Improved Left Ventricular Diastolic Filling in Patients with Coronary Artery Disease After Percutaneous Transluminal Coronary Angioplasty

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SUMMARY
Left ventricular (LV) diastolic filling is abnormal at rest in many patients with coronary artery disease (CAD), even in the presence of normal resting LV systolic function. To determine the effects of improved myocardial perfusion on impaired LV diastolic filling, we studied 25 patients with one-vessel CAD by high-temporal-resolution radionuclide angiography before and after percutaneous transluminal coronary angioplasty (PTCA). No patient had ECG evidence of previous myocardial infarction. Despite normal regional and global LV systolic function at rest in all patients, LV diastolic filling was abnormal (peak LV filling rate [PFR] < 2.5 end-diastolic volumes (EDV)/sec or time to PFR > 180 msec) in 17 of 25 patients. Twenty-three patients had abnormal LV systolic function during exercise. After successful PTCA, LV ejection fraction and heart rate at rest were unchanged, but LV ejection fraction during exercise increased, from 52 ± 8% (± SD) to 63 ± 5% (p < 0.001). LV diastolic filling at rest improved: PFR increased from 2.3 ± 0.6 to 2.8 ± 0.5 EDV/sec (p < 0.001) and time to PFR decreased from 181 ± 22 to 160 ± 18 msec (p < 0.001). Thus, a reduction in exercise-induced LV systolic dysfunction after PTCA, reflecting a reduction in reversible ischemia, was associated with improved LV diastolic filling at rest.

These data suggest that in many CAD patients with normal resting LV systolic function and without previous infarction, abnormalities of resting LV diastolic filling are not fixed, but appear to be reversible manifestations of impaired coronary flow.

ABNORMALITIES of left ventricular diastolic function occur frequently in patients with coronary artery disease after acute myocardial infarction,1–6 during active myocardial ischemia,2,4–14 and even under resting conditions in the absence of myocardial fibrosis or ischemia.1,2,6,15,16 Impaired left ventricular diastolic filling, assessed by radionuclide angiography, has been detected at rest in many patients who have no evidence of previous infarction or active ischemia and in whom resting regional and global left ventricular systolic function is normal.16 In these patients, the mechanism of diastolic abnormalities has not been fully explained. Impaired diastolic filling may reflect irreversible alterations in left ventricular distensibility, or reversible changes in left ventricular relaxation and filling resulting from subclinical ischemia or reduced coronary flow.

Percutaneous transluminal coronary angioplasty (PTCA) improves both myocardial perfusion17 and left ventricular systolic performance18 during exercise. To determine the effects of improved myocardial perfusion on impaired left ventricular filling at rest, and to investigate the reversibility of these diastolic abnormalities, we studied patients with one-vessel coronary artery disease and normal resting systolic function before and after PTCA.

Methods

Patient Selection
We studied 25 patients with coronary artery disease, ages 33–64 years (mean 51 years) referred for PTCA. Twenty were men and five were women. All 25 patients had a history of exertional angina pectoris. No patient had evidence of previous acute myocardial infarction by history or by 12-lead ECG. Each patient underwent left-heart catheterization before the decision was made to proceed with elective PTCA. At catheterization, each patient exhibited normal left ventricular function and greater than 50% reduction in luminal diameter of only one major coronary artery. In 16 of the 25 patients, the luminal diameter was reduced by at least 75%. No patient had any other associated cardiac abnormality. This series does not represent a consecutive series of all patients undergoing PTCA at our institution,18 but does represent a consecutive series from February 1979 to September 1981 of all patients who underwent radionuclide angiographic studies both before and after PTCA who fulfilled the following selection criteria: one-vessel coronary artery disease without other associated cardiac abnormality; no evidence of previous myocardial infarction by history or ECG; normal left ventricular regional and global systolic function on contrast left ventriculography and radionuclide angiography; all cardiac medications could be withdrawn for radionuclide studies both before and after the procedure; and successful PTCA. PTCA was considered successful if there was a 40% or greater reduction of the degree of stenosis (for example, an 80% stenosis reduced to 48% was considered a successful angiographic result). To measure coronary stenosis, three arteriographic projections of the coronary stenosis were projected onto paper, measured with calipers and averaged.

Initial radionuclide angiographic studies were performed within 48 hours before PTCA, except in two patients who were studied within 10 days before
PTCA. In patients who had been receiving antianginal medications, these studies were performed at least 24 hours after the cessation of propranolol and at least eight hours after the cessation of any nitrates. Patients in whom medical therapy could not be withdrawn before PTCA were excluded from study. Radionuclide studies were repeated 48 hours after PTCA in 17 patients and between 1 week and 1 month after PTCA in the other eight.

After the pre-PTCA radionuclide study, 16 patients received oral verapamil, 80–120 mg every 8 hours for 16–24 hours before PTCA (total of three or four doses). Verapamil was then discontinued at the completion of angioplasty. We allowed a 48-hour interval between the last dose of verapamil and the post-PTCA radionuclide study.

**Percutaneous Transluminal Coronary Angioplasty**

PTCA was performed using the procedure initially described by Gruentzig and co-workers. In 24 patients, angioplasty catheters of the Gruentzig design (Gruentzig Delica, USCI) were used and in one patient the Simpson-Roberts angioplasty catheter (Advanced Catheter Systems) was used. Improvement in coronary artery stenosis was assessed by angiographic measurement of luminal diameter and by direct measurement of the coronary artery pressure gradient and distal coronary artery pressure.

**Gated Blood Pool Cardiac Scintigraphy**

Radionuclide cineangiography was performed in the supine position using red blood cells labeled in vivo with 15–20 mCi of technetium-99m. Imaging was accomplished using a conventional Anger camera equipped with a high-sensitivity, parallel-hole collimator oriented in a modified left anterior oblique position to isolate the left ventricle. The cardiac image sequence spanning the average cardiac cycle was constructed by computer-based ECG gating, using the list-mode data acquisition system. High-temporal-resolution (10–20 msec/frame) left ventricular time-activity curves were generated from the cardiac image sequence after background correction. Extrasystolic and postextrasystolic cycles were excluded, and the diastolic portion of the time-activity curve was constructed by combined forward gating and reverse gating from the R wave. The time-activity curve represents a measure of relative left ventricular volume changes with time.

Left ventricular ejection fraction was determined by computer analysis of the time-activity curve. Regional left ventricular systolic function was determined subjectively by visual inspection of the cardiac image sequence, displayed in movie format, and by inspection of the count-based stroke volume functional map, constructed by computer subtraction of the end-systolic image from the end-diastolic image. Peak left ventricular ejection rate and filling rate were computed by fitting third-order polynomial functions to the systolic ejection and rapid diastolic filling portions of the time-activity curves using a least-squares technique. Both peak ejection rate and peak filling rate were computed in left ventricular counts per second, normalized for the number of counts at end-diastole, and expressed as end-diastolic counts per second (EDV/sec). This does not imply knowledge of actual left ventricular end-diastolic volume. The time to peak filling rate was measured from end-systole (minimum volume on the time-activity curve) to the time of peak left ventricular filling rate. Left ventricular ejection time was measured from R wave to end-systole.

Ejection fraction, peak ejection rate, and ejection time were used to measure left ventricular systolic function. Variables used to describe left ventricular diastolic filling were peak filling rate and time to peak filling rate. The validity of determining these variables from gated time-activity curves has been described, as have the normal values of these variables.

Studies were performed at rest and during maximal supine exercise. Exercise studies were performed using a bicycle ergometer with a restraining harness to minimize patient motion under the camera. Exercise loads were increased by 25 W every 2 minutes until the development of angina, limiting dyspnea or fatigue or high-grade ventricular arrhythmias. Patients who developed angina continued exercise until angina reached at least the severity that typically caused the patient to stop exercise. Heart rate and blood pressure (by cuff sphygmomanometry) were monitored during exercise. For pre-PTCA studies, imaging was begun shortly after the onset of exercise, but only the portion of the data series that occurred during maximal exercise, encompassing approximately the last 2 minutes of exercise, was selected for analysis. Adequate pre-PTCA exercise data were obtained in all patients. For post-PTCA studies, exercise images were obtained for each patient during the identical time period and at the identical work load as the pre-PTCA study; if patients could exercise beyond this previous maximal level, an additional image sequence was acquired representing the new maximal exercise level.

**Late Follow-up Studies**

Follow-up cardiac catheterization and radionuclide angiography were performed in 19 patients. In 12 patients who were asymptomatic after PTCA, they were carried out as routine follow-up studies 4–8 months (median 6 months) after the procedure, and in the other seven patients they were carried out because of persistent angina after PTCA in one patient and development of recurrent angina after an initial symptom-free period (range 2–6 months) in the rest. These latter studies were performed 2 weeks to 6 months after the procedure. Follow-up coronary arteriography was performed in three patients who did not undergo repeat radionuclide testing; one asymptomatic patient at 6 months and two patients with recurrent angina at 2 and 4 months. One patient was lost to follow-up and one died in an automobile accident before routine follow-up studies could be performed. The remaining patient is clinically stable without angina and has not returned for routine repeat coronary arteriography and radionu-
Reproducibility of Radionuclide Measurements
The reproducibility of the radionuclide angiographic variables describing left ventricular systolic function and diastolic filling at rest was determined in 41 patients with angiographically demonstrated coronary artery disease (> 50% stenosis of at least one major coronary artery). After a single injection of technetium-99m, two separate radionuclide studies, separated by 20–30 minutes, were performed at rest. Between the two studies, the patient rested in the supine position. All studies were performed at least 24 hours after the cessation of propranolol and 6 hours after the cessation of nitrate medications.

Statistical Analysis
Data were analyzed by the t test using paired data and by linear regression analysis as appropriate. The effects of changes in resting heart after PTCA on the observed changes in the diastolic filling variables at rest were assessed by analysis of covariance, using heart rate as the covariate.

Results
Left Ventricular Function Before PTCA

Left Ventricular Function at Rest
Before PTCA, left ventricular ejection fraction at rest in the 25 patients ranged from 45–66% (mean 55 ± 6% [± sp]), and was within the normal range of 45–72% in every patient (fig. 1). No patient had qualitative regional wall motion abnormalities at rest, reflecting our patient selection criteria. Both peak left ventricular ejection rate (range 1.9–3.7 EDV/sec) and left ventricular ejection time (range 280–420 msec) were normal.27

Peak left ventricular filling rate at rest was 1.1–3.2 EDV/sec (mean 2.3 ± 0.6 EDV/sec) and was below the lower limit of normal (2.5 EDV/sec) in 14 patients. Time to peak filling rate was 126–227 msec (mean 181 ± 22 msec) and was above the upper limit of normal (180 msec) in 14 patients, including three who had normal peak filling rates. Thus, abnormal left ventricular diastolic filling at rest, defined as subnormal peak filling rate, prolonged time to peak filling rate, or both, was observed in 17 of 25 patients (fig. 2), despite normal regional and global systolic function at rest in all 25 patients. Neither peak filling rate nor time to peak filling rate at rest correlated with resting heart rate (r = −0.04 and r = 0.11, respectively).

Left Ventricular Function During Exercise
During maximal supine exercise, 21 patients developed angina pectoris. In the other patients, exercise was terminated because of leg fatigue. The left ventricular ejection fraction decreased or did not change during exercise compared with the resting value in 13 patients and increased in 12 patients (fig. 1). For the total group, the change in ejection fraction from rest to exercise was not significant (55 ± 6% rest, 52 ± 8% exercise). Twenty-one patients showed regional wall motion abnormalities during exercise. Twenty-three had abnormal left ventricular function during exercise.
(less than 5% increase in ejection fraction compared with the value at rest or regional wall motion abnormalities or both). In the four patients who did not develop angina during exercise, the left ventricular ejection fraction was higher than the resting value, although three of four had regional wall motion abnormalities.

**Percutaneous Transluminal Coronary Angioplasty**

Before PTCA, the severity of the coronary artery stenosis ranged from 50% to 100% reduction in luminal diameter (mean 76 ± 15%). Reflecting our selection criteria, the degree of coronary stenosis improved in all 25 patients: Immediately after PTCA, coronary artery stenoses ranged from 0 to 53% (mean 30 ± 12%). The mean pressure difference across the coronary stenosis, measured in 24 patients, was reduced in all after PTCA, from 56 ± 16 to 25 ± 13 mm Hg (p < 0.001), and the coronary artery pressure distal to the stenosis, recorded in 24 patients, increased in all but one patient (mean 35 ± 15 mm Hg before and 63 ± 12 mm Hg after PTCA; p < 0.001).

**Effect of PTCA on Left Ventricular Function**

**Left Ventricular Function at Rest**

Resting heart rate and systemic blood pressure, measured in the supine position at the time of the radionuclide studies, were not different before and after PTCA. PTCA also did not affect left ventricular systolic performance at rest (table 1), as measured by ejection fraction, ejection time and peak ejection rate.

No patient had regional wall motion abnormalities at rest either before or after PTCA (fig. 1). The diastolic filling variables, however, were significantly influenced by PTCA (table 1, fig. 3): Peak left ventricular filling rate increased from 2.3 ± 0.6 to 2.8 ± 0.5 EDV/sec (p < 0.001), and time to peak filling rate decreased from 181 ± 22 to 160 ± 18 msec (p < 0.001). Eighteen patients showed concordant evidence of improved diastolic filling at rest (both increased peak filling rate and reduced time to peak filling rate) after PTCA. Both peak filling rate and time to peak filling rate were within the normal range after PTCA in 17 of 25 patients (fig. 2). Figures 4 and 5 are examples of improved diastolic filling at rest after PTCA.

Although the heart rate at rest was not significantly influenced by PTCA, it increased 2–18 beats/min after PTCA in 15 patients and did not change or decreased by 1–21 beats/min in 10 patients. Since both peak filling rate and time to peak filling rate are affected by changes in heart rate, the diastolic filling variables were analyzed separately in the subgroup of patients whose resting heart rate increased after PTCA and those whose heart rate decreased or was unchanged (table 2). Significant changes were noted in diastolic filling within each subgroup, but neither the values before and after PTCA nor the change between before and after PTCA were different between the two subgroups. Moreover, the change in heart rate did not correlate with the change in peak filling rate or time to peak filling rate (r = −0.15 and r = 0.03, respectively). By analysis of covariance, using heart rate as the

**Table 1. Effect of Percutaneous Transluminal Coronary Angioplasty on Left Ventricular Function**

<table>
<thead>
<tr>
<th></th>
<th>Before PTCA</th>
<th>After PTCA</th>
<th>p</th>
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<tbody>
<tr>
<td><strong>Rest</strong></td>
<td></td>
<td></td>
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<tr>
<td>Heart rate (beats/min)</td>
<td>69 ± 12</td>
<td>73 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>134 ± 18</td>
<td>131 ± 18</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>80 ± 7</td>
<td>78 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>LV systolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>55 ± 6</td>
<td>55 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Peak LV ejection rate (EDV/sec)</td>
<td>2.8 ± 0.6</td>
<td>2.8 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection time (msec)</td>
<td>344 ± 35</td>
<td>341 ± 36</td>
<td>NS</td>
</tr>
<tr>
<td>LV diastolic filling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak LV filling rate (EDV/sec)</td>
<td>2.3 ± 0.6</td>
<td>2.8 ± 0.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time to peak LV filling rate (msec)</td>
<td>181 ± 22</td>
<td>160 ± 18</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Exercise (identical work load)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>114 ± 12</td>
<td>118 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>182 ± 22</td>
<td>179 ± 26</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>95 ± 10</td>
<td>91 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>52 ± 8</td>
<td>63 ± 5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LV ejection fraction response to exercise (%)*</td>
<td>−2 ± 7</td>
<td>8 ± 5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are mean ± sd.

*LV ejection fraction during exercise minus ejection fraction at rest.

Abbreviations: LV = left ventricular; PTCA = percutaneous transluminal coronary angioplasty.
covariate, peak filling rate was significantly higher after PTCA (p < 0.01 for adjusted and unadjusted means), and heart rate was not a significant determinant of results (r = 0.53); time to peak filling rate was lower after PTCA (p < 0.001 for adjusted and unadjusted means), and heart rate was not a significant determinant of results (p = 0.55). Changes in resting ejection fraction also did not correlate with the change in diastolic filling variables (r = 0.20 and r = −0.10, respectively).

**Left Ventricular Function During Exercise**

After PTCA, all patients achieved at least the exercise work load attained during the pre-PTCA study. Only three patients developed angina at this work load. Sixteen patients exercised to higher work loads than on the pre-PTCA study. Fourteen of these patients terminated exercise because of fatigue and two developed angina at the new maximal work load.

Exercise data before and after PTCA at the same work load are presented in table 1 and figure 1. Exercise heart rate and blood pressure were not different before and after PTCA. Left ventricular ejection fraction during exercise was significantly higher after PTCA (52 ± 8% vs 63 ± 5%, p < 0.001) and increased by at least 5 percentage points compared with the pre-PTCA exercise value in all but four patients. Three patients had regional wall motion abnormalities during exercise after PTCA. Ejection fraction after PTCA was greater during exercise than at rest (63 ± 5% vs 55 ± 6%, p < 0.001). Thus, the left ventricular exercise response (exercise ejection fraction minus rest ejection fraction) significantly increased after PTCA, from −2 ± 7% to 8 ± 5% (p < 0.001) and increased by 5 or more percentage points in all but

**Figure 3.** Effect of percutaneous transluminal coronary angioplasty (PTCA) on left ventricular (LV) diastolic filling at rest. The dashed lines indicate the lower limit of normal for peak filling rate (2.5 EDV/sec) and the upper limit of normal for time to peak filling rate (180 msec).

**Figure 4.** (A) Left ventricular time-activity curves at rest from one patient before and after percutaneous transluminal coronary angioplasty (PTCA). (B) Schematic representations of the two curves. Before and after PTCA, heart rate (57 vs 58 beats/min), ejection fraction (53% vs 55%), peak ejection rate (2.3 vs 2.2 EDV/sec), and ejection time (400 vs 380 msec) are similar. However, after PTCA, peak filling rate is greater (1.1 vs 2.3 EDV/sec) and time to peak filling rate (TPFR) is lower (186 vs 166 msec). EDV = end-diastolic volume.

**Figure 5.** Time-activity curves obtained at rest in three patients before and after percutaneous transluminal coronary angioplasty (PTCA), demonstrating improved diastolic filling and unaltered systolic function after PTCA.
five patients. Twenty-four patients showed improvements in exercise-induced left ventricular systolic dysfunction, measured by an increase in exercise ejection fraction, an increase in ejection fraction response to exercise, or a reduction in regional wall motion abnormalities during exercise.

Data obtained during maximal exercise after PTCA were also analyzed, whether the maximal work load represented a higher work load than the pre-PTCA study (16 patients) or the same work load (nine patients). The exercise ejection fraction (63 ± 6%) and the ejection fraction response to exercise (8 ± 6%) were both significantly greater during maximal exercise after PTCA than before PTCA (both p < 0.001).

Although the diastolic filling variables were computed for the exercise studies and demonstrated increases in peak filling rate after PTCA, these data are not presented because of the significant increases in exercise ejection fraction after PTCA. Changes in left ventricular ejection fraction significantly affect changes in peak filling rate.16, 28 Changes in peak filling rate during exercise cannot be evaluated independent of the changes in ejection fraction.

Late Follow-up Studies

In 12 asymptomatic patients, follow-up coronary arteriography demonstrated long-term arteriographic improvement after PTCA (table 3). In 11 patients, insignificant coronary arterial narrowing (< 50% reduction in luminal diameter) was observed at the site of angioplasty. One patient showed 52% narrowing at the site of angioplasty, compared with 94% narrowing before and 47% narrowing immediately after PTCA. In these patients, improvement in the diastolic filling variables persisted, and both peak left ventricular filling rate and time to peak filling rate at the time of the late post-PTCA study were significantly different from pre-PTCA values (table 3). In seven patients with persistent or recurrent angina, coronary arteriography demonstrated restenosis at the site of angioplasty, with > 60% reduction in luminal diameter (> 75% in four of the seven). In these patients, neither peak filling rate nor time to peak filling rate on the late post-PTCA study were different from values before PTCA (table 3).

Reproducibility of Radionuclide Measurements

In the 41 patients with coronary artery disease who were studied twice at rest to determine reproducibility of the radionuclide measurements, none of the variables describing left ventricular systolic function or diastolic filling significantly changed between the two studies (table 4). The average change between studies was 0.6 ± 1.9% for left ventricular ejection fraction, 0.01 ± 0.14 EDV/sec for peak filling rate, and 0 ± 19 msec for time to peak filling rate. The maximum change in peak filling rate was 0.3 EDV/sec; the maximum change in time to peak filling rate was 35 msec.

### Table 2. Effect of Percutaneous Transluminal Coronary Angioplasty on Left Ventricular Diastolic Filling Relative to Changes in Heart Rate

<table>
<thead>
<tr>
<th></th>
<th>Before PTCA</th>
<th>After PTCA</th>
<th>Change between before and after PTCA</th>
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</thead>
<tbody>
<tr>
<td>Peak LV filling rate (EDV/sec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with unchanged or decreased HR after PTCA (n = 10)</td>
<td>2.1 ± 0.7</td>
<td>2.7 ± 0.5</td>
<td>0.6 ± 0.6</td>
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<tr>
<td>Significance between subgroups</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Patients with increased HR after PTCA (n = 15)</td>
<td>2.4 ± 0.5</td>
<td>2.8 ± 0.4</td>
<td>0.4 ± 0.4</td>
</tr>
<tr>
<td>Time to peak LV filling rate (msec)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with unchanged or decreased HR after PTCA (n = 10)</td>
<td>183 ± 19</td>
<td>162 ± 17</td>
<td>21 ± 15</td>
</tr>
<tr>
<td>Significance between subgroups</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Patients with increased HR after PTCA (n = 15)</td>
<td>181 ± 23</td>
<td>159 ± 20</td>
<td>22 ± 17</td>
</tr>
</tbody>
</table>

*Significance between before and after PTCA.

Abbreviations: HR = heart rate; LV = left ventricular; PTCA = percutaneous transluminal coronary angioplasty.

### Table 3. Long-term Effect of Percutaneous Transluminal Coronary Angioplasty on Left Ventricular Diastolic Filling

<table>
<thead>
<tr>
<th></th>
<th>Patients with long-term coronary arteriographic improvement (n = 12)</th>
<th>Patients with coronary artery restenosis (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before PTCA</td>
<td>Late after PTCA</td>
</tr>
<tr>
<td>Coronary artery stenosis (%)</td>
<td>80 ± 16</td>
<td>26 ± 17</td>
</tr>
<tr>
<td>Peak LV filling rate (EDV/sec)</td>
<td>2.2 ± 0.5</td>
<td>2.6 ± 0.3</td>
</tr>
<tr>
<td>Time to peak LV filling rate (msec)</td>
<td>188 ± 19</td>
<td>173 ± 23</td>
</tr>
</tbody>
</table>

Abbreviations: See table 1.
Discussion

Impaired left ventricular diastolic function often occurs under resting conditions in patients with coronary artery disease, including many patients who show no evidence of either previous acute myocardial infarction or active myocardial ischemia, and in whom left ventricular regional and global systolic function are normal. Left ventricular diastolic dysfunction in patients after myocardial infarction results from myocardial fibrosis, with alterations in the diastolic characteristics of the left ventricle. During active myocardial ischemia, diastolic dysfunction presumably develops from impaired early diastolic left ventricular relaxation or increased diastolic tone, resulting in abnormal left ventricular filling and altered diastolic pressure-volume relationships. However, the mechanisms for impaired diastolic function at rest are not completely understood in patients without previous myocardial infarction or active ischemia in whom resting indexes of left ventricular systolic function are normal. Periods of myocardial ischemia may produce irreversible changes in left ventricular compliance or in left ventricular relaxation and filling without altering systolic function. Alternatively, clinically apparent myocardial ischemia, so mild as not to cause angina or affect contractile function, may result in reversible alterations in left ventricular relaxation and filling. Finally, reduced rate of coronary flow in early diastole, resulting from coronary artery stenosis, may decrease the mechanical effect that rapid filling of the coronary reservoir in early diastole may have in augmenting myocardial relaxation. If either of these latter two mechanisms is operative, impaired left ventricular relaxation and filling should improve after reduction in coronary artery stenosis.

Studies of oral verapamil therapy demonstrated that impaired left ventricular diastolic filling under resting conditions may be reversible in some patients with coronary artery disease. These results might reflect either reduction in subclinical myocardial ischemia or improved coronary flow. However, verapamil also caused changes in left ventricular loading conditions, including effects on heart rate, blood pressure and left ventricular contractile performance (and, although not measured, possible alterations in left ventricular volumes and left atrial pressure) that might directly affect diastolic filling of the left ventricle. PTCA would appear to be an ideal procedure with which to study reversibility of impaired left ventricular diastolic filling after PTCA, separating by only a few days. Such techniques have been used to demonstrate an improvement in myocardial perfusion during exercise and reduction in exercise-induced left ventricular systolic dysfunction after PTCA.

We selected patients without evidence of previous myocardial infarction and with normal regional and global left ventricular systolic function at rest. Thus, we attempted to exclude patients with evidence of myocardial fibrosis, in whom impaired left ventricular diastolic filling might be irreversible because of fixed anatomic changes. We also selected patients with stenosis of only one coronary artery so that left ventricular function after PTCA would not be influenced by potentially ischemic myocardium in the distribution of coronary arteries that were not dilated. All patients were studied free from medication effects. Despite normal resting systolic function in all 25 patients, 17 (68%) had abnormal diastolic filling at rest. In a previous study, diastolic filling abnormalities were noted in 26 of 33 patients (79%) with one-vessel coronary artery disease, normal resting systolic function and no evidence of previous myocardial infarction.

After PTCA, judged to be successful by coronary arteriography, resting heart rate, blood pressure, and left ventricular systolic function were unchanged from pre-PTCA values (table 1, fig. 1). Left ventricular systolic function during exercise improved after PTCA in 24 patients (table 1, fig. 1), reflecting a reduction in exercise-induced ischemia, as previously described. Although systolic function at rest was not altered by PTCA, diastolic filling at rest improved in 18 patients (table 1, figs. 3–5) and was normal in 17 patients (fig. 2).
These data demonstrate reversibility of impaired resting left ventricular diastolic filling in patients with coronary artery disease. Although 16 patients received verapamil after the pre-PTCA radionuclide study (to prevent coronary spasm during angioplasty), they received only three to four doses. In every patient, verapamil was discontinued at least 8 half-lives of the drug before the post-PTCA study. Hence, verapamil could not account for the differences between the pre- and post-PTCA studies. Moreover, diastolic filling also improved in eight of nine patients who did not receive verapamil.

Although the mechanisms for improved left ventricular diastolic filling at rest after PTCA are not established, the data support two possible mechanisms. Impaired diastolic filling at rest may be the manifestation of subclinical ischemia or the residual manifestation of previous acute ischemia. Improved resting diastolic filling after PTCA may reflect a reduction or elimination of reversible myocardial ischemia. In this regard, the changes in left ventricular diastolic-filling (table 1, fig. 3) were paralleled by the changes in exercise ejection fraction and ejection-fraction response to exercise (table 1, fig. 1), which reflect the extent of reversible myocardial ischemia.

A second possible mechanism may relate to the effect of early diastolic coronary flow on the rate of left ventricular relaxation. Brutsaert and co-workers have hypothesized that rapid filling and distention of the coronary bed is an important mechanical driving force for augmenting and sustaining left ventricular relaxation. Although total flow in a stenosed coronary artery may be normal at rest, the rate and extent of flow in early diastole may be compromised, resulting in prolonged relaxation and alterations in the timing and rate of rapid diastolic filling. If so, then PTCA might improve left ventricular relaxation and filling at rest independent of any potential effect on myocardial ischemia.

Two other factors may contribute to our results. Temporal dyssynchrony between normal and ischemic myocardium may result in impaired left ventricular relaxation and filling, and regional dyssynchrony would improve after normalization of myocardial perfusion in the ischemic zone. Thus, improved global left ventricular filling after PTCA might result from improved regional left ventricular function. Second, in the absence of quantitative volume measurements, we cannot exclude the possibility that PTCA produced changes in resting left ventricular end-diastolic volume. Since peak filling rate cannot be expressed as absolute volume changes, but only as changes relative to end-diastolic volume (a limitation of our technique), changes in end-diastolic volume after PTCA might alter the peak filling rate. However, since resting ejection fraction, heart rate, and blood pressure were unchanged after PTCA, we do not feel that major changes in left ventricular end-diastolic volume occurred or contributed importantly to increased rate of diastolic filling. Moreover, the peak ejection rate, also measured relative to end-diastolic volume, was not changed after PTCA, while peak filling rate increased (table 1).

Our data suggest that improved left ventricular diastolic filling after PTCA is not dependent on changes in ventricular volume, but reflects either reduced myocardial ischemia or improved coronary flow.

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