The Noninvasive Identification of Left Main and Three-vessel Coronary Artery Disease by Myocardial Stress Perfusion Scintigraphy and Treadmill Exercise Electrocardiography

HAROLD DASH, M.D., BARRY M. MASSIE, M.D., ELIAS H. BOTVINICK, M.D., AND BRUCE H. BRUNDAE, M.D.

SUMMARY The usefulness of exercise electrocardiography (ECG) and myocardial stress perfusion scintigraphy (SPS) in the noninvasive identification of patients with left main or three-vessel coronary artery disease (CAD) was assessed. Ninety-six patients with chest pain were divided into three groups. Group 1 consisted of 44 patients with left main or three-vessel CAD. Group 2 included 37 other patients with CAD. Group 3 comprised 15 patients with normal coronary arteries. Standard criteria for positive and nondiagnostic SPS and ECG were used. Markedly positive patterns of SPS and ECG suggestive of left main or three-vessel CAD were defined.

Forty-two (95%) group 1 patients had positive SPS and 28 (64%) had positive exercise ECG (p < 0.005). Twenty-four (65%) group 2 patients had positive SPS (p < 0.005 compared with group 1) and 14 (38%) had positive ECG (p < 0.05 compared with group 1). No group 3 patient had a positive SPS and three (20%) had positive ECG.

Markedly positive SPS and ECG each detected only 19 (43%) and 15 (34%) group 1 patients, respectively. ECG or SPS were markedly positive in 30 (68%) group 1 patients, significantly increasing the diagnostic yield (p < 0.005). The specificity of markedly positive SPS (95%) for left main or three-vessel CAD was higher than markedly positive ECG (86%), but not statistically different.

SPS is more sensitive than ECG for the diagnosis of CAD in patients with left main or three-vessel CAD. However, SPS and ECG have low sensitivity for the accurate identification of this subgroup of patients with high-risk anatomy. Two scintigraphic patterns have been characterized that are specific for left main or three-vessel CAD. These patterns, in conjunction with ECG, allow noninvasive identification of 68% of symptomatic patients with left main or three-vessel CAD.

MYOCARDIAL PERFUSION SCINTIGRAPHY has become an important adjunct in the evaluation and diagnosis of coronary artery disease (CAD) in patients with chest pain syndromes. Most studies have shown that stress perfusion scintigraphy has greater sensitivity and specificity for the diagnosis of CAD than treadmill exercise electrocardiography.1-9 During the past several years, data have accumulated that suggest that coronary artery bypass surgery decreases morbidity and mortality in selected subsets of patients with critical coronary lesions.10-14 Thus, the detection of these high-risk patients has become an important goal of the noninvasive techniques currently used to assess patients with CAD.

We and others have examined the capacity of exercise testing to identify patients with left main and multivessel coronary stenoses.15-21 However, no study has evaluated the accuracy with which stress perfusion scintigraphy identifies these patients. This study was, therefore, undertaken to assess the value and compare the limitations of these two noninvasive techniques in the identification of patients with two types of coronary anatomy known to carry high risk for subsequent cardiovascular morbidity and mortality: left main and three-vessel CAD.

Methods

Study Population

The study population consisted of 96 patients with chest pain syndromes who were evaluated retrospectively. All patients underwent treadmill exercise electrocardiography in conjunction with thallium-201 myocardial stress perfusion scintigraphy within 1 month of selective coronary angiography. Patients with previous coronary artery bypass surgery or valvular heart disease were excluded. The 96 patients who met the criteria for the protocol were studied at the University of California, San Francisco, between June 1975 and January 1978. Prior myocardial infarction was defined as the presence of electrocardiographic Q waves of 0.04 second or more in duration, or a history of prolonged chest pain and a hospital discharge diagnosis of myocardial infarction.

Angiography

Selective coronary arteriograms were performed in multiple projections according to the Judkins technique and interpreted by two observers. Significant
CAD was diagnosed if at least one major coronary artery had a stenosis of at least 75% of the luminal diameter of the vessel. These lesions were considered hemodynamically significant, and no attempt was made to quantitate further the degree of stenosis. By definition, patients with three-vessel disease had proximal stenoses jeopardizing blood flow to part of the anterior descending, circumflex and posterior descending arteries.

The patients were divided into three groups, according to their coronary anatomy. Group 1 consisted of 44 patients with left main or three-vessel CAD. Group 2 included 37 patients with one- and two-vessel CAD. Group 3 consisted of 15 patients who had no significant coronary stenoses.

Treadmill Exercise Electrocardiography

Patients were tested in the fasting state. Cardiac medications were continued before the exercise study, if clinically indicated. After giving informed consent, each patient had a standard 12-lead ECG, followed by continuous monitoring with a CM5 bipolar precordial lead at rest, while standing, with hyperventilation, and during graded treadmill exercise. The exercise test was performed according to the Bruce protocol. All patients exercised until limiting symptoms or serious arrhythmias appeared. In the absence of resting ST-T changes, a test was positive for ischemia if, 0.08 second from the J point, horizontal or downsloping ST-segment depression ≥ 1 mm (compared with baseline) developed during exercise or recovery. A test was defined as markedly positive when the exercise ECG showed horizontal downsloping ST-segment depression ≥ 2 mm (compared with baseline) before the onset of stage III of the exercise protocol.

A test was considered negative only when the patient achieved 85% of the maximum predicted heart rate for age, without associated positive ST-segment changes. In the presence of baseline ST-T abnormalities, the exercise ECG was not classified as positive or negative, but was listed as "nondiagnostic." Nondiagnostic tests occurred in patients with inadequate heart rate responses, bundle branch block and digitalis therapy.

Myocardial Perfusion Scintigraphy

Myocardial perfusion scintigraphy was performed after the intravenous injection of 2 mCi of thallium-201 during peak exercise. Exercise was continued for another 30–60 seconds, and scintigraphy begun within 10 minutes after exercise. Images were obtained in the anterior, 45° left anterior oblique and left lateral projections. Imaging was performed with either a Searle Pho Gamma IV or an Ohio Nuclear Series 120 scintillation camera, using a converging collimator for the first part of the study and a high-sensitivity, parallel-hole collimator for the last 6 months. A 20% window was centered at 75 kev. Images were taken to 200 thousand counts in the anterior projection and to an equal time in remaining projections. Patients with abnormal exercise scintigrams returned 4 hours later for a redistribution study or within a week for a rest perfusion study.

Two observers interpreted the original, unenhanced scintigrams without knowledge of the patients' clinical, electrocardiographic or angiographic findings. Rare differences in findings were resolved after joint discussion. Scintigrams were considered abnormal when relatively decreased perfusion of a region of the left ventricular image was present. Isolated linear apical defects and lone defects of the inferior wall in the left lateral projection are often seen normally and were not considered abnormal. A positive stress perfusion scintigram indicative of exercise-induced ischemia was defined as a defect in the stress myocardial image not present at rest or redistribution. A stress perfusion scintigam was considered nondiagnostic if perfusion appeared normal, but the patient failed to achieve 85% of maximum predicted heart rate.

We used the stress perfusion scintigrams to infer the coronary anatomy of the patients. Anterior defects in the anterior and lateral views or a septal defect in the left anterior oblique view suggested left anterior descending disease; a posterolateral defect on the left anterior oblique view, circumflex artery stenosis; and inferior defects, posterior descending disease (i.e., dominant right or circumflex lesions). Accordingly, we identified two stress perfusion patterns suggestive of left main or three-vessel disease (fig. 1). The scintigrams in the upper panel show defects in the anterior and posterolateral walls and the interventricular septum consistent with significant left main coronary occlusion. The scintigrams in the lower panel show the accumulation of radioisotope at the base of the heart and the relative diminution of radioactivity in the main body of the left ventricle, and are in marked contrast to a normal scintigram. Such a pattern suggests ischemia in all distal myocardial beds consistent with stenoses of all three major coronary vessels. A patient whose exercise perfusion image manifested one of these patterns was designated as having a markedly positive stress perfusion scintigram.

Sensitivity and Specificity

In our study, a positive test suggested the presence of CAD, and a markedly positive test suggested the presence of the high-risk lesions of left main or three-vessel disease. For the purpose of this study, the terms "sensitivity" and "specificity" refer only to the identification of left main or three-vessel CAD in patients with documented CAD, not to the diagnosis of CAD in all patients with chest pain syndromes. Thus, only patients in groups 1 and 2 are included in the analysis, and only the markedly positive tests are considered.

Sensitivity (%) = 100 - 
\[
\frac{\text{true markedly positive tests}}{\text{all group 1 patients}} \times 100
\]

Specificity (%) = 100 - 
\[
\frac{\text{false markedly positive tests}}{\text{all group 2 patients}} \times 100
\]
Statistics

The treadmill exercise ECGs and the stress perfusion scintigrams are related tests performed on the same patients. Statistical tests used to evaluate the differences between test results included McNemar's test and an analysis of differences between proportions. Comparisons of patient groups were evaluated with chi-square analysis.

Results

Table 1 is a comparison of the frequency of positive tests in the patients with normal coronary arteries (group 3) with that of patients with CAD (groups 1 and 2). The exercise ECG was positive in 42 patients (52%) with CAD, and stress scintigraphy was positive in 66 (81%) ($p < 0.001$). However, 25 patients (31%) with CAD had nondiagnostic treadmill exercise tests because of suboptimal heart rate response or resting ST-segment abnormalities; only two patients (2%) had nondiagnostic stress perfusion scintigrams. If nondiagnostic tests are excluded from analysis, stress scintigraphy identified CAD in 84% of the patients in groups 1 and 2, while exercise electrocardiography identified 75% (NS). No patient with normal coronary arteries had a positive stress perfusion scintigram; three (20%) had positive treadmill tests, none of which were markedly positive.

Table 2 lists the frequency of positive tests in the two groups of patients with CAD. Stress scintigraphy identified 42 group 1 patients (95%) as having CAD, while the exercise ECG was positive in 28 group 1 patients (64%) ($p < 0.005$). Fourteen group 2 patients (38%) had a positive stress ECG and 24 (65%) had positive scintigrams. More group 1 patients had positive treadmill ECGs ($p < 0.05$) and positive stress perfusion scintigrams ($p < 0.005$) than group 2 patients.

Table 3 lists the frequency of markedly positive tests in groups 1 and 2. A markedly positive exercise ECG and stress perfusion scintigram both had a relatively low sensitivity for the diagnosis of left main or three-vessel disease and detected 34% and 43% of group 1 patients, respectively (NS). Figures 2 and 3, studies from two patients with high-risk CAD, illustrate the two markedly positive scintigraphic patterns. A markedly positive scintigram was somewhat more specific for the diagnosis of left main or three-vessel disease, appearing in only two (specificity of 95%) group 2 patients with one- or two-vessel disease, compared with a markedly positive exercise ECG, which was present in five (specificity of 86%) group 2 patients. The difference, however, was not statistically

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**Table 1. Relation Between Test Results and Presence or Absence of Coronary Disease**

<table>
<thead>
<tr>
<th></th>
<th>Groups 1 and 2 (coronary disease)</th>
<th>Group 3 (normal coronary arteries)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 81)</td>
<td>(n = 15)</td>
</tr>
<tr>
<td>ECG+</td>
<td>42 (52%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td></td>
<td>$p &lt; 0.001$</td>
<td></td>
</tr>
<tr>
<td>SPS+</td>
<td>66 (81%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>ECG+ or SPS+</td>
<td>71 (88%)</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>ECG ND</td>
<td>25 (31%)</td>
<td>6 (40%)</td>
</tr>
<tr>
<td>SPS ND</td>
<td>2 (2%)</td>
<td>4 (27%)</td>
</tr>
</tbody>
</table>

Abbreviations: ECG = exercise electrocardiogram; SPS = stress perfusion scintigram; + = positive; ND = nondiagnostic.
**TABLE 2. Relation Between Positive Tests and Coronary Anatomy**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>LM (n = 6)</th>
<th>3V D (n = 38)</th>
<th>All high risk (n = 44)</th>
<th>Group 2</th>
<th>1 or 2 VD (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG+</td>
<td>3 (50%)</td>
<td>25 (66%)</td>
<td>28 (64%)**</td>
<td></td>
<td>14 (38%)**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*p &lt; 0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPS+</td>
<td>6 (100%)</td>
<td>36 (95%)</td>
<td>42 (95%)†</td>
<td></td>
<td>24 (65%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*p &lt; 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG+ or SPS+</td>
<td>6 (100%)</td>
<td>37 (97%)</td>
<td>43 (98%)‡</td>
<td></td>
<td>28 (76%)‡</td>
</tr>
</tbody>
</table>

* p < 0.05.
† p < 0.005.
‡ p < 0.01.

Abbreviations: ECG = exercise electrocardiogram; SPS = stress perfusion scintigram; + = positive; LM = left main anatomy; 3 VD = three-vessel disease; 1 or 2 VD = one- or two-vessel disease.

**TABLE 3. Relation Between Markedly Positive Tests and Coronary Anatomy**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>LM (n = 6)</th>
<th>3 VD (n = 38)</th>
<th>All high risk (n = 44)</th>
<th>Group 2</th>
<th>1 or 2 VD (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG MP</td>
<td>3 (50%)</td>
<td>12 (36%)</td>
<td>15 (34%)**</td>
<td></td>
<td>5 (14%)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*p = NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPS MP</td>
<td>2 (33%)</td>
<td>17 (36%)</td>
<td>19 (43%)†</td>
<td></td>
<td>2 (5%)†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*p &lt; 0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG or SPS MP</td>
<td>4 (67%)</td>
<td>26 (64%)</td>
<td>30 (68%)‡</td>
<td></td>
<td>6 (16%)‡</td>
</tr>
</tbody>
</table>

* p < NS.
† p < 0.001.
‡ p < 0.001.

Abbreviations: ECG = exercise electrocardiogram; SPS = stress perfusion scintigram; MP = markedly positive; LM = left main anatomy; 3 VD = three-vessel disease; 1 or 2 VD = one- or two-vessel disease.

**Figure 2.** Left main pattern. Perfusion scintigrams and exercise ECGs from a patient with three-vessel disease are shown. Although the resting ECG has minimal baseline ST-segment abnormalities, the exercise ECG is markedly positive, with ST-segment depression > 2 mm, compared with rest. The rest perfusion scintigram is probably normal. The stress perfusion scintigram shows the left main pattern, with defects of the septum and posterolateral wall on the left anterior oblique (LAO) projection (arrows). There are also anterior and apical defects (arrows) on the left lateral (LLAT) and anterior (ANT) projections. Perfusion of the inferior wall appears relatively normal despite the presence of a high-grade right coronary stenosis. This patient illustrates the relative nature of myocardial perfusion scintigraphy: A region of the left ventricle with decreased perfusion secondary to proximal coronary stenosis may appear "normal" at scintigraphy because adjacent vascular beds have greater degrees of hypoperfusion.
significant. Figure 4 shows a markedly positive exercise ECG in a patient with left anterior descending and right coronary stenoses. His scintigram shows only a subtle inferior wall defect.

A markedly positive stress perfusion scintigram or exercise ECG was present in 30 of the high-risk group 1 patients (68%); the two tests together identified significantly more such patients than either test alone ($p < 0.05$), and thus increased the sensitivity of the exercise study.

Table 3 also lists the data for the subgroups of patients with left main or three-vessel disease. Although relatively specific for group 1 patients, the two markedly positive perfusion patterns were seen in each subgroup, as might be expected, because four of the six patients classified as having left main anatomy also had three-vessel disease. The one patient with an isolated left main stenosis who had a markedly positive scintigram had the left main pattern.

Most patients in groups 1 and 2 had poor exercise tolerance and tended to develop ischemic changes early in exercise. Twenty-six of the 28 group 1 patients with positive treadmill ECGs had ischemic ST-segment changes before stage III, compared with 11 of 14 group 2 patients (NS). Eleven group 1 patients (25%) exercised beyond stage II, compared with 16 group 2 patients (43%) (NS).

Nondiagnostic treadmill ECGs were common; they occurred in 12 group 1 patients (27%) and 13 group 2 patients (35%) (NS). Of these 25 patients, eight had submaximal heart rate responses, nine had resting ST-segment abnormalities preventing interpretation of the ECG, and eight had both. Ten of these patients were taking digitalis preparations and 10 were taking propranolol. An additional 27 patients with ischemic electrocardiographic responses were also taking propranolol. The proportion of patients in group 1 who took propranolol (48%) was not significantly different from that in group 2 (43%). Only two patients had nondiagnostic stress perfusion scintigrams; and both were taking propranolol at the time of the study.

Of the patients with CAD, 30 group 1 patients (68%) had a prior myocardial infarction, compared with 19 group 2 patients (51%) (NS). Of the 49 patients with prior myocardial infarction, 36 (73%) had abnormal rest perfusion scintigrams.

### Discussion

Many investigators agree that symptomatic patients with left main coronary disease have an improved life expectancy after bypass graft surgery.10-12 Although the effect of surgical therapy on the long-term survival of patients with three-vessel disease remains controversial,13-16, 25, 26 reports of the natural history of patients with these lesions suggest a higher mortality than in patients with lesser degrees of coronary obstruction.27-29 Thus, the noninvasive identification of patients with these patterns of potentially high-risk CAD has assumed increasing therapeutic and prognostic importance.

### Relationship of Coronary Anatomy to Results of Exercise Electrocardiography

In the present study, only 52% of all patients with CAD had a positive exercise ECG, a finding probably related to our inclusion of patients with resting ST-segment abnormalities or suboptimal stress. If patients with nondiagnostic treadmill ECGs are excluded from analysis, 75% of the patients in groups 1 and 2 had positive treadmill tests, a finding comparable to that reported in the literature.30, 31, 30, 31 Additionally, the use of a single bipolar CMx precordial lead may have contributed somewhat to the low percentage of positive stress tests. The use of multiple leads may increase the yield of positive tests.

Sixty-four percent of our group 1 patients (left main or three-vessel disease) had a positive treadmill test, compared with 38% of group 2 patients (one- or two-vessel disease) ($p < 0.05$). Other investigators31, 30, 31 have also noted an increase in the frequency of positive tests with more widespread proximal CAD.

Although more patients with left main or three-vessel disease had positive exercise ECGs, a positive
treadmill test could not in itself differentiate patients with these potentially high-risk lesions from those without. Several investigators have examined the relationship between the extent of coronary involvement and the magnitude and pattern of ST-segment depression, the duration of exercise, and the blood pressure response to exercise. The markedly positive treadmill test had low sensitivity and relatively high specificity in the current study. Thirty-four percent of the group 1 patients with high-risk anatomy had markedly positive treadmill tests, compared with 14% of the group 2 patients. Cheitlin et al. found a higher frequency of exercise ECGs showing at least 2-mm ST-segment depression among patients with left main or three-vessel disease than we did. The discrepancies may be related to differences in protocol and interpretation. In contrast to Cheitlin et al., we did not routinely discontinue propranolol or other cardiac medications before testing, and our definition of a markedly positive test was more stringent.

Five group 2 patients (14%) with one- or two-vessel disease had markedly positive treadmill exercise ECGs. Thus, the specificity of the markedly positive treadmill test for the diagnosis of left main or three-vessel disease was 86%. The anatomy of the coronary lesions in these patients is of interest. One had a left anterior descending artery stenosis proximal to all branch points with normal right and circumflex system. Three patients had disease of the right coronary artery with stenosis of either the left anterior descending or the left circumflex artery (fig. 4). The fifth patient had stenosis of the left anterior descending and circumflex arteries proximal to any branches. In each case, the obstructed vessels were large and the amount of myocardium jeopardized by the coronary lesions appeared extensive. Goldschlager et al. showed that a downsloping pattern of ST-segment depression suggests more severe coronary disease. Approximately 60% of their patients with three-vessel disease and 67% with left main obstruction had such stress-induced ST-segment changes. However, these patients constituted only 56% of those with the downsloping pattern. Although our study is not strictly comparable, their findings suggest that the downsloping pattern is more sensitive and less specific for the diagnosis of left main or three-vessel CAD than the markedly positive treadmill ECG, as we have defined it.

McNee et al. found that 60% of the patients with positive exercise ECGs in stage I or II of the Bruce protocol had three-vessel disease, and that only 11% of the patients with three-vessel disease were able to exercise to stage III without ischemic ST-segment changes. Our results were similar; however, most of our symptomatic patients had poor exercise tolerance and tended to develop ischemic changes early in exercise, indicating that these findings, too, have a rather low specificity for the diagnosis of three-vessel CAD.

On the other hand, hypotensive responses during exercise are strongly associated with high-risk coronary lesions, such as left main or three-vessel disease. However, exertional hypotension in such patients is uncommon and thus, like the markedly positive treadmill test, has a rather low sensitivity for the diagnosis of potentially high-risk CAD.
**Relationship of Coronary Anatomy to Scintigraphic Findings**

In our study, 95% of the group 1 patients and 65% of the group 2 patients had positive stress perfusion scintigrams. Overall, stress scintigraphy was positive in 81% of the patients, similar to the results reported by others.\(^5\)\(^6\) Contrary to our previous findings in a smaller population with CAD,\(^7\) our results support those of others who have noted that the sensitivity for diagnosing CAD increases with the degree of coronary vascular involvement.\(^8\)\(^9\)

Myocardial perfusion scintigraphy in our patients had a low sensitivity for the accurate detection of left main or three-vessel disease. Only 43% of the patients in group 1 had markedly positive scintigrams, a sensitivity similar to that of treadmill exercise electrocardiography. Lenaers et al.\(^34\) performed segmental analysis of stress perfusion scintigrams and correctly identified 32% of their patients with three-vessel disease by scintigraphic criteria, while the remaining 68% had lesser degrees of scintigraphic abnormalities. These results are similar to ours.

We examined several factors that might explain the low sensitivity of the markedly positive stress perfusion scintigrams in the group 1 patients. The percentage of group 1 patients taking propranolol or digoxin, the proportion failing to achieve 85% of their maximal predicted heart rate, and the frequency of prior myocardial infarction were all similar among patients with or without markedly positive stress perfusion scintigrams. However, it is still possible that the failure to obtain a markedly positive test in individual patients was related to the failure to discontinue drugs that may alter thallium uptake by myocardial cells,\(^35\) or to suboptimal stress.

There are several reasons for the low frequency of the markedly positive scintigraphic pattern in the setting of high-risk coronary anatomy. There is no reason to believe that all myocardial areas supplied by narrowed coronary vessels will produce ischemia at stress; thus, not all will show scintigraphic abnormalities. Also, scintigraphy is a relative technique, and the scintigram will reveal the most underperfused regions of the myocardium while adjacent, “best” perfused regions may not be normally perfused.\(^3\) Thus, scintigraphy may sensitively detect only the most severely hypoperfused segments, and other areas with smaller degrees of hypoperfusion may appear relatively normal. The degree of coronary stenosis, the presence of functional collateral vessels, and the presence of infarcted, nonperfused myocardium will affect the relative perfusion pattern. Gould\(^36\) recently showed in animals that a defect in the thallium-201 myocardial perfusion image will not appear until the blood flow ratio of normal to stenotic coronary arteries approaches 2:1. It is possible that similar flow ratios are necessary in man before the perfusion image will become abnormal.

A patient with three-vessel disease (fig. 2) illustrates the relative nature of perfusion scintigraphy. Although his right coronary artery had a significant stenosis, the inferior wall of the stress perfusion scintigram appears normal compared with the perfusion of other regions of his heart. Previous authors have commented on the unusual occurrence of normal stress perfusion scintigrams in patients with widespread three-vessel disease.\(^3\)\(^7\) Such a finding might occur in the setting of a homogeneous decrease in myocardial perfusion during exercise. There was one such patient in our study, and he had a markedly positive treadmill exercise ECG.

In our study, scintigraphy was not sensitive for the identification of left main or three-vessel disease, but it was specific — only two group 2 patients had a markedly positive stress scintigram (specificity 95%). One patient had a total occlusion of his left anterior descending artery just distal to a small first diagonal branch and a small septal perforator. He also had a tight proximal stenosis of a very large circumflex marginal branch. The second patient had isolated anterior descending and circumflex stenosis proximal to any branch points. These two patients, like most of the patients in group 2 with markedly positive treadmill ECGs, had extensive areas of myocardium jeopardized by proximal coronary stenoses. The specificity of the markedly positive stress perfusion scintigram in our study was somewhat greater than that of the markedly positive exercise ECG, but the difference was not statistically significant.

In our study, stress perfusion scintigraphy and exercise electrocardiography together identified over two-thirds of the group 1 patients, a significant increase in sensitivity compared with either test alone \((p < 0.05)\), indicating the importance of using both sets of test data in evaluating these patients.

Although the markedly positive perfusion patterns were specific for left main or three-vessel disease, the type of pattern did not necessarily predict a patient’s exact coronary anatomy, partly because of the overlap among the anatomic subgroups with these high-risk lesions. Thus, of the six patients with left main obstruction, four also had disease of the right coronary artery. None of the patients with isolated left main stenosis had the three-vessel disease pattern on stress perfusion scintigraphy. In fact, the three-vessel disease pattern was seen only in patients with three-vessel disease. While the predicted scintigraphic pattern of left main coronary disease did occur in relation to high-risk left main coronary anatomy, it was frequently associated with three-vessel disease, probably because of the scintigraphic tendency to underestimate the degree of vascular involvement and the high incidence of right coronary artery disease seen in relation to simultaneously occurring left anterior descending and left circumflex lesions. Although a reliable indicator of more extensive three-vessel disease in this study, this "left main" scintigraphic pattern in association with two-vessel, left anterior descending and left circumflex coronary lesions should be expected. The left main scintigraphic pattern did occur in two patients with proximal left anterior descending and left circumflex lesions. Such coronary anatomy has been called “left main equivalent” disease. It may threaten large myocardial regions, and some\(^38\) feel...
that it is related also to "high prognostic risk."

One possible limitation of this study should be mentioned. Despite attempts to be rigid regarding patient selection, in a retrospective clinical review, the representativeness of the patient population may be questioned. Our study population comprised a highly symptomatic subgroup of patients with CAD. Sixty percent of the patients had prior myocardial infarction and 54% had left main or three-vessel disease. Yet, the patients in this study were representative of those with chest pain syndromes catheterized at our institution. Thus, although probable, it is not certain that the findings here are applicable to all patients with CAD.

The results of our study indicate that the noninvasive diagnosis of the high-risk patterns of left main and three-vessel CAD is limited by the sensitivity of available tests. Exercise electrocardiography and myocardial stress perfusion scintigraphy have low sensitivity for the precise diagnosis of these high-risk lesions. Nonetheless, we have characterized two types of stress perfusion scintigraphic patterns that are highly specific for high-risk anatomy. Additionally, the exercise ECG and the myocardial stress perfusion scintigram are complementary tests. By using maximal stress testing in conjunction with myocardial perfusion imaging, the clinician will be able to identify approximately two-thirds of symptomatic patients with left main or three-vessel CAD before coronary angiography.

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References

Evaluation of Myocardial Ischemic Damage of Various Ages by Computerized Transmission Tomography

Time-dependent Effects of Contrast Material

CHARLES B. HIGGINS, M.D., PAUL T. SIEMERS, M.D., WALTER SCHMIDT, AND JOHN D. NEWELL, M.D.

SUMMARY The potential role of computerized transmission tomography (CTT) in the detection and quantitation of acute myocardial ischemic damage was assessed in 42 excised canine hearts at 2 hours, 8 hours, and 48 hours after coronary occlusion. The CTT scan detected myocardial damage that was 2–48 hours old each time the presence of regional ischemia was confirmed by histochemical staining or epicardial electrocardiographic mapping. Intravenous administration of contrast material enhanced the x-ray attenuation of areas of ischemic damage of 8 and 48 hours duration compared with normal myocardium, but enhanced only normal myocardium in those of 2 hours duration. Volumetric estimation of the extent of damage from the CTT scans in dogs with ischemia of 48 hours duration showed a close linear relationship with the morphometric volume in the absence of contrast material. Quantitation of the area of ischemic damage from the CTT scan after contrast administration resulted in substantial underestimation of the volume of damaged tissue.

THE CAPACITY of computerized transmission tomography (CTT) to detect regions of myocardial ischemic damage has been shown in the nonbeating canine heart.7 Ischemically damaged myocardial tissue appears on the CTT scan as an area of decreased x-ray attenuation compared with the surrounding normal myocardium. The mechanism of this altered x-ray attenuation has been related to edema formation within the ischemically damaged tissue.8,4 Studies from our laboratory have revealed that the CTT scan was not only sensitive in detecting areas of myocardial damage 48 hours after coronary arterial ligation, but was also relatively accurate in quantitating the actual volume of this area.7

After coronary arterial occlusion, ischemic changes evolve in the jeopardized myocardium, including loss of integrity of the myocardial cellular membranes, increased microvascular permeability, inflammatory cellular infiltrate, and finally, fibrotic replacement of myocardial cells.8,11 This dynamic process is characterized in the early phase by edema of the infarcted myocardium and in the late phase by fibrous replacement of myocardial tissue. Consideration of this time-related dynamic process suggests that the CTT image of a myocardial infarction and its interaction with radiographic contrast material may change with time.

The purpose of the current study was to: 1) determine the capacity of the CTT scan to detect myocardial ischemic changes at various time intervals after
The noninvasive identification of left main and three-vessel coronary artery disease by myocardial stress perfusion scintigraphy and treadmill exercise electrocardiography.
H Dash, B M Massie, E H Botvinick and B H Brundage

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