Noninvasive prediction of the angiographic extent of coronary artery disease after myocardial infarction: comparison of clinical, bicycle exercise electrocardiographic, and ventriculographic parameters

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ABSTRACT To assess alternative criteria for the prediction of multivessel coronary artery disease after myocardial infarction, we compared the clinical, bicycle electrocardiographic, and radionuclide ventriculographic (ejection fraction and wall motion) responses in 110 patients undergoing coronary angiography after myocardial infarction. Ninety-seven of the 110 patients had multivessel coronary artery disease (two or more diseased vessels). Clinical or electrocardiographic abnormalities were observed in 41 of 97 (sensitivity = 43%) patients with multivessel disease, and in only two of 13 (specificity = 85%) patients without multivessel disease. The average information content of these combined clinical and electrocardiographic variables relative to perfect discrimination was 5%. Among the scintigraphic parameters, the conventional criterion for ejection fraction abnormality, a rise of less than 5% had a sensitivity of 72% and a specificity of 62% for multivessel coronary artery disease, while a fall in ejection fraction of 5% or more had a sensitivity of 39% and specificity of 92% for multivessel coronary artery disease. The presence of an exercise wall motion abnormality in the nonadjacent noninfarcted (remote) region had a sensitivity of 82% and specificity of 55% for multivessel coronary artery disease. A more stringent criterion, worsening of remote wall motion with exercise, had a sensitivity of 52% and specificity of 75%. When this latter criterion was combined with a fall in ejection fraction, the sensitivity for multivessel coronary artery disease increased to 62%, specificity remained 75%, and information content increased from 5% to 10%. We conclude that conventional diagnostic criteria for abnormal clinical, bicycle electrocardiographic, or scintigraphic results do not identify patients with additional coronary artery disease after infarction with high accuracy. Two alternative ventriculographic parameters—a fall in ejection fraction and wall motion worsening—are similar to clinical parameters in specificity, but have a higher sensitivity and information content. Circulation 70, No. 2, 192-201, 1984.

IN MOST exercise radionuclide laboratories the same criteria for abnormality appear to be used in patients referred for diagnosis of coronary artery disease as in those with previous myocardial infarction referred for functional evaluation. Thus, 32 of 41 studies1-41 either

pooled patients referred for diagnosis and postinfarction patients in determining the sensitivity and specificity of exercise radionuclide ventriculography or applied the same criterion of abnormality to the separate populations.8-39

The question asked of the test in a patient being diagnosed (‘Is disease present?’) differs from that in a postinfarction patient (‘Is additional disease present?’). For the postinfarction patient, in whom disease is almost always present, the goal of testing is to predict prognosis. However, in the absence of a large body of data regarding prognosis, a decision to perform angiography often follows from noninvasive tests that indicate disease is present in more than one vascu-
lar territory. However, conventional criteria for diagnosis may not optimize the identification of postinfarction patients with multivessel disease. The purpose of our study, then, was to evaluate alternative criteria for exercise ejection fraction and segmental wall motion in predicting the extent of angiographic coronary artery disease in postinfarction patients and to compare the accuracy of these predictions to those based on clinical evaluation and bicycle stress electrocardiography.

Methods

Patient selection criteria. The study population consisted of patients meeting the following selection criteria. Each patient had a history of a single prior transmural myocardial infarction as confirmed by resting electrocardiographic examination and angiographic evidence of coronary artery disease. Infarct location was anterior (anterior, anterolateral, anteroseptal) in 58 patients and posterior (posterior, posterolateral, inferior, inferolateral) in 52. Patients with electrocardiographic evidence of both anterior and posterior infarction were excluded, as were patients with normal coronary arteriograms, valvular disease, or previous coronary bypass surgery. All patients underwent both exercise radionuclide ventriculography and coronary angiography within 3 months of infarction and there were no intervening cardiac events. Testing was performed 6 weeks or longer after infarction. One hundred and ten patients met these criteria, including 97 men and 13 women ranging in age from 26 to 83 years (mean 56 ± 11).

Assessment of chest pain. Seventy patients had a history of chest pain. Before testing, an examining cardiologist assigned one of four chest pain symptom classifications to each patient, according to the characteristics of the pain (substernal location, exertional precipitation, and prompt relief by rest or nitroglycerin). If all three characteristics were present, pain was classified as typical angina (34 patients), if two were present, it was classified as atypical angina (13 patients), and if less than two characteristics were present, pain was considered nonanginal (23 patients). The 40 remaining patients were asymptomatic.

Exercise protocol. Exercise was performed on an upright bicycle ergometer in conjunction with radionuclide ventriculography. B-Blocking drugs were withheld for at least 24 hr before testing; long-acting nitrates were withheld for the day of testing. Before imaging each patient was injected with 25 mCi of red blood cells labeled with technetium-99m in vitro. Patients performed graded stress tests beginning at a workload of 200 kilopond-meters (rpm) per minute and increasing by 200 rpm every 3 min of exercise. Exercise was maximal, and was terminated by the physician only for severe chest pain, serious arrhythmia, or exertional hypotension (≥10 mm Hg fall in systolic blood pressure from any previous recorded level during stress). Cardiac rhythm, ST segments, and heart rate were continuously monitored during and after exercise, and blood pressure was recorded at rest, during the third minute of each exercise level, and after exercise.

Exercise electrocardiography. The electrocardiographic response to exercise was not evaluated in patients with electrocardiographic evidence of left ventricular hypertrophy, left bundle branch block, or in patients taking digitals (18 patients). The depth of ST segment depression was measured at 0.08 sec after the J point relative to the PR segment. The stress test was considered positive if horizontal or downsloping ST segment depression of 1.0 mm or more was noted during exercise or recovery. If ST segment depression was present at rest, an additional 1.0 mm was required for abnormality.

Imaging protocol. With a mobile scintillation camera/computer system equipped with an all-purpose collimator, multipledetected imaging was performed immediately before stress testing and during the last 2 min of each exercise stage. Images were obtained in the 40 to 50 degree left anterior oblique view, with the exact angle of obliquity determined by that which best separated the left and right ventricles. Acquisition was obtained over 20 frames of equal duration distributed uniformly over the cardiac cycle (approximately 100,000 counts per frame).

Image analysis. Left ventricular end-diastolic, end-systolic, and background regions of interest were manually assigned, and rest and exercise left ventricular ejection fractions were calculated as the number of stroke counts divided by the background-corrected end-diastolic counts. The exercise ejection fraction response was characterized as a “rise” if it increased by at least 0.05 from that at rest,22-27 as “flat” if it changed less than 0.05 from that at rest, and as a “fall” if it decreased by 0.05 or more from that at rest.

Left ventricular images were evaluated in a closed-loop computer video display after spatial and temporal smoothing for image enhancement.44 Segmental wall motion was assessed by at least two experienced observers without knowledge of clinical data on the patients. For each image, the left ventricle was divided into five segments, and segmental wall motion was scored on a five-point scale as follows: 3 = normal wall motion; 2 = mild hypokinesis; 1 = moderate hypokinesis; 0 = akinesia; −1 = dyskinesis.43 Differences in determinations were mediated by joint interpretation.

The two following criteria for wall motion abnormality were compared: (1) any peak exercise abnormality (score <3), which is the conventional diagnostic criterion,2-21 and (2) any exercise-induced “worsening” of normal or resting hypokinetic segments, defined as a decrease of at least one grade from rest to peak exercise. A change from akinesis to dyskinesis, however, was not considered worsening.

Coronary angiography. Coronary angiography was performed in multiple projections by the Judkins technique. The extent of narrowing of luminal diameter was determined by a consensus reading of at least two experienced angiographers. Coronary artery disease was defined as 50% or more narrowing of luminal diameter of a major branch of any coronary vessel. Multivessel disease was defined as coronary artery disease of at least two of the three major coronary arteries (left anterior descending, left circumflex, and right). According to this definition, isolated left main disease was considered to be a form of multivessel disease. Regional wall motion abnormalities were attributed to specific coronary vascular distributions; the left anterior descending coronary artery was considered to supply the anterior circulation, while the left circumflex and right coronary arteries were considered to supply the posterior circulation. The two septal segments were assigned to the distribution of the anterior circulation, and the two posterolateral segments to the distribution of the posterior circulation. The segment between these regions, representing the inferior wall or apex or both, depending on the orientation of the heart, was termed the inferoapex and was analyzed separately. For the prediction of multivessel disease, wall motion parameters were evaluated in the nonadjacent, noninfarcted myocardial region, termed the remote region. Specifically, the posterolateral segments were evaluated in the patients with prior anterior infarction and the septal segments were evaluated in the patients with prior posterior infarction.

Data analysis. Age, exercise duration, rest and peak exercise heart rate, systolic blood pressure, and ejection fraction values were compared as continuous variables with an unpaired t test for multivessel vs single-vessel disease patient groups. The remaining clinical, electrocardiographic, and scintigraphic pa-
rameters were analyzed as dichotomous variables with the chi-square test or Fisher’s exact test. A p value of .05 or less was considered significant. The accuracy of a given sensitivity/specificity combination was defined by its average information content, I, expressed as a percentage relative to the information provided by coronary angiography:

\[ I = \sum \left[ ap \log_2 (ap) + bq \log_2 (bq) - (ap + bq) \log_2 (ap + bq) \right] - \sum p_i \log_2 p_i, \]

where a = true positive rate; b = false-positive rate; p = prevalence (from 0 to 1); q = 1 − p.

Results

Angiographic findings. The 110 patients were divided into four subgroups based on angiographic findings. Thirteen patients had single-vessel and 97 patients had multivessel disease, including 32 with double-vessel and 52 with triple-vessel coronary artery disease (and no left main coronary artery stenosis). The 13 other patients with multivessel disease had left coronary artery disease; all had concomitant left anterior descending and left circumflex coronary artery disease, and 10 had additional right coronary artery disease. In each patient with single-vessel disease, the angiographically determined location of disease corresponded to the location of infarction as determined by resting electrocardiography. Of 58 patients with anterior infarction, 50 (86%) had additional disease of the posterior circulation, and of 52 patients with posterior infarction, 40 (78%) had additional disease of the anterior circulation.

Clinical and electrocardiographic response. The clinical profiles of the patients and rest/exercise hemodynamic findings according to the extent of coronary artery disease are summarized in table 1. A history of typical angina was twice as common in patients with multivessel disease as in patients with single-vessel disease (p < .01), but most clinical and hemodynamic findings did not vary significantly.

The frequency of clinical and electrocardiographic abnormalities induced by graded bicycle exercise for each angiographic subgroup is illustrated in figure 1. Fifty-six patients experienced chest pain, ST depression, or hypotension during exercise, while the other 54 stopped exercise only because of fatigue. Exercise-induced chest pain and ST depression each occurred with low frequency in all patient subgroups, except among patients with left main coronary artery disease. Exertional hypotension was uncommon in all subgroups, occurring in only six patients in this study. Although clinical and electrocardiographic abnormali-

<table>
<thead>
<tr>
<th>Extent of coronary artery disease</th>
<th>SVD</th>
<th>DVD</th>
<th>TVD</th>
<th>Left main</th>
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<tr>
<td>n</td>
<td>13</td>
<td>32</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49 ± 13A</td>
<td>54 ± 10</td>
<td>59 ± 11</td>
<td>64 ± 09</td>
</tr>
<tr>
<td>% Male</td>
<td>88</td>
<td>81</td>
<td>88</td>
<td>78</td>
</tr>
<tr>
<td>Chest pain (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>38</td>
<td>41</td>
<td>35</td>
<td>31</td>
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<tr>
<td>Nonanginal</td>
<td>38</td>
<td>22</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Atypical</td>
<td>8</td>
<td>6</td>
<td>15</td>
<td>15</td>
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<tr>
<td>Typical</td>
<td>16A</td>
<td>31</td>
<td>33</td>
<td>38</td>
</tr>
<tr>
<td>Rest HR</td>
<td>75 ± 12</td>
<td>74 ± 12</td>
<td>75 ± 12</td>
<td>73 ± 18</td>
</tr>
<tr>
<td>Rest BP</td>
<td>128 ± 18</td>
<td>131 ± 23</td>
<td>130 ± 16</td>
<td>137 ± 30</td>
</tr>
<tr>
<td>Peak HR</td>
<td>134 ± 22</td>
<td>141 ± 23</td>
<td>130 ± 16</td>
<td>130 ± 24</td>
</tr>
<tr>
<td>Peak BP</td>
<td>176 ± 35</td>
<td>183 ± 34</td>
<td>172 ± 29</td>
<td>176 ± 36</td>
</tr>
<tr>
<td>Min ox</td>
<td>10 ± 4</td>
<td>10 ± 4</td>
<td>9 ± 3</td>
<td>8 ± 3B</td>
</tr>
</tbody>
</table>

SVD = single-vessel disease; DVD = double-vessel disease; TVD = triple-vessel disease; HR = heart rate; BP = systolic blood pressure; Min ox = minutes of exercise.

\(^{A}p < .01\) vs multivessel disease; \(^{B}p < .05\) vs single-vessel disease.

ties were associated with multivessel disease — 22 of 23 (96%) patients with exercise chest pain, 22 of 25 (88%) patients with ST depression, and all six patients with exertional hypotension had multivessel disease — the relatively low sensitivities of these variables made them poor predictors of extent of disease. Even when these variables were analyzed in combination, the ability to predict multivessel disease was poor. Only 42 (43%) of the 97 patients with multivessel disease had any clinical abnormality (i.e., chest pain, ST depression, or hypotension), while two (15%) of the 13 patients with single-vessel disease also had one abnormality or more; information content was only 5%. There were no significant differences in clinical or exercise electrocardiographic parameters among patients with single- or multivessel disease.

Response of ejection fraction. Figure 2 illustrates the magnitude of change in ejection fraction from rest to peak exercise, characterized as a rise, flat, or a fall. Although the mean value of change in ejection fraction was significantly lower in patients with multivessel disease (−0.05 ± 0.08) compared with in patients with single-vessel disease (+0.02 ± 0.09; p < .05), there was a wide overlap of functional responses. The change in ejection fraction during exercise ranged from −0.27 to +0.19 in patients with multivessel disease, and from −0.13 to +0.18 in patients with single-vessel disease. The conventional diagnostic criterion for an abnormal ejection fraction response (less than 0.05 rise) did not accurately distinguish patients with from those without multivessel disease. An ab-
abnormalities, and 37 of 40 (93%) with anterior circulation disease and posterior infarction had septal abnormalities (p < .05). However, only nine of 20 patients without multivessel disease had completely normal wall motion in the remote region at peak exercise (specificity = 45%). When wall motion worsening in the remote region was used to predict multivessel disease, sensitivity decreased to 52% and specificity increased to 75%. Seven patients had the combination of disease of the posterior circulation involving both the left circumflex and right coronary arteries and no disease of the anterior circulation. Four of these patients had a septal wall motion abnormality at peak exercise, but only one patient had worsening of wall motion in the septum with exercise, again reflecting the greater specificity of this criterion. Two of these patients also had worsening of wall motion in the posterior circulation.

When worsening of wall motion was analyzed in combination with a fall in ejection fraction, the sensitivity for predicting multivessel disease increased to

![Figure 1](http://circ.ahajournals.org/)

**FIGURE 1.** The frequency of clinical and electrocardiographic abnormalities induced by graded bicycle stress in each angiographic subgroup of patients with prior infarction. A stepwise increase in the frequency of abnormality with increasing extent of coronary artery disease (CAD) is observed. SVD = single-vessel disease; DVD = double-vessel disease; TVD = triple-vessel disease; LMain = left main disease.

Normal response was observed in 70 of 97 multivessel disease patients (sensitivity = 72%), but was also noted in five of 13 single-vessel disease patients (specificity = 62%). A flat response was observed in 33% (32 of 97) of patients with multivessel disease and in 31% (four of 13) of patients with single-vessel disease. A fall in ejection fraction, on the other hand, was observed in 38 patients with multivessel disease (sensitivity = 39%), and in just one patient with single-vessel disease (specificity = 92%). Thus, a fall in ejection fraction was a specific but relatively insensitive predictor of multivessel disease in this population. As a group, the patients with left main disease had the poorest responses, and no patient in this group had a greater than 5% increase in exercise ejection fraction.

**Response of wall motion.** Since the assessment of exercise wall motion was limited to a single view, wall motion analysis was confined to the region remote from that of infarction (figure 3). A remote wall motion abnormality was noted in 74 of 90 postinfarction patients with multivessel disease (sensitivity = 82%): 37 of 50 (74%) with posterior circulation disease and anterior infarction had posterolateral wall motion abnormalities, and 37 of 40 (93%) with anterior circulation disease and posterior infarction had septal abnormalities (p < .05). However, only nine of 20 patients without multivessel disease had completely normal wall motion in the remote region at peak exercise (specificity = 45%). When wall motion worsening in the remote region was used to predict multivessel disease, sensitivity decreased to 52% and specificity increased to 75%. Seven patients had the combination of disease of the posterior circulation involving both the left circumflex and right coronary arteries and no disease of the anterior circulation. Four of these patients had a septal wall motion abnormality at peak exercise, but only one patient had worsening of wall motion in the septum with exercise, again reflecting the greater specificity of this criterion. Two of these patients also had worsening of wall motion in the posterior circulation.

When worsening of wall motion was analyzed in combination with a fall in ejection fraction, the sensitivity for predicting multivessel disease increased to

![Figure 2](http://circ.ahajournals.org/)

**FIGURE 2.** The ejection fraction response to exercise, shown as the change from rest to peak exercise (ΔEF), with reference to extent of coronary artery disease (CAD) and infarct location (anterior infarction = closed circles; posterior infarction = open circles). The area above and including the upper dashed line represents a rise in EF, the area between the dashed lines represents a flat EF response, and the area below and including the lower dashed line represents a fall in EF. MI = myocardial infarction; other abbreviations as in figure 1.
62% and specificity remained 75%. This combination was more sensitive, although slightly less specific, than the combined clinical and exercise electrocardiographic variables (table 2). The average information content of ventriculographic parameters was twice that of the combined clinical and exercise electrocardiographic parameters, but this difference was not statistically significant.

Analysis of the inferoapex. Since 93 (85%) of the 110 patients had resting inferoapical wall motion abnormalities, we analyzed only exercise-induced worsening in this region with respect to the prediction of multivessel disease. In patients with prior anterior infarction, worsening in the inferoapical region was not associated with disease of the posterior circulation (p = .697). In patients with prior posterior infarction, however, inferoapical worsening was associated with disease of the anterior circulation (p = .017). Therefore, in patients with prior posterior infarction, inclusion of the inferoapical region as part of the remote (noninfarct) region increased sensitivity for multivessel disease from 60% to 73%, while specificity remained 75%.

**FIGURE 3.** Sensitivities and specificities of wall motion parameters for predicting disease of the remote coronary circulation after infarction. Two criteria were examined: any remote abnormality at peak exercise (*top*) and remote exercise-induced worsening (*bottom*). Striped bars summarize results in patients with anterior infarction, solid bars those in patients with posterior infarction. MI = myocardial infarction.

### Discussion

Our results indicate that no single clinical, electrocardiographic, or scintigraphic abnormality is both highly sensitive and specific for the prediction of multivessel disease in patients with prior infarction. The nonscintigraphic variables we evaluated were all insensitive as predictors of multivessel disease. For example, exercise-induced chest pain and ST depression were each noted in less than 25% of the patients with multivessel disease, while exercise-induced hypotension was observed in only 6%. Even the combined analysis of these parameters — the presence of any abnormality — was insensitive in identifying the presence of multivessel disease; abnormalities were detected in less than half of such patients.

The ejection fraction response to exercise showed considerable overlap among angiographic subgroups. The conventional definition of an abnormal rest/exercise ejection fraction response in patients without infarction (less than 0.05 rise), was not effective in separating the subgroups of patients with prior infarction because it was nonspecific. Nevertheless, no patient with left main disease had a greater than 0.05 rise in exercise ejection fraction. In contrast, an ejection fraction fall during exercise was much more specific, but much less sensitive, for detecting multivessel disease.

We examined two criteria for interpretation of regional wall motion relative to the prediction of additional disease — the presence of any exercise abnormality in the myocardial region remote from the site of

| TABLE 2 | Comparison of variables in the prediction of multivessel disease after infarction |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| | Sensitivity | Specificity | Information content |
| | n/total (%) | n/total (%) | (%) |
| **Clinical response** | | | |
| Exercise chest pain | 22/90 44 | 19/20 95 | 6 |
| Exercise ST depression | 22/73 30 | 16/19 84 | 2 |
| Exercise hypotension | 6/90 7 | 20/20 100 | 3 |
| Any abnormality | 40/90 44 | 16/20 80 | 5 |
| **EF response** | | | |
| Flat or fall (<0.05 rise) | 68/90 76 | 13/20 65 | 12 |
| Fall (≥0.05) | 39/90 43 | 19/20 95 | 15 |
| **Wall motion response** | | | |
| Remote region abnormality | 74/90 82 | 11/20 55 | 10 |
| Remote region worsening | 47/90 52 | 15/20 75 | 5 |
| Worsening or EF fall | 56/90 62 | 15/20 75 | 10 |

EF = ejection fraction.

a Data reanalyzed to correspond to wall motion analysis.

b p < .05 for anterior vs posterior infarction.

c Excludes 18 patients, as described in text.
Infarction, and the presence of exercise-induced worsening in these regions. The former, more liberal, criterion proved to be relatively sensitive, but non-specific, while the latter was less sensitive but more specific for the presence of multivessel disease. As with other cardiac tests, then, a predictable tradeoff in sensitivity and specificity for the detection of multivessel disease results from revising the criteria for abnormality.

In our study, the development of worsening wall motion was more sensitive than clinical or electrocardiographic abnormalities in detecting multivessel disease after infarction. These data correlate with the empirical observations of others. Various investigators have reported that chest pain is a late manifestation of myocardial ischemia, and that it is commonly preceded by the development of hemodynamic and electrocardiographic abnormalities. For example, demonstrated that abnormalities in left ventricular function were present at the first level of exercise in 22 of 25 patients with coronary artery disease before angina pectoris or electrocardiographic abnormalities developed. Similarly, Kimchi et al. observed that wall motion abnormalities during the first stage of exercise occurred twice as frequently as ST depression. The higher sensitivity that we observed for exercise wall motion abnormalities in this study, therefore, is not surprising. Our ability to identify multivessel disease in patients with prior anterior infarction, however, may be limited by our use of a single 45 degree left anterior oblique view, since the myocardial region supplied by the right coronary artery is not visualized. For example, in a patient with anterior infarction, left anterior descending coronary artery disease, and additional right coronary artery disease, one would not expect to see a posterolateral wall motion abnormality with exercise. In this regard it is not surprising that our results in predicting additional disease in patients with inferior infarction were superior to those in patients with anterior infarction. We have noted that the addition of a second, anterior view exercise study aids in the evaluation of the extent and location of coronary artery disease.

**Comparison to previous studies.** Although few reports on exercise radionuclide ventriculography were specifically designed to assess its ability to predict extent of disease after infarction, we were able to extract the combined experience with 963 such patients from a total of 21 studies (table 3). A number of trends are evident. First, as in our study, no nonscintigraphic parameter is both highly sensitive and specific in predicting the presence of multivessel disease. Results of the few studies reporting the frequency of exercise-induced chest pain or ST segment depression during bicycle exercise are in accord with those of our study. Second, both exercise-induced chest pain and ST depression occurred almost twice as frequently with treadmill exercise as with bicycle exercise. This is also consistent with our experience. In a previous study we evaluated 36 patients undergoing treadmill and bicycle exercise within 2 weeks of each other and found the frequencies of chest pain and ST depression to be 17% and 28%, respectively, during bicycle exer-

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**TABLE 3**

Summary of the pooled medical literature: prediction of multivessel disease

<table>
<thead>
<tr>
<th>Information</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Information content (%)</th>
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<tbody>
<tr>
<td></td>
<td>n/total %</td>
<td>n/total %</td>
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<tr>
<td>Bicycle stress</td>
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<tr>
<td>Chest pain</td>
<td>36/96 38</td>
<td>29/40 73</td>
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<tr>
<td>ST depression</td>
<td>16/47 34</td>
<td>18/22 82</td>
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<tr>
<td>Treadmill stress</td>
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<tr>
<td>Chest pain</td>
<td>76/133 57</td>
<td>56/65 86</td>
<td>15</td>
</tr>
<tr>
<td>ST depression</td>
<td>217/365 59</td>
<td>107/145 74</td>
<td>8</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3/17 18</td>
<td>23/23 100</td>
<td>9</td>
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<tr>
<td>Stress-redistribution thallium scintigraphy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple visual defects</td>
<td>41/73 56</td>
<td>23/25 92</td>
<td>20</td>
</tr>
<tr>
<td>Multiple quantitative defects</td>
<td>24/36 67</td>
<td>20/24 83</td>
<td>18</td>
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<tr>
<td>Exercise radionuclide ventriculography</td>
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<tr>
<td>Abnormal EF response</td>
<td>115/139 83</td>
<td>39/71 55</td>
<td>11</td>
</tr>
<tr>
<td>EF fall</td>
<td>71/138 51</td>
<td>43/61 70</td>
<td>3</td>
</tr>
<tr>
<td>Remote wall motion worsening</td>
<td>19/51 37</td>
<td>23/23 100</td>
<td>22</td>
</tr>
<tr>
<td>EF fall or remote wall motion worsening</td>
<td>38/51 75</td>
<td>18/23 78</td>
<td>20</td>
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</table>

EF = ejection fraction.

*Less than 0.05 rise with exercise.
exercise, but 50% and 70%, respectively, during treadmill exercise. Thus, had we used treadmill rather than bicycle exercise the accuracy of predicting multivessel disease by electrocardiography may have improved. Third, scintigraphic parameters appear to be more sensitive than clinical parameters in predicting the presence of multivessel disease.65 This higher sensitivity, however, was dependent on the criterion employed. Wasserman et al. observed a lower sensitivity and higher specificity for exercise-induced worsening of wall motion than that in this study, but they applied a more stringent definition of worsening — a score that decreased by at least two grades in the remote region.

With an experimental design parallel to that of this study, Wasserman et al. reported a somewhat higher sensitivity and correspondingly lower specificity for an ejection fraction fall of 0.05 or more. This difference may represent the effect of the exercise protocol on the ejection fraction response, or may represent a difference in patient populations. With respect to the former possibility, our patients performed upright exercise, while their’s performed supine exercise. Most studies comparing upright and supine exercise, however, indicate a similar ejection fraction response in the two positions. With respect to the latter possibility, our study population had a significantly higher prevalence of multivessel disease (88% vs 69%, p = .002) and a higher proportion of females (15% vs 5%, p = .062).

Several studies have used submaximal exercise testing early after infarction (before hospital discharge) (table 4). These studies suggest that the sensitivity of scintigraphy for detection of multivessel disease might be somewhat higher (and specificity somewhat lower) than that of conventional “late” (postdischarge) evaluation. Results were similar, however, in the two studies in which the same patients were examined both early and late. One study compared the ventriculographic response to exercise at 3 and 8 weeks after infarction, while the other compared the results of thallium stress testing at 2 weeks and 3 months after infarction. These results imply that the same radionuclide test criteria might be useful for both periods.

**Limitations of the present study.** In assessing the noninvasive test parameters we used a highly conventional method of classification of the coronary anatomy based on the presence or absence of multivessel disease. This classification is justified by a clinical fact of life: the physician often decides to catheterize a patient on the basis of noninvasive test results indicating disease in at least one vessel outside the infarct zone. Second, since we sought to compare our results to those of previous investigations, we adopted the classification most often used in these studies. We recognize, however, that this classification is both arbitrary and simplistic. There is a continuum of the extent and severity of coronary artery disease that is not represented by single vs multivessel disease assignments because of such factors as degree of stenosis, proximity of stenosis to the coronary orifice, length and number of stenoses, and the adequacy of collateral circulation. Newer methods for expressing the degree of coronary artery disease are being devised and these may ultimately provide better correlation between angiographic data and noninvasive test results.

### Table 4

<table>
<thead>
<tr>
<th>Summary of the pooled medical literature: prediction of multivessel disease before hospital discharge</th>
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<tr>
<td></td>
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<td></td>
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<tr>
<td>Bicycle stress</td>
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<td>Chest pain61, 74</td>
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<td>ST depression61, 74</td>
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<tr>
<td>Treadmill stress</td>
</tr>
<tr>
<td>Chest pain65-77</td>
</tr>
<tr>
<td>ST depression65-77</td>
</tr>
<tr>
<td>Stress-redistribution thallium scintigraphy</td>
</tr>
<tr>
<td>Multiple visual defects64, 78</td>
</tr>
<tr>
<td>Increased lung uptake79</td>
</tr>
<tr>
<td>Multiple quantitative defects65, 75</td>
</tr>
<tr>
<td>Exercise radionuclide ventriculography</td>
</tr>
<tr>
<td>Abnormal EF73. A</td>
</tr>
<tr>
<td>EF fall73</td>
</tr>
</tbody>
</table>

EF = ejection fraction.

*Less than 0.05 rise with exercise.
A second limitation of this study derives from the assumption that knowledge of coronary anatomy accurately predicts cardiac prognosis. Thus, while cardiac events occur more often in patients with angiographically more severe disease, resting left ventricular function remains a potent predictor of prognosis independent of anatomy. Our current experience with thallium-201 and exercise blood pool scintigraphy suggest that these studies may provide independent predictors of prognosis. Jones et al., recently reported that combined knowledge of exercise ejection fraction and coronary anatomy better predicted benefit from coronary bypass surgery than knowledge of anatomy alone. Patients with coronary artery disease and normal exercise ejection fraction responses fared no better after surgery than their medical cohorts without surgery. Furthermore, Gibson et al. demonstrated that low-level stress-redistribution thallium scintigraphy is more accurate than coronary angiography in predicting subsequent cardiac events over a 36 month period. Of note is the fact that, in their study, new events occurred in 13 of 58 (22%) postinfarction patients with single-vessel coronary artery disease and 12 of these had a high-risk thallium pattern. Similarly, with the use of exercise radionuclide ventriculography, Nicod et al. found that 11 of 16 postinfarction patients with single-vessel disease had a major cardiac event within a follow-up period of 8 months, and the prognostic outcome was correctly predicted in 13 of these patients by the change in ejection fraction. In the present study, such single-vessel disease patients with exercise-induced ischemia after infarction would have been classified as “false positive” for additional disease. Additional work is needed to clarify whether consideration of the more relevant clinical question regarding prognosis obviates the limitations of this technique in predicting multivessel coronary artery disease.

We conclude that abnormal clinical responses, including chest pain, ST depression, and hypotension during bicycle exercise yield high specificity but low sensitivity for detection of multivessel coronary artery disease in patients with prior myocardial infarction. In contrast, the conventional diagnostic criteria for radionuclide ventriculography are relatively sensitive but nonspecific for identifying additional disease in patients with prior infarction. Two alternative scintigraphic criteria, however, appear to be more specific predictors of remote disease in patients with myocardial infarction: worsening of wall motion in the distribution of the remote circulation and an ejection fraction fall during exercise. These data imply that the interpretation of scintigraphic (and probably other) tests can be improved by independent optimization of criteria in diagnostic and postinfarction populations.

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