DIAGNOSTIC METHODS

VENTRICULAR PERFORMANCE

Alteration of diastolic filling rate during exercise radionuclide angiography: a highly sensitive technique for detection of coronary artery disease

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ABSTRACT Diastolic and systolic parameters of left ventricular performance were characterized from high-frequency time-activity curves obtained in 10 normal volunteers (mean age 29 ± 4 yr), in 25 patients with normal coronary arteries, and in 50 patients with coronary artery disease (CAD) at rest and during three stages of exercise radionuclide angiography. In the normal volunteers ejection fraction was 65 ± 5% (SD) at rest and 78 ± 5% with exercise (p < .001). In patients with normal coronary arteries ejection fraction was 64 ± 5% at rest and 72 ± 8% with exercise (p < .0001). In patients with CAD resting ejection fraction was 60 ± 10% and that during exercise was 61 ± 13% (p = NS). Peak diastolic filling rate in the first half of diastole, peak systolic ejection rate, and times to peak rates and to end-systole were measured. In the normal subjects resting peak distolic filling rate was 3.1 ± 0.6 end-diastolic counts/sec and it increased in all subjects with exercise to 3.6 ± 0.7 (p < .05). In patients with normal arteries and those with CAD peak diastolic filling rate was 2.3 ± 0.8 at rest and with exercise this parameter increased to 3.2 ± 1.1 (p < .001) in patients with normal arteries and fell to 1.7 ± 0.6 in those with CAD (p < .001). Peak systolic ejection rate decreased from 2.5 ± 0.8 to 1.9 ± 0.8 with exercise in patients with CAD (p < .001). The sensitivity of wall motion and ejection fraction response to exercise for detection of CAD in patients was 62% (80% excluding those with one-vessel disease), with no false-positive results. Sensitivity and specificity of peak systolic ejection rate were 66% and 67%, respectively. Peak diastolic filling rate exercise/rest ratio was greater than 1 for patients with normal and 1 or less for patients with diseased arteries, with sensitivity of 98% and specificity of 94%. Thus, alteration of peak diastolic filling rate during exercise is a very sensitive and specific indicator of ischemic heart disease.

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MYOCARDIAL PERFORMANCE can be critically assessed during exercise with radionuclide angiography.1–3 In normal subjects the heart responds to stress with increased contractility and stroke volume, while in patients with coronary artery disease (CAD), with the onset of ischemia abnormalities develop in contractile performance during systole1–3 and in relaxation and filling of the ventricle during diastole.15–20 Exercise radionuclide angiography has been demonstrated to be a sensitive technique for the detection of abnormalities in cardiac contraction with the onset of ischemia.1–14 Contractile parameters may be apparently normal, however, in some individuals with CAD — especially those with good ventricular function and single-vessel disease, but also in some patients with double- or triple-vessel disease.3 Diastolic performance has been demonstrated to be very sensitive to ischemia.15–33 Careful assessment of diastolic properties during stress, however, has not been previously well characterized by radionuclide angiography, and might prove to enhance the sensitivity of detection of ischemia. We therefore sought to evaluate and characterize the detection of ischemic heart disease by alteration in diastolic as well as systolic parameters during exercise. Accordingly, diastolic and systolic parameters of left ventricular performance were characterized from high-frequency time-activity curves obtained at rest and during exercise radionuclide angiography in young healthy volunteers (to assess the effect of age), in patients with normal coronary arteries, and in patients with CAD. Peak diastolic filling rate in the first half of diastole,
peak systolic filling rate, and times to peak rates and to end-systole were measured.

Methods

Study population. The study population included 85 individuals, none of whom had significant valvular, pericardial, or primary myocardial disease or mitral valve prolapse. Ten were normal volunteers (five men and five women) with a mean age of 29 ± 4 years. The patient population included 25 individuals (17 men and eight women with a mean age of 52 years) with normal coronary arteries and 50 patients (48 men and two women, mean age of 57) with CAD. Coronary disease was defined as luminal obstruction of 50% or more. However, all but one of the patients had 70% or more obstruction of at least one coronary vessel; the remaining individual with single-vessel disease of the left anterior descending coronary artery had 50% proximal stenosis. Of the 50 patients with CAD, 17 had single-vessel disease. Nine of these patients had single-vessel left anterior descending, seven had right coronary artery, and one had circumflex CAD. Twenty patients had two-vessel disease, and 13 had triple-vessel disease. Patients were selected for good ventricular performance and were those consecutively sent to the nuclear laboratory in whom the diagnosis of ischemic heart disease was not evident or confirmed by history, electrocardiography, resting ventricular function, or segmental wall motion abnormalities. We therefore hoped the patient population for study would be one in which there would be diagnostic challenge and in which a more sensitive diagnostic technique would be of some value. Resting ejection fraction was 66 ± 5% (SD) in the normal volunteers, 64 ± 5% in the patients with normal coronary arteries, and 60 ± 10% in the patients with CAD. Nine of the patients with ischemic heart disease had previous inferior infarcts and two had anterior infarcts with segmental wall motion abnormalities. Approximately the same percentage of patients in the group with normal coronary arteries and the group with CAD were treated with medication. In the CAD population, 44% had been treated with nitrates, 38% with β-blockers, and 28% with calcium antagonists. Of the group with normal coronary arteries, 36% had been treated with nitrates, 32% with β-blockers, and 12% with calcium antagonists.

Radionuclide angiography. The radionuclide studies were carried out proximate to coronary arteriography in the patients and in most instances were done just before catheterization. Exercise during radionuclide angiography was performed on a calibrated supine bicycle ergometer (Quinton Corp.) at low-intermediate, and peak exercise levels. The peak exercise level achieved was 870 ± 323 kilopond-meters (kpm) in volunteers, 540 ± 222 kpm in patients with normal arteries, and 557 ± 194 kpm in patients with CAD. Heart rate rose from 77 ± 17 to 169 ± 28 beats/min in volunteers, from 69 ± 10 to 127 ± 22 beats/min in patients with normal arteries, and from 64 ± 12 to 113 ± 22 beats/min in patients with CAD.

Radionuclide angiography was performed in subjects at rest and during each level of supine bicycle exercise. Resting views were obtained in an anterior and in steep and shallow left anterior or oblique projections after labeling of red blood cells in vivo with 30 mCi of 99mTc-sodium pertechnetate. Exercise radionuclide angiography was accomplished with the camera positioned for optimal left ventricular visualization in a shallow left anterior oblique projection (approximately 35 degrees left anterior oblique with 15 degree caudal tilt). Resting studies were carried out at a preset count density of 275 counts per pixel (64 × 64 matrix) over the left ventricle. During exercise, stablishment of the heart rate was allowed during the first minute before data acquisition was begun. Radionuclide data were acquired for a minimum of 2 min at each exercise level with 2 to 4 min of data acquisition at peak exercise. As the heart rate stabilized at each exercise level, data were acquired during this plateau at an R-R interval of ± 20%. There was no substantial variation in R-R interval during the exercise plateau phase in any of these patients selected for good ventricular function, and no irregular beats were noted during data acquisition in any of the subjects.

Radionuclide data were acquired at 32 frames per cardiac cycle at rest and during exercise for the construction of time-activity curves with average framing intervals of 28 ± 5 msec at rest and 16 ± 4 msec during exercise. The determination of ejection fraction and analysis of wall motion and construction of time-activity curves with computer calculation of diastolic and systolic parameters was carried out by an experienced observer without knowledge of clinical or catheterization results. Most studies were performed and interpreted just before catheterization. Ejection fractions were calculated with a separate region of interest for end-diastole and end-systole. Both ejection fraction and wall motion were assessed in subjects at rest and during each level of exercise. The time-activity curve was constructed after spatial and temporal smoothing of the data with a commercial software program (Technicare Corp.) and background subtraction. Vigorous background subtraction was carried out so as to bring background beyond the ventricular edge close to zero counts in order to create a sharp delineation of the ventricular boundary to optimize tracking of the region of interest by the computer software. The designated left ventricular region of interest was divided into four quadrants by the computer, with individual setting of threshold in each of the four quadrants. The ventricle was then tracked with a semiautomated program algorithm with a variable region of interest for each frame for construction of the time-activity curve. The data were reformatted in some cases beginning at the termination of the cycle with the last frame from end-diastole to the onset of systole, which allowed better tracking of the left ventricle by the program algorithm to assess diastolic filling and the calculation of slopes. In a few patients with very high ejection fractions in whom there was difficulty in exactly tracking the ventricle with the program algorithm, regions of interest could be manually designated for each and every frame of the cardiac cycle. The performance of the program algorithm in tracking the ventricle was carefully observed for each patient to make certain that accurate tracking of the ventricle was accomplished. The time-activity curve was generated with an on-line PDP-11/60 computer running under ISM-11 (Intersystems Corp.), a dialect of standard MUMPS (ANSI × 11.1, 1977). Curve data in this system were smoothed with a 5-point parabolic algorithm implemented by a digital filter.

Shown in figure 1 is a stylized time-activity curve with the measurements made by the computer in resting and exercising subjects. Measurement of peak diastolic filling rate was made in the first half of diastole. Also calculated were peak systolic ejection rate and time to peak rates and to end-systole at rest and during stress. Peak slopes were calculated by the computer in a standard fashion by fitting a second-degree polynomial to the curve. The time-activity curve could likewise be alternatively directly generated by the data acquisition computer in the Nuclear Cardiology Laboratory with programs written for determination of peak slopes and times. With this system the generated curve data were smoothed by applying a 3-point digital filter to the curve. Slopes were calculated by use of a 7-point least squares fit. All slopes were normalized to end-diastolic counts or volumes per second. Peak diastolic filling rate was obtained at that point at which the slope was maximum during the first half of diastole, which was calculated from the linear distance from end-systole to the end of ventricular filling. Time to peak slope was measured from end-systole on the time-activity curve.
FIGURE 1. Representative time-activity curve for a cardiac cycle. Counts are normalized to end-diastolic counts or volumes per second along the vertical axis, and time (in msec) is on the horizontal axis. Measured are peak diastolic filling rate (PDFR) in the first half of diastole, peak systolic ejection rate (PSER), times to peak rates (TPDFR, TPSER), and ejection times (TES).

curve. Peak systolic ejection rate was obtained at that point at which slope became steepest during systole. Time to peak slope was taken as the time from onset of contraction to peak slope. The ejection time was measured from the onset of contraction to end-systole as the nadir of the curve that represented the frame containing the least counts over the left ventricle.

The numerical values of the slopes and times employed for calculation of mean values are from the nuclear cardiology computer system. Directional changes were the same for both computer systems used and actual values were not significantly different with either system.

Observer variability for calculation of rates was 4% (difference in observations/mean of observations), with no difference in the direction of change of rate from rest to exercise. The correlation coefficient for blinded separate observation for generation of curves and calculation of data was $r = .91$. The $r$ value for rest to exercise change between initial and repeated measurements was .82, and the coefficient of variation (SD/mean $\times 100$) between the separate individual determination of slopes was 9%.

Statistical analysis of the data was performed by analysis of variance and by paired t test when appropriate. Analysis of covariance was also used to determine if heart rate was a contributing factor to the differences among the groups. Results were considered significant if the t or F values were significant at $p < .05$. Statistics were run after data entry into the university main-frame computer system and selected Statistical Analysis System programs were used for the analysis.

Results

Ejection fraction and wall motion. In 10 volunteers the ejection fraction was 66 ± 5% (SD) at rest and 78 ± 5% with exercise ($p < .001$). The patients were selected for good ventricular performance, and in those with normal coronary arteries the ejection fraction was 64 ± 5% at rest and 72 ± 8% with exercise ($p < .0001$). In patients with coronary disease, ejection fraction at rest was 60 ± 10% and that with exercise was 61 ± 13% ($p = NS$; figure 2). As a group, patients with ischemic heart disease demonstrated a typical abnormal response to exercise, with no change in ejection fraction. The majority of the 17 patients with single-vessel disease, however, and some of the patients with two- or three-vessel disease responded to stress with an increase in ejection fraction (figure 3). In this selected population the sensitivity of detection of CAD as judged by an inappropriate ejection fraction response to the level of stress ($<5\%$ increase with maximal stress with an increase in end-systolic volume) and/or
the development of segmental wall motion abnormalities with exercise was only 62% (if patients with single-vessel disease are excluded sensitivity = 80%). There were no false-positive results in this patient population.

**Peak diastolic filling rate.** Peak diastolic filling rate during the first half of diastole was 3.1 ± 0.6 end-diastolic volumes/sec in normal volunteers at rest and increased in all subjects with exercise to 3.6 ± 0.7 (p < .05; figure 4). In the patients with normal coronary arteries and those with ischemic heart disease peak diastolic filling rate was the same at rest: 2.3 ± 0.8 end-diastolic volumes/sec in both groups. With exercise, peak diastolic filling rate increased to 3.2 ± 0.1 (p < .001) in normal patients while it fell to 1.7 ± 0.6 (p < .001) in those with CAD. The change in slope during the first half of diastole with exercise in patients with normal arteries vs those with coronary disease was highly significant and was independent of rate by analysis of covariance. Exercise peak diastolic filling rate fell to 1.9 ± 0.6 end-diastolic volumes/sec in patients with single-vessel disease, to 1.7 ± 0.7 end-diastolic volumes/sec in those with two-vessel disease, and to 1.5 ± 0.6 end-diastolic volumes/sec in those with three-vessel disease (figure 5). Figure 6 demonstrates the ratio of exercise to resting peak diastolic filling rate for the volunteers and patients. The rest/exercise peak diastolic filling rate ratio was greater than 1 for all of the volunteers and for 23 of 25 patients with normal coronary arteries and was 1 or less for 49 of the 50 patients with CAD, including patients with single-vessel disease and those with normal ejection fraction and wall motion responses to exercise.

Data from a subset of 20 patients without previous infarction chosen at random from our population were analyzed to assess the diagnostic value of the peak rate of ventricular filling obtained during the entire diastolic phase without limiting this calculation to early diastole. This peak diastolic filling rate decreased during exercise in 40% of the patients with ischemic heart disease. For this subgroup peak diastolic filling rate was 2.5 ± 0.6 at rest and 2.6 ± 1 during exercise but, focusing on early diastole, the filling rate was 2.5 ± 0.8 at rest and 1.8 ± 0.6 end-diastolic volumes/sec during exercise (p < .002). Of 10 randomly selected patients with normal coronary arteries, 80% had an increase in peak rate computed from the entire diastolic filling curve: filling rate was 2.3 ± 0.8 and 2.7 ± 1 end-diastolic volumes/sec at rest and with exercise, respectively. Presence or absence of alteration of peak filling rate during the first half of diastole during exercise accurately separated all of these individuals into the appropriate normal or abnormal group. That is to say, in these patients, the early filling rate increased in those with normal and fell in those with diseased coronary arteries, but this was not true when the peak rate was not limited to early diastole. In those patients with
coronary disease that was not detected by the change in peak diastolic rate the fastest rate was recorded in the second half of diastole and in all of those with normal arteries who were missed the fastest rate was recorded at a time beyond the first half of diastole while they were at rest.

Nine of the 85 patients in our study had previous myocardial infarction (seven inferior and two anterior infarctions) and eight of these had normal or only mildly decreased ejection fractions. Early filling rate in the first half of diastole fell in all of these patients with exercise. The peak filling rate of the diastolic curve when not limited to early diastole fell in 78% with exercise and peak rates that increased did not do so within the early diastolic filling period.

**Peak systolic ejection rate.** Changes in peak systolic ejection rate from rest to exercise are illustrated in figure 7 for volunteers and the patients. Mean peak systolic ejection rate did not significantly change from rest to exercise in either the volunteers or the patients with normal coronary arteries in this group of individuals with mean resting ejection fractions greater than 60%. However, like peak diastolic filling rate the peak ejection rate was higher in the younger volunteers than in the patients. Resting values for ejection rate were similar in the patient group, but in those with coronary disease it fell from 2.5 ± 0.8 to 1.9 ± 0.8 end-diastolic counts/sec with exercise (p < .0001).

Ejection time and times to peak rates. With increasing heart rate during exercise, the location of end-systole was shifted to a later position in the cardiac cycle since there was a decrease in the relative percentage of the cycle length available for diastolic filling. The position of end-systole relative to cycle length increased about 10% in patients with normal arteries and in those with CAD as heart rate increased and shortening cycle length decreased. At rest, the time to end-systole was similar for both groups of patients. During exercise time to end-systole decreased 82 msec in those with normal coronary arteries vs a decrease of 12 msec in those with CAD (p < .01). Time to peak systolic ejection rate decreased 16 msec in patients with normal coronary arteries and increased 25 msec in those with CAD (p = .007). The time to peak diastolic filling rate in the first half of diastole was not useful in distinguishing between the two groups of patients.

**Exercise response and predictive indexes.** Thus, with stress a normal response is distinguished from that in patients with CAD by the fact that there is an increase in peak diastolic filling rate in the first half of diastole in those with normal arteries while peak filling rate does not increase in those with diseased coronary arteries. There is a decrease in peak systolic ejection rate and an increase in time to peak ejection rate with coronary disease, while normally there is a decrease in time to end-systole (table 1).

The sensitivity of wall motion and ejection fraction response to exercise for detection of coronary disease in this patient population selected for good ventricular...
TABLE 1
Directional change of parameters during exercise in normal subjects and patients with CAD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>CAD</th>
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<tr>
<td>PDFR</td>
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<tr>
<td>PSER</td>
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<td>TES</td>
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PDFR = peak diastolic filling rate; PSER = peak systolic ejection rate; T = time; TES = time to end-systole.

Performance was 62% (80% when those with single-vessel disease were excluded) with no false-positive results. Sensitivity for a decrease in peak systolic ejection rate was 66% and specificity was 67%. For peak diastolic filling rate, the sensitivity was 98% and the specificity 94% (table 2).

Discussion

In normal individuals cardiac performance improves with stress while in patients with CAD, with the onset of significant ischemia, contractile performance deteriorates with an increase in end-systolic volume. Ejection fraction does not increase and may fall and segmental wall motion abnormalities develop. Also, abnormalities occur in diastolic relaxation and filling with a decrease in ventricular compliance. This study sought to characterize the alterations in performance of the heart in delivering an increased stroke volume and in diastolic filling during stress and how these parameters of left ventricular performance might be altered by ischemia.

Using nuclear techniques, investigators have found ejection rates and first-third ejection fraction to be lower than normal in patients with ischemic heart disease. Left ventricular relaxation, an active energy-dependent process, is also altered by ischemia. Ischemia results in a decrease in negative dP/dt, prolongation of isovolumetric relaxation, and an increase in left ventricular end-diastolic pressure. Myocardial ischemia thus not only alters the contractile properties of the heart but also the compliance of the left ventricle with a shift in the pressure volume curve.

In this study, peak systolic ejection rate did not substantially change with exercise in the normal groups. Peak ejection rate, however, was higher in the younger volunteers than in the patients. In our study patients were selected for good ventricular function with mean resting ejection fractions greater than 60%. Ejection rates were quite steep in the young healthy volunteers and remained so during stress. That ejection fractions in our patients with normal arteries were quite high may explain why we did not observe an increase in ejection rate with stress, as others have reported. We did note, however, an increase in ejection rate during stress in these patients, with lower ejection fractions (in the 50% range). Resting peak systolic ejection rate was similar in the two patient groups, but in those with coronary disease, peak systolic ejection rate fell with exercise and the time to peak rate increased. Similar observations regarding resting values and magnitude and direction of change of systolic slope with exercise have also been reported by other investigators. Ejection time was similar at rest for patients with and without coronary disease, but the time to deliver a stroke volume decreased more significantly during exercise in those with normal than in those with diseased arteries. This is consistent with the enhanced contractile state during exercise with increasing catecholamine levels in normal individuals. The sensitivity of ejection rate for detection of coronary disease was similar to that of development of ejection fraction and wall motion abnormalities during exercise, although ejection rate was less specific. Some patients with coronary disease increased their rate of ejection while in some normal individuals this rate fell. Peak ejection rate and its directional change with exercise is probably dependent on a number of factors, including resting ejection fraction, contractility, level of exercise, and degree of ischemic dysfunction produced as well as afterload.

Bonow et al., using gated radionuclide angiography, reported that diastolic filling rates at rest distinguished patients with coronary disease from normal subjects, and Hayes et al. found that the time to peak filling rate occurred later in diastole in patients with CAD during stress. In this study we elected to assess the change in diastolic filling rate with exercise during the first half of the diastolic portion of the time-activity curve. At this point a well-defined slope and rate of ascent is present. During exercise, end-diastolic volume increases in most people and end-systolic volume...
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decreases, stroke volume widens, and ejection fraction increases. With increased heart rate, the time for diastolic filling of the heart decreases and the proportion of the cardiac cycle available for filling is decreased, with most of the cycle devoted to systolic ejection. It would seem, therefore, that the rate of filling should become more rapid during exercise to accommodate a larger end-diastolic volume with increasing venous return in a shorter time frame. With a decrease in compliance due to ischemia, changes in the rate of diastolic filling might be more pronounced in the early portion of diastole rather than towards the end of ventricular filling. This exact approach of assessing the directional change of rate in the first half of diastole with exercise has not been previously employed by other investigators.

Use of the peak filling rate during the entire diastolic phase during exercise has not been shown to be reliable in distinguishing individual patients with ischemic heart disease. This has been our experience as well. Peak filling rates have been found by Mancini et al., using gated technique, to be significantly lower at rest and during exercise in patients with CAD, but they also found a large overlap between normal subjects and patients with CAD. While resting rates were found in early diastole, peak exercise rates in this study were taken from late diastole.

Austin and Jones and Reduto et al. studied filling rates at rest and with exercise in patients in the upright position by a first-pass technique with a multicrystal gamma camera, while we assessed patients by a gated technique while they were in the supine position and ventricular volumes are different in the two positions. With the body in the supine position, the heart does more volumetric work at a lower heart rate, while in the upright position at comparable workloads delivery of cardiac output is more rate related since the heart operates at a somewhat lower volume with the legs in a dependent position. The first-pass technique in which the multicrystal gamma camera is used with conventional software also has major limitations. Three to five beats are averaged with a paucity of counts over the left ventricle, variability in individual beats may occur, spatial resolution is poor, and difficulty with satisfactory temporal resolution has been encountered. Marked statistical chatter in the data may be produced by use of a satisfactory timing interval during exercise and major smoothing of this statistical noise is required. Also, other studies in which diastolic function was assessed by a first-pass technique did not use exactly the same time frame for diastolic assessment as that used in our study. It was found by Reduto et al., however, that during the first third of diastole normal subjects had a significantly greater increase in slope during exercise than did patients with ischemic heart disease; this is supportive of our findings. Austin and Jones found an increase in filling rate from rest to exercise in normal subjects and in patients with CAD. The timing of peak filling rate from their data during exercise was determined in late diastole (73% of diastolic duration). Contribution or blending of atrial kick into the diastolic curve is probably an important factor at this point in diastole during stress. They found that filling rates were higher during exercise in normal subjects, but there was considerable overlap in the rates between groups.

In our study it was found that in patients with normal coronary arteries and in patients with coronary disease who had good ventricular function there was no difference in the rate of early diastolic filling at rest when there was no evidence of ischemia. Resting filling rate was 2.3 ± 0.8 end-diastolic volumes/sec in both groups. Austin and Jones also reported no significant difference in resting filling rates in patients with three-vessel disease and in patients with normal coronary arteries. We found that young healthy volunteers had higher rates of filling at rest and during exercise than did the older individuals (in their 50s) who were patients, suggesting that ventricular compliance diminishes with age. Our findings in patients at rest differ from those published by NIH investigators, who demonstrated lower than normal filling rates in patients with ischemic heart disease. Our resting values for peak filling rate are, however, similar to those found by these investigators. For patients with ischemic heart disease and normal ejection fractions, the rates are nearly identical in the two studies (2.1 ± 0.5 and 2.3 ± 0.8); in their normal population the rates were similar to our findings in young healthy volunteers (3.3 ± 0.6 vs 3.1 ± 0.6 end-diastolic volumes/sec). If the normal population in a study comparing normal subjects with those with ischemic heart disease includes young healthy volunteers and the heart disease population is weighted with patients with previous myocardial damage and decreased ventricular compliance, then a marked separation in the groups at rest will appear if peak filling rates are considered.

We demonstrated a difference in the directional change from rest to exercise in peak filling rate in the first half of diastole in patients with normal coronary arteries and in those with ischemic heart disease. In normal individuals, during stress filling of the ventricle during early diastole became more rapid and peak diastolic filling rate increased. In patients with ische-
mic disease, during stress ventricular compliance decreases and the rate of filling in early diastole does not increase. Thus, with stress in patients with CAD the rate of ejection falls and there is an increase in the time to peak ejection rate. In normal subjects there is a more rapid delivery of stroke volume, a decrease in the time to end-systole, and an increase in the early diastolic filling rate. This directional alteration of peak diastolic filling rate during exercise appears to be a very sensitive indicator of ischemic heart disease. Further experience will be necessary, however, to define the ultimate clinical utility and practical functional use and accuracy of the rest/exercise peak filling rate ratio in appropriate patients.

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References
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