Effects of Left Ventricular Peak Filling Rate on Exercise Capacity 3 to 6 Weeks After Acute Myocardial Infarction*

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Study objectives: To investigate the importance of early left ventricular (LV) diastolic filling on maintenance of exercise performance, we examined peak filling rate and its relation to exercise capacity during upright bicycle exercise in patients with recent myocardial infarction.

Design: Retrospective analysis of data of cardiopulmonary exercise testing characteristics in patients with recent myocardial infarction.

Setting: Coronary care unit in a university hospital.

Patients: Fifty-one patients 3 to 6 weeks after acute myocardial infarction.

Interventions: Upright bicycle exercise using a symptom-limited graded exercise protocol.

Measurements and results: Peak filling rate increased significantly from 1.55±0.52 at rest to 3.43±1.1 end-diastolic volume per second at peak exercise. Despite no significant relation between peak filling rate at rest and peak oxygen consumption, peak filling rate at peak exercise correlated significantly with peak oxygen consumption (r=0.50; p<0.002), stroke volume (r=0.51; p<0.002), and cardiac output (r=0.56; p<0.002) at peak exercise. Although both end-systolic and end-diastolic volumes increased from rest to peak exercise, the increases in end-systolic volume correlated inversely with the changes in peak filling rate during exercise (r=−0.45; p<0.02), but the increases in end-diastolic volume did not.

Conclusions: During maximal upright bicycle exercise, exercise capacity and exercise hemodynamic responses were mainly dependent on early LV diastolic filling, and preserved LV systolic contraction, resulting in a cardiac suction effect following early diastole, seemed to have an important role in the enhancement of early LV diastolic filling in patients with recent myocardial infarction.

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Key words: exercise capacity; myocardial infarction; peak filling rate

Abbreviations: LV=left ventricular

Measurements of left ventricular (LV) function that predict exercise capacity in patients with LV dysfunction remain elusive. Previous studies have shown that measurements of LV systolic function are poor predictors of exercise capacity.1-7 In contrast, several investigators have focused on abnormalities of LV diastolic function rather than systolic function as the cause of exercise intolerance.8-14 Recently, we have also demonstrated that during supine bicycle exercise, LV diastolic dysfunction has an important role in determining exercise hemodynamic responses and exercise capacity in patients with LV dysfunction.15 However, these results obtained during supine bicycle exercise cannot actually be extrapolated to upright bicycle exercise because the changes in LV diastolic filling during exercise are greatly influenced by body positions.16,17

The present study was designed to examine the relation between LV peak filling rate assessed by radionuclide angiography and exercise performance during maximal upright bicycle exercise, and to further characterize the importance of early LV diastolic filling on maintenance of exercise capacity during upright position exercise in patients with recent myocardial infarction.

Materials and Methods

Patients

We analyzed 51 patients who fulfilled the following criteria: (1) emergency coronary arteriography performed in the acute phase...
for the purpose of revascularization that revealed single-vessel disease; (2) no history of previous myocardial infarction; and (3) normal exercise test results. LV ejection fraction ranged from 31 to 79% (mean, 49±12%) at entry in the study. All patients included in this study had had their first acute Q-wave myocardial infarction 3 to 6 weeks before the study, and none had postinfarction angina, critical arrhythmia, or uncontrolled congestive heart failure. The location of myocardial infarction was anterior in 34 patients and inferior in 17 patients. Before entry into the study, each patient underwent a complete physical examination, and patients were excluded from the study if they had mitral regurgitation evaluated by color Doppler echocardiography, physical or radiographic signs of obstructive lung disease, or intermittent claudication that limited their exercise capacity. Treatment with all medications was discontinued for at least 48 h before the study. The risks of the study were fully explained and written informed consent was obtained from each patient.

Study Protocol

Patients were studied in the upright position at rest and during bicycle ergometric exercise. Upright bicycle exercise was performed to familiarize patients with an isokinetic bicycle ergometer 2 or 3 days before the study (Cat-eye Ergociser 1C-1200: Osaka, Japan). On the day of the study, a 7F Swan-Ganz catheter was inserted through the internal jugular vein and advanced to the pulmonary artery under fluoroscopic control. Thirty minutes later, bicycle exercise testing was performed with ECG monitoring and expired gas analysis. Exercise began at a workload of 25 W with the pedal speed maintained at 60 revolutions per minute and increased by 25 W every 3 min until exhaustion. Continuous expired gas analysis was performed (with an Oxycon-4; Minjinhardt Company, Bunnik, Holland). Oxygen consumption was measured at rest and continuously during exercise, and averaged measurements during the last 30 s of each exercise stage were used for analysis. The baseline hemodynamic measurements were obtained with both legs on the bicycle pedals. Heart rate was recorded continuously during exercise. Pulmonary artery wedge pressure was recorded intermittently at each exercise stage (DS-3300 System; Fukuda Denki; Tokyo, Japan).

Radionuclide Angiography

First-pass radionuclide angiography was performed at rest and peak exercise using a multicrystal gamma camera (Baird Atomic System 77; Baird Corp; Boston, Mass). For each radionuclide acquisition, 740 megabequerels of technetium-99m pertechnetate was injected as a bolus and counts were recorded at 25-ms intervals. After correction for background activity and electric dead time, data from three to six individual beats were combined to produce an average representative cardiac cycle. Indexes of LV function were derived by computer analysis of background-corrected time activity curve. LV ejection fraction was computed on the basis of relative end-diastolic and end-systolic counts. Peak filling rate was determined by fitting third-order polynomial functions to the rapid diastolic filling portions of the time activity curve by a least square technique. Peak filling rate was computed in LV counts per second, normalized for the number of counts at end-diastole, and expressed as end-diastolic volume per second. LV volume was calculated by the area length method of Dodge et al with the ellipse of revolution modified for the single anterior plane projection as 0.85×A×L, where A is the area obtained by planimetry and L is the longest diameter measured from the aortic valve to the apex of the left ventricle.

From these data, stroke volume and cardiac output were calculated as follows: stroke volume = radionuclide ejection fraction × end-diastolic volume and cardiac output = stroke volume × heart rate. LV end-systolic volume was calculated as follows: end-systolic volume = end-diastolic volume − stroke volume. LV end-diastolic pressure-volume ratio was calculated as follows: pulmonary artery wedge pressure/end-diastolic volume, and this was used as an index of global LV diastolic function.

Statistical Analysis

All data are presented as mean±SD. Paired t test was used for paired data for statistical analysis. The least-squares regression was used to assess the relationship between the two variables. Probability values of <0.05 were considered to be significant.

RESULTS

In all 51 patients, upright bicycle exercise was limited by exercising muscle fatigue and not by dyspnea. No patient developed angina or ischemic ST segment changes during exercise. Hemodynamic and metabolic measurements at rest and peak exercise are summarized in Table 1.

Relationship Between Peak Filling Rate and Exercise Capacity

Peak oxygen consumption ranged from 13 to 29 mL/min/kg (mean, 20.7±4.05 mL/min/kg). During exercise, LV ejection fraction did not change significantly (49±12% at rest to 51±15% at peak exercise), whereas end-diastolic pressure-volume ratio elevated significantly from 0.06±0.01 to 0.16±0.04 mm Hg/mL at peak exercise (p<0.002), and peak filling rate elevated significantly from 1.55±0.52 at rest to 3.43±1.1 end-diastolic volume per second at peak exercise (p<0.002). Both LV ejection fraction and end-diastolic pressure-volume ratio at rest and peak exercise did not correlate significantly with peak oxygen consumption. Al-

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<td>Heart rate, beats/min</td>
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*p<0.001; all p values indicate differences from resting values.
though there was no significant correlation between peak filling rate at rest and peak oxygen consumption, peak filling rate at peak exercise had a significant positive correlation with peak oxygen consumption \((r=0.50; p<0.002)\) (Fig 1). Furthermore, peak filling rate at peak exercise correlated significantly with stroke volume \((r=0.51; p<0.002)\) and cardiac output \((r=0.56; p<0.002)\) at peak exercise (Fig 1).

**Relationship of Peak Filling Rate to End-Systolic and End-Diastolic Volume**

During exercise, end-diastolic volume increased by \(30\pm22\%\) \((123\pm32\text{ mL})\) at rest to \(157\pm39\text{ mL}\) at peak exercise; \(p<0.001\) and end-systolic volume increased by \(26\pm31\%\) \((66\pm31\text{ mL})\) at rest to \(82\pm41\text{ mL}\) at peak exercise; \(p<0.001\). A significant negative correlation was found between the changes in peak filling rate and the increases in end-systolic volume from rest to peak exercise \((r=-0.45; p<0.02)\) (Fig 2, left). However, the changes in peak filling rate did not correlate with the increases in end-diastolic volume during exercise \((r=-0.19; p>0.2)\) (Fig 2, right).

**DISCUSSION**

The pathophysiologic basis of limited exercise capacity in patients with LV dysfunction has not been clearly elucidated. The present study confirms the previous observation\(^1-7\) of patients with heart failure that exercise capacity was not related to LV ejection fraction. However, we found that peak filling rate at peak exercise had significant positive correlations with peak oxygen consumption, and stroke volume and cardiac output at peak exercise. These observations suggest that during maximal

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21745/)

Figure 1. Relationship between peak filling rate and peak oxygen consumption, and stroke volume and cardiac output at peak exercise.

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21745/)

Figure 2. Relationship of the changes in peak filling rate to the increases in end-systolic volume (A, left) and the increases in end-diastolic volume (B, right).
upright bicycle exercise, early LV diastolic filling has an important role in determining exercise hemodynamic responses and exercise capacity in patients with recent myocardial infarction.

During exercise, LV diastolic filling must increase to maintain or augment the stroke volume. There are two potential stages to augment LV diastolic filling during exercise: early in diastole after mitral valve opening and late in diastole during atrial systole. Although previous studies have emphasized the importance of LV diastolic filling on maintenance of exercise capacity, the relative contributions of early and late diastolic filling to increasing exercise capacity are uncertain. Several studies have demonstrated a significant relationship between peak filling rate obtained by nuclear techniques and exercise capacity in heart failure. In contrast, others have demonstrated a significant relationship between late peak transmural flow velocity using Doppler echocardiography and exercise capacity in patients with LV dysfunction. The discordant results of the previous studies may be due to large differences in the type of exercise (isometric or dynamic), patient position, mechanism of LV failure (ischemic or nonischemic), and level of left atrial pressure. In this study, LV peak filling rate at peak exercise had significant correlations with peak oxygen consumption, and stroke volume and cardiac output at peak exercise (Fig 1), whereas LV diastolic pressure-volume ratio as an index of global LV diastolic function did not correlate with these variables. These results suggest that during upright bicycle exercise, exercise hemodynamic responses and exercise capacity were mainly dependent on early diastolic filling in patients with recent myocardial infarction.

Previous studies have demonstrated that the process of early diastolic function is intimately related to LV systolic function. Courtis et al. and Sonnenblick have demonstrated that LV systolic function determines subsequent early diastolic filling by means of a cardiac suction effect. The magnitude of this suction effect is related to the elastic potential energy stored by the myocardium during systole, and the greater suction effect generates a larger gradient for early diastolic filling and a greater LV filling rate. However, Tomai et al. have reported that cardiac suction has a minimal role in the enhancement of early diastolic filling during exercise in patients with dilated cardiomyopathy because of structural alterations of the myocardium. In the present study, we observed significant increases in both end-systolic and end-diastolic volumes from rest to peak exercise. However, only increases in end-systolic \( (r = -0.45; p < 0.02) \) but not increases in end-diastolic volumes \( (r = -0.19; p > 0.2) \) were related to the changes in peak filling rate during exercise (Fig 2), indicating that LV systolic contraction was closely associated with early LV filling during exercise. Although patients with severe LV systolic dysfunction were not included in this study, our results suggest that preserved LV systolic contraction, resulting in a suction effect during the following early diastole, seemed to contribute to the enhancement of early diastolic filling during exercise in patients with recent myocardial infarction.

Three limitations of our study should be addressed. First, our patient group was considered to be a relatively low-risk population. It remains to be seen whether the results obtained in this study can be extrapolated to a high-risk population. Second, it is possible that the correlation of the changes in peak filling rate with the increases in end-systolic volume may be an indication of less ventricular damage or impairment rather than any other physiologic effect. Although we cannot define whether the enhancement of early LV diastolic filling was due to a cardiac suction effect or the Frank-Starling mechanism in patients with less ventricular damage, our finding that the changes in peak filling rate correlated significantly with the increases in end-systolic volume supports the fact that smaller LV end-systolic volume generated greater subsequent early LV diastolic filling. Third, we did not measure LV early diastolic pressure, which would have provided the most compelling evidence of cardiac suction. However, because the relation between end-systolic volume and LV minimal pressure is well known, it is reasonable to speculate that the relation between LV end-systolic volume and peak filling rate can reflect a relation between LV systolic function and LV early diastolic pressure.

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