Abnormal transoesophageal Doppler coronary flow reserve in patients with dilated cardiomyopathy: relationship to exercise capacity

Z. CHATI, J. F. BRUNTZ, G. ETHÉVENOT, E. ALIOT and F. ZANNAD
Department of Cardiology, Hôpital Jeanne d'Arc, B.P. 303 54201, Nancy, France, and the Centre d'Investigation Clinique (CIC) INSERM-CHU, Hôpital Jeanne d'Arc, B.P. 303 54201, Nancy, France

1. In patients with dilated cardiomyopathy, abnormal myocardial blood flow may contribute to poor myocardial function.

2. The aim of this study was to investigate the possible contribution of abnormal myocardial blood flow to the limitation of exercise capacity in patients with dilated cardiomyopathy.

3. Coronary flow reserve was assessed in 16 patients with dilated cardiomyopathy and 9 matched normal control individuals. All participants had angiographically normal coronary arteries. At rest and after dipyridamole infusion (0.56 mg/kg intravenously), peak systolic and diastolic coronary flow velocities were measured in the proximal left anterior descending coronary artery using transoesophageal pulsed Doppler echocardiography, guided by colour flow imaging. Coronary flow reserve was calculated as the ratio of hyperaemic to basal diastolic and systolic peak coronary flow reserve.

4. Baseline diastolic and systolic coronary flow velocities were significantly higher in patients (50 ± 6 and 30 ± 4 cm/s respectively) compared with control individuals (37 ± 3 and 20 ± 1 cm/s respectively) (mean ± S.E.M.) (P < 0.05). Diastolic and systolic peak coronary flow reserve were significantly lower in patients (1.60 ± 0.14 and 1.40 ± 0.09 respectively) compared with control individuals (2.89 ± 0.15 and 2.17 ± 0.17 respectively) (P < 0.001). Although peak VO₂ and exercise time were significantly lower in patients compared with control individuals, coronary flow reserve did not correlate to exercise capacity in patients with dilated cardiomyopathy.

5. These results confirm the abnormalities of coronary flow reserve previously observed in patients with dilated cardiomyopathy, but suggest that such abnormalities do not contribute to the limitation of exercise capacity in these patients.

INTRODUCTION

In chronic heart failure (CHF), exercise capacity is often limited by the onset of fatigue or dyspnoea [1]. The lack of a close correlation between the parameters of left ventricular (LV) systolic function at rest and exercise capacity expressed as peak oxygen consumption (VO₂) may be explained by poor cardiac reserve adaptation during exercise, which is unsuspected at rest.

In patients with dilated cardiomyopathy (DCM), abnormal myocardial blood flow may contribute to poor myocardial performance [2], and may therefore also contribute to exercise capacity limitation. The aim of this study was to investigate the possible relationship between coronary blood flow and exercise capacity in patients with DCM.

Under pharmacological evaluation, coronary flow reserve (CFR) has traditionally been measured using invasive techniques [2-4]. Several studies which have evaluated coronary blood flow using positron emission tomography (PET) scanning have revealed abnormalities of myocardial blood flow distribution [5,6] and decreased CFR in patients with DCM compared with control individuals [2,7]. PET scanning is, however, expensive and is not generally available.

Alternatively, transoesophageal pulsed Doppler echocardiography (TEE) has been shown to be a safe and rapid method for the evaluation of coronary blood flow [8]. In the study reported here, CFR patterns in patients with DCM were assessed using TEE and compared with those from matched normal control individuals in order to assess the possible contribution of CFR to the limitation of exercise capacity.

METHODS

Selection and characterization of patients and controls

All patients who underwent coronary artery angiography for CHF and suspected DCM in the Department of Cardiology, Hôpital Jeanne d’Arc, Nancy, France, between February 1995 and March 1996, were screened for enrolment in the study. DCM was diagnosed using transthoracic two-dimensional

Keywords: coronary flow reserve, dilated cardiomyopathy, exercise capacity, transoesophageal Doppler echocardiography.

Abbreviations: CFR, coronary flow reserve; CFV, coronary flow velocity; CHF, chronic heart failure; DCM, dilated cardiomyopathy; LAD, left anterior descending; LV, left ventricular; LVEF, left ventricular ejection fractions; PET, positron emission tomography; TEE, transoesophageal pulsed Doppler echocardiography.

Correspondence: Dr Z. Chati.
Doppler echocardiography (TTE) in patients who had a dilated, hypocontractile left ventricle in the absence of other forms of cardiac disease. Eighteen patients with DCM, who had angiographically normal coronary arteries, but in whom LV ejection fraction (LVEF) was less than 40%, were enrolled in the study. All were outpatients with CHF (New York Heart Association class II or III). All patients were stabilized for at least 1 month using angiotensin-converting enzyme inhibitor and diuretic treatment, with or without digoxin.

All individuals who underwent coronary artery angiography for atypical angina pectoris during the same period were also screened for participation in the study. Eleven healthy matched individuals with angiographically normal coronary arteries, no history of either cardiac or pulmonary disease, and normal resting and stress ECGs were enrolled in the study as controls.

Informed consent was obtained from all individuals, and the study protocol was approved by the ethics committee of the University Hospital of Nancy.

### TTE

TTE examinations were performed using a commercially available 2.5/2.0-MHz TTE probe (Hewlett-Packard Sonos 1000, Andover, MA, U.S.A.). LV internal dimensions (LVID) at end-diastole and end-systole, the thickness of the interventricular septum (IVS) and the LV posterior wall (PWT), and the dimensions of the left atrium at end-systole were measured (cm) using standard M-mode ECGs according to the recommendations of the American Society of Echocardiography (ASE) [9]. LV mass was calculated at end-diastole by the method of Troy et al. [10]:

\[
\text{Mass (g)} = 1.04 [(\text{IVS} + \text{LVID} + \text{PWT})^3 - (\text{LVID})^3]
\]

The resulting mass was then corrected using the following equation [11] to correlate with necropsy findings:

\[
\text{LV mass (g)} = 0.8 \times \text{(LV mass ASE)} + 0.6
\]

LV mass was indexed using body surface area [12].

Mitral flow velocities were recorded during TTE with the sample volume located at the tips of mitral leaflets. The peak and velocity time integral of maximal early (E) and late (A) diastolic filling velocities was measured, and the E:A wave ratio was calculated in the 13 patients and all control individuals who had sinus rhythm.

Pulmonary arterial pressure was evaluated from the maximum velocity of tricuspid regurgitation [13].

### TEE

After an 8-h fast, all individuals were premedicated (5 mg of sublingual midazolam). After topical anaesthesia (10% lignocaine spray), a commercially available 5/3.7-MHz TEE multiplane probe (Hewlett-Packard Sonos 1000) was inserted. All individuals were placed in the left lateral decubitus position, and the probe was positioned to provide a basal short-axis view of the aortic valve. The transducer was then manipulated to obtain a horizontal view of the left main coronary artery just above the aortic valve, and the left coronary bifurcation, which was generally Y-shaped. Transducer position was then adjusted to visualize the left anterior descending (LAD) coronary artery.

**Coronary flow velocity (CFV)—data at baseline.** After identification of the LAD, aided by colour-flow Doppler, the echo-Doppler beam was placed in a position as parallel as possible to that of the artery; angles of less than 30° to flow were consistently achieved. Doppler measurements were mainly performed in the horizontal plane (0°). Angles of 45° were sometimes used to improve LAD colour-flow Doppler. A pulsed Doppler sample volume (5 mm in length) was placed in the proximal LAD and the CFV was recorded. The selection of an adequate sample volume length and the alignment of the ultrasound beam with the long axis of the proximal portion of the LAD ensured that heart motion did not alter the positioning of the Doppler beam within the coronary artery, a method validated in previous studies [8,14]. The Doppler signal in the LAD was characterized by a small systolic component and a larger diastolic component (Figure 1). Baseline heart rate, systolic blood pressure, diastolic blood pressure and CFV measurements were made while the pulsed Doppler sample volume remained stationary in the LAD. Measurements of the baseline peak systolic CFV (sCFV) and diastolic CFV (dCFV), made using a computerized light pen, were averaged over five Doppler flow velocity signals.

**CFR.** All measurements of CFV indexes, heart rate and blood pressure were reassessed after an infusion of dipyridamole (0.56 mg/kg intravenously over 4 min). This dose was selected because it has previously been shown to be safe and to produce predominantly distal coronary artery dilation with no discernible change in proximal non-stenotic coronary arteries [4]. The value for each parameter was determined from the average of three measurements. Consequently, the CFR ratio was calculated as the ratio of hyperaemic to basal diastolic peak CFR (dCFR) and systolic peak CFR (sCFR).

All echocardiography studies were performed by the same two experienced echocardiographers. An inter-/intra-observer variability study of CFV measurements was not performed because previous studies [8,14], including one from the authors [15], have demonstrated that short-term inter-/intra-observer variability in blood flow measurements is minimal. Inter-/intra-observer variability, expressed as absolute differences, has been shown not to exceed 2.0 cm/s (95% confidence interval 0.9–3.1), for both dCFV and sCFV [15].
Coronary flow reserve in dilated cardiomyopathy

Coronary angiography

Angiography was performed using the Seldinger technique.

Exercise test with measurement of peak VO₂

Within 48 h of the CFR study, all individuals underwent an exercise test on an ergometric bicycle. Data were analysed using an IBM AT computer connected to a rapid cycle-by-cycle respiratory gas analyser (Medical Graphics Desktop diagnostics/CPX, St. Paul, MN, U.S.A.). A protocol using an increasing workload was selected, giving successive increments of 25 W for 3 min, thus enabling the measurement of peak VO₂, total duration of exercise and the anaerobic threshold (determined graphically) [16]. Exercise was continued until the patient was exhausted (dyspnoea, fatigue). During the 2 weeks before the study, all individuals were familiarized with this test, so that they obtained a performance level that could be reproduced (within a margin of 15%) before participating in the study. All tests were run in the morning before the individual took his/her usual medication.

Statistical analysis

All data are expressed as means ± S.E.M. All between-group comparisons were performed using the Mann–Whitney U-test for unpaired series and Wilcoxon’s test for paired series. The Spearman correlation test was used to examine the relation between CFR data and exercise capacity parameters. A stepwise regression was calculated between CFR and TTE parameters and exercise capacity parameters. A value of P < 0.05 was considered statistically significant.

RESULTS

After 29 studies, 16 of the 18 patients and 9 of the 11 control individuals (86% of total participants) had produced TEE recordings that were technically adequate for analysis. Two patients and two controls were excluded from analysis because of the loss of recorded data (one from each group) and because of throat irritation from the transoesophageal probe (one from each group).

Clinical characteristics and haemodynamic values

Table 1 lists the clinical characteristics and haemodynamic values of patients and control individuals. There were significant differences in heart rate and

<table>
<thead>
<tr>
<th></th>
<th>DCM (n = 16)</th>
<th>Control (n = 9)</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>56 ± 2</td>
<td>56 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>16/0</td>
<td>6/3</td>
<td>0.01</td>
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<tr>
<td>Weight (kg)</td>
<td>75 ± 3</td>
<td>75 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173 ± 2</td>
<td>169 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at baseline</td>
<td>88 ± 4</td>
<td>69 ± 4</td>
<td>0.008</td>
</tr>
<tr>
<td>after dipyridamole</td>
<td>103 ± 5*</td>
<td>84 ± 5*</td>
<td>0.02</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at baseline</td>
<td>119 ± 6</td>
<td>139 ± 5</td>
<td>0.04</td>
</tr>
<tr>
<td>after dipyridamole</td>
<td>120 ± 5</td>
<td>136 ± 5</td>
<td>0.04</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at baseline</td>
<td>74 ± 3</td>
<td>80 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>after dipyridamole</td>
<td>72 ± 4</td>
<td>83 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>Rate–pressure product</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at rest</td>
<td>10330 ± 532</td>
<td>9627 ± 681</td>
<td>NS</td>
</tr>
<tr>
<td>after dipyridamole</td>
<td>12296 ± 628</td>
<td>11593 ± 875</td>
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</table>
systolic blood pressure between the two groups at baseline and at the time of peak coronary dilator effect of dipyridamole. Although in both groups heart rate increased significantly after dipyridamole infusion compared with baseline (P < 0.05), there were no differences in systolic and diastolic blood pressure at baseline and after dipyridamole infusion in either group.

Baseline TTE values

Statistically significant differences were seen in LV mass, end-diastolic diameter, end-systolic diameter, LVEF and pulmonary arterial pressure between patients with DCM and control individuals (Table 2). There were no significant differences in the E:A ratio or the isovolumic relaxation time (Table 2).

Table 2 Baseline Doppler-echocardiographic values

<table>
<thead>
<tr>
<th></th>
<th>DCM</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass index (g/m²)</td>
<td>174 ± 16</td>
<td>90 ± 5</td>
<td>0.0003</td>
</tr>
<tr>
<td>LV EDD (mm)</td>
<td>65 ± 3</td>
<td>47 ± 2</td>
<td>0.0006</td>
</tr>
<tr>
<td>LV ESD (mm)</td>
<td>54 ± 3</td>
<td>29 ± 2</td>
<td>0.0001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>30 ± 2</td>
<td>63 ± 2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pulmonary arterial pressure (mmHg)</td>
<td>3.1 ± 0.3</td>
<td>2.2 ± 1</td>
<td>0.0001</td>
</tr>
<tr>
<td>E:A</td>
<td>1.33 ± 0.21</td>
<td>0.93 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Isovolumic relaxation time (ms)</td>
<td>114 ± 9</td>
<td>117 ± 8</td>
<td>NS</td>
</tr>
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</table>

Table 3 Coronary flow velocities at baseline and after dipyridamole

<table>
<thead>
<tr>
<th></th>
<th>DCM</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>dCFV at baseline (cm/s)</td>
<td>5.1 ± 5</td>
<td>3.7 ± 3</td>
<td>0.04</td>
</tr>
<tr>
<td>dCFV after dipyridamole (cm/s)</td>
<td>8.9 ± 10*</td>
<td>10.5 ± 8*</td>
<td>NS</td>
</tr>
<tr>
<td>dCFV at baseline/LV mass (cm·s⁻¹·g⁻¹)</td>
<td>0.135 ± 0.028</td>
<td>0.416 ± 0.036</td>
<td>0.05</td>
</tr>
<tr>
<td>dCFV after dipyridamole/LV mass (cm·s⁻¹·g⁻¹)</td>
<td>0.544 ± 0.062*</td>
<td>1.207 ± 0.124*</td>
<td>0.0004</td>
</tr>
<tr>
<td>dCFR</td>
<td>1.69 ± 0.14</td>
<td>2.89 ± 0.15</td>
<td>0.0002</td>
</tr>
<tr>
<td>dCFR/LV mass</td>
<td>0.011 ± 0.001</td>
<td>0.034 ± 0.003</td>
<td>0.0001</td>
</tr>
<tr>
<td>sCFV at baseline (cm/s)</td>
<td>30 ± 4</td>
<td>20 ± 1</td>
<td>0.02</td>
</tr>
<tr>
<td>sCFV after dipyridamole (cm/s)</td>
<td>42 ± 6*</td>
<td>44 ± 5*</td>
<td>NS</td>
</tr>
<tr>
<td>sCFV at baseline/LV mass (cm·s⁻¹·g⁻¹)</td>
<td>0.189 ± 0.024</td>
<td>0.231 ± 0.016</td>
<td>0.06</td>
</tr>
<tr>
<td>sCFV after dipyridamole/LV mass (cm·s⁻¹·g⁻¹)</td>
<td>0.254 ± 0.030*</td>
<td>0.513 ± 0.066*</td>
<td>0.001</td>
</tr>
<tr>
<td>sCFR</td>
<td>1.38 ± 0.08</td>
<td>2.17 ± 0.17</td>
<td>0.0008</td>
</tr>
<tr>
<td>sCFR/LV mass</td>
<td>0.009 ± 0.001</td>
<td>0.023 ± 0.003</td>
<td>0.0001</td>
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</table>

CFV

At rest, sCFV and dCFV were significantly higher in patients with DCM compared with control individuals (P < 0.05) (Table 3). dCFV and dCFV indexed by LV mass only positively correlated with heart rate at rest in patients with DCM (r = 0.60, P = 0.02 and r = 0.73, P = 0.004 respectively). dCFV indexed by LV mass in patients with DCM at rest, however, correlated to rate–pressure product (r = 0.56, P = 0.03). At the time of peak coronary dilator effect of dipyridamole, sCFV and dCFV significantly increased in both groups (P < 0.05) (Figure 1). This response, however, was higher in control individuals compared with patients with DCM (Figure 2 and Table 3). Consequently, sCFR and dCFR were significantly lower in patients with DCM than in control individuals (P < 0.001) (Table 3). By stepwise regression, however, CFR correlated to LVEF, LV mass and LV diameter, but not to heart rate, in patients as well as in control individuals. All measurements of CFV and CFR indexed by LV mass were lower in patients compared with control individuals (Table 3). There was no correlation between coronary flow measurements and LVEF or diastolic LV function.

Exercise capacity

Statistically significant differences in peak VO₂, anaerobic threshold and exercise duration were observed between patients with DCM and control individuals (P < 0.05) (Table 4). At exercise peak, however, heart rate and systolic and diastolic blood pressure were similar in both groups (Table 4).

Relationship between CFR and exercise capacity

No significant correlation between CFR and CFR indexed by LV mass and exercise capacity was observed, either in patients with DCM or in the control group (Figure 3).

DISCUSSION

CFR assessment by TEE

This study is the first to assess and confirm CFR abnormalities using TEE in patients with DCM. Moreover, this study is the first to investigate the relationship between these CFR abnormalities and exercise capacity in this disease. The major finding reported here is the confirmation, using TEE, of abnormalities in CFR in patients with DCM previously demonstrated using PET scanning [2,7] and intracoronary pulsed Doppler [17]. The results also show that there is no correlation between CFV parameters, at rest and after infusion of dipyridamole, and exercise capacity.

The method of choice for the non-invasive estimation of myocardial perfusion reserve is PET scanning, which allows accurate and sequential measure-
Coronary flow reserve in dilated cardiomyopathy

Figure 2  Spectral Doppler flows obtained from a transoesophageal view of the proximal LAD artery

The patient with DCM shows a 2-fold increase in diastolic velocity; the control individual shows a 3.17-fold increase in diastolic velocity. A, systolic velocity; B, diastolic velocity.

Table 4  Exercise test parameters

<table>
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<tr>
<th>Parameter</th>
<th>DCM</th>
<th>Control</th>
<th>P</th>
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<tbody>
<tr>
<td>Peak VO₂ (ml·min⁻¹·kg⁻¹)</td>
<td>16.9±1.7</td>
<td>24.1±2.6</td>
<td>0.03</td>
</tr>
<tr>
<td>Anaerobic threshold</td>
<td>9.6±1.0</td>
<td>13.2±1.1</td>
<td>0.03</td>
</tr>
<tr>
<td>Exercise duration (s)</td>
<td>628±52</td>
<td>896±98</td>
<td>0.02</td>
</tr>
<tr>
<td>HR, peak exercise (beats/min)</td>
<td>142±8</td>
<td>137±10</td>
<td>NS</td>
</tr>
<tr>
<td>SBP, peak exercise (mmHg)</td>
<td>152±19</td>
<td>183±13</td>
<td>NS</td>
</tr>
<tr>
<td>DBP, peak exercise (mmHg)</td>
<td>77±4</td>
<td>88±8</td>
<td>NS</td>
</tr>
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</table>

Pharmacological coronary vasodilatation using dipyridamole infusion is widely accepted as an effective means of inducing maximal coronary hyperaemia in patients undergoing myocardial perfusion imaging [20]. Dipyridamole appears to produce coronary vasodilatation by elevating interstitial adenosine concentration through the blockade of cellular uptake of adenosine [4].

CFR abnormalities in DCM

Elevated filling pressures, decreased CPP, increased heart rate and LV mass beyond that resulting from microcirculatory growth can partially account for the impairment of CFR in patients with DCM [21]. Intrinsic microvascular disease can also be present [21]. In the study reported here, sCFV and dCFV at rest were higher in patients with DCM than in control individuals. This phenomenon could not be explained by differences in systolic or diastolic blood pressure between the two groups: at rest, systolic blood pressure was higher in the control group compared with the DCM group, whereas diastolic blood pressure was similar in both groups. An abnormally high CFV has been reported in hypertrophied ventricles, in the presence or absence of myocardial ischaemia [22,23]. This high CFV may result from an increase in absolute blood flow combined with an inadequate increase in the cross-sectional area of the vessel (relative functional coronary stenosis) [24], and this may also explain the high CFV observed using TEE.

Previous investigations, in which myocardial blood flow and flow reserve were measured in non-rejecting allografts, demonstrated normal hyperaemic but increased resting blood flow, so that myocardial flow...
Correlation of CFR and exercise capacity expressed by peak VO$_2$ in patients with DCM

**Figure 3**

sCFR, systolic CFR; dCFR, diastolic CFR.

reserve was lower than in normal volunteers [25,26]. This increase in resting blood flow was attributed to an increase in cardiac work at rest, as evidenced by increased rate–pressure product [25–27]. Furthermore, increasing blood flows during acute transplant rejection at rest were shown to correlate directly with the rate–pressure product [28]. In the study reported here, no significant difference in rate–pressure product was detected between patients with DCM and the control group at rest.

Although heart rate was significantly higher in patients with DCM compared with control individuals, and although it correlated with dCFV and dCFV/LV mass, the rate–pressure product correlated only with dCFV/LV mass in patients with DCM at rest. Thus, an increase in cardiac work at rest may explain the high CFV observed in patients with DCM in the study reported here. Furthermore, decreased CFR may be explained by the increase in coronary blood flow with regard to the increase in LV mass. Thus, there is a relative functional coronary insufficiency in DCM.

Since elevated filling pressures may influence CFV [21], LV diastolic dysfunction may be one mechanism to explain CFV and CFR abnormalities in patients with DCM. Furthermore, previously published results have supported the hypothesis that abnormalities of LV diastolic function are important contributors to exercise intolerance in patients with CHF [30]. Indeed, patients with CHF and a resting Doppler restrictive filling pattern (high E:A ratio) have been shown to have more severely reduced exercise tolerance [31]. However, in the study reported here, no correlation between CFV or CFR and mitral flow velocity patterns and exercise capacity parameters was observed. Previous Doppler echocardiographic studies have demonstrated a marked variability in mitral flow velocity patterns [32]. According to the classification used by Appleton et al. [32], the patients with DCM in the study reported here had ‘normalized patterns’ (E:A ratio = 1.33). Patients with diastolic dysfunction may be difficult to classify, although the combination of an appropriate clinical history, data from other diagnostic procedures, one or more abnormal mitral flow velocity variables and serial recordings may provide
important clues as to their diastolic abnormality [32]. Consequently, the contribution of diastolic dysfunction to CFR abnormalities and the limitation of exercise capacity in patients with DCM cannot be excluded from the results reported here.

**CFV and exercise capacity**

The lack of a relationship between central haemodynamics and exercise capacity in CHF had been further substantiated by the demonstration that improvement in any one of these variables shows no parallel consistent improvement in the others [33]. LV systolic dysfunction at rest, however, poorly correlates to exercise capacity as expressed by peak oxygen consumption \( \left( V_{O_2} \right) \) [34,35]. This finding may be explained by poor cardiac reserve adaptation during exercise, which is not evident at rest.

Since the abnormal myocardial blood flow values found in DCM have been shown to correlate significantly with reductions in myocardial performance [2], and since cardiac index at exercise correlates significantly to exercise capacity as expressed by peak \( V_{O_2} \) [36], the cardiac reserve as expressed by CFR may influence exercise tolerance. However, in the study reported here, CFV and CFR abnormalities do not correlate with exercise capacity in patients with DCM. The explanation for this lack of relationship may be that peripheral abnormalities, especially skeletal muscle metabolism, rather than central mechanisms, have a prominent role in exercise capacity limitation [35]. A better CFR at exercise could, possibly by enhancing the cardiac index, increase peak leg blood flow and improve exercise tolerance. For example, Sullivan et al. [37] have demonstrated that exercise training improves maximal exercise tolerance in patients with CHF by producing an improvement in peripheral adaptation that includes increased peak blood flow to active skeletal muscles and more efficient peripheral oxygen extraction. Conversely, Mancini et al. [33] have reported that dobutamine does not improve oxygen delivery to working skeletal muscle in patients with CHF, despite its ability to increase cardiac output and limb blood flow. Presumably, an increase in cardiac output at exercise cannot, separately, improve exercise tolerance. Several peripheral mechanisms therefore appear to contribute to the determination of exercise capacity in CHF.

**Study limitations**

The major limitation in the determination of CFV using TEE is the recording of coronary blood flow in the absence of any motion artefacts. It is difficult, however, to accept the idea that signals could be obtained from a moving structure as clearly as from the same structure when totally free from motion artefacts. Moreover, several studies have shown that TEE is useful for the evaluation of coronary artery velocities [8,14,15,18,24]. Indeed, although the heart is moving throughout the cardiac cycle, it is relatively motionless during diastole, when the majority of coronary blood flow occurs, and this facilitates the measurement of stable coronary Doppler signals [14]. Whereas Iliceto et al. [14] obtained adequate Doppler flow signals in the proximal LAD in only 69% of patients investigated, success rates of 89% [8], 81% [24] and 83% [15] have been reported. These figures compare well with the success rate reported in this study (86%).

Although these findings add to the speculations concerning CFV in DCM, the small study size means that relevant and definitive conclusions should be extended with caution to all CHF populations.

A third study limitation relates to the lack of haemodynamic evaluation. For technical reasons, haemodynamic cardiac performance changes caused by dipyridamole infusion or during exercise were not assessed.

**CONCLUSIONS**

This study confirms that CFV may be measured using TEE, and demonstrates that myocardial blood flow abnormalities assessed by CFV and CFR in patients with DCM do not contribute to the limitation of exercise capacity. The contribution of peripheral mechanisms could play a major role in the determination of exercise capacity in CHF. Further studies should aim to evaluate the consequences of CFV abnormalities on haemodynamic cardiac performance changes and on exercise capacity in a larger group of patients with DCM.

**ACKNOWLEDGMENT**

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**REFERENCES**

artery disease from non-ischemic dilated cardiomyopathy utilizing positron emission tomography. J Am Coll Cardiol 17: 373-83.