Comparison of Rest and Exercise Radionuclide Angiography and Exercise Treadmill Testing for Diagnosis of Anatomically Extensive Coronary Artery Disease

CHRISTIAN T. CAMPOS, A.B., H. WILLY CHU, M.D., HARRY J. D’AGOSTINO, JR., M.D., AND ROBERT H. JONES, M.D.

SUMMARY The accuracy of rest and exercise radionuclide angiography (RNA) and exercise treadmill testing (ETT) for diagnosis of three-vessel or left main coronary artery disease (extensive CAD) was determined in 544 patients. ETT and RNA sensitivities were similar (88% vs 92%, NS), but ETT was more specific than RNA (46% vs 34%, p < 0.01). The prevalence of extensive CAD in patients with a positive treadmill (41%) increased only 3% when the RNA was also positive. However, in the 292 patients with a negative or indeterminate ETT, a positive RNA increased this prevalence from 16% to 23%, while a negative RNA decreased this prevalence to 5%. These results support the initial use of ETT followed by RNA if the treadmill is negative or indeterminate for diagnosis in a population with a high prevalence of extensive CAD. This approach separates patients into subgroups with a high or low probability of extensive CAD.

SURVIVAL in patients with coronary artery disease (CAD) has been related to the number of diseased coronary vessels and to the presence of significant left main coronary artery stenosis.1-3 The identification of patients with a high probability of three-vessel or left main disease is an important goal of noninvasive testing. Exercise-induced left ventricular functional abnormalities appear to result from ischemia and can be used to diagnose CAD in patients with chest pain.4-10 Moreover, the magnitude of abnormality of left ventricular function during exercise appears to be related to the anatomic extent of coronary artery disease.11 The purpose of the present study is to document the relative diagnostic accuracy of radionuclide angiography (RNA) and exercise treadmill testing (ETT) in evaluating patients for the presence of three-vessel or left main CAD.

Methods

Study Population

Between January 1, 1977, and June 30, 1981, 3005 patients underwent cardiac catheterization and coronary arteriography for suspected coronary artery disease at Duke University Medical Center. Bruce multistage exercise treadmill tests were performed in 1495
(50%) of these 3005 patients. Seventy-eight of these 1495 patients were excluded from this investigation because of previous cardiac surgery or concomitant congenital or significant valvular heart disease. Rest and exercise RNA studies were performed within 3 months of cardiac catheterization and arteriography in 544 of the remaining 1417 patients. Data from these 544 patients were obtained from the Duke University Medical Center computerized information storage and retrieval system.12

Cardiac catheterization included right- and left-heart pressure measurements, biplane left ventriculograms and selective coronary arteriograms in multiple views of both the right and left coronary systems. Arteriograms were interpreted in conference by two or more experienced cardiologists who were not investigators in this study. A 75% or greater narrowing of the luminal diameter was required to diagnose significant CAD in any coronary vessel, including the left main coronary artery. Stenoses of less than 75% of the vessel diameter were considered insignificant. Coronary arteries were considered normal if no areas of stenosis were apparent.

Exercise Treadmill Test Technique

Exercise treadmill testing was performed using the Bruce graded multistage protocol.13 Exercise end points were moderate chest pain, severe fatigue or dyspnea, claudication, serious arrhythmias, marked ST-segment changes on the ECG or achievement of 85% of the maximal predicted heart rate (220 - age).

Positive ST-segment changes were defined as: (1) horizontal or downsloping ST-segment depression of 0.1 mV or greater persisting at least 0.08 second in the absence of preexisting ST-segment abnormalities; (2) ST-segment elevation of 0.1 mV or more than in the control tracing in any lead except aVR; (3) in the presence of ST-segment depression of 0.05 mV or more in the control tracing, additional depression equal to or greater than 0.2 mV was required for the test to be interpreted as positive. The ETT was negative only when the patient achieved 85% of the maximal predicted heart rate and failed to develop any positive ST-segment changes. The test was indeterminate when no positive ST-segment changes occurred but the patient failed to achieve 85% of the maximal predicted heart rate. Other reasons for an indeterminate test included left bundle branch block or the development of a serious arrhythmia during exercise.

Since exercise duration during ETT is considered to provide additional diagnostic information,14 the effect of incorporating the maximum stage into the definition of a positive ETT was examined. No increase in the sum of ETT sensitivity and specificity was obtained and, therefore, the positive ETT definition used in this study did not incorporate the exercise duration.

Radionuclide Angiographic Technique

RNA studies were performed at rest and during exercise as previously described14 with patients in the upright, sitting position on a bicycle ergometer (Fitron, Lumex Inc.), using a multicrystal gamma camera (System Seventy-Seven, Baird, Inc.) positioned anterior to the precordium. The rest RNA was performed by injecting a 15-mCi bolus of technetium-99m pertechnetate and recording counts at 25-msec intervals for 30 seconds. Exercise was then begun at a work load of 200 kilopond-meter (kpm)/min and was increased by 100 kpm/min each minute. The exercise RNA was obtained upon occurrence of any of these end points: pain suggestive of myocardial ischemia, ECG evidence of ischemia, severe fatigue or dyspnea, or achievement of 85% of the maximal predicted heart rate.

Measurements determined included left ventricular ejection fraction (LVEF), end-diastolic volume and end-systolic volume (ESV). These measurements have been shown to be accurate and reproducible.15,16 Regional wall motion was assessed qualitatively using static and cinematic images of a representative cardiac cycle. An exercise-induced wall motion abnormality was defined as the appearance of a wall motion abnormality not present at rest or an increase in the severity or extent of a wall motion abnormality present at rest.

The RNA was considered abnormal if the resting LVEF was less than 0.50, ESV increased more than 20 ml during exercise, exercise LVEF was more than 0.05 below the predicted value, or an exercise-induced wall motion abnormality developed. These criteria were initially developed in our laboratory to identify patients with a 75% or greater stenosis of one or more coronary arteries.11 Since different criteria might better identify patients with three-vessel or left main disease, the previously described methods of defining optimal criteria were repeated to identify patients with anatomically extensive CAD. No alternative set of criteria increased the sum of RNA sensitivity and specificity; therefore, the above criteria initially published by our laboratory were used to recognize anatomically extensive CAD.

Determination of RNA and ETT Diagnostic Accuracy

The diagnostic accuracy of RNA was determined by applying the RNA criteria to the entire population and to selected subgroups of the population. The diagnostic accuracy of the ETT was assessed by calculating its sensitivity and specificity in patients with positive or negative treadmill results. Combined use of the RNA and the ETT was evaluated by determining the prevalence of three-vessel or left main CAD in patients grouped by the RNA and ETT results and by calculating the sensitivity and specificity of combinations of both tests.

Mortality data were obtained at 6 months and at yearly intervals after the initial evaluation. These data were obtained by staff cardiologists during a clinic visit or by a research associate by telephone. Follow-up was 97% complete.

Statistical Analysis

Differences between groups were assessed for significance by chi-square analysis. In all instances where chi-square analysis was used, p values have been included in the text. A p value less than 0.01 was considered significant.
Results

Patients studied by RNA and ETT in addition to cardiac catheterization were similar to all patients undergoing cardiac catheterization for suspected CAD except that fewer had New York Heart Association (NYHA) class IV or progressive chest pain or a history of congestive heart failure (table 1). Catheterization results showed no significant differences between these two groups (table 2). The resting LVEF determined by RNA ranged from 0.16 to 0.92 (mean 0.59 ± 0.14) (± sd). The study population was similar to the group that underwent ETT in addition to cardiac catheterization. Of the 544 patients, 99 (18%) had completely normal coronary arteries, 46 (8.5%) had atherosclerotic changes that did not cause a 75% or greater occlusion of the diameter of a major coronary artery, 114 (21%) had one-vessel CAD, 135 (25%) had two-vessel disease, 126 (23%) had three-vessel disease, and 24 (4.4%) had left main CAD.

Diagnostic Accuracy of the ETT

The ETT was indeterminate in 151 (28%) of the 544 patients. When these 151 patients were excluded, the ETT had a sensitivity of 88% and a specificity of 46% for the diagnosis of three-vessel or left main CAD. When the ETT was applied for the diagnosis of left main disease only, the sensitivity was 91% and the specificity was 38%. The ETT was 84% sensitive and 61% specific for the diagnosis of two-vessel, three-vessel or left main CAD. Application of the ETT for the diagnosis of any significant CAD resulted in a sensitivity of 77% and a specificity of 76% (table 3). Comparable ETT sensitivities and specificities were obtained when patients without a previous myocardial infarction documented by characteristic ECG or enzyme changes or both were considered (table 4). Similar ETT sensitivities and specificities were observed in patients with a resting LVEF greater than or equal to 0.50 and no resting wall motion abnormalities.

Diagnostic Accuracy of the RNA

An abnormal radionuclide result was based solely upon a resting LVEF less than 0.50 in 45 of the 544 patients (8.3%). In 13 of the 544 patients (2.4%), the only abnormality observed during RNA was the development of an exercise-induced wall motion abnormality. Overall, an exercise-induced wall motion abnormality was present in 236 of the 544 patients (43%).

Applying the abnormal RNA criteria to the entire population of 544 patients resulted in a sensitivity of 92% and a specificity of 34% for the diagnosis of three-vessel or left main CAD. When the RNA was applied for the diagnosis of left main coronary artery disease only, the sensitivity was 83% and the specificity was 27%. The RNA was 88% sensitive and 43% specific for the diagnosis of two-vessel, three-vessel or left main disease. Application of the RNA for the diagnosis of significant CAD yielded a sensitivity of 85% and a specificity of 59% (table 5). The RNA sensitivities and specificities were similar in patients without a previous myocardial infarction (table 6) and in patients

---

**Table 1. Clinical Characteristics, Management and Outcome of Patients Evaluated for Suspected Coronary Artery Disease from January 1, 1977, to June 30, 1981**

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>3005 patients with cath (%)</th>
<th>1495 patients with ETT + cath (%)</th>
<th>544 patients with ETT + RNA + cath (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 years</td>
<td>9.6</td>
<td>11</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>&gt; 70 years</td>
<td>1.3</td>
<td>1.1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>96</td>
<td>97</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>Typical angina</td>
<td>59</td>
<td>56</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Atypical angina</td>
<td>32</td>
<td>37</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Nonanginal chest pain</td>
<td>5.5</td>
<td>6.8</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>Class IV angina</td>
<td>56*</td>
<td>52</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Progressive angina</td>
<td>41*</td>
<td>32</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>History of CHF</td>
<td>8.9*</td>
<td>5.0</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>40</td>
<td>34</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>History of hypertension</td>
<td>40</td>
<td>38</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>History of diabetes</td>
<td>11</td>
<td>9.1</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>69</td>
<td>68</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Peripheral bruises</td>
<td>12</td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Subsequent operation</td>
<td>36</td>
<td>29</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Subsequent death</td>
<td>7.3</td>
<td>5.6</td>
<td>5.5</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.005; all other differences not significant.

Abbreviations: cath = catheterization and coronary arteriography; ETT = exercise treadmill test; RNA = radionuclide angiocardiography; CHF = congestive heart failure.

---

**Table 2. Results of Cardiac Catheterization and Coronary Arteriography in Patients Evaluated for Suspected Coronary Artery Disease from January 1, 1977, to June 30, 1981**

<table>
<thead>
<tr>
<th>Cardiac function</th>
<th>3005 patients with cath (%)</th>
<th>1495 patients with ETT + cath (%)</th>
<th>544 patients with ETT + RNA + cath (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-V O₂ &gt; 5.5 vol%</td>
<td>12</td>
<td>7.4</td>
<td>7.6</td>
</tr>
<tr>
<td>Normal LV contractility</td>
<td>54</td>
<td>60</td>
<td>57</td>
</tr>
<tr>
<td>Diffusely abnormal LV contractility</td>
<td>5.9</td>
<td>3.1</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Coronary anatomy

<table>
<thead>
<tr>
<th>Coronary anatomy</th>
<th>20</th>
<th>23</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>7.7</td>
<td>8.9</td>
<td>8.5</td>
</tr>
<tr>
<td>Insignificant CAD</td>
<td>28</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>1-vessel CAD</td>
<td>21</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>2-vessel CAD</td>
<td>28</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Left main CAD</td>
<td>5.2</td>
<td>4.7</td>
<td>4.4</td>
</tr>
</tbody>
</table>

All differences were not significant.

Abbreviations: cath = catheterization and coronary arteriography; CAD = coronary artery disease; ETT = exercise treadmill test; RNA = radionuclide angiocardiography; LV = left ventricular; A-V O₂ = arteriovenous oxygen difference.
with a normal resting LVEF and no resting wall motion abnormalities.

Excluding patients who did not achieve an adequate exercise end point during RNA did not significantly alter the sensitivity (91% vs 92%) or the specificity (32% vs 34%) of the RNA for the diagnosis of anatomically extensive CAD (NS). Three-vessel or left main disease was less prevalent in patients who achieved 85% of their target heart rate (15%) and more prevalent in patients who developed angina (39%) or ECG ischemic changes (51%) during the RNA than in the overall population (28%).

Patients who took propranolol within 24 hours of the RNA had a higher prevalence of anatomically extensive CAD (33%) than patients who did not (26%). Despite this higher disease prevalence, the RNA was less sensitive (84% vs 94%) and less specific (31% vs 35%) for the diagnosis of severe CAD in patients who took propranolol. Excluding the 96 patients who were taking propranolol at the time of the RNA did not significantly change the sensitivity (94% vs 92%) or the specificity (35% vs 34%) of the RNA (NS).

**Comparison of RNA and ETT**

The RNA was more sensitive than the ETT ($p = 0.008$) for the diagnosis of significant CAD, but both tests were equally sensitive (NS) for the diagnosis of all other degrees of CAD. The ETT was more specific than the RNA ($p < 0.01$) for the diagnosis of all degrees of CAD.

In the 544 patients studied, the ETT was positive in 252, negative in 141 and indeterminate in 151 patients. The RNA was positive in 398 patients and negative in 146 patients. The prevalence of three-vessel or left main CAD was 41% in patients with a positive ETT, 35% in patients with a positive RNA and 44% in patients with both a positive ETT and a positive RNA. The prevalence of three-vessel or left main disease was 10% in patients with a negative ETT, 8% in patients with a negative RNA and 0% in patients with both tests.

**TABLE 3. Sensitivity and Specificity of the Exercise Treadmill Test in Patients with Adequate Exercise**

<table>
<thead>
<tr>
<th>Extent of CAD</th>
<th>Disease prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main CAD</td>
<td>22/393 (6%)</td>
<td>20/22 (91%)</td>
<td>139/371 (38%)</td>
</tr>
<tr>
<td>Three-vessel or left main CAD</td>
<td>118/393 (30%)</td>
<td>104/118 (88%)</td>
<td>127/275 (46%)</td>
</tr>
<tr>
<td>Two-vessel or greater CAD</td>
<td>216/393 (55%)</td>
<td>182/216 (84%)</td>
<td>107/177 (61%)</td>
</tr>
<tr>
<td>Any significant CAD</td>
<td>298/393 (76%)</td>
<td>229/298 (77%)</td>
<td>72/95 (76%)</td>
</tr>
</tbody>
</table>

*Abbreviation: CAD = coronary artery disease.*

**TABLE 4. Sensitivity and Specificity of the Exercise Treadmill Test in Patients with Adequate Exercise and No Previous Myocardial Infarction**

<table>
<thead>
<tr>
<th>Extent of CAD</th>
<th>Disease prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main CAD</td>
<td>12/233 (5.2%)</td>
<td>11/12 (92%)</td>
<td>92/221 (42%)</td>
</tr>
<tr>
<td>Three-vessel or left main CAD</td>
<td>65/233 (28%)</td>
<td>58/65 (89%)</td>
<td>86/168 (51%)</td>
</tr>
<tr>
<td>Two-vessel or greater CAD</td>
<td>107/233 (46%)</td>
<td>91/107 (85%)</td>
<td>77/126 (61%)</td>
</tr>
<tr>
<td>Any significant CAD</td>
<td>153/233 (66%)</td>
<td>121/153 (79%)</td>
<td>61/80 (76%)</td>
</tr>
</tbody>
</table>

*All differences were not significant ($p \geq 0.01$) compared with the exercise treadmill test results of table 3. Abbreviation: CAD = coronary artery disease.*

**TABLE 5. Sensitivity and Specificity of Radionuclide Angiocardiography**

<table>
<thead>
<tr>
<th>Extent of CAD</th>
<th>Disease prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main CAD</td>
<td>24/544 (4.4%)</td>
<td>20/24 (83%)</td>
<td>142/520 (27%)</td>
</tr>
<tr>
<td>Three-vessel or left main CAD</td>
<td>150/544 (28%)</td>
<td>138/150 (92%)</td>
<td>134/394 (34%)</td>
</tr>
<tr>
<td>Two-vessel or greater CAD</td>
<td>285/544 (52%)</td>
<td>251/285 (88%)</td>
<td>112/259 (43%)</td>
</tr>
<tr>
<td>Any significant CAD</td>
<td>399/544 (73%)</td>
<td>338/399 (85%)</td>
<td>85/145 (59%)</td>
</tr>
</tbody>
</table>

*Abbreviation: CAD = coronary artery disease.*

**TABLE 6. Sensitivity and Specificity of Radionuclide Angiocardiography in Patients with No Previous Myocardial Infarction**

<table>
<thead>
<tr>
<th>Extent of CAD</th>
<th>Disease prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main CAD</td>
<td>14/333 (4.2%)</td>
<td>11/14 (79%)</td>
<td>114/319 (36%)</td>
</tr>
<tr>
<td>Three-vessel or left main CAD</td>
<td>85/333 (26%)</td>
<td>75/85 (88%)</td>
<td>107/248 (43%)</td>
</tr>
<tr>
<td>Two-vessel or greater CAD</td>
<td>148/333 (44%)</td>
<td>124/148 (84%)</td>
<td>93/185 (50%)</td>
</tr>
<tr>
<td>Any significant CAD</td>
<td>208/333 (63%)</td>
<td>167/208 (80%)</td>
<td>76/125 (61%)</td>
</tr>
</tbody>
</table>

*All differences were not significant ($p \geq 0.01$) when compared with the radionuclide angiocardiography results of table 5. Abbreviation: CAD = coronary artery disease.*
negative (fig. 1). Similar prevalences were observed when only patients without a previous myocardial infarction were considered (fig. 2). Patients with both tests positive had a higher prevalence of three-vessel or left main disease and patients with both tests negative had a lower prevalence of three-vessel or left main disease than when either test was considered individually.

These data were used to calculate the sensitivity and specificity of all possible combinations of using both tests for the diagnosis of three-vessel or left main CAD (table 7). When both a positive ETT and a positive RNA were necessary for the diagnosis of three-vessel or left main disease, the sensitivity was 65% and the specificity was 68%. When three-vessel or left main CAD was considered to be present, unless both the ETT and the RNA were negative, the sensitivity was 100% and the specificity was 15%. Interpretation of either test being positive as indicative of three-vessel or left main disease yielded a sensitivity of 96% and a specificity of 29%.

Follow-up Data

Follow-up information on life-death status was known in 527 (97%) of the 544 patients in this study. Seventeen patients were lost to follow-up shortly after initial evaluation. After a mean follow-up period of 21 months, there were 29 deaths: 20 patients (69%) with a positive ETT and a positive RNA, two patients (7%) with a negative ETT and a positive RNA, six patients (21%) with an indeterminate ETT and a positive RNA, and one patient (3%) with an indeterminate ETT and a negative RNA (fig. 3).

**Discussion**

Prospective randomized studies have demonstrated an improved survival in surgically treated patients with three-vessel or left main CAD. Recognition of patients with anatomically extensive CAD is more clinically important than identification of patients with any significant coronary disease, as the former group would probably benefit from early cardiac catheterization and surgery, whereas the latter group is so heterogeneous that no single therapy is clearly indicated. Clinical information combined with exercise electrocardiography has attained a sensitivity of 0.70–0.90 and a specificity of 0.30–0.40 for diagnosis of severe CAD. Exercise thallium-201 myocardial imaging has demonstrated a sensitivity of 0.90–0.95 and a specificity of 0.10–0.30 in recognizing patients with three-vessel or left main CAD. Our laboratory recently determined that rest and exercise radionuclide angiography is highly sensitive (0.90) and moderately specific (0.58) for the diagnosis of any significant CAD. Since the magnitude of abnormality of left ventricular function correlated with the anatomic extent of the coronary disease, we felt that the RNA might be a very sensitive indicator of anatomically extensive CAD. This investigation was undertaken to assess the relative accuracy of the RNA and the ETT for diagnosis of anatomically extensive CAD in a large population of patients with non-infarct-related chest pain.
group of patients evaluated for suspected coronary disease.

The study population had a lower prevalence of NYHA class IV angina, progressive angina or a history of congestive heart failure than the 3005 patients who underwent cardiac catheterization. This difference reflects the fact that patients with more severe CAD undergo cardiac catheterization directly without prior exercise stress testing by ETT or RNA. Since no significant differences were found between the study group and the 1495 patients undergoing ETT in addition to cardiac catheterization, the study population appears representative of all patients undergoing exercise stress testing for suspected coronary artery disease at this institution.

The sensitivity and specificity data show that the ETT and the RNA are comparable for diagnosis of differing anatomic extents of coronary artery disease. The RNA is more sensitive (85% vs 77%) but less specific (59% vs 76%) than the ETT in recognizing patients with a 75% or greater stenosis of one or more coronary arteries. This agrees with our previous report, and the present study extends this analysis to more severe degrees of coronary arterial involvement. The RNA is as sensitive as, but less specific than, the ETT for the diagnosis of two-vessel or greater CAD, of three-vessel or left main disease, and of left main coronary disease only. The low RNA specificity has been noted previously, and the reason for an abnormal left ventricular response to exercise in patients with chest pain and normal coronary arteriograms is an important topic for further investigation. In the present study, the low RNA specificity was largely due to abnormal tests in patients with one- or two-vessel CAD. The RNA is also significantly less specific in women and the present study population included 148 (27%) women. Similar limitations of test specificity in women have been observed with the ETT.

Our results indicate that sequential use of the ETT and the RNA is the best approach to identify patients with anatomically extensive CAD in a population with a high prevalence of severe CAD. The prevalence of three-vessel or left main CAD was 41% in patients with a positive ETT. A positive RNA increased this prevalence by only 3% and a negative RNA reduced this prevalence to 22%. This small amount of additional diagnostic information does not justify performance of a RNA in patients with a positive ETT. The RNA proved most effective in the large number of patients with a negative or indeterminate treadmill. In this study, this subgroup had a 16% prevalence of severe CAD. A positive RNA increased this prevalence to 23%, while a negative RNA decreased this prevalence to 5%.

If a positive ETT, or a negative or indeterminate ETT and a positive RNA were used as selection criteria for cardiac catheterization, 425 of the 544 patients in this study would have undergone cardiac catheterization. One hundred forty-four (34%) of these 425 patients actually had anatomically extensive CAD. One hundred nineteen patients (22% of the total population) would not have undergone cardiac catheterization and only six of these patients (5%) had three-vessel or left main CAD. Five of these patients, including the patient with left main disease, are alive 24–36 months after their initial evaluation and one patient is lost to follow-up. Requiring a positive ETT or a positive RNA for cardiac catheterization increased the likelihood that patients undergoing this invasive procedure would have anatomically extensive CAD (34% vs 28% if all patients underwent cardiac catheterization directly).

Sequential use of the ETT and the RNA would have saved 119 patients the risk and inconvenience of cardiac catheterization. This approach would have also reduced the cost of diagnosis in these patients. Based on average costs at Duke University Medical Center, cardiac catheterization on all 544 patients would cost $1,556,928 ($2862 per cardiac catheterization including hospitalization). By using the ETT and the RNA sequentially to eliminate catheterizations, 544 ETTS would be performed ($200 per ETT); 292 RNAs would be done ($612 per rest and exercise RNA), and 425 cardiac catheterizations would be performed for a total cost of $1,503,854. Sequential use of the ETT and the RNA would have cost $53,074 less than performing cardiac catheterization on all patients. These estimated savings may be conservative in that loss of work days and cost of hospital resources not reflected in the daily room charge were not figured into the cost of cardiac catheterization. One hundred nineteen cardiac catheterizations would have been eliminated and only six patients excluded from cardiac catheterization would have had anatomically extensive CAD.

Preliminary follow-up data suggest that the RNA may be more effective than the ETT in assessing prognosis. Twenty of the 29 patients (69%) who died after initial evaluation had a positive ETT, while 28 of these patients (97%) had a positive RNA (chi-square = 7.33, p = 0.006). The majority of deaths occurred in patients with a positive ETT and a positive RNA, indicating that this subgroup is at higher risk for subsequent death. Nine deaths (31%) occurred in patients with a negative or indeterminate ETT, and a positive RNA identified eight of these nine patients. Sequential use of the ETT and the RNA would have identified 28 of the 29 patients who subsequently died as having probable severe CAD. The one patient missed by this approach had insignificant CAD and died 1 day after urgent myocardial revascularization performed for preinfarction angina. Coronary artery spasm was probably a significant factor in this death. These preliminary follow-up data further support the sequential use of the ETT and the RNA in the evaluation of a population with a high prevalence of anatomically extensive CAD.

References
2. Humphries JO, Kuller L, Ross RS, Friesinger GC, Page EE: Natural history of ischemic heart disease in relation to arteriographic
findings. Circulation 49: 489, 1974
3. Buggraf GW, Parker JO: Prognosis in coronary artery disease —
angiographic, hemodynamic and clinical factors. Circulation 51:
146, 1975
4. Sharma B, Goodwin JF, Raphael MJ, Steiner RF, Rainbow RG,
Taylor SH: Left ventricular angiography on exercise: a new method
of assessing left ventricular function in ischemic heart disease. Br
Heart J 38: 59, 1976
5. Borer JS, Bacharach SL, Green MV, Kent KM, Epstein SE, John-
ston GS: Real-time radionuclide cineangiography in the noninva-
sive evaluation of global and regional left ventricular function at
rest and during exercise in patients with coronary artery disease. N
6. Rerych SK, Scholz PM, Newman GE, Sabiston DC Jr, Jones RH:
Cardiac function at rest and during exercise in normals and patients
7. Berger HJ, Reduto LA, Johnstone DE, Borkowski H, Sands J,
Cohen L, Langou R, Gottschalk A, Zaret B: Global and regional
left ventricular response to bicycle exercise in coronary artery
disease: assessment by quantitative radionuclide angiograph-
8. Jengo JA, Oren V, Conant R, Brizendine M, Nelson T, Uszler JM,
Mena I: Effects of maximal exercise stress on left ventricular func-
tion in patients with coronary artery disease using first pass radio-
nuclide angiography: a rapid, noninvasive technique for de-
termining ejection fraction and segmental wall motion. Circulation
59: 60, 1979
9. Borer JS, Kent KM, Bacharach SL, Green MV, Rosing DR,
Seides SF, Epstein SE, Johnston GS: Sensitivity, specificity and
predictive accuracy of radionuclide cineangiography during exercise
in patients with coronary artery disease. Comparison with exercise
electroangiography. Circulation 60: 572, 1979
10. Newman GE, Rerych SK, Upton MT, Sabiston DC Jr, Jones RH:
Comparison of electroangiography and left ventricular functional
PM, Upton MT, Peter CA, Austin EH, Leong K, Gibbons RJ,
Cobb FR, Coleman RE, Sabiston DC Jr: Accuracy of diagnosis of
coronary artery disease by radionuclide measurement of left ven-
12. Rosati RA, McNeer JF, Starmer CF, Mittler BS, Morris JJ Jr,
Wallace AG: A new information system for medical practice. Arch
Intern Med 135: 1017, 1975
13. Bruce RA, Horstein TR: Exercise stress testing in evaluation of
patients with ischemic heart disease. Prog Cardiovasc Dis 11: 371,
1969
14. McNeer JF, Margolis JR, Lee KL, Kisslo JA, Peter RH, Kong YH,
Behar VS, Wallace AG, McCants CB, Rosati RA: The role of the
exercise test in the evaluation of patients for ischemic heart disease.
Circulation 57: 64, 1978
15. Upton MT, Rerych SK, Newman GE, Bounous EP Jr, Jones RH:
The reproducibility of radionuclide angiographic measurements of
left ventricular function in normal subjects at rest and during exercise.
Circulation 62: 126, 1980
16. Rerych SK, Scholz PM, Sabiston DC Jr, Jones RH: Effects of
exercise training on left ventricular function in normal subjects: a
longitudinal study by radionuclide angiography. Am J Car-
diol 45: 244, 1980
17. Takaro T, Hultgren HN, Lipton MJ, Detre KM, and participants in
the study group: The VA cooperative randomized study of surgery
for coronary arterial occlusive disease. II. Subgroup with signif-
icient left main lesions. Circulation 54 (suppl III): III-107, 1976
18. Murphy ML, Hultgren HN, Detre K, Thomsen J, Takaro T, and
participants of the Veterans Administration Cooperative Study:
Treatment of chronic stable angina. A preliminary report of survi-
val data of the randomized Veterans Administration Cooperative
19. European Cooperative Surgery Study Group: Coronary artery by-
pass surgery in stable angina pectoris: survival at two years. Lancet
1: 889, 1979
20. Weiner DA, McCabe CH, Ryan TJ: Identification of patients with
left main and three vessel coronary artery disease with clinical and
21. Detry JMR, Kapita BM, Cosyns J, Sotiaux B, Brasseau LA, Rous-
seau MF: Diagnostic value of history and maximal exercise electro-
angiography in men and women suspected of coronary artery
22. Weiner DA, Ryan TJ, McCabe CH, Kennedy JW, Schloss M,
Tristani F, Chairman BR, Fisher LD: Exercise stress testing —
correlations among history of angina, ST-segment response and
prevalence of coronary artery disease in the coronary artery surgery
23. Rehn T, Griffith LS, Achuff SC, Bailey IK, Bulkey BH, Burow R,
Pitt B, Becker LC: Exercise thallium-201 myocardial imaging in
left main coronary artery disease: sensitive but not specific. Am J
Cardiol 48: 217, 1981
24. Iskandrian AS, Segal BL: Value of exercise thallium-201 imaging
in patients with diagnostic and nondiagnostic exercise electrocar-
25. Bailey IK, Griffith LSC, Rouleau J, Strauss HW, Pitt B: Thallium-
201 myocardial imaging at rest and during exercise — comparative
sensitivity to electrocardiography in coronary artery disease. Cir-
culation 55: 79, 1977
26. Barolky SM, Gilbert CA, Farughi A, Nutter DO, Schlant RC:
Differences in electrocardiographic response to exercise of women
Comparison of rest and exercise radionuclide angiography and exercise treadmill testing for diagnosis of anatomically extensive coronary artery disease.

C T Campos, H W Chu, H J D'Agostino, Jr and R H Jones

_Circulation_. 1983;67:1204-1210
doi: 10.1161/01.CIR.67.6.1204

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/67/6/1204