Accuracy of Exercise $^{201}$TI Myocardial Scintigraphy in Asymptomatic Young Men

Robert S. Schwartz, MD; William G. Jackson, MS; Paul V. Celio, MD; Londe A. Richardson, MD; and James R. Hickman Jr., MD

**Background.** Little is known about the diagnostic usefulness of $^{201}$TI scintigraphy for detecting asymptomatic coronary artery disease in apparently healthy men. We thus evaluated planar $^{201}$TI exercise myocardial scintigraphy in 845 asymptomatic male military aircrew undergoing coronary arteriography because of abnormal noninvasive tests suggesting possible myocardial ischemia.

**Methods and Results.** Patients were stratified by prior disease risk into six subgroups using age ($<45$ and $\geq 45$ years) and ratio of total to high density lipoprotein cholesterol ($<4.5, 4.5-6.0$, and $>6.0$). Significant coronary artery disease ($\geq 50\%$ diameter stenosis in any major coronary artery) was present in 143 (16.9\% prevalence). Overall sensitivity and specificity of $^{201}$TI scintigraphy adjusted for verification bias were estimated to be $45\pm4\%$ and $78\pm1\%$, respectively. These values are lower than corresponding values accepted for clinical populations. Positive and negative predictive values varied across subgroups. A normal thallium scan indicated low risk of disease, but an abnormal test was likely to be a false-positive result. A logistic equation was retrospectively fit to the data for estimating the probability of disease given age, cholesterol ratio, and thallium results. Within each quintile of estimated risk, the average risk did not differ significantly from the observed disease prevalence.

**Conclusions.** Exercise $^{201}$TI scintigraphy is limited by the frequent occurrence of false-positive tests in detecting asymptomatic, anatomic coronary artery disease in young men in accordance with Bayesian probability theory. (Circulation 1993;87:165–172)

**Key Words** • exercise • $^{201}$TI • scintigraphy • coronary artery disease • Bayes' theorem

Exercise $^{201}$TI myocardial scintigraphy is widely used for detecting reversible myocardial ischemia. Although its accuracy is established in the symptomatic, clinical population, little is known about its value in detecting the asymptomatic, younger individual who may have coronary artery disease and myocardial ischemia.

The possibility of asymptomatic coronary disease is typically of concern in individuals with elevated cardiac risk factors, in those wishing to begin a vigorous exercise program, or in those engaged in hazardous occupations such as military or commercial aviation. Such populations generally have a low coronary artery disease prevalence and lack many risk factors traditionally associated with significant disease. Accurate noninvasive detection of coronary artery disease thus is more difficult because noninvasive methods such as the exercise treadmill test, which function adequately in clinical populations, show significant decrease in predictive value when applied to lower prevalence groups. This is in accordance with Bayesian probability theory, and there is substantial literature describing this problem.

Although thallium scintigraphy has been proposed as a method of detecting asymptomatic coronary artery dis-
significant coronary artery disease in the asymptomatic male given his age, cholesterol ratio, and thallium scintigraphic result; and 3) to provide quantitative data for the practicing cardiologist on thallium performance in the asymptomatic, younger man.

Methods

Study Population

All US Air Force aircrew members aged ≥35 years are regularly screened for health problems including coronary artery disease. Some individuals are disqualified from flying for obvious health problems, whereas others are referred to the US Air Force School of Aerospace Medicine (USAFSAM) when diagnoses are uncertain or when special testing is required. Individuals so referred are asymptomatic from a cardiac standpoint. Individuals referred for possible cardiac diagnoses are required to undergo both treadmill testing and exercise thallium scintigraphy. If either the treadmill or thallium is abnormal, coronary arteriography is required to remain on flying status. Aviators referred for noncardiac diagnoses (e.g., ophthalmological problems) are not required to undergo either treadmill or thallium testing. All treadmill testing is symptom limited, and a test is interpreted as abnormal if there is ST segment depression of ≥1.0 mm at 80 msec after the J point, regardless of the slope.

Cardiac catheterization is mandatory to remain on flying status if an individual has 1) any abnormal noninvasive test for reversible ischemia (symptom-limited treadmill test, exercise thallium scintigraphy, or MUGA radionuclide ventricular angiography), 2) coronary artery fluoroscopy positive for calcification, 3) three or more consecutive ventricular premature beats with exercise or on Holter ambulatory monitoring, or 4) acquired left bundle branch block on any ECG record.

The arteriographical study population consisted of 845 consecutive male aircrew members undergoing cardiac catheterization because of possible coronary artery disease. All patients were asymptomatic from a cardiac standpoint.

201T1 Scintigraphy

All patients fasted for at least 8 hours before testing. For each study, 2.2 mCi 201T1 i.v. was injected within 1 minute of peak exercise (determined by symptom-limited treadmill test the previous day) after the USAFSAM (modified Balke) protocol. Imaging began within 6 minutes of injection and was repeated at 4 hours. Images were obtained in the anterior, 45° left anterior oblique, and 67° left anterior oblique positions during 6-minute scans. All images were read before catheterization by experienced nuclear cardiologists without knowledge of patient identity, coronary arteriographical results, diagnosis, clinical history, or results of other noninvasive tests. Images were interpreted visually and graded normal if there were no perfusion defects and no reperfusion abnormalities. Studies were considered nondiagnostic if there were areas of unmatched reperfusion abnormalities or areas of delayed washout. A scan was interpreted as abnormal if there were fixed perfusion defects or if any area showed reperfusion abnormalities. Potential imaging artifacts resulting from sources such as apical thinning, upper septal defects in cases of left bundle branch block, and inferior wall attenuation were considered in image interpretation.

Coronary Arteriography

Coronary arteriography was performed using the Judkins technique. Each arteriogram was reviewed by at least two experienced staff cardiologists. In general, angiographers were not specifically blinded to thallium results. Obstructing lesions were visually graded by diameter stenoses. For this study, “significant” coronary diameter disease was defined as one or more stenoses of ≥50% diameter in any major coronary artery, including large diagonal and marginal vessels. A patient was defined as having “mild” disease if arteriographic lesions were found, none of which was ≥50% diameter stenosis.

Statistical Analysis

The 845 patients were stratified by both age (<45 and ≥45 years) and by cholesterol ratio (<4.5, 4.5–6.0, and >6.0) to form six subgroups ranging in size from 68 to 266 patients. Within each stratum, unadjusted sensitivity and specificity, positive and negative predictive values, and odds ratios were calculated by standard methods, omitting nondiagnostic examinations. These calculations were then performed again including the nondiagnostic examinations. Homogeneity of these sensitivities, specificities, and positive predictive values across strata were tested with Pearson’s χ² statistic for contingency tables. Estimates of overall sensitivity and specificity (ignoring strata), adjusted for “verification bias,” were computed using the method described by Begg and Greenes. As noted above, bias results when evaluating a diagnostic test when that test itself is used to determine which patients will receive the verifying test. In this situation, positive tests will be overrepresented in the patients who went on to verification. This causes observed sensitivity to subsequently be increased over “true” sensitivity and observed specificity to be decreased over “true” specificity.

The debiasing method of Begg and Greenes used in this study accounts for the selection bias induced when an abnormal thallium test itself leads to cardiac catheterization. Briefly, in this method, correction for selection bias is done as follows. The decision by a clinician to proceed further (to “verify”) in the evaluation of a patient is not only influenced by the test under study but also by visible clinical factors. In an unverified group of individuals, all of whom have the same noninvasive test results, disease status will be conditionally independent of whether the verifying test is performed.

Figure 1 graphically depicts the patient groups studied. There were 2,175 patients evaluated, 845 of whom underwent coronary arteriography. Of these 845, there were 191 patients with nondiagnostic thallium results, leaving 654 with definitive (normal or abnormal) results. The remaining 1,330 patients were those who underwent thallium scintigraphy during the same time period but did not undergo coronary arteriography. In this 1,330-patient group without coronary arteriography, 961 had definitive thallium results. Of these 961, 416 had completely normal noninvasive test results (i.e., all patients in this group had normal thallium scintigraphy). The group for adjusted estimates of sensitivity and specificity thus consisted of 654 plus 961, or 1,615, patients.
Homogeneity of odds ratios across groups was tested by the Breslow-Day technique. The overall odds ratio of Mantel and Haenszel was computed and tested against unity (1.0), and confidence limits were calculated.

An unstratified analysis for estimating risk of significant disease was computed by age and cholesterol ratio in a logistic multiple regression model. Age and cholesterol ratio were used as continuous prediction variables and thallium result as a binary variable (abnormal, 1; normal, 0). The regression parameter for thallium and its standard error were used to compute an estimate with confidence limits for the odds ratio of significant disease given an abnormal thallium scintigram relative to a normal test result.

Results

Population Data

Of the 2,175 asymptomatic patients with thallium test results, 845 underwent coronary arteriography. The reasons for arteriography in this group of 845 are listed in Table 1. Age, cholesterol, and triglyceride characteristics for these 845 patients are shown in Table 2. Tables 3 and 4 show coronary artery disease data for this group. Significant coronary artery disease was present in 143 of 845 (population prevalence, 16.9%). An individual must have had a significant (≥50% diameter stenosis) lesion in one, two, or three of the major coronary arteries to be included in the one-, two-, or three-vessel disease categories, respectively.

Thallium Test Performance

Of 845 thallium tests performed in catheterized patients, 268 (31.7%) were interpreted as normal, 191 (22.6%) were nondiagnostic, and 386 (45.7%) were abnormal. Table 5 shows thallium results by coronary artery disease category for the two age groups subdivided by cholesterol ratio.

In the 845-patient group undergoing catheterization, 73 (8.6%) had normal thallium and treadmill tests (recommended for arteriography because of positive coronary fluoroscopy, ventricular tachycardia, left bundle branch block, etc.). 223 (26.4%) had abnormal thallium and normal treadmill tests, 195 (23.1%) had normal thallium and abnormal treadmill tests, and 163 (19.3%) had both thallium and treadmill tests abnormal. The remaining 191 patients (22.6%) had other abnormal or nondiagnostic noninvasive tests.

Table 6 shows ²⁰¹¹TI performance in terms of unadjusted sensitivities and specificities and predictive values stratified by risk subgroup. The Pearson χ² for the unadjusted sensitivities across all six subgroups was 1.47 with 5 degrees of freedom (df) (p=0.92). Unadjusted specificities, also compared across all six subgroups, resulted in a χ² value of 1.65 (5 df, p=0.90). Thus, there were no significant differences across risk strata among the unadjusted sensitivities and specificities.

Table 7 shows results of sensitivity and specificity for the group of patients who had thallium scans read as

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

**Figure 1.** Separation of the overall 2,175 patients into subgroups for study.

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**Table 1. Reasons for Coronary Arteriography in 845 Aviators**

<table>
<thead>
<tr>
<th>Reason</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal thallium scintigraphy only</td>
<td>163</td>
<td>19.2</td>
</tr>
<tr>
<td>Abnormal treadmill exercise test only</td>
<td>284</td>
<td>33.6</td>
</tr>
<tr>
<td>Abnormal coronary fluoroscopy only</td>
<td>45</td>
<td>5.3</td>
</tr>
<tr>
<td>Ventricular tachycardia only</td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td>Left bundle branch block only</td>
<td>8</td>
<td>0.9</td>
</tr>
<tr>
<td>Atypical symptoms only</td>
<td>8</td>
<td>0.9</td>
</tr>
<tr>
<td>Two or more of the above</td>
<td>271</td>
<td>32.0</td>
</tr>
<tr>
<td>Other*</td>
<td>60</td>
<td>7.1</td>
</tr>
</tbody>
</table>

*The reasons for “other” were not available but include patient request for arteriography and patients with diagnoses of atrial fibrillation or mitral valve prolapse. These diagnoses do not require coronary arteriography to remain on flying status.
TABLE 2. Age, Cholesterol, and Triglycerides in 845 Asymptomatic Men With Exercise Thallium Tests and Coronary Arteriography by Disease Category

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients with no disease (n=579)</th>
<th>Patients with disease (n=266)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; range)</td>
<td>40.7±5.8 (22–65)</td>
<td>45.2±5.4 (27–61)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl; range)</td>
<td>206±38 (117–364)</td>
<td>233±44 (130–473)</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl; range)</td>
<td>47±12 (20–96)</td>
<td>42±10 (20–78)</td>
</tr>
<tr>
<td>Cholesterol ratio (mg/dl; range)</td>
<td>4.71±1.53 (2.1–14.9)</td>
<td>5.77±1.75 (2.4–14.8)</td>
</tr>
<tr>
<td>Triglycerides (mg/dl; range)</td>
<td>138±93 (29–972)</td>
<td>167.3±89 (18–620)</td>
</tr>
</tbody>
</table>

HDL, high density lipoprotein.

Values are given as mean±SD.

Disease was defined as any diameter stenosis of ≥10%.

Triglyceride data were available on only 541 of the nondiseased patients and 257 of the diseased patient groups.

nondiagnostic compared with those with normal thallium scans. The χ² value for unadjusted sensitivities across the six groups here was 1.47 (5 df, p=0.92). Similarly, χ² for unadjusted specificities across the same groups was 6.36 (5 df, p=0.27). Once again, there were no significant differences among the unadjusted sensitivities and specificities across strata.

Overall estimates of sensitivity and specificity adjusted for “verification bias” were computed by the method of Begg and Greenes. The frequencies needed to adjust for verification bias in normal versus abnormal thallium scans and normal versus nondiagnostic thallium scans are given in Table 8. Table 9 summarizes the calculations of biased and debiased sensitivity and specificity. The debiased sensitivity for an abnormal thallium was 45%, markedly lower than that in symptomatic populations, reflecting the possibility that the magnitude of disease in asymptomatic groups is less than in clinical populations.

Positive predictive values were compared across all six subgroups. The χ² statistic was 41.3 with 5 df, (p<0.001) providing evidence that positive predictive value varied with population subgroup and, thus, disease prevalence. The odds ratio for disease given an abnormal versus a normal thallium scan was calculated for each subgroup and results are shown in Table 10. The test for homogeneity of odds ratios across strata yielded a χ² value of 1.34 with 5 df (p=0.93), indicating no significant change across these subgroups. The average odds ratio across all patients with definite thallium results and coronary arteriography was 3.85 with confidence limits (2.34, 6.35).

Logistic Regression Results

Fitting the thallium and angiographic data to a logistic multiple regression model resulted in the following expression to calculate significant disease likelihood given age, cholesterol ratio, and thallium result:

\[
\text{Disease likelihood} = \frac{1}{1 + e^{(3.4 - \text{age} - \text{cholesterol ratio} - \text{thallium})}}
\]

where a is 0.0901 (age coefficient: p<0.001), r is 0.3766 (cholesterol ratio coefficient, p<0.001), th is 1.2637 (thallium coefficient, p<0.001), normal thallium is thal (0), and abnormal thallium is thal (1). The “Appendix” demonstrates the use of this expression with an example. The estimated odds ratio based on the thallium coefficient in the logistic risk equation is 3.54, with 95% confidence limits of (2.08, 6.02), values close to those calculated in the stratified analysis.

Disease probability was calculated using this equation, ignoring thallium results, and then compared with disease probability when thallium results were known. Figure 2 shows these probabilities for asymptomatic 30-, 40-, and 50-year-old men. Disease probability resulting from a normal or abnormal thallium scan can thus be directly assessed given the cholesterol ratio.

The 654 patients with definite thallium results and coronary arteriography were studied to assess the fit of the regression equation to the observed patient data. Five risk quintiles were created by placing the 131 patients with the lowest risk in one group, the 131 with the next lowest risk in a second group, and similar placement for the remaining patients. In the highest risk quintile there were 130 patients. Within each quintile, the mean calculated risk was compared with the observed disease prevalence. Confidence limits (95%) for disease prevalence within the population represented by each quintile were also calculated; the results are shown in Figure 3. In each case, the mean calculated risk was found to lie within the 95% confidence limits.

Discussion

Little is known about the natural history of asymptomatic coronary artery disease and myocardial ischemia, despite much recent attention. A comprehensive understanding of these processes could be beneficial since early detection might avoid unexpected and catastrophic ischemic events in some patients. Assuming that asymptomatic coronary disease precedes angina pectoris or myocardial infarction, the likelihood that a US male will experience myocardial infarction or death from coronary disease before age 65 is nearly 20%, making this problem a national public health issue.

TABLE 3. Coronary Artery Disease in 845 Asymptomatic Men With Exercise Thallium Tests and Coronary Arteriography

<table>
<thead>
<tr>
<th>Coronary artery disease</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No disease detected</td>
<td>579</td>
</tr>
<tr>
<td>Mild disease only (all lesions &lt;50%)</td>
<td>123</td>
</tr>
<tr>
<td>Significant disease (one or more lesions ≥50% stenosis)</td>
<td>143</td>
</tr>
</tbody>
</table>

TABLE 4. One-, Two-, and Three-Vessel Coronary Artery Disease in 143 Asymptomatic Men With Significant Coronary Artery Disease (One or More Lesions ≥50% Stenosis)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-vessel disease</td>
<td>69</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>50</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>24</td>
</tr>
</tbody>
</table>
Exercise $^{201}$TI scintigraphy has been suggested as a method for detecting completely asymptomatic coronary disease, but few studies have addressed the diagnostic value of this procedure in such populations. Thallium exercise testing is well established in the symptomatic, clinical patient population, with sensitivity estimates varying from 58% to >90%. Similarly, specificity is estimated from 85% to 100%. Gerson and associates combined results in a meta-analytic review of previous studies and calculated an overall sensitivity and specificity of 83.6% and 88.4%, respectively, based on a total of 2,413 patients. Studies using quantitative thallium scintigraphy report even better results, substantially improved over the treadmill test.

This study used planar thallium imaging because single-photon emission computed tomography (SPECT) imaging was not available during the years of this study. The SPECT method demonstrates higher photon sensitivity with no overlap of myocardial regions examined. However, there may be more false-positive tests due to patient motion. Comparative studies have suggested improved detection of multivessel disease using SPECT. The usefulness of SPECT thallium imaging in detecting asymptomatic coronary artery disease is also unknown, but concern arises when considering the potentially increased number of false-positive responses.

The clinical patient groups used in prior studies are generally older and symptomatic and have higher coronary artery disease prevalence (62.6% in Gerson's pooled results). Studies of patients from clinical catheterization populations are thus highly selected, strongly biased toward patients with disease.

The excellent test performance previously reported does not necessarily apply to lower prevalence patient groups such as younger, asymptomatic men. The asymptomatic group of aviators in this study was substantially closer to the asymptomatic general population than clinical patient groups used for prior studies. This is borne out by an observed coronary artery disease prevalence of 16.9%, roughly one fourth the prevalence in most clinical studies. This patient group thus provided a unique chance to evaluate the accuracy of exercise thallium in a low prevalence population.

The observed sensitivity and specificity for significant disease were substantially lower than for clinical populations as were predictive values, as anticipated by Bayesian probability. In all risk subgroups, unadjusted positive predictive value and specificity were <50% and, as expected, were worst in the lowest-risk subgroups. Thus, there is at least a 50% likelihood that an abnormal thallium study in an asymptomatic patient is false-positive, even if the patient is at higher risk in terms of age and cholesterol ratio. If he is <45 years old and has a cholesterol ratio <4.5, the probability that an abnormal thallium is false-positive may be >90%. Based on individual reasons (such as occupation) for performing thallium scintigraphy and the resulting low disease probabilities regardless of scintigraphic result, the physician must decide whether to perform thallium testing at all in this patient group (i.e., no diabetics, no untreated hypertension, etc.).
TABLE 8. Thallium Scan Results Among 2,175 Asymptomatic Aviators

<table>
<thead>
<tr>
<th>Positive criterion</th>
<th>No. of positives</th>
<th>TP</th>
<th>FP</th>
<th>TN</th>
<th>FN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic or abnormal</td>
<td>1,100</td>
<td>96</td>
<td>290</td>
<td>412</td>
<td>47</td>
</tr>
<tr>
<td>Abnormal</td>
<td>540</td>
<td>123</td>
<td>454</td>
<td>48</td>
<td>20</td>
</tr>
</tbody>
</table>

TP, true-positives in the angiographical subset; FP, false-positives in the angiographical subset; TN, true-negatives in the angiographical subset; FN, false-negatives in the angiographical subset.

Bias appeared in this study population since some aviators were referred for coronary arteriography by the very diagnostic test (thallium scintigraphy), which was being evaluated. The observed thallium performance values were adjusted using the method of Beggs and Greenes. This method stratifies patients according to measured risk factors and then assumes within each stratum that disease prevalence is independent of arteriographic verification. Observed prevalence data are used to estimate disease prevalence in the unverified group, those patients who did not undergo arteriography.

With this independent adjustment method, this study found sensitivities and specificities that were in general agreement with adjusted values calculated by Diamond and Beggs, Greenes, and Iskandrian et al., which also discuss SPECT performance.

A reassuring finding was that predictive values were dependent on disease prevalence. Conversely, unadjusted sensitivity and specificity were not dependent on prevalence, all in accordance with Bayes’ theorem.

The logistic risk equation derived to estimate the probability of significant disease in this asymptomatic young population used age and cholesterol ratio combined with thallium result. The stratification by age and cholesterol ratio permitted better thallium performance since higher-risk subgroups could be selected where disease prevalence was higher. The logistic regression modeling also indicated no interaction between thallium scintigraphic results and either age or cholesterol ratio. Thus, the thallium stress test performs equally well regardless of age or cholesterol ratio as measured by the odds ratio. An abnormal thallium stress test conferred an independent risk for significant coronary disease 2.83-fold that of a normal test.

In an earlier study from this institution, Uhl et al. showed substantially better results using exercise thallium testing to detect significant coronary disease in a smaller series of 191 asymptomatic men (41 with disease), reporting a predictive value of 74%, sensitivity of

TABLE 9. Biased and Debiased Sensitivities and Specificities

<table>
<thead>
<tr>
<th>Test result</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biased</td>
<td>Debiased</td>
</tr>
<tr>
<td>Abnormal</td>
<td>67±4</td>
<td>45±4</td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>19±5</td>
<td>30±6</td>
</tr>
<tr>
<td>Abnormal or nondiagnostic</td>
<td>86±3</td>
<td>75±4</td>
</tr>
</tbody>
</table>

TABLE 10. Odds Ratios for Abnormal Versus Normal Thallium Scintigraphy (845 Asymptomatic Men)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cholesterol ratio</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;45</td>
<td>&lt;4.5</td>
<td>2.67</td>
</tr>
<tr>
<td>4.5–6.0</td>
<td></td>
<td>4.06</td>
</tr>
<tr>
<td>&gt;6.0</td>
<td></td>
<td>3.90</td>
</tr>
<tr>
<td>≥45</td>
<td>&lt;4.5</td>
<td>2.79</td>
</tr>
<tr>
<td>4.5–6.0</td>
<td></td>
<td>6.9</td>
</tr>
<tr>
<td>&gt;6.0</td>
<td></td>
<td>3.01</td>
</tr>
</tbody>
</table>

FIGURE 2. Calculated probability of significant coronary artery disease versus cholesterol ratio and thallium scan results for an asymptomatic man aged 30 (panel A), 40 (panel B), and 50 (panel C). In each case, the middle curve shows a separate logistic regression equation derived using age and cholesterol ratio only and ignoring thallium test result. Generally, these curves lie closer to the “abnormal” thallium curve, indicating that more information is gained from a negative than from a positive thallium result. ABN, abnormal thallium result; NOR, normal result; none, calculation ignoring thallium result; HDL, high density lipoproteins.
95%, and specificity of 95%. Differences between the current study and this previous research might be from the following causes. In Uhl et al’s study, all aviators had an abnormal treadmill test as opposed to the current study. In Uhl et al’s study, there also were fewer cases of “subcritical” disease (7.8% versus 14.6% in the present study). It is thus possible that in the present study, lesions that were graded as anatomically “insignificant” were physiologically important and created thallium scintigraphic abnormalities, resulting in some cases being misclassified as false-positive. Each of these factors may have contributed separately to the different results and conclusions. Regardless, earlier hopes for thallium scintigraphy as a potent independent predictor of asymptomatic coronary artery disease have not materialized after further study of a larger and less-selected patient group. This is principally due to the large number of false-positive tests.

Conclusions

Compelling clinical or occupational circumstances are sometimes encountered where detection of coronary artery disease in an asymptomatic man is quite important. The decision to undertake cardiac catheterization in such a patient is usually made when an abnormal noninvasive test suggests potential coronary artery disease. This study indicates that in completely asymptomatic men, many normal or minimally diseased individuals could undergo cardiac catheterization based on thallium test results. Pretest stratification by age and cholesterol ratio may partially alleviate this problem.

When evaluating the possibility of coronary artery disease in the asymptomatic individual engaged in a hazardous occupation, test sensitivity should be valued over specificity. The physician must have a clear understanding of noninvasive test performance before committing a patient to a test whose poor specificity may lead to coronary arteriography (see “Appendix” for an example). The “need to know” regarding coronary artery disease in any asymptomatic patient thus must be balanced against the risks and expense of cardiac catheterization and the patient’s likelihood of having significant disease. Detecting completely asymptomatic coronary artery disease remains a significant medical problem due to the imperfect nature of diagnostic tests and the comparatively low disease prevalence found in asymptomatic populations.

Acknowledgments

We gratefully acknowledge the skilled technical assistance of Major Anna K. MacDonald, RN, and TSgt. Michael W. Glass, and Mr. Thomas D. Kay for expertise in techniques of nuclear cardiology.

Appendix

The logistic regression equation is demonstrated by calculating the likelihood of significant coronary artery disease in an asymptomatic man aged 42 years, with a cholesterol ratio of 6.2 and an abnormal 20Tl test. In this case, a is 0.0901, r is 0.3766, th is 1.2637, age is 42, thallium is 1 (normal, 0; abnormal, 1), and the cholesterol ratio is 6.2. Therefore, the likelihood of significant disease l is as follows:

\[ l = 1 / \left[ 1 + e^{(a + 0.0901 - 0.3766 \times 1.2637 - 0.3766 \times 6.2 - 1.2637 \times 42)} \right] \]

or

\[ l = 1 / \left[ 1 + e^{(8.34 - 0.0901 - 0.3766 \times 1.2637 - 0.3766 \times 6.2 - 1.2637 \times 42)} \right] = 0.277(27.7\%) \]

Conversely, a normal thallium test would result in a likelihood of significant disease calculated as follows:

\[ l = 1 / \left[ 1 + e^{(8.34 - 0.0901 - 0.3766 \times 1.2637 - 0.3766 \times 6.2 - 1.2637 \times 0)} \right] = 0.098(9.8\%) \]

The occurrence of an abnormal thallium scan has thus increased the risk of significant coronary artery disease in this case by 2.83. With regard to clinical decision making using this example, the likelihood of obstructive disease is higher than 1:4 if the scan is abnormal. This would be clearly important information if such a patient were involved in a hazardous occupation or wished to embark on a vigorous exercise program. Conversely, in the case of a negative study, the likelihood of obstructive coronary disease dropped to <1:10, a substantially more comfortable margin. These data probably would not be the sole basis on which to base a clinical decision but would give an important quantitative perspective in interpreting the test results.

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Circulation. 1993;87:165-172
doi: 10.1161/01.CIR.87.1.165
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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