>
<td>0.005</td>
</tr>
<tr>
<td>CO bs</td>
<td>ns</td>
</tr>
<tr>
<td>ESVI bs</td>
<td>0.0005</td>
</tr>
<tr>
<td>%EF</td>
<td>0.0006</td>
</tr>
<tr>
<td>%CO</td>
<td>0.013</td>
</tr>
<tr>
<td>%ESVI</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Abbreviations as in previous Table.
of systolic dysfunction, being more pronounced in idiopathic cardiomyopathy than ischaemic cardiomyopathy[24]. Chronically increased sympathetic nervous system activity may also greatly contribute to exercise intolerance by markedly attenuating the beta-adrenergic responsiveness of the heart to exercise, thus limiting the cardiac output response to exercise, increasing peripheral vascular resistance and decreasing blood flow to skeletal muscles[23,24,28,29]. A direct relationship of the degree of beta1-receptors down-regulation to peak VO2 was also found in patients with idiopathic cardiomyopathy[30]. Thus, impaired myocardial response to dobutamine and exercise intolerance may share a common pathophysiological mechanism in chronic heart failure.

**Figure 2** Linear correlation (continuous line) along with its 95% confidence intervals (dotted lines) between peak VO2 and %ESVI.

**Figure 3** Peak VO2 in patients with %ESVI <15% and >15% respectively.

**Table 4** Univariate and multivariate predictors of the occurrence of events during the follow-up

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate P</th>
<th>Multivariate P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>EF bs</td>
<td>0.05</td>
<td>ns</td>
</tr>
<tr>
<td>CO bs</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>ESVI bs</td>
<td>0.05</td>
<td>ns</td>
</tr>
<tr>
<td>Peak VO2</td>
<td>0.0005</td>
<td>ns</td>
</tr>
<tr>
<td>%EF</td>
<td>0.003</td>
<td>ns</td>
</tr>
<tr>
<td>%CO</td>
<td>0.009</td>
<td>ns</td>
</tr>
<tr>
<td>%ESVI</td>
<td>0.003</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Abbreviations as in previous Table.

**Figure 4** Survival curves for patients divided according to %ESVI <15% (---) or >15% (——).
In this study we evaluated cardiac reserve by low-dose dobutamine in patients with chronic heart failure secondary to idiopathic cardiomyopathy stratified by peak VO₂. All patients had left ventricular systolic dysfunction. Peak VO₂ is an objective and accurate measure of the severity of chronic heart failure. Its determination has therefore a prominent role in the risk stratification and clinical decision-making process. The efficient use of peak VO₂ in individual patients may, however, be limited by non-cardiac factors, such as skeletal muscle deconditioning, patient motivation and concomitant non-cardiac exercise limiting conditions. Low dose dobutamine echocardiography is insensitive to these factors.

As expected, the cardiac response to dobutamine, as assessed by two-dimensional echocardiography, was significantly worse in the chronic heart failure patient group than in normal subjects. The dobutamine-induced mean percentage decrease in end-systolic volume index was 19.4 ± 12% vs 30.4 ± 14%, respectively. In the chronic heart failure patients, the cardiac response to dobutamine worsened proportionally as Weber’s class deteriorated, the worst response being observed in Weber’s class C patient group. The mean percentage decrease in end-systolic volume index induced by the dobutamine infusion was 28.7 ± 9% in class A, 18.6 ± 8% in class B, and only 6.4 ± 6% in class C. As patients with substantial exercise intolerance are at higher risk for death or clinical deterioration, we also identified the echocardiographic variable during the dobutamine infusion most closely related to a peak VO₂ <15 ml kg⁻¹ min⁻¹. At multivariate analysis, a less than 15% decrease in end-systolic volume index following dobutamine infusion emerged as the only variable independently related to substantially impaired exercise tolerance. Moreover, when we classified the patients into two groups on the basis of their change in end-systolic volume index following the dobutamine infusion, we observed a significant difference in peak VO₂ achieved by the two groups.

The reserve of pump function can only be evaluated during exercise or inotropic stimulation. In nearly all previous studies investigating the relationship between the reserve of pump function and exercise capacity, exercise was used as the cardiovascular stimulus to evaluate cardiac reserve. A significant correlation between peak VO₂ and peak cardiac output was observed, leading to the conclusion that peak VO₂ is closely linked to circulatory dysfunction during exercise, although some patients with a reduced peak VO₂ may exhibit only mild or moderate haemodynamic dysfunction. Both cardiac output and VO₂ are, however, closely linked to exercise levels.

In the present study, the reserve of pump function was evaluated by measuring the changes in cardiac function following low-dose dobutamine infusion, providing a measure of cardiac reserve independent of exercise as a stimulus. The changes in cardiac function following inotropic stimulation with dobutamine were found to be related to exercise capacity and the lowest changes in end-systolic volume index were closely linked to substantial exercise intolerance. Most of the patients with a substantially reduced peak VO₂ exhibited minimal or no change in end-systolic volume index following the dobutamine infusion. On the basis of these data, it may be inferred that the reduced reserve of pump function significantly contributes to exercise intolerance in patients with chronic heart failure secondary to idiopathic cardiomyopathy. Previous studies showed that dobutamine infusion, despite improving left ventricular function and haemodynamics, increases peak VO₂ only minimally in patients with severe heart failure. However, as the mechanisms underlying exercise limitation are multiple, complex, long-standing and even heterogeneous, it seems very unlikely that an immediate increase in exercise tolerance by acutely improving only one of its determinants can be obtained in severely ill patients.

The prognostic significance of low-dose dobutamine responsiveness was also assessed. During a mean follow-up of 13 months, clinical progression of the disease, defined as death or rehospitalization for worsening heart failure, occurred in 28% of the patients. At multivariate analysis, the dobutamine-induced percentage change in end-systolic volume index was the only echocardiographic discriminant factor. The patients who presented clinical deterioration or died were those with the lowest decrease in end-systolic volume index. Independently of the cut-off value used, the prognostic accuracy for end-systolic volume index decrease following dobutamine infusion was not significantly different from that for peak VO₂. Our findings are consistent with a previous study by Ansalone et al. who found the end-systolic volume during dobutamine infusion to be independently correlated with prognosis.
in 30 patients with idiopathic cardiomyopathy. In another recent study\textsuperscript{[9]}, the prognostic value of low-dose dobutamine in patients with severe chronic heart failure caused by ischaemic dilated cardiomyopathy was also ascertained. These data suggest that low-dose dobutamine, which is insensitive to factors such as skeletal muscle deconditioning or poor motivation, is a valuable alternative technique to peak VO\textsubscript{2} determination for assessing the severity of the disease and prognosis of patients with chronic heart failure secondary to idiopathic cardiomyopathy. Whether the accuracy of risk assessment may be improved by the integrated (for example, reserving low-dose dobutamine for those patients whose exercise tolerance is limited by non-cardiac factors) or combined use of low-dose dobutamine and cardiopulmonary exercise testing should be investigated in further prospective studies.

Conclusions

This study indicates that in patients with chronic heart failure secondary to idiopathic cardiomyopathy, the cardiac response to low-dose dobutamine, as assessed by echocardiography, is correlated with peak VO\textsubscript{2}, an objective and accurate measure of the severity of the disease, and clinical outcome.

References

[29] Colucci WS. The sympathetic nervous system in congestive heart failure. In: Hosenpud JD, Greenberg BH, eds. Congestive heart failure: pathophysiology, diagnosis and


