Relationship Between Doppler-Derived Left Ventricular Diastolic Function and Exercise Capacity in Patients With Myocardial Infarction

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Doppler echocardiographic indices of left ventricular (LV) diastolic function are widely used to evaluate the cardiac function of patients with cardiac disease. However, there have been few reports about the relationship between Doppler indices and exercise capacity and so 44 patients with myocardial infarction were investigated by cardiopulmonary exercise testing and 2-D and Doppler echocardiography. Diastolic performance was assessed using Doppler transmirtal flow velocity and pulmonary venous flow velocity. The ratio of peak E wave velocity and peak A wave velocity (E/A) correlated with peak oxygen consumption (peak VO2) (R=0.72), and there was a negative correlation between the deceleration time of E velocity (Dct) and peak VO2 or anaerobic threshold (AT) (R=−0.65, −0.62, respectively). The ratio of peak S wave velocity and peak D wave velocity (S/D) negatively correlated with peak VO2 (R=−0.58). Left ventricular ejection fraction did not correlate to exercise capacity. These results suggest that the Doppler echocardiographic indices of LV diastolic function correlate with exercise capacity in patients with mild cardiac dysfunction.

**Key Words:** Cardiopulmonary exercise test; Diastolic function; Doppler echocardiography; Exercise capacity; Myocardial infarction

Redced exercise capacity is an important symptom in patients with cardiac dysfunction, and cardiopulmonary exercise testing provides precise indices of exercise capacity. The utility of cardiopulmonary exercise testing in patients with cardiac disease has been reported, especially for assessing functional state. However, left ventricular (LV) systolic function was not shown to relate to exercise capacity although some studies have reported a correlation between LV diastolic function and exercise capacity in patients with cardiac disease. Many of those studies used cardiac catheterization or the radionuclide method to evaluate diastolic function, which depend on high fidelity, invasive measurements of instantaneous pressure, volume, mass, and wall stress that cannot be done on a routine clinical basis. With Doppler echocardiography, diastolic function can be evaluated non-invasively and repeatedly but there are only a few reports about the relationship between Doppler echocardiographic indices and exercise capacity.

The present study evaluated the correlation between Doppler echocardiographic indices of LV diastolic function and exercise capacity derived from cardiopulmonary exercise testing by measuring the gas exchange in patients with myocardial infarction (MI).

**Method**

**Study Population**

The study recruited patients with MI [New York Heart Association (NYHA) functional class I or II] in whom the onset had been from 6 to 12 months prior to the study. The series comprised 44 patients [31 men, 13 women; average age, 60.1±3.6 (range, 52–67) years] who met the following criteria: (1) they had been stable symptomatically on the same medication for at least 2 months before the tests; (2) they could undergo cardiopulmonary exercise testing with an ergometer to exhaustion, limited only by fatigue or dyspnea and not by angina; (3) they did not have multivessel coronary artery disease; (4) they did not have obstructive pulmonary disease as assessed by a spirometer; (5) they did not have overt heart failure, valvular or other cardiac disease; and (6) they showed an ‘abnormal relaxation pattern’ in their transmirtal flow pattern on Doppler echocardiography.

All patients were in sinus rhythm. Informed consent was obtained from each patient and no complications occurred as a result of the study.

**Echocardiograms**

An echocardiographic examination was performed with each patient resting in the left lateral position, using a 3.5 MHz imaging transducer connected to a SONOS 5500 (Agilent Technologies, Andover, USA). Left ventricular end-diastolic volume (LVEDV), LV end-systolic volume (LVESV) and ejection fraction (LVEF) were measured using a modified Simpson’s rule according to the recommendations by the American Society of Echocardiography. Doppler recordings of the mitral inflow and the right upper
pulmonary vein were obtained in the apical 4-chamber view to assess LV filling dynamics and pulmonary venous flow, respectively. For the assessment of LV diastolic filling, the pulsed-wave Doppler sample volume was positioned between the tips of the mitral leaflets to derive the following variables: peak early (E) and late (A) transmitral filling velocities (cm/s), their ratio (E/A ratio), the deceleration time of E velocity (Dct; ms), and isovolumic relaxation time (IRT; ms). For the assessment of pulmonary venous flow, the pulsed-wave Doppler sample volume was positioned 0.5 cm to 1.0 cm into the right upper pulmonary vein to measure the peak velocity of the forward systolic (S) and diastolic (D) flows (cm/s), their ratio (S/D ratio), and the amplitude of the atrial flow reversal (PVA; cm/s).

Exercise Testing and Gas Exchange Analysis

An upright electromagnetically braked cycle ergometer (EM840; Siemens, Munich, Germany) was used in the exercise test. The workload began at 20 W for 3 min and increased by 10 W every minute, using a ramp protocol. In each case, the patient was encouraged to perform maximal exercise. Expired gas was measured at rest and during exercise using an automated breath-by-breath gas exchange spirometer (Minato RM300; Minato-Ikagaku, Tokyo, Japan), which calculated oxygen consumption (V̇O₂), carbon dioxide production (V̇CO₂), minute pulmonary ventilation (V̇E), respiratory exchange ratio, and the ventilatory equivalents for O₂ (V̇E/V̇O₂). Peak V̇O₂ was defined as the highest V̇O₂ achieved during exercise. Throughout the exercise tests, heart rate and blood pressure were monitored. The ECG and SaO₂ were monitored continuously and recorded each minute. The anaerobic threshold (AT) was obtained using the V-slope method and expressed as V̇O₂ at that point. Software equipped with Minato’s gas exchange spirometer performed the V-slope calculation.

Statistical Analysis

Data are expressed as mean values±SD. Relationships between exercise capacity and variables derived from Doppler echocardiography were evaluated by correlation coefficient and univariate linear regression analysis. Results were considered to be significant at p<0.05.

**Results**

**Echocardiograms (Table 1)**

The LVEF ranged from 36% to 80% (mean, 57.7±

12.0%), so a wide variation in LV systolic function was found in the present patients, ranging from normal to moderately depressed conditions.

The mean E wave velocity was 65.8±21.6 cm/s (range, 28–110 cm/s); mean A wave velocity was 64.6±20.1 cm/s (range, 30–113 cm/s); mean E/A ratio was 0.71±0.17 (range, 0.40–0.95); and mean Dct was 235±34.1 ms (range, 180–325 ms). Rapid E wave deceleration was not observed in the present series of patients; hence, the ‘restriction to filling pattern’ of transmitral flow was not observed either.

The mean S/D ratio was 1.31±0.41 (range, 0.26–2.07) and PVA ranged between 18 cm/s and 77 cm/s (mean, 34.6±9.8 cm/s).

**Relationship Between Echocardiographic Data and Exercise Capacity**

Neither E (R=0.09) nor A (R=0.06) correlated significantly with peak VO₂ or with AT (R=0.09 for E, R=0.10 for A), whereas E/A correlated with peak VO₂ (R=0.72; Fig 1),

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**Table 1 Echocardiographic Data in the 44 Patients**

<table>
<thead>
<tr>
<th>Variable (cm/s)</th>
<th>Mean±SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>57.7±12.0</td>
<td>36–80</td>
</tr>
<tr>
<td>E</td>
<td>65.8±21.6</td>
<td>28–110</td>
</tr>
<tr>
<td>A</td>
<td>64.6±20.1</td>
<td>30–113</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.71±0.17</td>
<td>0.40–0.95</td>
</tr>
<tr>
<td>Dct (ms)</td>
<td>235±34.1</td>
<td>180–325 ms</td>
</tr>
<tr>
<td>IRT (ms)</td>
<td>90.5±16.2</td>
<td>64–135</td>
</tr>
<tr>
<td>S (cm/s)</td>
<td>50.1±9.3</td>
<td>19–70</td>
</tr>
<tr>
<td>D</td>
<td>51.4±11.2</td>
<td>25–82</td>
</tr>
<tr>
<td>S/D ratio</td>
<td>1.31±0.41</td>
<td>0.26–2.07</td>
</tr>
<tr>
<td>PVA (cm/s)</td>
<td>34.6±9.8</td>
<td>18–77</td>
</tr>
</tbody>
</table>

EF, LV ejection fraction; E, peak E wave velocity; A, peak A wave velocity; Dct, deceleration time of E velocity; IRT, isovolumic relaxation time; S, peak S wave velocity; D, peak D wave velocity; PVA, peak velocity of pulmonary vein atrial flow reversal.

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Fig 1. The ratio of peak E wave velocity and peak A wave velocity (E/A) correlated with peak oxygen consumption (peak V̇O₂) (R=0.72).

Fig 2. The deceleration time of E wave (Dct) had an inverse correlation with peak V̇O₂ (R=-0.65).
but did not correlate with AT (R=0.38). There was a significant negative correlation between Dct and peak VO₂ (R=−0.65; Fig 2) and with AT (R=−0.62; Fig 3), whereas IRT did not correlate with either peak VO₂ (R=0.32) or with AT (R=0.24). Forward systolic flow (R=0.02) and diastolic flow (R=0.20) did not correlate with either peak VO₂ or with AT (R=0.17 for S, R=0.08 for D), and S/D showed a negative correlation with peak VO₂ (R=−0.58; Fig 4), but did not correlate with AT (R=0.12). Neither PVA nor EF showed any correlation with peak VO₂ (R=−0.31 for PVA) (R=0.001 for EF; Fig 5) or with AT (R=−0.28 for PVA) (R=0.01 for EF; Fig 6). Similarly, EDV and ESV did not correlate with peak VO₂ or AT either.

Discussion

Reduced exercise tolerance is the most common symptom for cardiac dysfunction, but the correlation between objective measurements of physical capacity and systolic function is poor.7–7 The importance of diastolic function and cardiac filling pressure in limiting physical capacity in patients with cardiac disease remains controversial. The mechanisms underlying exercise intolerance in patients with cardiac dysfunction are not understood precisely, although it has been suggested that reduced stroke volume, cardiac output, and EF may lead to increased muscle glycolysis, lactate accumulation, and leg fatigue.29,30 Parameters of systolic function have been shown to be useful in the diagnosis, prognosis, and response to therapy for patients with cardiac disease, but the relationship between LV systolic function and exercise capacity has been reported as poor.5–7 Conversely, diastolic dysfunction seems to play an important role in exercise capacity.7,15 The present study demonstrated that Doppler echocardiographic indices of LV diastolic function at rest correlate with exercise capacity derived from cardiopulmonary exercise testing in patients with MI.

Two-dimensional echocardiography allows the visualization of the entire heart through multiple tomographic planes in real time and has become the non-invasive method of choice for evaluating chamber size and function. However, to date, invasive cardiac catheterization has been required for the assessment of hemodynamics. Doppler echocardiography can be used to determine various hemodynamic parameters, such as transvalvular gradients, rates of pressure change, and changes in cardiac pressure.17,31,32 In addition, pulsed-Doppler examination of atrioventricular valve flow provides valuable information about the diastolic filling of the heart.33 Thus, Doppler echocardiography has become a powerful non-invasive method with the ability to provide information about diastolic function. Some studies on the relationship between transmirtal flow and exercise capacity have shown a significant relationship between E/A and exercise capacity.12–14,34 As well as transmirtal flow, pulmonary venous flow was suggested recently as being useful for evaluating LV diastolic function;35–37 however, to date, there are few reports about the relationship between pulmonary venous flow and exercise capacity. In the present study, a significant relationship was found between measurements of pulmonary venous flow pattern
and exercise capacity.

All patients in the present series showed the ‘abnormal relaxation pattern’ in their transmural flow. As the severity of cardiac dysfunction ranged within a narrow spectrum, which means that only patients with mild cardiac dysfunction were included, the transmural flow patterns in the present study were all ‘abnormal relaxation patterns’.

With progression of cardiac dysfunction, left atrial pressure increases, thus increasing the driving pressure across the mitral valve. There is a gradual increase in E velocity on the mitral flow velocity curve. As LV compliance decreases, Dct shortens and a ‘pseudonormal pattern’ appears. In more advanced cardiac dysfunction, left atrial pressure is higher and ventricular compliance is poor, producing a ‘restriction to filling pattern’. If such patterns were included in the study population, the relationships between E/A, Dct and exercise capacity would be complicated. However, any abnormalities in diastolic filling of the heart in the range of abnormal relaxation patterns may be a contributing factor to quantifying diastolic dysfunction. Therefore, parameters such as E/A and Dct may be useful for evaluating exercise intolerance in patients with mild cardiac dysfunction.

As well as progression of disease, diastolic function is also affected by age. In a study of healthy subjects, Benjamin et al reported that E/A ranges from a mean of 2.08±0.55 for subjects in their third decade to 0.84±0.29 for those in their eighth decade. They also reported that E/A<1 is abnormal in subjects aged less than 40 years, but is common in subjects aged more than 70 years. Although Doppler indices of LV diastolic function change dramatically with age, all patients in the present series were in their sixth and seventh decades. As the age range was narrow, the effect of aging in the present series is thought to be small.

Cardiac dysfunction symptoms may first manifest as dyspnea or fatigue during activity. Therefore, in patients with cardiac dysfunction, estimates of functional capacity, such as exercise duration or peak work rate achieved, are less reliable than measuring gas exchange directly. Consequently, measuring cardiopulmonary indices during exercise has become the standard for assessing functional capacity in cardiac dysfunction. In stable cardiac dysfunction, VO2max and AT measurements are highly reproducible and hence are recommended when evaluating cardiac dysfunction. Although some patients may be unable to achieve a true VO2max, most can safely attain an AT. The AT is usually a minimum target in testing and, properly measured, is reproducible in repeated testing. Little has been said about the relationship between diastolic function and AT.

In the present study, a correlation between Dct and AT was found; however, from the results it was not clear whether LV diastolic function correlated with AT. There are still technical problems in determining AT; hence, further studies on the correlation between diastolic function and AT are necessary.

Although the present study indicated that Doppler echocardiographic indices of LV diastolic function are highly predictive for exercise capacity in patients with MI, its pathophysiology is still unclear. Several investigators have previously suggested some possible mechanisms for exercise intolerance associated with diastolic dysfunction. One of these is that the impairment of exercise capacity may relate to alterations in resting LV diastolic distensibility? E/A, Dct, and S/D could be considered as parameters of myocardial distensibility and, in the present study, may have correlated with exercise capacity; however, peripheral muscular function; which can be another determinant of exercise capacity, was not evaluated. Moreover, even though Doppler-derived measurements have been used as simple and reproducible indices of LV diastolic function, there are some physiological factors other than diastolic function that affect these indices. Therefore, these parameters cannot be simply interpreted as complete measurements of myocardial distensibility. Further studies on the relationship between Doppler echocardiographic LV diastolic indices and exercise capacity are required.

**Study Limitations**

The present study evaluated patients with ‘abnormal relaxation’ in their transmural flow velocity pattern. Only patients with mild diastolic dysfunction were recruited. If the study population had included patients with more severe diastolic dysfunction showing ‘pseudonormal patterns’ and ‘restrictive patterns’, correlations between E/A, Dct and exercise capacity would not have been found. The results are applicable only to patients with mild diastolic dysfunction.

**Conclusions**

For patients with mild cardiac dysfunction, E/A, Dct, and S/D correlated with peak VO2, and Dct also correlated with AT. These results indicate that LV diastolic function plays a role in exercise intolerance for patients with mild cardiac dysfunction.

**References**

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