Value and Limitations of Segmental Analysis of Stress Thallium Myocardial Imaging for Localization of Coronary Artery Disease

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SUMMARY This study was done to determine the value of thallium-201 myocardial scintigraphic imaging (MSI) for identifying disease in the individual coronary arteries. Segmental analysis of rest and stress MSI was performed in 133 patients with arteriographically proved coronary artery disease (CAD). Certain scintigraphic segments were highly specific (97–100%) for the three major coronary arteries: anterior wall and septum for the left anterior descending (LAD) coronary artery; the inferior wall for the right coronary artery (RCA); and the proximal lateral wall for the circumflex (LCX) artery. Perfusion defects located in the anterolateral wall in the anterior view were highly specific for proximal disease in the LAD involving the major diagonal branches, but this was not true for “septal” defects. The apical segments were not specific for any of the three major vessels. Although MSI was abnormal in 89% of these patients with CAD, it was less sensitive for identifying individual vessel disease: 63% for LAD, 50% for RCA and 21% for LCX disease (narrowings > 50%). Sensitivity increased with the severity of stenosis, but even for 100% occlusions was only 87% for LAD, 58% for RCA and 38% for LCX. Sensitivity diminished as the number of vessels involved increased: with single-vessel disease, 80% of LAD, 54% of RCA and 33% of LCX lesions were detected, but in patients with triple-vessel disease, only 50% of LAD, 50% of RCA and 16% of LCX lesions were identified. Thus, although segmental analysis of MSI can identify disease in the individual coronary arteries with high specificity, only moderate sensitivity is achieved, reflecting the tendency of MSI to identify only the most severely ischemic area among several that may be present in a heart. Perfusion scintigrams display relative distributions rather than absolute values for myocardial blood flow.

EXERCISE THALLIUM-201 myocardial perfusion imaging is being used increasingly to evaluate patients with suspected or known coronary artery disease. Although several studies have now shown thallium scintigraphy to be more sensitive than exercise electrocardiography for detecting patients with ischemic heart disease, much less is known about the value of the technique for identifying narrowings in the individual coronary arteries. This study was done to determine to what extent the sites of perfusion defects in rest and exercise thallium scintigrams reflect the sites of coronary artery narrowings found by coronary arteriography.

Methods

Rest and exercise thallium-201 myocardial scintigraphic imaging (MSI) and coronary arteriography were performed in over 250 patients at The Johns Hopkins Hospital during a 2-year period. Informed consent was obtained from all patients. One hundred forty-one of these patients had a narrowing of greater than 50% in at least one major coronary artery; eight patients with left main disease were excluded, leaving 133 patients who form the subject of this report. There were 116 males and 17 females, mean age 49.7 years (range 31–74 years). Ninety-six patients (72%) had at least one previous myocardial infarction. The indications for coronary arteriographic study were as follows: angina pectoris in 63 patients, chest pain of uncertain etiology in 13 patients, positive exercise test without chest pain in five patients, exercise-induced ventricular arrhythmias in three patients, and follow-up of myocardial infarction survivors (part of a separate research project) in 49 patients. In the latter group, 16 were having angina pectoris and 33 were not.

We identified a second group of 26 patients in whom no major coronary artery was narrowed by more than 50%. There were 12 males and 14 females, mean age 47.8 years (range 26–63 years). Twenty-three patients were being evaluated for chest pain syndromes, including 20 with abnormal rest or exercise ECGs. The other three patients did not have chest pain, but had a history of ischemic-type ST-segment changes during exercise.

Coronary Arteriography

All patients underwent left ventriculography and selective coronary arteriography in multiple projections using the Judkins technique. Angiographic studies were analyzed without knowledge of the thallium-201 MSI or the electrocardiographic find-
ings. Narrowings in the right (RCA), left anterior descending (LAD) and circumflex (LCX) coronary arteries were graded visually according to the percentage of the lumen diameter involved (50% or less, 51–70%, 71–90%, 90–99%, or 100%). Significant disease in a coronary artery was defined as greater than 50% narrowing in either its mainstem portion or in one or more of its major marginal or diagonal branches. The coronary circulation was classified as a right-dominant, left-dominant or balanced distribution if the posterior descending artery branched from the RCA, LCX, or both vessels, respectively. To assess observer reproducibility, 15 studies chosen at random were reread several months after the first readings.

Rest and Exercise TI-201 MSI

Thallium scintigrams were acquired using standard techniques. For rest studies, 1.5–2.0 mCi of thallium-201 was injected intravenously and 10 minutes later imaging was performed in anterior, 40° left anterior oblique (LAO), and 60° LAO views, using an Ohio Nuclear Series 120 scintillation camera with an all-purpose, parallel-hole collimator. Images contained 400,000 counts full field and were stored on magnetic disk in a 128 × 128 matrix (Medical Data Systems Simultaneity System). The resolution of this system was measured to be 0.56 line pairs/cm using a thallium-201 flood source with 4.5-cm water attenuation. For exercise studies, patients performed graded exercise on a bicycle ergometer or treadmill according to standard protocols. Exercise was terminated when chest pain or ischemic ST changes occurred, the patient became exhausted, or the heart rate reached 90% of the maximum predicted value. Thallium was injected intravenously 1 minute before the end of exercise, and the patient was imaged 5 minutes later, as described above.

Scintigraphic images were analyzed subjectively without background correction or computer processing. Studies from the patients with coronary disease were mixed with studies from the patients with angiographically proved insignificant coronary artery disease, normal subjects and patients with known coronary artery disease who were not part of this protocol. Matching views from rest and exercise studies were displayed as pairs and interpreted by three observers without knowledge of the clinical, angiographic or electrocardiographic findings. Each image was divided into five roughly equal segments for a total of 15 segments numbered 1–15 (fig. 1). The thallium uptake of each segment was classified as normal or reduced (mildly reduced = 1, moderately reduced = 2, severely reduced = 3) by a consensus of the observers. To assess observer reproducibility, 22 studies selected randomly were analyzed on two different days.

Rest and Exercise Electrocardiography

Resting ECGs were examined for the presence of abnormal Q waves, defined by a duration ≥ 0.04 sec-

FIGURE 1. Location of the 15 scintigraphic segments. ANT = anterior, LAO = left anterior oblique.

ond and depth > 25% of the R wave in the same lead. Twelve-lead exercise ECGs were analyzed for ischemic ST-segment changes, defined as ≥ 1 mm horizontal or downsloping ST-segment depression, lasting at least 0.08 second and appearing in three consecutive beats with a steady baseline.

Data Analysis

Detailed analysis was carried out in the group of patients with significant coronary disease. Sensitivity was defined as the number of true-positive tests × 100, divided by the sum of true-positive and false-negative tests. Specificity was defined as the number of true-negative tests × 100, divided by the sum of true-negative and false-positive tests. Data were analyzed using the chi-square test of correlated proportions and Yates corrected chi-square when appropriate (whenever any of the expected frequencies were less than 5).

Results

Insignificant Coronary Narrowings

Twenty-six patients had no major coronary artery narrowed by more than 50%. In 21 patients (81%) the exercise and rest scintigraphic studies were normal. Fifteen of the 21 had completely normal coronary arteries, with normal left ventricular (LV) function in 11 patients (two with incidental mitral valve prolapse without regurgitation) and abnormal LV function in four (diffuse hypokinesis in three and regional hypokinesis in one). The other six patients with normal MSI had mild coronary artery abnormalities: two with 30–40% isolated LAD narrowing; one with calcium in the LAD without luminal narrowing; one with multiple narrowings (< 50%) in the main left coronary artery, LAD, LCX and LAD diagonal arteries; and one with an abnormal LCX arising from the RCA (no narrowings). Five patients, all female, had abnormal scintigraphic studies. In all cases, however, there were associated abnormalities of coronary anatomy, LV function, or both (table 1).

Significant Coronary Narrowings

Of the 133 patients with greater than 50% narrowing in one or more major coronary arteries, 56 patients had involvement of a single artery: 35 patients with LAD disease, 13 with RCA disease and eight with LCX disease (six with right distribution, two with
left or balanced distribution). Thirty-five patients had significant narrowings of two vessels, including 16 with LAD and RCA narrowings, 11 with LAD and LCX narrowings and eight with RCA and LCX narrowings. Forty-two patients had narrowings of all three coronary arteries.

Eighty-three patients (62%) had a defect in the resting myocardial scintigraphic study, compared with 58 patients who had Q waves on the ECG. Sixty-two patients developed angina pectoris during exercise, 57 had ischemic ST depression, and 84 (63%) had either angina or ST depression. In comparison, 74 patients (56%) developed a new perfusion defect or significant extension of preexisting rest defects. A total of 119 patients (89%) had thallium-201 MSI defects either at rest or exercise, while 94 (71%) had Q waves at rest or ST-segment depression during exercise.

Observer Variability

Twenty-two scintigraphic studies from the group of patients with significant coronary disease were examined twice to assess observer reproducibility (table 2). Each of the 15 segments was analyzed to determine whether there was 1) agreement on the two readings (normal-normal or abnormal-abnormal); 2) disagreement related to placement of defects in different but contiguous segments (type 1 disagreement); and 3) disagreement unrelated to defect contiguity (type 2 disagreement). Agreement was generally good, with most frequent disagreements occurring in the high septum and high lateral wall in the LAO 40° view (segments 6 and 10) and the high posterolateral wall in the LAO 60° view (segment 15).

In terms of vascular areas (see below), 39 separate thallium defects were detected on the first reading (18 LAD, 14 RCA, seven LCX and 27 areas normal). On the second reading, 62 of the 66 vascular areas were interpreted identically; one new defect (LCX) was found on the second reading, while three defects (one LCX, two RCA) present the first time were missed. Fifteen angiographic studies were also read twice to determine the reproducibility of our estimates of

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**Table 1. Abnormal Scintigrams in Patients with Insignificant Coronary Narrowings**

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Abnormal segments*</th>
<th>Defect type</th>
<th>Coronary anatomy</th>
<th>LV ejection fraction</th>
<th>Regional LV function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>F</td>
<td>6, 7, 12</td>
<td>Fixed</td>
<td>LAD 30% stenosis</td>
<td>43%</td>
<td>Anteropapical HK</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>F</td>
<td>9, 10</td>
<td>Transient</td>
<td>N</td>
<td>72%</td>
<td>Lateral AK</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>F</td>
<td>1, 2, 11</td>
<td>Transient</td>
<td>LAD small, does not reach apex</td>
<td>69%</td>
<td>Apical AK</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>F</td>
<td>3</td>
<td>Transient</td>
<td>N</td>
<td>78%</td>
<td>Severe LV hypertrophy (?? cardiomyopathy)</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>F</td>
<td>†</td>
<td>†</td>
<td>N</td>
<td>53%</td>
<td>Diffuse HK</td>
</tr>
</tbody>
</table>

*See figure 1.
†Inconsistent defects: segments 4, 5, 6, 7, 10 and 11 abnormal at exercise, normal at rest; segments 2, 7, 12 and 13 normal at exercise, abnormal at rest.

Abbreviations: N = normal; HK = hypokinesis; AK = akinesis; LAD = left anterior descending coronary artery; LV = left ventricular.

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**Table 2. Observer Variability in Myocardial Scintigraphic Imaging Interpretation**

<table>
<thead>
<tr>
<th>Rest</th>
<th>Anterior</th>
<th>LAO 40°</th>
<th>LAO 60°</th>
</tr>
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<tr>
<td></td>
<td>1 2 3 4 5</td>
<td>6 7 8 9 10</td>
<td>11 12 13 14 15</td>
</tr>
<tr>
<td>Agree</td>
<td></td>
<td>21 21 22 22 20</td>
<td>20 21 21 21 20</td>
</tr>
<tr>
<td>Type 1 disagreement</td>
<td>0 1 0 0 0</td>
<td>1 1 1 0 1</td>
<td>0 2 1 0 1</td>
</tr>
<tr>
<td>Type 2 disagreement</td>
<td>1 0 0 0 2</td>
<td>1 0 0 1 1</td>
<td>0 0 2 0 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Anterior</th>
<th>LAO 40°</th>
<th>LAO 60°</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>1 2 3 4 5</td>
<td>6 7 8 9 10</td>
<td>11 12 13 14 15</td>
</tr>
<tr>
<td>Agree</td>
<td></td>
<td>21 21 20 19 21</td>
<td>19 22 20 20 19</td>
</tr>
<tr>
<td>Type 1 disagreement</td>
<td>0 1 1 2 0</td>
<td>0 0 1 1 0</td>
<td>1 3 3 0 0</td>
</tr>
<tr>
<td>Type 2 disagreement</td>
<td>1 0 0 1 1</td>
<td>3 0 1 1 3</td>
<td>0 0 1 0 4</td>
</tr>
</tbody>
</table>

For meaning of agree, type 1 disagreement and type 2 disagreement, see text.
Abbreviation: LAO = left anterior oblique.
narrowing in the individual coronary arteries. For each patient the three major coronary arteries (LAD, RCA, LCX) were considered separately, providing a total of 45 arteries for analysis. On the first reading 10 arteries were narrowed by 0–29% (most severe stenosis), six arteries by 30–49%, two arteries by 50–69%, 18 arteries by 70–99% and nine arteries by 100%. On the second reading, all arteries were classified identically except for two: both were LCX arteries read as 70–99% narrowed the first time and 50–69% narrowed the second time.

Patients with Single-vessel Disease

Figure 2 shows the location of thallium defects relative to coronary artery anatomy in the 56 patients with single-vessel disease. Both exercise-induced and fixed defects were included. Thirty-two of the thirty-five patients with single LAD narrowing had defects. Defects were located in the anterolateral wall and apex in the anterior view (segments 1–3), the septum and apex in the 40° LAO view (segments 6–8), and the anteroseptal wall and apex in the 60° LAO image (segments 11–13).

Ten of thirteen patients with RCA narrowings had thallium defects. All 13 had a right coronary artery distribution. Defects were located in the inferior wall (segments 4 and 5), in the posterolateral wall (segment 9) and in the posteroinferior wall (segments 14 and 15), as well as in the apex (segments 3, 8 and 13).

Three of six patients with LCX narrowings and right distribution had defects involving the posterolateral wall (segments 9 and 10), the posteroinferior wall (segments 14 and 15) and the apex in the anterior view (segment 3). The anterolateral wall (segments 1 and 2) was also involved once. One of the two patients with LCX narrowing and a left distribution had defects involving segments 3, 4, 5, 9, 13 and 14, a distribution similar to that seen in patients with RCA narrowings. None of the patients with single-vessel LCX disease had a balanced distribution.

Specificity of Individual Segments

Figure 3 shows for the group of patients with significant coronary disease the specificity of each segment for disease in each of the three major coronary arteries. The specificity of a given segment for a particular vessel was found by examining those patients within the group without disease in that vessel. For example, the specificity of segment 3 for LAD disease was found by determining whether a defect was present in segment 3 in patients with RCA or LCX disease, but no significant LAD disease. Specificity was defined as the percentage of these patients in which segment 3 was normal.

In 29 patients free of LAD disease, segments 1, 2, 6, 7, 11 and 12, representing the anterolateral, septal and anterior walls, had a specificity of 97–100% for the LAD. In 49 patients free of RCA disease, segments 4 and 5, representing the inferior wall, had a specificity of 98–100% for the RCA. In 64 patients free of LCX disease, segment 10 had a specificity of 100% for the LCX. In 35 patients free of either RCA or LCX disease, segments 9, 14 and 15 had a specificity of 97–100% for RCA or LCX disease. The apical segments 3, 8 and 13 had relatively poor specificity for any of three arteries.

Sensitivity of Individual Segments

To calculate the sensitivity of each segment for lesions in the individual coronary arteries, the largest portion of the patient population with coronary disease was used in which the contribution of disease in vessels other than the one being examined could be excluded (see legend, table 2). For example, to calculate the sensitivity of detecting LAD disease, all patients with LAD disease were used for specific LAD segments, whether or not disease existed in other vessels. However, for specific RCA or specific LCX segments, patients with coexisting disease of the RCA or LCX, respectively, were excluded. For nonspecific

LOCATION OF PERFUSION DEFECTS IN SINGLE VESSEL DISEASE

FIGURE 2. Distribution of thallium perfusion defects in patients with single-vessel left anterior descending (LAD), right coronary artery (RCA) or left circumflex (LCX) disease. Dots indicate number of patients with defect in each scintigraphic segment. R Dist and L Dist = right and left coronary distribution, respectively; ANT = anterior; LAO = left anterior oblique.
segments, only patients with single-vessel LAD disease were examined.

For LAD disease, sensitivity was highest (52%) in segment 12 and almost as high in apical segments 3 and 13, where specificity was less (table 3). For RCA disease, sensitivity was highest (43–46%) in segments 4 and 5. For LCX disease, sensitivity was poor, being only 33% in apical segment 3 and 21% in the specific segment 10.

The relationship between segments and arteries was also evaluated by contingency-table analysis (table 3). Results indicated that perfusion defects in segments 2, 3, 6, 7, 11 and 12 were statistically associated with LAD disease, defects in segments 4, 5 and 14 with

![Table 3. Sensitivity of Individual Segments for Disease in Individual Coronary Arteries](http://circ.ahajournals.org/)

<table>
<thead>
<tr>
<th>Coronary artery lesion (&gt; 50%)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>8%</td>
<td>18%</td>
<td>51%</td>
<td>2%</td>
<td>0%</td>
<td>34%</td>
<td>35%</td>
<td>26%</td>
<td>3%</td>
<td>0%</td>
<td>28%</td>
<td>52%</td>
<td>46%</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>p &lt;</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.001</td>
<td>0.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>RCA</td>
<td>0%</td>
<td>0%</td>
<td>15%</td>
<td>46%</td>
<td>43%</td>
<td>0%</td>
<td>0%</td>
<td>23%</td>
<td>14%</td>
<td>0%</td>
<td>5%</td>
<td>5%</td>
<td>31%</td>
<td>31%</td>
<td>17%</td>
</tr>
<tr>
<td>p &lt;</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.01</td>
</tr>
<tr>
<td>LCX (right distribution)</td>
<td>8%</td>
<td>8%</td>
<td>33%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>21%</td>
<td>21%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>7%</td>
</tr>
<tr>
<td>p &lt;</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>NS</td>
<td>0.001</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>LCX (left and balanced distribution)</td>
<td>0/3</td>
<td>0/3</td>
<td>1/2</td>
<td>4/5</td>
<td>1/5</td>
<td>0/3</td>
<td>0/3</td>
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<td>0/3</td>
<td>0/3</td>
<td>1/2</td>
<td>2/5</td>
<td>0/5</td>
</tr>
</tbody>
</table>

Subsets of the population were analyzed for each segment and vessel. For the left anterior descending (LAD) analysis, anterior and anterolateral segments 1, 2, 6, 7, 11 and 12 (specific LAD segments) included all patients with LAD disease, including those with coexisting disease in other vessels (104 patients); inferior wall segments 4 and 5 (specific right coronary artery [RCA] segments) excluded those with RCA disease (46 patients remaining); segment 10 representing proximal lateral wall (specific for left circumflex artery [LCX]) excluded those with LCX disease (51 patients remaining); and segments 3, 8, 9, 13, 14 and 15 (non-specific segments; apical, posterolateral and posteroinferior) excluded those with RCA or LCX disease (35 patients remaining). Similarly, for the RCA, segments 4 and 5 included all patients with RCA disease (68 patients), while segments 1, 2, 6, 7, 11 and 12 excluded those with coexisting LAD disease (20 patients remaining), segments 9, 10, 14 and 15 excluded those with LCX disease (29 patients remaining) and segments 3, 8 and 13 excluded those with LAD or LCX disease (13 patients remaining). For the LCX analysis, segment 10 included all patients with LCX disease (53 patients), segments 4, 5, 9, 14 and 15 excluded those with RCA disease (14 patients remaining), segments 1, 2, 6, 7, 11 and 12 excluded those with LAD disease (13 patients remaining), and segments 3, 8 and 13 those with either LAD or RCA disease (six patients remaining). Similar subsets of the population were analyzed for the group with LCX disease and a left or balanced distribution. Patients with RCA and LCX disease with a left or balanced distribution were excluded from the analysis of the RCA and LCX, right distribution groups. The relationship between segments and arteries was evaluated by contingency-table analysis relating normal or abnormal segments to the presence or absence of disease in the artery considered, using the subsets of population defined. This table indicates the level of significance (p value) for each segment-artery combination.
RCA disease, and defects in segment 10 with LCX disease.

Influence of the Location of Narrowings

Proximal obstruction of the LAD above the first septal perforator did not significantly influence the frequency of defects in segments 6 or 7, the so-called septal segments. The frequency of defects in segment 6 was 37% (24 of 61) when the first septal perforator was involved and 28% (11 of 39) when it was not. For segment 7, the values were 37% and 31%, respectively. These differences were not statistically significant.

Involvement of the first major diagonal branch of the LAD, either by a proximal mainstem lesion above the diagonal origin or a significant lesion of the diagonal itself, was associated with defects in segment 1 or 2 (fig. 4). The sensitivity of segments 1 and 2 for proximal LAD disease, however, decreased with the number of vessels involved (11 of 23 [48%] with single-vessel disease; five of 22 [23%] with double-vessel disease; and three of 35 [9%] with triple-vessel disease) ($\chi^2 = 11.8; p < 0.01$; two degrees of freedom).

The level of LAD obstruction did not influence the overall sensitivity for detecting LAD disease in specific segments 2, 6, 7, 11 and 12. A defect was present in one or more of the segments in 41 of 61 (67%) patients with disease above the first septal perforator, compared with 28 of 43 (65%) patients with lesions below the septal perforator. Similar results were found for lesions above or below the first diagonal.

The level of RCA obstruction (proximal RCA, middle RCA or distal RCA) did not appear to influence the relative distribution of perfusion defects in scintigraphic segments 4, 5, 8 and 14. However, the frequency of defects in segments 4, 5 and 14 depended on the level of obstruction. Perfusion defects were found in 26 of 31 (84%) patients with proximal RCA lesions, nine of 23 (39%) patients with middle lesions and two of nine (22%) patients with distal lesions (all patients with a right-dominant circulation). In patients with a left-dominant or balanced distribution, three of 13 (23%) with RCA disease had perfusion defects in these segments, including two of three with concomitant RCA and LCX disease.

Patients with LCX disease, with or without coexisting LAD lesions, were examined to determine whether there were any scintigraphic differences between narrowings in the mainstem LCX and narrowings limited to the LCX marginal branches. No differences could be found.

Sensitivity of MSI Relative to Severity of Coronary Artery Narrowings

Using only segments with $> 97%$ specificity, we determined the sensitivity of thallium-201 MSI for detecting lesions of different severity in individual coronary arteries (table 4). For each major vessel, sensitivity increased as the stenosis became more severe. However, at each level of severity, the order of sensitivity for individual vessels was generally LAD $>$ RCA $>$ LCX. This was partly because the LAD tended to be more severely involved in any given heart than the other two vessels. The data were therefore reanalyzed by selecting narrowings that were either isolated or the most severe relative to other arteries in that heart (table 4). Sensitivity increased for LAD and LCX, but the detection rate for LCX disease remained less than that for LAD or RCA disease, suggesting that other factors were also important.

The sensitivity of thallium-201 MSI for detecting lesions in individual coronary arteries was also examined as a function of the number of vessels involved (table 5). Sensitivity tended to decrease as the number of vessels with disease increased. For the LAD, sensitivity decreased from 80% in single-vessel disease to 50% in triple-vessel disease ($p < 0.01$).

Prediction of LAD, RCA or LCX Lesions

The ability of thallium-201 MSI to predict narrowings $> 50%$ in the LAD, RCA and LCX was tested for the group of patients with significant coronary disease using various combinations of myocardial segments. The scheme depicted in figure 5 accounted for all abnormal thallium scintigrams and provided the best predictivity by chi-square analysis (greatest number of true positives + true negatives, and smallest number of false positives + false negatives). The detection rate was 84% for LAD disease, 62% for RCA disease and 38% for LCX disease. However, as a trade-off for increased sensitivity, specificity fell. The false-positive rate was 27% for patients without LAD disease, 6% for those without RCA disease, and 8% for those without LCX disease. The false positives for LAD disease were mainly related to defects in segment 3 (apex in the anterior view); however, because of the high prevalence of LAD disease, the greatest predictivity was achieved by including segment 3 as an LAD segment.

Discussion

Our results indicate that stress myocardial perfusion imaging has high sensitivity for detection of coronary artery disease in general, but only moderate
sensitivity for detection of stenosis in individual coronary arteries. In our patients with significant coronary disease, the frequency of abnormal rest or post-exercise scintigrams was 89%, a figure consistent with previous reports. The high value undoubtedly reflects our patient population, which included a large percentage of patients (72%) with previous myocardial infarction. In patients without prior infarction, the sensitivity for detection of disease in general, as well as for stenoses in individual coronary arteries, would be expected to be lower. As in other studies, thallium-201 scintigraphy was more sensitive than electrocardiography for detecting coronary artery disease.

In our patients with coronary disease, we found that segmental analysis of scintigrams in three views allowed identification of areas highly specific for the individual coronary arteries. The anterolateral wall in the anterior view, septum in the 40° LAO view and anteroseptal wall in the 60° LAO view were 97–100% specific for LAD disease. Similarly, the inferior wall in the anterior view was 98–100% specific for RCA disease, and the proximal lateral wall in the 40° LAO view was 100% specific for LCX disease. In addition, involvement of the anterolateral wall in the anterior view was highly specific for lesions involving early diagonal branches of the LAD, either a mainstem lesion before the first large diagonal branch or a lesion in the diagonal branch itself. No significant difference in defect localization was found between LAD disease occurring before or after the first septal perforating artery. Also, no differences in localization could be detected for proximal vs distal RCA disease or for mainstem LCX vs LCX marginal disease. It is possible that analysis of larger numbers of patients, especially those with single-vessel disease, or use of additional imaging views might have shown differences in these anatomic subgroups.

These specificity figures pertain to our patients with significant coronary disease; i.e., given that a patient has disease, the specificity reflects the chance that a thallium defect in a certain location represents a > 50% narrowing in a given major coronary artery. When a larger patient population is considered, including the type of patient included in our group with < 50% narrowings, the specificity values will be lower. As seen in table 1, defects may occur in areas of regional LV dysfunction (patients 1–3, and possibly 5) even with normal or minimally narrowed arteries.

### Table 4. Sensitivity of Specific Segments Relative to Severity of Lesions

<table>
<thead>
<tr>
<th>Grade of lesion</th>
<th>All lesions</th>
<th>( {\text{LAD}} )</th>
<th>( {\text{RCA}} )</th>
<th>( {\text{LCX (RD)}} )</th>
<th>Single-vessel disease</th>
<th>Most severe lesions only</th>
</tr>
</thead>
<tbody>
<tr>
<td>51–70%</td>
<td>3/20 (15%)</td>
<td>2/10 (20%)</td>
<td>1/15 (7%)</td>
<td>1/4 (15%)</td>
<td>1/3 (33%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>71–90%</td>
<td>14/25 (56%)</td>
<td>6/11 (55%)</td>
<td>2/15 (13%)</td>
<td>7/8 (88%)</td>
<td>2/4 (50%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>91–99%</td>
<td>9/15 (69%)</td>
<td>5/11 (45%)</td>
<td>3/10 (30%)</td>
<td>4/6 (67%)</td>
<td>3/6 (50%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>100%</td>
<td>40/46 (87%)</td>
<td>21/36 (58%)</td>
<td>5/13 (38%)</td>
<td>32/36 (89%)</td>
<td>14/25 (56%)</td>
<td>2/5 (40%)</td>
</tr>
<tr>
<td>Overall (&lt; 50%)</td>
<td>66/104 (63%)</td>
<td>34/68 (50%)</td>
<td>11/53 (21%)</td>
<td>44/54 (81%)</td>
<td>20/38 (53%)</td>
<td>5/14 (36%)</td>
</tr>
</tbody>
</table>
| Abbreviations: LAD = left anterior descending coronary artery; RCA = right coronary artery; LCX = left circumflex coronary artery; RD = right distribution.

### Table 5. Influence of Number of Diseased Vessels on Sensitivity of Stress Myocardial Scintigraphic Imaging for Detecting LAD, RCA, and LCX Lesions

<table>
<thead>
<tr>
<th></th>
<th>One-vessel disease</th>
<th>Two-vessel disease</th>
<th>Three-vessel disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>28/35 (80%)*</td>
<td>17/27 (63%)</td>
<td>21/42 (50%)*</td>
</tr>
<tr>
<td>RCA</td>
<td>7/13 (54%)</td>
<td>11/23 (48%)</td>
<td>16/32 (50%)</td>
</tr>
<tr>
<td>LCX (RD)</td>
<td>2/6 (33%)</td>
<td>4/15 (27%)</td>
<td>5/32 (16%)</td>
</tr>
</tbody>
</table>

*Difference between values statistically significant \( x^2 = 7.425; p < 0.01 \).

Abbreviations: LAD = left anterior descending coronary artery; RCA = right coronary artery; LCX = left circumflex coronary artery; RD = right distribution.

### Figure 5. Localization scheme accounting for all positive thallium scintigrams (above) and comparison of lesions predicted by myocardial scintigraphic imaging (MSI) using this scheme, and true lesions (> 50%) found by angiography (below). Values represent number of patients in each category. \( x^2 \) for LAD = 32.24, for RCA = 34.94, and for LCX = 13.72. See figure 2 for abbreviations.
Coronary arteries may be abnormal despite being patent, and produce perfusion abnormalities (patient 3). Patients with severe LV hypertrophy may have "false-positive" defects, such as the apical defect in patient 4. Finally, technical problems, such as camera non-uniformity or attenuation of a portion of the heart activity by the breast, may lead to a mistaken interpretation of thallium defect.

Comparison of our results with reports by Lenaers and Hamilton reveals certain disagreements that are probably explained by differences in data analysis. Lenaers et al. lumped all patients together, including those with triple-vessel disease, main left disease and no disease, to determine the correlation of thallium defects and disease in specific coronary arteries. This approach led to some apparently spurious correlations due to contribution of disease in vessels other than the one being examined. By comparison, we emphasized patients with single-vessel disease and used specific myocardial segments in patients with multivessel disease to exclude the effects of disease in other arteries. Disagreements between our studies concern the relation between the apexes and the RCA and LCX, the posterolateral wall and the LAD, the anterolateral wall and the LCX, and the posterior segments and the LCX. Despite differences on individual segments, our studies agree surprisingly well regarding which segments should be used to predict coronary artery lesions.

Hamilton et al. reported a separation of the three major coronary perfusion beds in the 45° LAO view, but did not provide a detailed analysis of individual patients. In our study the apex in the LAO 40° view had only a 78% specificity for RCA disease, while the sensitivity of this segment in patients with single-vessel RCA disease was only three of 13. There was no statistical association between this segment and RCA disease in our population. Because the LAO 40° view is greatly affected by heart position and rotation, the scintigraphic apex would be expected to correspond to different myocardial segments in different patients. The apex in this view probably is most representative of the RCA vascular bed in those patients with a horizontal heart position.

The most important limitation of thallium-201 scintigraphy for identifying disease in individual coronary arteries is its relatively low sensitivity, a problem noted by several investigators. We found that the detection rate was dependent on the severity of narrowing, but even for 100% occlusions, was only 87% for LAD, 58% for RCA, and 38% for LCX disease using the specific myocardial segments. Including certain nonspecific segments (fig. 5) increased the overall detection rate from 63% to 84% for the LAD, 50% to 62% for the RCA, and 21% to 38% for the LCX (50% lesions). The sacrifice in specificity resulted in 27% false positives for the LAD, 6% for the RCA and 8% for the LCX. Why there were higher sensitivities for LAD disease compared with RCA or LCX disease is not completely clear. The anteriorly located LAD bed is closer to the camera than the more posterolateral LCX region and therefore would be expected to be more easily visualized. In addition, the LAD bed is generally larger than either the RCA or LCX beds, and consequently should be associated with a larger mass of ischemic myocardium.

There are several obvious problems in trying to predict individual coronary artery disease by thallium imaging. First, significant numbers of patients with coronary disease have normal exercise scintigrams. This occurred in 16 of our patients, including 10 patients with single-vessel disease. The normal scintigraphic appearance may be the result of inadequate exercise, inadequate sensitivity of the technique, or diffuse ischemia resulting in a homogeneous pattern.

Second, in patients with multivessel disease, only a single region of myocardium may become ischemic during exercise among the several areas with narrowed arteries. As the first, and presumably most severely involved region becomes ischemic, symptoms or electrocardiographic changes may cause the patient to stop exercising. At this point, perfusion abnormalities may be less obvious or nonexistent in the other areas and therefore may not be visible by MSI.

Third, the correspondence between scintigraphic segments and coronary artery disease is not rigorous, because the anatomical position of the heart in the chest and the coronary artery distribution vary from patient to patient. In a retrospective study such as this, defects in the inferior, posterior or lateral walls could be assigned specifically to lesions in the RCA or LCX. However, when the type of coronary artery distribution is unknown, defects in these regions should probably only be used to identify disease in the "posterior descending coronary artery" or "lateral wall marginal system," which are usually branches of the RCA and LCX, respectively.

Fourth, the significance of individual coronary artery lesions is affected by various factors that complicate comparison with the angiographic data. For example, the presence of left main coronary artery disease (excluded in this study) can modify the significance of lesions in the distal vessels. The presence of coronary collaterals may improve flow to the distal coronary beds and account for preservation of a "normal" scintigraphic appearance. Increased metabolic demands as in aortic stenosis may account for the appearance of defects in spite of angiographically nonsignificant lesions.

Our data indicate that thallium-201 scintigraphy has the greatest difficulty identifying individual coronary artery lesions in patients with multiple vessel disease. The sensitivity for detecting LAD disease decreased from 80% to 50% as the number of diseased vessels increased from one to three. In large part, this is probably due to an important technical limitation of thallium scintigraphy. Because myocardial scintigrams reflect only relative differences in perfusion, patients with multivessel disease may appear to have defects only in the most ischemic areas. Other scintigraphic segments may also have reduced perfusion, but appear normal because of their relatively higher tracer uptake. Methods for quantifying the absolute level of perfusion in each scintigraphic segment will be required before this technical limitation can be overcome.
Finally, it should be pointed out that this study was done using "state-of-the-art" methods. Conventional planar images were obtained in multiple views using standard imaging equipment and techniques. For exercise studies, attention was paid to minimizing the time between the end of exercise and the beginning of data acquisition. Analysis of the scintigrams was done subjectively, but by experienced observers. New techniques for data acquisition and analysis may improve detection of coronary artery lesions. Approaches currently being evaluated include the use of vasodilators to create myocardial perfusion abnormalities,13 special collimators and cameras for tomographic imaging,14,15 computer methods to quantify regional thallium uptake and provide objective image interpretation16 and methods for measuring regional thallium washout rates to help identify areas with low flow.17 Although promising, these approaches will have to be shown to provide significant advantages before they become adopted widely. Until then, the conventional methods used in our study will remain standard and our results will be broadly applicable in the clinical setting.

References