Comparative Sensitivity of the Exercise Electrocardiogram, Thallium Imaging and Stress Radionuclide Angiography to Detect the Presence and Severity of Coronary Heart Disease

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SUMMARY The relative sensitivity and specificity of individual and combined noninvasive tests to detect coronary heart disease were evaluated in 75 patients with chest pain admitted for cardiac catheterization and coronary arteriography. Of the 75 patients, 56 had coronary heart disease. Exercise-induced ST-segment abnormalities ($\geq 1$ mm) were found in 58%. In contrast, computer-processed exercise thallium-201 perfusion imaging detected 82% ($p < 0.01$) and assessment of regional ejection fraction determined at rest and during isometric exercise by radionuclide angiography detected 82% ($p < 0.02$). Pathologic Q waves were present in 20%. Of nine patients with single-vessel disease, only one had exercise ST-segment abnormalities, while four had abnormalities in thallium-201 perfusion and five in regional ejection fraction. Of 16 patients with two-vessel disease, 10 had ST-segment abnormalities, 14 had defects on thallium-201 imaging and 13 had abnormalities in regional ejection fraction. Similarly, of 31 patients with three-vessel coronary heart disease, 23 had exercise-induced ST-segment changes, while 28 had thallium-201 perfusion defects and 28 had abnormalities in regional ejection fraction.

Combined noninvasive testing using pathologic Q waves and exercise ST-segment abnormalities detected 71% of patients with coronary heart disease. Addition of exercise thallium-201 imaging resulted in 88% of patients being detected, and addition of regional ejection fraction detected 96%. If an abnormality in any of the four tests was considered, 55 of 56 patients (98%) with coronary heart disease were detected.

In 19 patients with normal coronary arteries, the specificity of the exercise ECG was 84%, exercise thallium-201 imaging 89% and assessment of regional ejection fraction 79%. However, if all noninvasive tests were considered, the specificity decreased to 58%.

Thus, either exercise thallium-201 imaging or assessment of regional ejection fraction is superior to exercise-induced ST-segment abnormalities. Combined testing results in a very high sensitivity, but there is a concomitant reduction in specificity.

IN RECENT YEARS, there has been a concerted effort to develop noninvasive techniques that accurately delineate both the presence and severity of coronary heart disease in patients with chest discomfort syndromes. Traditionally, the rest and exercise ECGs have been the most widely used noninvasive, objective, diagnostic tests for evaluating such patients. Although pathologic Q waves on the resting ECG are highly predictive of coronary heart disease, they are relatively insensitive, and are absent in more than one-half of such patients. Exercise electrocardiography has received the greatest attention and provides improved diagnostic and prognostic capability. However, its sensitivity, specificity and quantitative ability are suboptimal, and its overall value has been questioned.

Radioactive tracer techniques that allow delineation of areas of myocardial scar or ischemia have provided a new approach to noninvasive diagnosis. Myocardial perfusion scanning with thallium-201, a potassium analog, combined with exercise has improved sensitivity and specificity compared with exercise-induced electrocardiographic ST-segment changes alone.

A second radionuclide approach uses radionuclide angiographic assessment of left ventricular function at rest and during exercise. This technique relies on detecting resting or exercise-induced abnormalities in segmental wall motion. Abnormality in segmental wall motion correlates well with the presence of coronary heart disease. The present study was undertaken to evaluate the relative sensitivity and specificity of thallium-201 myocardial imaging combined with exercise vs radionuclide angiographic assessment of segmental wall motion at rest and during isometric (handgrip) exercise in the same group of patients.

Methods

Patients who underwent evaluation for chest discomfort syndromes form the basis of this report. No patient was taking cardioactive medications at the time of study. All patients underwent exercise testing with thallium-201 and radionuclide angiographic assessment of left ventricular function within 2 weeks of cardiac catheterization, including coronary...
arteriography and ventriculography. Patients found to have a cardiomyopathy or valvular dysfunction by cardiac catheterization were excluded.

Exercise thallium-201 imaging was performed in the nuclear cardiology laboratory with the patients in the postabsorptive state using a mechanically braked bicycle ergometer. A 20-gauge cannula was inserted into a forearm vein. A standard 12-lead ECG was recorded using a three-channel automatic machine with a frequency response of 0.05–100 Hz. After careful skin preparation, silver silver-chloride electrodes were applied, and a 12-lead baseline ECG, blood pressure and the effect of hyperventilation on the ECG were recorded. The patients exercised on a mechanically braked bicycle ergometer (Monark) at an initial zero load (<30 seconds), and the work load was increased by 300 kilo-seconds/min every 3 minutes. Thallium-201 (New England Nuclear) was administered intravenously in a dose of 2.0 mCi just before or at peak exercise, which was then maintained for another 60 seconds. If pain developed before maximum stress was attained, thallium-201 was administered and the load reduced; however, exercise was maintained for 60 seconds unless pain continued to increase. Specific treatment with nitrates or analgesics was not required, and there were no complications. Stress was continued until limited by chest pain, significant ventricular arrhythmias (bigeminy, multifocal ventricular premature depolarizations or couplets) or fatigue.

During and after exercise, a 12-lead ECG and blood pressure were recorded. Imaging was begun within 5–10 minutes of intravenous administration of thallium-201 using a computer-assisted, multicrystal gamma camera (Baird Atomic System Seventy-Seven) with a high-resolution, parallel-hole coliminator. Spectrometer settings were adjusted for thallium-201 and 250,000–300,000 counts whole image were obtained immediately after exercise in the 30° and 60° left anterior oblique and anteroposterior projection for 8–12 minutes in each view. Images were recorded on computer disc for processing and on magnetic tape for long-term storage. In addition, redistribution images were obtained 2–3 hours after exercise and compared with the exercise images.

Radionuclide angiograms were obtained on a different day. After administration of 200 mg of potassium perchlorate, the patient was positioned in the right anterior oblique view and 12–18 mCi of technetium-99m pertechnetate in a volume less than 0.7 ml was rapidly administered into an antecubital vein and flushed with 10–15 ml of D5W to obtain a bolus injection. Counts were recorded at a framing interval of 20 frames/sec during the “first pass” of the isotope. The data were recorded on computer disc for processing and magnetic tape for long-term storage.

The initial raw data were qualitatively reviewed to determine the presence of contraction abnormalities. After 10 minutes, patients considered to have normal or borderline normal left ventricular contraction were asked to squeeze a hand dynamometer (CH Stoelting and Company) to the maximum extent possible and then maintain contraction at one-third of the predetermined maximum for 3–4 minutes while blood pressure and heart rate were monitored. Care was taken not to allow the patient to perform a Valsalva maneuver. Before the termination of handgrip and after an increase in systolic pressure of greater than 20 mm Hg had been obtained, a background frame was collected, a second injection of pertechnetate was administered, and a radionuclide angiogram was recorded as above. Chest pain or serious arrhythmias did not occur in any of the patients. Data acquisition required less than 30 seconds for each injection.

Right- and left-heart catheterization was performed using standard techniques. Contrast left ventriculography was performed with the patient in the right anterior oblique projection using 30–40 ml of meglumine diatrizoate (Renografin-76) injected into the left ventricle. Selective coronary cinearteriography was performed in multiple views using the Judkins or Sones technique. Hemodynamics were monitored and recorded on an Electronics for Medicine oscillographic recorder.

All thallium-201 images were initially corrected for field uniformity using a flood source performed on the day of testing and processed quantitatively by computer to aid in analysis of thallium images. Each view was first displayed as a 16-color isocount image and continuous gray scale without background subtraction. A horizontal profile was then taken to determine background contribution, which was subtracted and the image redisplayed (fig. 1). A quantitative analysis was accomplished by obtaining two profiles.
from each of the 30° and 60° left anterior oblique projections, which were then individually processed, background subtracted and displayed as a count pattern for the demarcated zone. For the anteroposterior view, two profiles were obtained, one including the inferior and apical regions and the second the anterior and inferior regions.14

Exercise tests, interpreted independently of either imaging or catheterization data, were considered positive if ≥1 mm horizontal or downsloping ST depression ≥0.08 second appeared in any lead, with the PR segment as baseline. Pathologic Q waves were considered present if a QS or a Q wave ≥0.04 second was recorded in leads V2-V6 or a Q wave greater ≥0.04 second was found in lead aVF. Isolated Q waves in lead III were not considered evidence of infarction.

All radionuclide angiographic data were first corrected for nonuniformity of field using a uniform source each day and for dead time. For the handgrip study, the background frame obtained immediately before exercise was used to correct for preexisting counts. The study was then reviewed in a serial format on an oscilloscope. Frames of data containing the left ventricle were displayed and, using a zone grid representing the individual crystals, a region of interest comprising the left ventricle was selected and a time-activity curve generated. The peaks (diastole) and valleys (systole) were used to derive a computer-generated representative cycle and end-diastolic and end-systolic frames.11, 15, 17

A computer-derived image of regional ejection fraction was based on the formula \( \frac{C_D - C_S}{C_D} - b \), where \( C_D \) = counts in diastole, \( C_S \) = counts in systole and \( b \) = background.11 The computer-derived end-diastolic and end-systolic images were used to derive an image of stroke volume (fig. 2). This frame was then divided by the background-corrected end-diastolic frame. The image thus obtained represents the relative contribution to ejection fraction of different zones of the left ventricle (fig. 3). In addition, to help localize abnormalities, a computer-derived end-diastolic perimeter was added to the image of relative regional ejection fraction. The left ventricle was further divided into anterior and inferior halves along a line from the midpoint of the aortic valve plane to the apex.

Figure 2. Computer-generated and smoothed images of end-diastole (ED), end-systole (ES) are displayed without background subtraction (A). Subtraction of end-systole from end-diastole results in stroke volume (B). Thus, zones of left ventricle contributing relatively more to stroke volume are represented by red and yellow, indicating the greatest number of counts. Color code as in figure 1.

Figure 3. Images of left ventricular ejection fraction obtained after dividing the computer-derived stroke volume image (figure 2B) by end-diastole corrected for background. The control (C) study reveals a uniform contribution to ejection fraction from the anterior and inferior regions of the left ventricle, as determined by the relatively uniform color patterns between these two zones. During handgrip (HG), this uniform contribution to ejection fraction is maintained, and yellow and red predominate in both anterior and inferior zones.
Changes in regional ejection fraction were quantified as follows. The computer generated the images of relative regional ejection fraction similarly for both the rest and handgrip studies. The full range (0–100%) of activity level was used. The computer displayed these counts normalized according to the maximum number of counts in any of the matrix elements of the image, over the full range according to a computer-generated, 16-color isocount display. This permitted assessment of relative regional differences in ejection fraction as small as 6.25%. For purposes of analysis, relative decrease of at least 25% (a four-color shift) involving one-third by area of either the anterior or inferior zones was considered indicative of an abnormal regional ejection fraction.

The severity of a coronary occlusion was assessed by comparing its diameter with the diameter of the vessel immediately proximal to it. The obliquity showing the maximal decrease in diameter was selected for analysis in each case; coronary arterial narrowing ≥75% was considered significant for purposes of analysis.

Interpretation of exercise electrocardiography and relative regional ejection fraction determined by radionuclide angiography, and thallium-201 perfusion imaging were interpreted without knowledge of coronary arteriography and were correlated with the independently determined presence of angiographically quantified coronary heart disease. Statistical analysis was performed using the t tests for paired and unpaired data and McNemar's test, when appropriate. All data are given as mean ± SEM. Sensitivity was defined as the number of true-positive responses divided by the number of true-positive and false-negative responses. Specificity was defined as the number of true-negative responses divided by the number of false-positive and true-negative responses. The predictive value of a positive test was the number of diseased persons with a positive test divided by the number of persons with a positive test. Predictive value of a negative test was the number of nondiseased persons with a negative test divided by the number of persons with a negative test.

Results

Seventy-five patients undergoing cardiac catheterization had both exercise thallium-201 imaging as well as rest and handgrip exercise radionuclide angiographic assessment of relative regional ejection fraction. Fifty-six patients had coronary heart disease: nine had single-vessel, 16 two-vessel and 31 three-vessel obstructive coronary disease, including eight patients who also had significant obstruction of the left main coronary artery. Segmental asynergy was present by contrast ventriculography in all 11 patients with pathologic Q waves on the surface ECG and in 23 of 45 patients without pathologic Q waves. Nineteen patients had normal coronary arteries and left ventricular contraction.

**Coronary Heart Disease:**

**Sensitivity of Individual Tests**

Of the nine patients with single-vessel disease, two had Q waves, one anteriorly and one inferiorly, while only one had significant ST-segment depression on the stress ECG (table 1). Exercise thallium-201 perfusion defects were seen in four patients (44%), while an abnormality in regional ejection fraction occurred in five patients (56%) (table 1).

Of the 16 patients with two-vessel disease, 13 had pathologic Q waves and 10 had exercise-induced ST-segment depression. Fourteen patients had thallium-201 perfusion defects, and 13 had abnormalities in regional ejection fraction (table 1 and fig. 4).

Of 31 patients with three-vessel disease, six had pathologic Q waves and 23 had exercise-induced ST-segment changes (table 1). Twenty-eight of the 31 patients had thallium-201 perfusion defects (fig. 5). Similarly, 28 had abnormalities of regional ejection fraction. Eight of the 31 patients with three-vessel disease also had a left main coronary artery obstruction. Only one had a pathologic Q wave, while six had exercise-induced ST-segment changes and seven had abnormalities in regional ejection fraction. All eight had thallium-201 perfusion defects.

Of the 11 patients with pathologic Q waves,

### Table 1. Relationship Between Presence and Severity of Coronary Heart Disease and Noninvasive Testing

<table>
<thead>
<tr>
<th>Number of obstructed coronary arteries*</th>
<th>0 (19)</th>
<th>1 (9)</th>
<th>2 (16)</th>
<th>3 (31)</th>
<th>LM (8)</th>
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<tr>
<td>Pathologic Q waves</td>
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<td>6</td>
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<tr>
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<td>≥ 1 mm</td>
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<td>1</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>&lt; 1 mm</td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>8</td>
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<td>4</td>
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</tr>
<tr>
<td></td>
<td>Normal</td>
<td>17</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Regional ejection fraction</td>
<td>Abnormal</td>
<td>4</td>
<td>5</td>
<td>13</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>15</td>
<td>4</td>
<td>3</td>
<td>3</td>
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</tbody>
</table>

*Number of patients in parentheses. All eight patients with left main (LM) disease had associated three-vessel disease.
exercise-induced ST-segment abnormalities were present in four. All 11 patients had thallium-201 perfusion defects immediately after exercise, including 10 at rest. In addition, of the nine patients with Q waves and two- or three-vessel coronary heart disease, five had perfusion defects indicative of multivessel disease. Similarly, abnormalities in regional ejection fraction were seen in 10 of 11, including eight at rest. Three of the nine with multivessel disease had abnormalities in two areas.

Thallium-201 perfusion defects were present in the redistribution images in 27 patients and appeared in the exercise images only in an additional 19 patients. Six of the 27 patients developed additional perfusion abnormalities with exercise. Assessment of relative regional ejection revealed abnormalities in 23 patients at rest and in an additional 23 during handgrip exercise. Of the 23 with abnormalities at rest, eight developed new abnormalities during exercise.

Overall, pathologic Q waves were present in 20%, and exercise-induced ST-segment changes were present in 58%. In contrast, thallium-201 perfusion defects were seen in 82% \((p < 0.01)\), while regional ejection fraction was abnormal in 82% \((p < 0.02)\). Global ejection fraction decreased slightly from \(48.0 \pm 1.8\%\) to \(44.6 \pm 1.7\%\) in patients with coronary heart disease. Overall, 79% of patients showed either no change \(<5\%)\) or a decrease in ejection fraction of more than 5%. There was no significant difference between the sensitivity of exercise thallium-201 imaging and assessment of regional ejection fraction.

Sensitivity of Combined Testing

Of the 56 patients with coronary heart disease, 11 had pathologic Q waves (fig. 6). Exercise-induced ST-segment abnormalities were seen in 29 of the remaining 45 patients, for a cumulative sensitivity of 71%.

Sixteen patients with coronary heart disease had neither pathologic Q waves nor exercise-induced ST-segment abnormalities (fig. 6). The relative regional ejection fraction method detected an additional 14 of these 16, for an overall sensitivity of 96% (fig. 6). In comparison, thallium-201 defects occurred in nine of these 16 patients, for an overall sensitivity of 88% (NS). If all tests were performed, at least one abnormal parameter was seen in 55 of the 56 patients. Only one patient with a single obstructive lesion of the left anterior descending artery was normal by all noninvasive tests (fig. 6).

The concordance of test results with thallium-201 imaging and assessment of regional ejection fraction is summarized in table 2. In only two of nine patients with single-vessel disease were both tests abnormal. In contrast, both thallium imaging and regional ejection fraction were abnormal in 11 of 16 (69%) with two-vessel disease, 25 of 31 (81%) with three-vessel disease and seven of eight (88%) with left main coronary disease.

The average heart rate of patients with exercise-induced ST-segment abnormalities was \(117 \pm 4\) beats/min and \(133 \pm 6\) beats/min for patients with a negative stress test. Of the patients with a negative stress test, the average heart rate was \(133 \pm 7\) beats/min for those with an exercise thallium-201 perfusion defect and \(135 \pm 10\) beats/min for those with a normal exercise perfusion scan. Handgrip resulted in an average increase in systolic pressure of \(38 \pm 2\) mm

![Figure 5. Thallium-201 imaging immediately after exercise showing perfusion defects in the inferior (anteroposterior [AP]) and lateral (left anterior oblique [LAO]) zones.](http://circ.ahajournals.org/Downloaded from)
DETECTION OF CORONARY HEART DISEASE/Bodenheimer et al.

Sensitivity of Combined Noninvasive Testing

56 Patients with CHD
→
Rest Electrocardiogram
→
Pathologic Q Wave
11
→
No Q Wave
45
→
Exercise ECG
→
Regional EF
ABNORMAL
14
NORMAL
2
→
Exercise Thallium-201
→
Regional EF
ABNORMAL
6
NORMAL
1

Figure 6. Sensitivity of sequential noninvasive testing in patients with coronary heart disease (CHD). EF = ejection fraction.

Hg in patients with an abnormal regional ejection fraction and 36 ± 4 mm Hg in those with a normal regional ejection fraction.

Normal Coronary Arteries

Of 19 patients with normal coronaries, ST segments were falsely abnormal in three. Defects were read on thallium-201 imaging in two and abnormalities of regional ejection fraction in four. The specificity of the stress ECG, thallium and regional ejection fraction, therefore, was 84%, 89% and 79%, respectively. No patient had pathologic Q waves (table 1). Global ejection fraction changed from 52.6 ± 2.4% to 48.4 ± 3.1%; only three of 19 patients had an increase in ejection fraction of more than 5%.

Specificity of Combined Testing

All three of the patients with exercise-induced ST-segment abnormalities had normal thallium-201 perfusion scans and normal regional ejection fraction studies.

Twelve of 16 remaining patients without exercise-induced ST-segment abnormalities had no regional ejection fraction studies, for a combined specificity of 63% (fig. 7). Similarly, 14 of these 16 patients had normal thallium-201 scans (fig. 1). All noninvasive tests were normal in 11 of the 19 patients (58%).

Predictive Value of Individual and Combined Testing

The predictive value of a positive test was similar for each test (table 3). However, when negative tests are considered, both thallium-201 imaging and assessment of regional ejection fraction were superior to

<table>
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<tr>
<th>Number of obstructed coronary arteries</th>
<th>0 (19)</th>
<th>1 (9)</th>
<th>2 (16)</th>
<th>3 (31)</th>
<th>LM (8)</th>
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<tr>
<td>Abn TL and REF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abn TL and normal REF</td>
<td>1</td>
<td>2</td>
<td>11</td>
<td>25</td>
<td>7</td>
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<tr>
<td>Normal TL and abn REF</td>
<td>1</td>
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<td>3</td>
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<td>Normal TL and REF</td>
<td>3</td>
<td>4</td>
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<td>Normal TL and REF</td>
<td>14</td>
<td>1</td>
<td>0</td>
<td>0</td>
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</tr>
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</table>

Number of patients is given in parentheses.
*All patients with left main occlusions included in patients with three-vessel obstructive coronary heart disease.
Abbreviations: Abn = abnormal; TL = thallium; REF = regional ejection fraction; LM = left main.

TABLE 2. Relationship Between Severity of Coronary Heart Disease and Concordance in Individual Patients of Exercise Thallium-201 and Regional Ejection Fraction
Discussion

Coronary heart disease results in a regional reduction in myocardial perfusion, which results in both ischemia and contraction abnormalities of the subserved left ventricular segment. If the reduction in coronary blood flow is sufficiently severe, a significant decrease in zonal myocardial perfusion and/or contraction will be present at rest.19, 20 These abnormalities may be associated with pathologic Q waves.21 However, myocardial perfusion is frequently adequate at rest, and left ventricular contraction may be normal or only minimally affected, even in the presence of multivessel obstructive coronary heart disease.22-23 Thus, the usefulness of techniques that evaluate myocardial perfusion, ischemia or segmental contraction are considerably enhanced when performed during stress as well as at rest.

Stress-induced changes in the ST segment are by far the most commonly used noninvasive method of detecting coronary heart disease. In the present study, ST-segment changes detected 58% of such patients. This is similar to the reported sensitivity of 53-64% in previous series of patients evaluated for chest pain.2-4 This relatively low sensitivity may reflect the indirect and multifactorial manner in which the ST segment reflects ischemia.

Recent studies have combined the stress ECG with a more direct assessment of regional myocardial perfusion using thallium-201. These studies have shown a 17-41% improvement in sensitivity, 6-8, 10 although one such study failed to show improved sensitivity.4 In the present study, sensitivity increased by 24% in patients with coronary heart disease (p < 0.01). When thallium imaging was combined with the stress ECG, all patients with left main disease and 30 of 31 patients with three-vessel disease were diagnosed.

Recent studies from our laboratory and others have shown that radionuclide angiography accurately delineates segmental asynnergy both at rest and during exercise.11, 12, 13, 17 In the present study, regional ejection fraction determined by radionuclide angiography detected 82% of all patients with coronary heart disease, including seven of eight patients with left main and 28 of 31 patients with three-vessel disease. This technique, therefore, was also significantly more sensitive than exercise-induced ST-segment abnormalities (p < 0.02).

Several important questions must be answered before deciding the relative value of these tests. One consideration is the form of stress used to unmask an abnormality in patients with coronary heart disease. Numerous studies have shown that both dynamic and isometric exercise accomplish this goal. Although clearly different, the presumed mechanism of either is to induce an increase in demand disproportionate to oxygen supply. Isometric handgrip exercise accomplishes this primarily by a rapid increase in afterload, with smaller although significant increases in heart rate. In contrast, dynamic exercise exerts its effect by marked increases in heart rate as well as blood pressure, with a higher pressure heart rate product than isometric exercise25 unless discontinued due to ischemia.26 While differences in induced ST-segment abnormalities are apparent, studies performed at cardiac catheterization show both forms of stress to be of value in detecting abnormalities in left ventricular function.27, 28

Different methods have been used to detect exercise-induced abnormalities. Borer et al. obtained excellent results by determining changes in global ejection fraction during dynamic exercise.29 Although changes in global left ventricular ejection fraction during handgrip exercise were of limited value in the present study, as has been noted during catheterization,26 assessment of relative changes in regional ejection fraction were of considerable value. In patients with coronary heart disease, this technique relies on the characteristic presence of segmental abnormalities that result in differences in contribution to ejection fraction between areas of the left ventricle. This technique is potentially limited however, because a diffuse global abnormality in contraction, such as a cardiomyopathy, may manifest itself as a uniform contribution to ejection fraction. In such a patient, thallium-201 imaging may be superior in determining whether the underlying cause is obstructive coronary disease.29

A major concern with radionuclide techniques is exposure to radiation. Thallium-201 results in a whole
body dose of 140 mrad at clinical doses, while technetium results in a whole body dose of 240 mrad/20 mCi. Thus, in doses required for diagnostic purposes, the radiation hazard is relatively small. However, repeated testing would clearly have to be evaluated in light of the overall radiation exposure. Other adverse reactions are rare.60

While the current study demonstrates that both thallium-201 imaging and radionuclide angiographic assessment of regional ejection fraction are more sensitive than the exercise ECG in the diagnosis of coronary heart disease (table 1), it is unclear which technique or combination of techniques is superior (fig. 6). Thallium-201 imaging combined with exercise-electrocardiographic evidence of pathologic Q waves and exercise-induced ST-segment abnormalities yielded a sensitivity of 88% (fig. 6). Similarly, assessment of regional ejection fraction in patients undergoing exercise electrocardiography resulted in an overall sensitivity of 96% (fig. 6). Concordance of these two tests in individual patients was good, particularly in the presence of more severe coronary heart disease (table 2). Thus, either isotope test enhances sensitivity, which can be increased to 98% if all four tests are performed. A significant portion of this additional yield is attributable to detection of patients with single-vessel disease.

Specificity is also an important factor in evaluating these tests individually or in combination. Although none of the normal patients in the present study had pathologic Q waves, false-positive results have been reported.1 Individual tests yielded similar specificity, but thallium-201 imaging was superior to exercise-induced ST-segment depression, a finding that is consistent with recent reports.10 When pathologic Q waves, ST-segment abnormalities, regional ejection fraction, and thallium-201 are all used, the sensitivity of 98% is associated with a specificity of 58% (table 4). Thus, it appears that while isometric studies have significantly improved the noninvasive diagnosis of coronary heart disease, significant limitations still exist, particularly in patients with single-vessel disease. Further technological advances in imaging devices and isotopes that provide improved resolution and count characteristics combined with optimal forms of exercise should further enhance noninvasive diagnosis of coronary heart disease.

**Table 4. Combined Noninvasive Testing for Detection of Coronary Heart Disease**

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<th>Sensitivity (n = 56)</th>
<th>Specificity (n = 19)</th>
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<tr>
<td>Q</td>
<td>20%</td>
<td>100%</td>
</tr>
<tr>
<td>Q + ST</td>
<td>71%</td>
<td>84%</td>
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<td>Q + ST + TL</td>
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<td>74%</td>
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<td>Q + ST + REF</td>
<td>96%</td>
<td>63%</td>
</tr>
<tr>
<td>All four</td>
<td>98%</td>
<td>58%</td>
</tr>
</tbody>
</table>

Abbreviations: Q = pathologic Q waves; ST = ST-segment abnormalities; TL = thallium-201; REF = regional ejection fraction.

**Acknowledgment**

We thank Kathy McNair and Regina Harrison for their help in the preparation of this manuscript.

**References**


Analysis of Regional Ischemic Left Ventricular Dysfunction by Quantitative Cineangiography

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SUMMARY The ability of left ventricular angiography to detect regional ischemic dysfunction was assessed in 10 closed-chest dogs during the course of acute balloon occlusion of the anterior descending coronary artery. During the 2-minute period of occlusion, serial cineangiography revealed a sequence of wall motion abnormalities over the anteroseptal region almost identical to that observed using directly implanted gauges. This sequence consisted of progressive reduction in regional systolic shortening with eventual replacement by systolic expansion. These changes preceded both electrocardiographic ST-segment and hemodynamic alterations, and were readily observed by gross subjective inspection of the cineangiograms, but with an intraobserver variability of 22%. Frame-by-frame motional analysis of the ventricular perimeter relative to its centroid of mass allowed more precise characterization of regional dysfunction. These data are consistent with previous studies demonstrating that regional wall motion abnormalities are both sensitive and specific markers of acute ischemia, and support the use of computerized left ventricular angiography for the quantitative assessment of clinical ischemic dysfunction.

REGIONAL ABNORMALITIES of left ventricular function have been demonstrated both during the course of acute coronary occlusion4,6 and graded reduction in coronary blood flow4,6 in the experimental animal by using a variety of analog techniques.4-10 The changes are best characterized as a sequence that begins as late systolic outward motion and ends with total replacement of active shortening by passive expansion.4,6,7 Such a sequence is highly specific for regional ischemia4,4,6,7 and invariably precedes electrocardiographic ST-segment shifts.4,6 It has been postulated4,5 that these alterations of regional function are directly analogous to qualitative angiographic contraction patterns such as "hypokinesis" and "dyskinesis."11 12 If this is the case, clinical left ventriculography might be used as a quantitative measure of regional ischemia. It is not known, however, if angiographic techniques reveal a similar sequence of altered regional function in response to acute ischemia, nor if such changes are detectable by qualitative inspection. The present study was designed to determine the effect of acute coronary occlusion on regional and global cardiac performance assessed by angiography in the closed-chest animal, and to correlate subjective qualitative angiographic assessment with quantitative analysis of a computerized two-dimensional analog representation.

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