Asynchronous left ventricular diastolic filling in patients with isolated disease of the left anterior descending coronary artery: assessment with radionuclide ventriculography

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ABSTRACT

To study the relationship between global and regional filling of the left ventricle, we conducted resting gated radionuclide ventriculographic studies in 15 control subjects (group 1) and 22 patients with isolated disease of the left anterior descending coronary artery (group 2). None had had a previous myocardial infarction. A computer program subdivided the image of the left ventricle into four regions. The time-activity and first-derivative curves of the global and regional left ventricles were computed. In the global left ventricle, the normalized peak filling rate (PFR) was decreased (p < .01) and the ratio of the time to PFR (time interval from global end-systole to PFR) to the diastolic time, TPFR/DT, was greater (p < .02) in group 2 than in group 1. In the regional left ventricle, in the side perfused by the stenosed vessel (septal and apical), PFR was slightly decreased in the apical (p < .05), but not the septal region (p = NS); TPFR/DT was greater in the apical (p < .02) and in the septal region (p < .01) in group 2. In the normally perfused lateral side, there were no significant differences in PFR or in TPFR/DT between group 1 and group 2. Total ΔPFR/DT, which was defined as the ratio of the sum of the absolute values of the time differences from global PFR to regional PFR (septal, apical, and lateral) to the diastolic time, was significantly greater in group 2 (0.09 ± 0.05 vs 0.16 ± 0.05; p < .001). This indicates the existence of asynchronous diastolic filling in the different regions of the left ventricle in group 2. A negative correlation existed between total ΔPFR/DT and global PFR (r = −.64, p < .001). Thus, in patients with one-vessel disease, asynchronous diastolic filling occurs due to the filling disturbance in the affected regions, which may cause impairment of the filling of the global left ventricle.


LEFT VENTRICULAR diastolic filling has been reported to be impaired in many patients with coronary artery disease in whom there is no evidence of previous myocardial infarction. However, little is known regarding the effect of the regional filling in the left ventricular cavity on the global left ventricular filling during diastole in these patients. Recent development of computer technology permits the acquisition and display of radionuclide images collected continuously throughout the cardiac cycle, and assessment of regional left ventricular function under a physiologic state with the use of a scintillation camera interfaced to a computer system has become an established and widely applied method for the noninvasive evaluation of regional left ventricular performance. We used this computer-assisted technique to quantitatively assess regional left ventricular function based on changing count rates, a variable that is directly proportional to changes in left ventricular blood volume. To evaluate the relationship between global and regional left ventricular filling, we performed electrophysiographically gated radionuclide ventriculography in patients at rest with single-vessel disease but without myocardial infarction.

Materials and methods

Patient population. The study group consisted of 37 patients (24 men and 13 women) referred to the Yamaguchi University...
Hospital between 1981 and 1983. All patients underwent electrocardiographically gated radionuclide ventriculography. They were classified as follows:

Group 1 consisted of 15 subjects who acted as controls (seven men and eight women, age range 20 to 64 years); group 2 consisted of 22 patients with significant single-vessel disease of the left anterior descending coronary artery and angina pectoris (18 men and four women, age range 33 to 66 years). Each of the patients in group 1 underwent cardiac catheterization for the evaluation of atypical chest pain and had a normal left ventriculogram and coronary arteriogram and normal values for hemodynamic variables at rest and during a supine bicycle exercise test or ergonovine maleate test. Clinical findings in all were normal. Physical examination (including determination of blood pressure), chest radiography, exercise electrocardiography, echocardiography, and stress myocardial scintigraphy with thallium-201 showed no abnormalities. All patients in group 2 underwent cardiac catheterization and had severe organic stenosis (>75% luminal diameter) of only the proximal left anterior descending branch. In all patients in group 2, the tracer uptake defects seen on the stress myocardial images obtained with thallium-201 were in the anteroapical or septal left ventricular wall and there were no deficits in other areas. None of the patients had a history or electrocardiographic or ventriculographic evidence of previous myocardial infarction. Patients with additional coronary artery lesions, congenital heart disease, hypertensive heart disease, arrhythmia, valvular heart disease, or cardiomyopathy were excluded from the study. Patients with angina at rest or unstable chest pain were also excluded. Radionuclide ventriculography was performed at least 72 hr after treatment with calcium antagonists or β-blockers had been stopped and at least 12 hr after treatment with nitrates was stopped. The test was performed during the 10 days before or after cardiac catheterization.

All patients in groups 1 and 2 were in normal sinus rhythm and they had no conduction disturbances. The radionuclide studies were preceded by resting myocardial scintigraphic studies with thallium-201 in all patients and subjects and the tracer uptake defects were not seen on the resting images from any of the 37. The mean age was similar in group 1 and group 2 (group 1, 50 ± 13 years; group 2, 54 ± 8 years; NS).

**Gated radionuclide ventriculography.** A conventional gamma camera (PHO/GAMMA LFOV, Searle Inc., Des Plaines, IL) equipped with a high-resolution all-purpose parallel-hole collimator was used for gated imaging. All patients were given 15 to 20 mCi of 99mTc-labeled human serum albumin. After the radionuclide had equilibrated with the intravascular space (about 10 min), the camera was positioned in the modified left anterior oblique projection (15 degrees caudal tilt) because the separation of the left ventricle from the right ventricle and left atrium was greatest in this view. In all studies, low-count (500,000 counts) scintigrams were acquired with a digital computer (Scintiview, Searle Inc.) until the camera obliquity showing the greatest separation of the right and left ventricles was found (typically a 40 to 60 degree projection). Then, counts were acquired during 600 beats in a multiple-gated mode on a magnetic disc with a digital computer (SCINTIPAC-1200, Shimadzu Seisakusho, Kyoto, Japan). Data were collected for 600 beats in all studies. Those photoevents falling within a 20% window centered on the photopeak of technetium-99m were recorded. A computer-based procedure gated to the electrocardiogram was used to collect and organize data into a series of images or frames (framing rate up to 31 frames/cardiac cycle) spanning the average cardiac cycle.

After data acquisition a summed-beats curve in which the number of summed beats in each frame was calculated explicitly was constructed and the average cardiac cycle length was defined as the interval between the first frame and the frame that summed approximately 300 beats on this curve (the last frame).
For the global time-activity curve (2), the end-systolic frame was defined as the frame with the minimum counts within the end-diastolic perimeter of the left ventricle. Crescent-shaped global and regional background regions of interest were traced manually with an electronic cursor along the lateral, apical, and septal portions adjacent to and inside the left ventricular end-diastolic perimeter applied to the end-systolic frame, specifically avoiding regions of high-count activity (figure 2). A computer program determined a geometric center of the area of the end-diastolic perimeter of the left ventricle and subdivided it into four regions (basal, septal, apical, and lateral), with two intersecting lines at an angle of 45 degrees to the longitudinal axis of the left ventricle at the geometric center of the area (figure 2). The background correction for the four regions (septal, apical, and lateral regions and global left ventricle) was estimated with an average count per cell in each of the four background regions of interest obtained in the end-systolic frame. Background-corrected global and regional time-activity curves were generated from the global left ventricle and each of three regions (septal, apical, and lateral) after three-point temporal smoothing using counts within a constant region of interest (fixed region of interest method). First-derivative curves (dV/dt) of these time-activity curves were computed for the entire cycle in the septal, apical, and lateral regions and the global left ventricle (figure 3). The dV/dt value in the i-th frame was calculated as: dV/dt (i) = (C (i+1) - C (i - 1))/2 × frame interval (sec), where the dV/dt value was obtained by the slope per second of two points (that is i + i-th frame and i - i-th frame) and C (i+1) and C (i-1) were counts at the i-th and i-th frames, respectively, on the time-activity curve. The dV/dt values at the first frame (ED) and the last frame (last) were calculated as follows: dV/dt (ED) = (C (ED +1) - C (ED))/1 × frame interval (sec) and dV/dt (last) = (C (last) - C (last - 1))/1 × frame interval (sec).

A maximum value of positive dV/dt during diastole was defined as the peak filling rate. End-systole was defined as the minimum volume at which the dV/dt value was zero. When the peak filling rate or the end-systolic volume in the two consecutive frames had the same values, they were considered to have occurred at the half period between the two frames. Since the basal region of the left ventricle tended to overlie the regions of the mitral and aortic valves, aorta, left atrium, and great vessels, this region was excluded from study.

The following indexes were obtained from the time-activity and first-derivative curves in the global left ventricle and in each of the three regions (septal, apical, and lateral) (figure 3):

Systolic phase indexes: (1) Ejection fraction (%) = 100 × (EDV - ESV)/(EDV - BG), where EDV, ESV, and BG are end-diastolic, end-systolic, and background counts, respectively. (2) Time to end-systole (msec) = the time interval between the electrocardiographic R wave and the frame with minimum counts at which the dV/dt value is zero.

Diastolic phase indexes: (1) Normalized peak filling rate (EDV/sec) = peak filling rate normalized to end-diastolic counts. (2) Time to peak filling rate (msec) = the time interval

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TABLE 2
Radionuclide ventriculographic variables

<table>
<thead>
<tr>
<th>Region</th>
<th>EF (%)</th>
<th>p value</th>
<th>TES (msec)</th>
<th>p value</th>
<th>PFR (EDV/sec)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G1</td>
<td>G2</td>
<td></td>
<td>G1</td>
<td>G2</td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>59±6</td>
<td>59±5</td>
<td>NS</td>
<td>349±27</td>
<td>352±32</td>
<td>NS</td>
</tr>
<tr>
<td>Septal</td>
<td>72±9</td>
<td>73±10</td>
<td>NS</td>
<td>344±31</td>
<td>337±32</td>
<td>NS</td>
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<td>Apical</td>
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<td>79±6</td>
<td>NS</td>
<td>352±29</td>
<td>357±31</td>
<td>NS</td>
</tr>
<tr>
<td>Lateral</td>
<td>74±9</td>
<td>78±8</td>
<td>NS</td>
<td>355±27</td>
<td>367±31</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

EF = ejection fraction; TES = time to end-systole; PFR = normalized peak filling rate; TPFR = time to peak filling rate; DT = diastolic time; G1 = control subjects; G2 = patients with angina pectoris.

between the global end-systole and the peak positive dV/dt. (3) Time to peak filling rate/diastolic time = time to peak filling rate normalized to diastolic time (R-R interval–global time to end-systole),7 since heart rate or diastolic time affects the measurement of diastolic variables.1 (4) Total ∆t = sum of the absolute values of the time differences from the peak positive dV/dt in the global left ventricle to that in each of the three regions. (5) Total ∆t/diastolic time = total ∆t normalized to diastolic time. This parameter is a quantification of asynchronous diastolic filling in the left ventricle and asynchronous filling is considered to increase with the increase in total ∆t/diastolic time.

Reproducibility of radionuclide technique. The reproducibility of radionuclide ventriculographic variables in measuring left ventricular systolic or diastolic function was determined in 12 patients with various heart diseases (previous myocardial infarction [n = 3], angina pectoris [n = 3], hypertensive heart disease [n = 3], valvular heart disease [n = 2], and hypertrophic cardiomyopathy [n = 1]). Two separate radionuclide studies were performed 20 to 30 min apart on patients at rest after a single injection of technetium-99m. In the interval between the two studies the patients rested in the supine position. All the studies were performed at least 72 hr after all treatment had been stopped.

Angiographic study. Hemodynamic data were obtained during cardiac catheterization, as previously described.13 Coronary angiographic examinations were performed by the Sones method. Significant coronary artery stenosis was considered to be present when a more than 75% narrowing of the luminal diameter was observed. A Millar catheter-tip micromanometer (Model PC-484A, pigtail) was used for pressure measurement and cineangiography.

Statistical analysis. The data are presented as mean ± SD. The lower and upper limits of the normal values were defined as the mean ± 2 SD. Statistical analysis was performed with the t test for unpaired data. The level of statistical significance was p < .05.

Results

All hemodynamic parameters are listed in table 1 and all radionuclide parameters are listed in tables 2 to 4. The mean resting heart rate was 72 ± 9 beats/min for group 1 and 67 ± 9 beats/min for group 2. The mean diastolic time was 490 ± 98 msec for group 1 and 528 ± 106 msec for group 2. There were no significant differences between group 1 and group 2 in mean resting heart rate, mean diastolic time, or values for hemodynamic variables obtained during cardiac catheterization (table 1).

![FIGURE 4](image-url) Normalized peak filling rate (PFR). G1 = control subjects; GII = patients with angina pectoris; other abbreviations as in figure 3. Bars represent mean ± SD.

![FIGURE 5](image-url) The ratio of the time to peak filling rate to the diastolic time. Abbreviation are as in figures 3 and 4. Bars represent mean ± SD.
TABLE 2  
(Continued)

<table>
<thead>
<tr>
<th>TPFR (msec)</th>
<th>TPFR/DT</th>
<th>Total Δt (msec)</th>
<th>Total Δt/DT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>G1</td>
<td>G2</td>
</tr>
<tr>
<td>G1 156 ± 20</td>
<td>199 ± 28</td>
<td>0.32 ± 0.05</td>
<td>0.39 ± 0.10</td>
</tr>
<tr>
<td>G2 168 ± 26</td>
<td>223 ± 22</td>
<td>0.35 ± 0.05</td>
<td>0.44 ± 0.09</td>
</tr>
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</table>

Systolic phase indexes. In the global left ventricle, there were no significant differences between group 1 and group 2 in ejection fraction or time to end-systole. There were also no differences in these parameters in any of the three regions between the two groups (table 2). End-systole of each region occurred within 40 msec before or after the global end-systole in all patients studied. When time to end-systole in one region (regional time to end-systole) was compared with that in another region within the same group, there was no significant difference among the three different regions in either group. To allow comparison of the time interval between global and regional end-systole when the heart rates varied, the time interval was normalized by dividing it by the global time to end-systole, and the value obtained was expressed as a percentage. There were no significant differences between the two groups in this value in the septal (group 1, 3 ± 3%; group 2, 4 ± 4%; NS), apical (1 ± 1%, 2 ± 3%; NS), or lateral (2 ± 2%, 4 ± 2%; NS) regions.

Diastolic phase indexes

**Global left ventricle.** Normalized peak filling rate in group 2 was significantly lower than that in group 1 (figure 4; table 2). This was not due to an increase in end-diastolic volume without a decrease in peak filling rate since there was no significant difference between the two groups in end-diastolic volume (table 1). The time to peak filling rate in group 2 was significantly prolonged when compared with that in group 1 (table 2). The time to peak filling rate/diastolic time was significantly greater in group 2 than in group 1 (figure 5; table 2). When an abnormal value was defined as one more than 2 SD from the mean, of the 22 patients in group 2, 11 patients (50%) had either a markedly decreased peak filling rate (<2.2 EDV/sec in 10 patients [45%]) or a significantly increased time to peak filling rate/diastolic time (>0.42 in six patients [27%]) (figure 6; table 3). Neither peak filling rate nor time to peak filling rate/diastolic time correlated with heart rate in the patients studied (r = .23, −.30, respectively).

**Regions of the left ventricle.** In the apical region, peak filling rate was significantly lower in group 2 than in group 1, while there were no significant differences between the two groups with respect to peak filling rates in the septal and lateral regions (figure 4; table 2). Although there was no significant difference in times to peak filling rate in the lateral region, the values were significantly prolonged in the apical region and in the septal region in group 2. There was also no significant difference in the ratios of time to peak filling rate/diastolic time in the lateral region, but the ratios were significantly greater in the apical and septal regions in group 2 (figure 5; table 2). In regional analysis of the 22

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFR</td>
<td>Global</td>
</tr>
<tr>
<td>45% (10/22)</td>
<td>9%     (4/44)</td>
</tr>
<tr>
<td>TPFR/DT</td>
<td>27%    (6/22)</td>
</tr>
<tr>
<td>50% (11/22)</td>
<td>39%    (17/44)</td>
</tr>
</tbody>
</table>

The lower and upper limits of the normal values were defined as the mean ± 2 SDs.

PFR + TPFR/DT = combined PFR and TPFR/DT; global = global analysis; regional = regional analysis; other abbreviations are as in table 2.

22 = number of patients with angina pectoris (group 2); 15 = number of control subjects (group 1); 44 = number of regions perfused by stenosed vessel; 67 = number of regions normally perfused.

TABLE 3

Prevalence of left ventricular diastolic filling abnormalities in patients with angina pectoris (group 2)

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td></td>
<td>Global</td>
</tr>
<tr>
<td>PFR</td>
<td>45%    (10/22)</td>
</tr>
<tr>
<td>TPFR/DT</td>
<td>27%    (6/22)</td>
</tr>
<tr>
<td>PFR + TPFR/DT</td>
<td>50%    (11/22)</td>
</tr>
<tr>
<td>Total Δt/DT</td>
<td>50%    (11/22)</td>
</tr>
</tbody>
</table>
patients in group 2, peak filling rate was outside the lower normal limits (<2 SD: septal 2.2, apical 2.4, and lateral region 2.8 EDV/sec) in one patient (5%) in the apical region, in three patients (14%) in the septal region, and in three patients (14%) in the lateral region (figure 6). Time to peak filling rate/diastolic time was outside the upper normal limits (>2 SD: septal 0.45, apical 0.43, and lateral region 0.38) in seven patients (32%) in the apical region, in eight patients (36%) in the septal region, and in three patients (14%) in the lateral region (figure 6). In regional analysis of 44 regions (22 apical and 22 septal regions) perfused by stenosed vessels, peak filling rate and time to peak filling rate/diastolic time values identified 9% (4/44) and 34% (15/44) of the affected regions, respectively, as abnormal (table 3). Total Δt in group 2 was significantly greater than that in group 1. Total Δt/diastolic time in group 2 was also significantly greater than that in group 1 (figure 7; table 2), and was outside the upper normal limits (>2 SD, 0.17) in 11 patients (50%) in group 2 (table 3). In figure 8, individual values for global peak filling rate were plotted against the values for total Δt/diastolic time. A negative correlation was found between these two parameters (r = −.64, p < .001).

Reproducibility of radionuclide technique. The reproducibility of the technique is demonstrated in table 4. There was excellent correlation between the global systolic and diastolic variables obtained from the first and second studies (r ≥ .93) and between the regional systolic and diastolic variables obtained from the first and second studies (r ≥ .90).

**Discussion**

Accuracy of the radionuclide method in assessing regional left ventricular function. The main problem when assessing regional wall movement in various parts of the ventricle is the fixing of a reference point to which wall movement can be related. As our reference point of the system we chose the geometric center of the area of the end-diastolic image and determined regional ventricular function by analyzing the regional time-activ-

![FIGURE 6. Relationship between the normalized peak filling rate (y) and time to peak filling rate/diastolic time (x). Abbreviations are as in figures 3 and 4. Dotted lines indicate normal range.](http://circ.ahajournals.org/)

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**TABLE 4**

Reproducibility of radionuclide measurements

<table>
<thead>
<tr>
<th></th>
<th>EF (%)</th>
<th>TES (msec)</th>
<th>PFR (EDV/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Global</td>
<td>.98</td>
<td>0.98</td>
<td>4</td>
</tr>
<tr>
<td>Regional</td>
<td>.98</td>
<td>0.94</td>
<td>5</td>
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</table>

The relationship between the radionuclide ventriculographic variables obtained from the first and second study was study 2 = A × study 1 + B. Abbreviations are as in table 2.
ity curves. If the reference point moves throughout the cardiac cycle, measurement of regional wall motion is avoided. \(^{15}\) Left ventricular segmental shortening is directed towards the center of the area, \(^{17}\) which is maintained at a relatively stable position throughout the cardiac cycle both in patients with normal and those with abnormal contractile dynamics. \(^{18-20}\) We also studied the dynamics of the left ventricular center of the area in a 60 degree left anterior oblique projection from projected cineventriculograms and found that the path length traversed by the center of the area during systole was small relative to the left ventricular longitudinal axis in control subjects and in patients with one-vessel left anterior descending coronary artery disease without previous myocardial infarction. \(^{21}\) Thus, it is reasonable to assume that the use of the center of the area as a reference point results in the least error.

The values obtained for diastolic parameters should be interpreted with caution since there were potential sources of error in our method stemming from the counts correction for undersampling at the last three of four frames; these frames of time-activity curves were not accurate. However, this counts correction probably did not affect our measurement of diastolic variables since global and regional peak filling rates occurred in the frames before the terminal fourth portion of the time-activity curves in all patients studied.

Previous authors who have examined regional function have found it necessary to use regional background correction. \(^{9-11}\) In this study, an average background count per cell contained within the global region of interest was 62 ± 4% (group 1) and 64 ± 4% (group 2) of the average global end-diastolic counts per cell. The percentages of background within regional regions of interest were as follows: septal region, 74 ± 5% and 74 ± 7%; apical region, 59 ± 6% and 61 ± 5%; lateral region, 64 ± 6% and 65 ± 6% for group 1 and group 2, respectively. There were no significant differences in the percent background in the global left ventricle or in any of the three regions between the two groups. Global ejection fractions calculated by this technique correlated well with those determined with biplane cineangiography (n = 30, \(r = .93, p < .001\)).

Prevalence of left ventricular diastolic filling abnormalities in patients in group 2. Comparing the regional and global analyses in our study, an analysis of regional peak filling rate offered no help in the discrimination of normal from diseased regions, since the degree of overlap in the regional peak filling rate in the affected (septal and apical) regions between the diseased group and the control group was considerable (figure 4; table 3). Miller et al., \(^{8}\) using radionuclide ventriculography, found that the global peak filling rate value identified 50% of patients with coronary artery disease and normal ejection fractions and wall motion as abnormal, while the regional peak filling rate value did not separate the control subjects and the patients with coronary artery disease. Our findings generally agree with those of Miller et al. This discrepancy between the global and the regional analyses of peak filling rate suggests that the abnormalities in global peak filling rate we found in patients in group 2 may be not attributable only to the abnormalities in regional peak filling rate.

Systolic phase function. There were no significant differences between group 1 and group 2 with regard to ejection fraction or time to end-systole in the global left ventricle and/or any of the three regions (table 2). The time interval between global and regional end-systole was short relative to the global time to end-systole in both groups. This indicates that the regional end-systole occurred very close to the global end-systole, and that in group 2 as well as in group 1 each region completed shortening synchronously during systole. A similar finding has been observed by Holman et al. \(^{10}\)

Global diastolic phase function. Normalized peak filling rate was significantly lower in group 2 than in group 1 (figure 4; table 2), which is in agreement with results obtained with gated radionuclide ventriculography. \(^{3,6,8}\) and with contrast ventriculography \(^1\) or first-pass radionuclide ventriculography. \(^{4,5}\) Time to peak filling rate in group 2 was significantly prolonged compared with that in group 1, which is in agreement with the findings of Bonow et al., \(^3\) Polak et al., \(^3\) and Miller et al. \(^8\) Time to peak filling rate/diastolic time was also significantly greater in group 2 (figure 5; table 2), in

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**TABLE 4**

(Continued)

<table>
<thead>
<tr>
<th>TPFR (msec)</th>
<th>TPFR/DT</th>
<th>Total Δt (msec)</th>
<th>Total Δt/DT</th>
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<tbody>
<tr>
<td></td>
<td>r</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>.99</td>
<td>1.10</td>
<td>–17</td>
<td></td>
</tr>
<tr>
<td>.98</td>
<td>0.95</td>
<td>12</td>
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agreement with the findings of Slutsky et al.7 These results indicate that left ventricular diastolic filling could be impaired at rest in many patients with coronary artery disease who have had no previous myocardial infarction.

**Regional diastolic phase function.** Differences in regional peak filling rates between group 1 and group 2 were only significant in the apical region, and differences in times to peak filling rate and in the ratios time to peak filling rate/diastolic time were significant in the septal and apical regions, which were perfused by the stenosed vessel. There were no significant differences in peak filling rate, time to peak filling rate, or time to peak filling rate/diastolic time in the normally perfused lateral region (figures 4 and 5; table 2). This indicates that the filling patterns in different intracavitary portions are quite different from those in the normal heart in patients with one-vessel disease, and that peak filling rate occurs significantly later in the involved side than in the normally perfused side in patients with stenosed vessels.

Figure 9 shows typical global and regional time-activity curves obtained in a control subject (group 1) and a patient with angina pectoris (group 2). As shown in figure 9, early diastolic portions of time-activity curves were assessed visually and abnormal filling patterns were noted in these portions in 20 of 22 patients in group 2, but not at all in patients in group 1. These abnormal filling patterns were not observed in the normally perfused lateral side of the heart in either group. It is well known that in the experimental preparation abnormal regional wall motion similar to that shown in figure 9 occurs in an ischemic zone during acute ischemia.22-24 Kumada et al.23 demonstrated that the ischemic segment exhibits a reduction in the duration of active shortening and subsequent late systolic lengthening with further shortening, and that ventricular asynchronous wall motion (in opposite directions) in ischemic and normal zones is present after experimental total coronary occlusion. They and other investigators emphasized that this temporal asynchrony was accompanied by marked impairment of left ventricular relaxation.23, 25

This phenomenon is observed not only after total coronary occlusion but also during partial coronary stenosis, which produces coronary flow reductions below approximately 50% of the control flow level.22 More recently, Gewirtz et al.26 reported that ischemia-
induced impairment of left ventricular relaxation reduced the diastolic filling rate of the left ventricle in experimental preparations. These findings strongly suggest that asynchronous wall motion can cause impairment of filling of the left ventricle. In our study, in the control subjects, peak filling rates in three regions occurred at a time close to the time of global peak filling rate so that total Δt/diastolic time was small (0.09 ± 0.04). In contrast, in the patients with one-vessel disease, peak filling rates in the affected regions (septal and apical) occurred significantly later than global peak filling rate, and also later than that in the normal lateral region, so that total Δt/diastolic time, a quantification of the asynchronous diastolic filling in the left ventricle, became greater (0.16 ± 0.05). This indicates that peak filling rate occurs asynchronously in the normally perfused and affected sides. In our study, diastolic asynchronous filling, determined by the values of total Δt/diastolic time, was present under resting conditions in 50% of patients in group 2 (table 3). Furthermore, the negative correlation between the global peak filling rate and the total Δt/diastolic time suggests that global peak filling rate may be reduced with progressive increase in asynchrony (figure 8). Miller et al., using phase-analysis methods, also found that diastolic asynchronous filling could be detected under resting conditions in 65% of patients with coronary artery disease and normal ejection fractions. St. John Sutton et al., using echocardiography, reported that the left ventricular peak filling rate was reduced with an increase in asynchrony between the septum and the posterior wall in patients with idiopathic hypertrophic subaortic stenosis.

There could be several possible explanations for the mechanism of the asynchronous regional filling observed in the present study. First, small foci of myocardial necrosis produced by repeated anginal episodes, too small to be detected by resting myocardial scintigraphy, may be present in patients with one-vessel disease and myocardial necrosis impairs diastolic filling. The second possible mechanism may relate to the effect of early diastolic coronary flow on the rate of left ventricular relaxation. Brutsaert et al. have hypothesized that rapid filling and distension of the coronary bed is an important mechanical driving force for augmenting and sustaining left ventricular relaxation. Even if total flow in a stenosed coronary artery is normal at rest, changes in the rate and extent of coronary flow in early diastole may cause prolonged relaxation and result in alterations in the timing and the rate of rapid diastolic filling.

Although left ventricular diastolic filling is complex and peak filling rates and filling periods are only two factors in this process, the present results indicate that asynchronous filling could be one of the causes of impairment of diastolic filling of the global left ventricle in some patients with coronary artery disease.

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