Can the Extent of Coronary Artery Disease Be Predicted from Thallium-201 Myocardial Images?

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The accuracy with which the extent of coronary artery disease can be predicted from stress thallium-201 myocardial images has been assessed in 81 patients with chest pain. Whereas the appearance of the myocardial images was both a sensitive means of detecting coronary artery disease (images abnormal in 43 of 47 patients with abnormal coronary arteriograms) and specific in excluding it (images normal in 31 of 34 patients with normal arteriograms), there was poor correlation between the extent of disease predicted from the Tl-201 images and the findings at arteriography. It is concluded that although stress Tl-201 myocardial imaging is a useful method for the noninvasive diagnosis of coronary artery disease, it cannot be relied upon to predict the number of abnormal vessels.

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Gamma-camera imaging of the left-ventricular myocardium following the injection of the potassium analog thallium-201 at the end of symptom-limited exercise is being increasingly recognized as a useful method for noninvasively detecting coronary artery disease (*1-6*). The mortality associated with ischemic heart disease is proportional to the extent of the disease (*7*), and the value of myocardial imaging would be greatly increased if the technique allowed accurate prediction of the number of abnormal vessels. The published studies on this point are relatively few and have yielded conflicting information (*2,6,8,9*). We have previously found that when the appearances of stress Tl-201 myocardial images are reviewed with knowledge of the findings at coronary arteriography, in patients with multiple vessel disease, abnormalities do not always appear on the Tl-201 image to correspond to each of the diseased vessels (*10*). We have therefore examined, in an extended series of patients with chest pain, the degree to which this affects the reliability of prediction of the number of abnormal vessels.

PATIENTS AND METHODS

Eighty-one consecutive patients referred by the participating cardiologists for myocardial imaging were studied. All had undergone selective coronary arteriography with left ventriculography for the assessment of chest pain. There were 67 male patients and 14 female. They ranged in age from 27 to 59 yr (mean = 45.3 yr).

Selective coronary arteriography was carried out by the percutaneous transfemoral route. Vessels were considered to be diseased when the luminal diameter was reduced by 50% or more in any of the standard projections. For the purposes of the study, the right coronary artery (RCA), the main left coronary artery, the left anterior descending (LAD), and left circumflex (LCX) coronary arteries were analyzed.

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TABLE 1. CORONARY ARTERY LESIONS ASSOCIATED WITH ABNORMALITIES OF PARTICULAR REGIONS OF MYOCARDIAL IMAGE

Myocardial region abnormal	Associated abnormal coronary artery*
Posteroseptal	LAD or RCA
Anteroseptal	LAD
Anterolateral	LAD
Lateral	LAD or LCX
Anterior	LAD
Posterolateral	LCX
Posterior	LCX or RCA
Inferior	RCA
Apical	Any vessel

* LAD = left anterior descending coronary artery
RCA = right coronary artery
LCX = left circumflex coronary artery

TABLE 2. COMPARISON BETWEEN PREDICTION OF MINIMUM EXTENT OF CORONARY ARTERY DISEASE (CAD) FROM STRESS THALLIUM-201 IMAGES, AND CORONARY ARTERIOGRAPHIC FINDINGS
(figures refer to numbers of patients)

Extent of CAD predicted from stress Tl-201 images	Extent of CAD at coronary arteriography			
	None	Single-vessel	Double-vessel	Triple-vessel
None	31	1	2	1
Single-vessel	3	9	13	7
Double-vessel	0	1	9	3
Triple-vessel	0	0	0	1

Myocardial imaging was performed after the i.v. injection of 2 mCi thallous chloride (Tl-201)* at the end point of a symptom-limited multistage exercise test. The accepted end points for the exercise test were chest pain, fatigue, breathlessness, hypotension, attainment of predicted maximal heart rate, or horizontal or downsloping ST segment depression of at least 1 mm and lasting 0.08 sec or more. Following injection of the tracer, the subject continued exercise for a further 30-45 sec. Images containing at least 300,000 counts, or lasting 7 min (whichever was the longer), were obtained in anterior, 30° and 60° left anterior oblique, and left lateral projections using a gamma camera† fitted with a high-resolution, low-sensitivity parallel-hole collimator. The images were displayed using a 128 by 128 matrix on a color-television screen with a 14-color activity scale, and were stored on magnetic tape using a computer‡ interfaced to the gamma camera.

The images were analyzed semiquantitatively using a regions-of-interest technique that we have previously described in detail (*11*). Briefly, using the computer, regions of interest are drawn on each myocardial image to correspond to the various myocardial areas, and an average count density is derived for the whole of each region. A region is considered abnormal if its average count density is less than 85% of the average count density for the maximally dense region in the same image.

Previous analysis of image appearances in patients with single- or double-vessel disease has enabled the association of image abnormalities in each of the myocardial segments with lesions of particular coronary arteries (*10*). Abnormalities of the posteroseptal myocardial area are associated with either right or left anterior descending coronary artery disease; anterior, anteroseptal, and anterolateral abnormalities with left anterior descending coronary artery lesions; inferior abnormalities with right coronary artery disease; posterior abnormalities with right or left circumflex coronary artery disease, and posterolateral abnormalities with left circumflex disease. Abnormalities of the apex are not specific for lesions of any particular vessel. These associations are summarized in Table 1. As can be seen, there is some overlap between the segments supplied by the various coronary vessels in different patients, presumably reflecting the normal variation in dominance of the right and left coronary circulations in different subjects.

RESULTS

The coronary arteriograms were normal in 34 patients. This is a rather high proportion of normal arteriograms (42%) and reflects the fact that this study was looking at the specificity as well as sensitivity of Tl-201 imaging for the diagnosis of coronary artery disease. Of 47 patients with abnormal arteriograms, 11 had single-vessel disease, 24 double-vessel disease, and 12 triple-vessel disease.

Stress Tl-201 myocardial images were normal in 31 of 34 patients with normal coronary arteriograms (specificity = 91.2%) and abnormal in 43 of 47 patients with abnormal arteriograms (sensitivity = 91.5%).

Since abnormalities in certain myocardial segments (e.g., posteroseptal) may be associated with lesions of more than one coronary artery, two strategies are possible in predicting the number of abnormal vessels from stress images, namely, predicting the minimum or the maximum number of abnormal vessels that would produce the observed image abnormalities. Because of the nonspecificity of the apex for any individual vessel, apical defects were not used in predicting the extent of disease.

The results of predicting the minimum number of abnormal vessels are summarized in Table 2. The three patients with normal arteriograms but an ab-

normal Tl-201 study all showed anterior abnormalities on their myocardial images, thus suggesting single-vessel (LAD) disease. In the patients with abnormal arteriograms, single-vessel disease was correctly predicted in nine of 11 patients, double-vessel disease in nine of 24, and triple-vessel disease in one of 12. The number of abnormal vessels was therefore accurately predicted in 19 of 47 patients (40.4%). The division between single- and multiple-vessel disease was correctly predicted in 22 of 47 (46.8%) patients with abnormal arteriograms.

Previous myocardial infarction may produce extensive abnormalities on Tl-201 images. The prediction of the minimum number of abnormal vessels was therefore repeated in the 29 patients with abnormal coronary arteriograms but no historical, electrocardiographic, or ventriculographic evidence of previous infarction. The results are summarized in Table 3. Single-vessel disease was accurately predicted in seven of nine patients, double-vessel disease in five of 14, and triple-vessel disease in one of six patients. The number of abnormal vessels was thus accurately predicted in 13 of 29 patients (44.8%) and the division into single-vessel or multiple-vessel disease in 13 of 29 patients (44.8%). These figures are not significantly different from the accuracy of prediction when patients with previous infarcts are included (by chi-square test, $p > 0.05$).

In Table 4 the results of the prediction of the maximum number of abnormal vessels from Tl-201 images are compared with the coronary arteriographic findings for all 81 patients. The three patients with abnormal Tl-201 images but normal arteriograms had myocardial image appearance suggesting single-vessel disease. The number of abnormal vessels was correctly predicted from the Tl-201 images in five of 11 patients with single-vessel disease, in nine of 24 with double-vessel disease, and in one of 12 with triple-vessel disease—an overall accuracy of 15 of 47 or 31.9%. The distinction between single- and multiple-vessel disease was correctly predicted in 23 of 47 (48.9%) patients with abnormal arteriograms.

In Table 5 the results of predicting the maximum number of possibly abnormal vessels are compared with the results of coronary arteriography for the 29 patients with abnormal arteriograms but no previous myocardial infarction. The number of abnormal vessels was correctly predicted in ten of 29 (34.5%) patients (three with single-, six with double-, and one with triple-vessel disease), and the distinction between single- and multiple-vessel disease was successfully made in 13 of 29 patients (44.8%). This does not differ significantly from the accuracy of prediction when patients with previous infarction are also included (by chi-square test, $p > 0.05$).

TABLE 3. COMPARISON BETWEEN PREDICTION OF MINIMUM EXTENT OF CAD FROM STRESS THALLIUM-201 IMAGES, AND CORONARY ARTERIOGRAPHIC FINDINGS, IN PATIENTS WITH ABNORMAL ARTERIOGRAMS AND NO PREVIOUS MYOCARDIAL INFARCTION
(figures refer to numbers of patients)

Extent of CAD predicted from stress Tl-201 images	Extent of CAD at coronary arteriography		
	Single-vessel	Double-vessel	Triple-vessel
None	1	1	1
Single-vessel	7	8	4
Double-vessel	1	5	0
Triple-vessel	0	0	1

TABLE 4. COMPARISON BETWEEN PREDICTION OF MAXIMUM EXTENT OF CAD FROM STRESS THALLIUM-201 IMAGES, AND CORONARY ARTERIOGRAPHIC FINDINGS
(figures refer to numbers of patients)

Extent of CAD predicted from stress Tl-201 images	Extent of CAD at coronary arteriography			
	None	Single-vessel	Double-vessel	Triple-vessel
None	31	1	2	1
Single-vessel	3	5	8	7
Double-vessel	0	5	9	3
Triple-vessel	0	0	5	1

TABLE 5. COMPARISON BETWEEN PREDICTION OF MAXIMUM EXTENT OF CAD FROM STRESS THALLIUM-201 IMAGES, AND CORONARY ARTERIOGRAPHIC FINDINGS, IN PATIENTS WITH ABNORMAL ARTERIOGRAMS AND NO PREVIOUS MYOCARDIAL INFARCTION
(figures refer to numbers of patients)

Extent of CAD predicted from stress Tl-201 images	Extent of CAD at coronary arteriography		
	Single-vessel	Double-vessel	Triple-vessel
None	1	1	1
Single-vessel	3	4	4
Double-vessel	5	6	0
Triple-vessel	0	3	1

DISCUSSION

The foregoing results suggest that stress Tl-201 myocardial imaging, although a sensitive method of diagnosing coronary artery disease, is of limited value in predicting the number of abnormal vessels. This confirms the findings of Lenaers et al. (*2*) and

Rehn et al. (*9*). Similar results were found by Massie et al. (*8*), though they still concluded that "stress perfusion scintigraphy is a useful adjunct in the identification of patients with high risk coronary artery disease." In complete contrast to our results are those of Wainwright et al. (*6*) who successfully predicted the extent of disease in nine out of 13 patients with single-vessel disease and in 50 out of 53 with multiple-vessel disease.

In our study the overall accuracy of prediction was not significantly different when either the maximum or the minimum number of abnormal vessels that would explain the Tl-201 findings was predicted. When the minimum number of abnormal vessels was predicted, single-vessel disease was predicted from the Tl-201 images in nine of 11 single-vessel patients and in 20 of 36 patients with multiple-vessel disease, whereas multiple-vessel disease was predicted in one of 11 patients with single-vessel disease and in 13 of 36 with multiple-vessel disease. When the "maximum vessel strategy" was used, single-vessel disease was predicted in five of 11 patients with single-vessel disease and in 15 of 36 patients with multiple-vessel disease, whereas multiple-vessel disease was predicted in five of 11 single-vessel patients and in 18 of 36 with multiple-vessel disease. The accuracy of prediction was not affected by the exclusion of patients with previous myocardial infarction.

Thus when the minimum number of abnormal vessels was predicted from the Tl-201 myocardial images, findings suggestive of multiple-vessel disease were accurate in all but one patient, but appearances of single-vessel disease did not reliably exclude multiple-vessel disease. By comparison, when the "maximum vessel prediction" is used, neither the multiple- nor single-vessel disease picture in the myocardial images is reliable.

Various reasons may be put forward to explain the poor accuracy of prediction of the extent of coronary artery disease from Tl-201 myocardial images. The first to be considered is whether the coronary arteriogram reliably indicates the extent of coronary artery disease. Several studies comparing coronary arteriography and autopsy findings have suggested that arteriography may tend to underestimate the severity of coronary artery disease (*12,13*). It is generally accepted, however, that coronary arteriography is a reliable tool in the detection of clinically significant coronary artery lesions (*13,14*) and that the extent of the disease as judged from the arteriographic findings is closely related to the patient's prognosis (*7,15*). Selective coronary arteriography, therefore, remains the test against which others must be judged. Note that in our study we have considered coronary artery stenosis of 50% or more of the lumen to be significant. This is the standard generally used by arteriographers in the United Kingdom, rather than the figure of 70% or greater, which is perhaps more widely accepted in the U.S.A.

A further consideration is whether the poor correlation between the two techniques is because the coronary arteriogram demonstrates an anatomical abnormality of the major coronary vessel, whereas the Tl-201 image reflects abnormalities of regional myocardial perfusion (*16*); and possibly alterations in the function of the myocardial cells' sodium-potassium pump (*17*). Animal and patient studies have demonstrated that the normal increment of myocardial blood flow that occurs during stress is reduced distal to coronary artery occlusions of greater than 50% of the luminal diameter (*18*). Recent experimental work has indicated that Tl-201 uptake in dog myocardium is relatively insensitive to reduction in myocardial perfusion unless it is accompanied by myocardial ischemia (*19*). It is likely, however, that in coronary artery disease, under conditions of stress, reduction in myocardial perfusion distal to a coronary lesion will be accompanied by myocardial ischemia and, therefore, should be associated with reduction in Tl-201 uptake by the myocardium.

A more likely source of the discrepancy of the findings between the two techniques is the fact that in coronary artery disease abnormalities of Tl-201 myocardial images reflect relative regional reduction in myocardial blood flow rather than absolute myocardial blood flow (*20*). Thus in multiple-vessel disease, the Tl-201 images may underestimate the extent of the abnormality, either a) because the patient's performance is limited by ischemia in the territory of the most abnormal vessel, before flow is reduced in less abnormal vessels, or b) because the relatively greater reduction in myocardial blood flow in the territory of the most abnormal vessels causes the other areas to be interpreted as normal, even though their flow is reduced in absolute terms.

As noted above, reduction of Tl-201 uptake in certain myocardial areas may be associated with lesions in more than one coronary artery, and when such image abnormalities are observed it is not possible to be certain whether this reflects lesions of one or both of the vessels. The uncertain anatomical relationship between the two techniques is not surprising in view of the variability of the territories supplied by the various coronary arteries, and especially the reciprocal nature of the areas of myocardium supplied by the right coronary artery and the left circumflex vessel (*21,22*). It does, however, increase the difficulty of predicting a specific coronary lesion from myocardial images.

A final point to be considered in explaining the low accuracy of prediction is the possible role of collateral vessels. Using intracoronary xenon-133, Frick et al. (*23*) studied the effect of angiographically detected collateral vessels on myocardial blood flow and found that in some patients the presence of collaterals did appear to prevent the development of stress-induced hypoperfusion distal to significant coronary stenosis. In other patients, however, the collaterals did not exert this "protective" effect. There is little information yet available on the effect of coronary collateral circulation on the appearance of Tl-201 myocardial images, but recently Rigo et al. (*24*) have found some evidence that collaterals sometimes, but by no means always, prevent the development of Tl-201 image abnormalities in the vascular territories of stenosed coronary arteries.

What implications do our findings have in clinical practice? When considering a patient with possible coronary artery disease, the clinician is faced with three questions. First, does this patient have coronary artery disease? There is a growing body of evidence to suggest that Tl-201 myocardial imaging is of considerable value in answering this question. Second, what is the extent of the coronary disease and does the patient fall into one of the high-risk groups such as triple-vessel disease or main left disease? There is debate on the utility of Tl-201 imaging in answering this question, but our own results suggest that it is of limited value. And third, could this patient benefit from coronary artery surgery? This decision depends on how much disability the patient's symptoms are causing, on the anatomical state of his coronary arteries, and on the degree to which cardiac performance is impaired. Thallium-201 myocardial imaging, therefore, cannot answer this third question.

FOOTNOTES

* Duphar Laboratories, Petten, The Netherlands.
† Ohio-Nuclear Series 100, Solon, OH.
‡ Varian 620L-100, Irvine, CA.

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