Predictive Value of Dipyridamole Thallium Imaging in a Patient with Myocardial Bridging but Without Fixed Obstructive Coronary Artery Disease

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CLINICAL HISTORY

A 44-yr-old male was referred to the cardiology clinic for evaluation of atypical chest pain and possible coronary angiography. He presented with a history of 4 wk of substernal chest pain which had been increasing in frequency, now occurring three to four times a day. The pain lasted 5–10 min, was associated with left arm tightness and dyspnea and occurred with exertion, when at rest or while asleep. He had become unable to maintain his normal lifestyle or sleep through the night. Coronary risk factors included a positive family history, with four uncles and two grandparents who died in their forties and fifties from myocardial infarction, smoking, hypertension with blood pressures of 155/100 to 165/100, hypercholesterolemia with total cholesterol 203–237 mg/dl and obesity (with a weight of 258 pounds). Medications at the time of presentation included extended release nifedipine 60 mg qd, isosorbide 10 mg qid, lasix 20 mg qd, potassium 20 mEq bid, atenolol 50 mg bid and allopurinol 300 mg qd. Previous surgery included fundoplication and internal fixation of a right ankle fracture, with both complicated by multiple infections and reoperations.

Physical examination was pertinent for blood pressure 140/80, pulse 80 and regular, diminished left carotid upstroke but no bruits, and a normal jugular venous pressure and waveform. The lungs were clear, the heart sounds distant without gallops, clicks, or murmurs and the peripheral pulses were normal. The electrocardiogram demonstrated sinus rhythm with a rate of 74, axis 45° and T-wave flattening in V2 and V3 (Fig. 1).

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Because of symptoms suggestive of angina and multiple risk factors for coronary artery disease, coronary angiography was considered. However, because of atypical features of the chest pain, a less invasive diagnostic study was finally recommended. The patient underwent dipyridamole-thallium scanning with exercise. A standard Bruce exercise test was not chosen because of a history of multiple ankle surgeries with residual pain. Sixty-eight milligrams of intravenous dipyridamole were administered over 4 min, using the standard dose of 0.56 mg/kg. Baseline vital signs were blood pressure 136/80 and pulse 63. Minimal blood pressure postinfusion was 122/70, with a maximal heart rate of 92. Exercise consisted of 2.5 min of walking at 1.7 mph on a flat surface (Bruce protocol Stage 0). No EKG changes were detected. Planar thallium imaging following initial administration of 120 MBq ^{201}Tl with delayed reinjection of 28 MBq revealed normal perfusion both post-dipyridamole and with reinjection (Fig. 2).

Because of the completely normal thallium study, the patient was informed that he did not have significant coronary artery disease, and that an angiogram would not be beneficial for the degree of risk involved. However, the patient continued to have increasingly frequent chest pain which could not be controlled with medical therapy and which continued to prevent a normal lifestyle. In light of these circumstances and the large number of risk factors for coronary disease, cardiac catheterization was performed.

The right coronary artery (RCA) was dominant, with a 30% mid-RCA stenosis. The left main and circumflex (LCX) arteries were normal. The left anterior descending artery (LAD) distal to the second septal and second diagonal arteries demonstrated 30% systolic bridging (Figs. 3 and 4). Left ventricular wall motion was normal, and there was no mitral regurgitation. Intracardiac pressures were right atrium 7 mmHg, pulmonary artery 20/8, pulmonary wedge pressure 8, left ventricle 110/14 and aorta 110/65. The cardiac output was 7.0 liters per minute.

In the month following angiography, the patient became free of chest pain, though none of his medications were

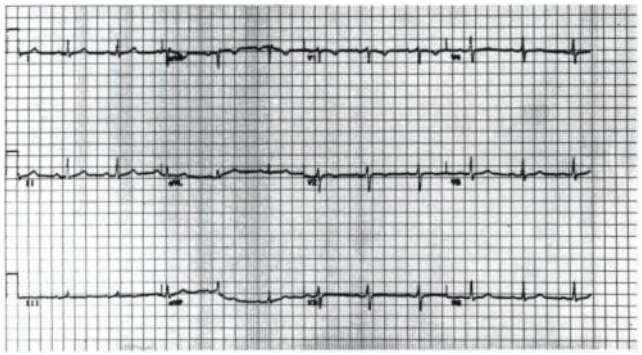

FIGURE 1. Resting electrocardiogram.

changed during that time. During the next 10 mo while on a regimen of 100 mg atenolol per day without calcium channel blocking agents or nitrates, the patient had neither chest pain nor other cardiac symptoms.

DISCUSSION

The patient presented here raises several interesting points regarding the diagnosis and management of coronary artery disease. These include the rationale behind dipyridamole-thallium imaging, critical interpretation of test results for coronary artery disease and the significance of myocardial bridging.

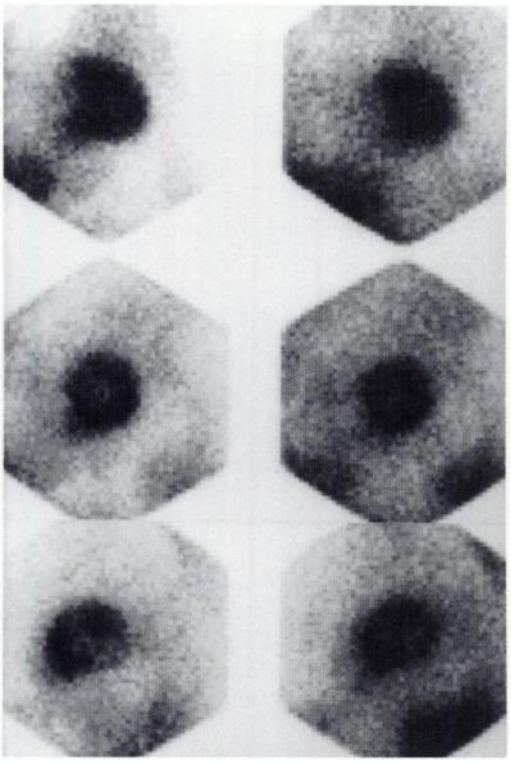

FIGURE 2. Immediate post-dipyridamole (left) and reinjection (right) thallium images in the anterior (top row), 45° left anterior oblique (middle row) and 70° left anterior oblique (bottom row) projections. The infero-basal zone of reduced thallium uptake is due to diaphragmmatic attenuation.

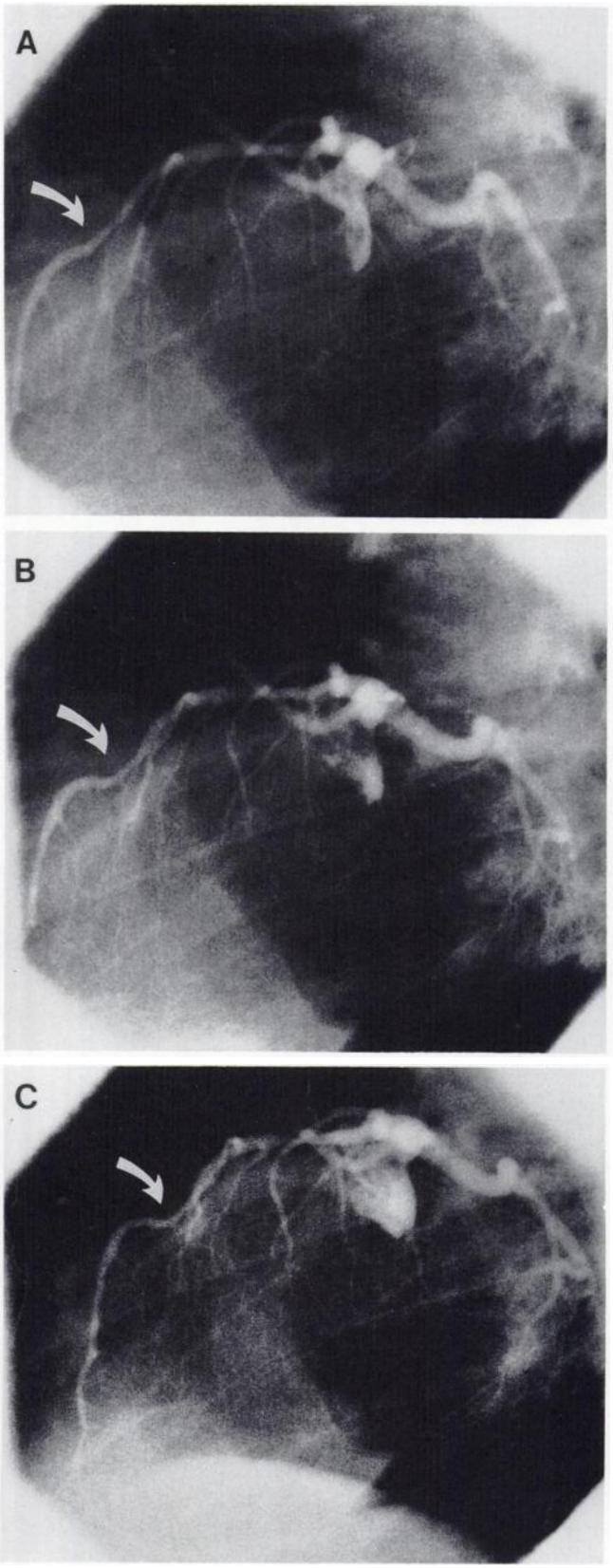

FIGURE 3. Left anterior oblique projection of the left coronary artery during end-diastole (A), mid-systole (B) and end-systole (C) shows progressive narrowing and angulation of the left anterior descending artery (arrows) with myocardial contraction.

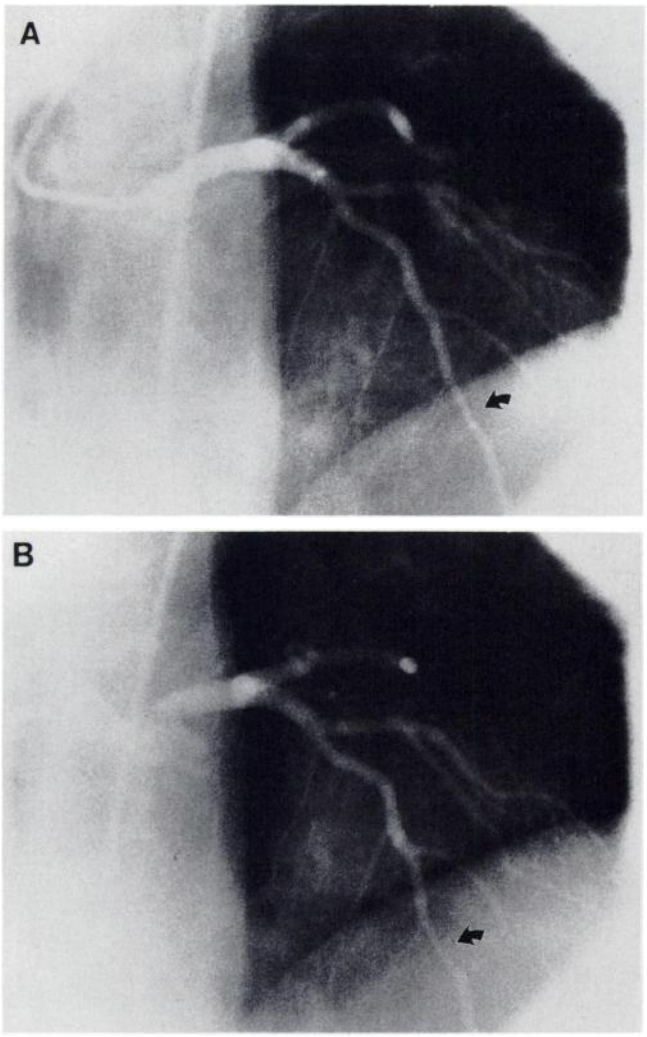

FIGURE 4. Right anterior oblique projection of the left coronary artery during end-diastole (A) and end-systole (B) demonstrates compression of the left anterior descending artery (arrows) with myocardial contraction. Same lesion as shown in Figure 3.

Basis of Dipyridamole-Thallium Cardiac Imaging

Thallium myocardial perfusion imaging is widely used for indirect assessment of both resting coronary blood flow and coronary flow reserve. Myocardial thallium uptake is linearly proportional to coronary blood flow at rest and moderately increased flow, but becomes nonlinear at high flow rates as thallium extraction fraction decreases (*1*). At high coronary flow, thallium extraction falls to about 50% of corresponding microsphere extraction, which may cause underestimation of disease severity (*2*). Myocardium with a restricted blood supply is detected by differential thallium uptake compared to normally perfused myocardium. In dogs, a flow differential of 2:1 has been found to be the threshold for detection of a stenotic vessel by planar thallium imaging (*1*). In a territory served by a stenotic vessel, the initial thallium extraction will be lower, since relative coronary blood flow is lower. Washout is likewise slower in myocardium supplied by the stenotic vessel, since the thallium concentration gradient between such an area of myocardium and the blood is lower than between normally perfused myocardium and blood. This helps to explain redistribution: as time passes, the thallium in normal myocardium washes out more rapidly than in stenotic areas, leading to a more equal distribution of thallium on delayed images (*1,3*). Thallium images are acquired immediately after dipyridamole or exercise and again in 3–4 hr, sometimes following thallium reinjection. Reversible perfusion defects indicate reversible ischemia. Fixed defects are considered to represent infarction, although some represent areas of reversible ischemia. This has been corroborated by perfusion and wall motion studies before and after revascularization and with studies using positron emission tomography (*4*).

Dipyridamole is a pyrimidine derivative which inhibits cellular uptake of adenosine, raising extracellular adenosine level to double the normal level when administered at a dose of 0.4 mg/kg over 8 min intravenously (*5*). This agent augments coronary blood flow to a greater degree than exercise and has been found to augment coronary blood flow three to five times the resting level, compared to one- to two-fold for exercise (*1,2,5*). Dipyridamole dilates coronary arterioles, which are the major resistance vessels of the coronary bed, to a greater extent than peripheral arterioles (*6*). In the presence of a coronary stenosis, this leads to increased epicardial but decreased subendocardial coronary blood flow, which causes a fall in the perfusion pressure distal to the stenosis, since the distal coronary vascular resistance diminishes (*3*). In comparison, both subendocardial and epicardial blood flow normally increase with vasodilation, and relative myocardial perfusion is maintained.

The current protocol for intravenous dipyridamole imaging involves the infusion of 0.56 mg/kg over 4 min, injection of 2–3.5 mCi (74–130 MBq) ^{201}Tl-chloride 3 min later and planar or SPECT imaging beginning 3 min after the injection. Repeat imaging 3–4 hr later is performed, often following reinjection of 1 mCi (37 MBq) ^{201}Tl. Low-level exercise may be used to reduce splanchnic uptake and hence to improve the target-to-background ratio. Dipyridamole is antagonized by caffeine, aminophylline and other xanthines, and is often routinely reversed with 50–100 mg aminophylline. Cardiac side effects include angina, ST changes and dysrhythmias. Noncardiac side effects include bronchospasm, lightheadedness and gastrointestinal symptoms. Dipyridamole is contraindicated in severe bronchospastic disease. Several studies attest to the safety of intravenous dipyridamole (*3*).

Epidemiology in the Interpretation of Dipyridamole-Thallium Imaging

Once a diagnosis is under consideration, for example, further investigation should be guided by consideration of the predictive value of such investigation. A test should only be performed if it will yield useful information. Testing for coronary artery disease, like any testing technique, depends on epidemiologic analysis for interpreta-

TABLE 1
Glossary of Statistical Terms

Sensitivity = TP/(TP+FN)
Specificity = TN/TN+FP
Positive Predictive Value (PPV) = TP/(TP+FP)
Negative Predictive Value (NPV) = TN/(TN+FN)
True-Positive rate = Sensitivity
False-Positive rate = 100+ Specificity
True-Negative rate = Specificity
False-Negative rate = 100− Sensitivity
Prevalence = Pretest Probability = (TP+FN)/All Patients

tion of results (Table 1). Sensitivity is defined as the probability that a test will be abnormal if disease is present. Specificity is defined as the probability that a test will be normal if disease is absent. A positive predictive value is related to but significantly different than sensitivity: it is the probability that disease is present when the test is positive. Likewise, a negative predictive value is the probability that disease is absent when the test is normal. For a given patient, the positive and negative predictive values are the two more clinically relevant statistics, since one is interested in the interpretation of that individual patient's test rather than in the determination of the sensitivity or specificity of that test (*7*).

The result of a particular test must also be interpreted with respect to the prior likelihood of disease in a particular patient. At a given prevalence, or pretest probability, of disease, the positive predictive value yields a post-test probability of disease if the test is abnormal. The post-test probability of disease if the test is normal is given by 100% minus the negative predictive value, since the negative predictive value gives the fraction of patients *without* disease. The greatest discriminating function of a test, i.e., the largest difference between post-test probabilities depending on whether the test is "positive" or "negative," occurs when the prevalence is moderate, between 40% and 60%. Sackett et. al. give an excellent discussion on this topic (*7*). It is important to know or at least to be able to estimate the prior likelihood of disease (since positive and negative predictive values and therefore the post-test probability vary with the pretest probability) at a given sensitivity and specificity of the test.

The concepts of sensitivity, specificity, predictive value and dependence of post-test probability on pretest probability is demonstrated in Table 2, which relates test results to disease presence.

In Table 2, sensitivity = a/(a+c), specificity = d/(b+d), positive predictive value = a/(a+b), negative predictive value = d/(c+d) and prevalence = (a+c)/(a+b+c+d). By assuming a sensitivity of 70% and specificity of 80% for dipyridamole-thallium testing in coronary artery disease, we can use Tables 3–5 to examine the contribution of this test to the detection of coronary artery disease depending on the pretest probability.

TABLE 2
Relationship of Test Results to Disease Presence

	Disease +	Disease −	
Test +	a	b	a+b
Test −	c	d	c+d
	a+c	b+d	a+b+c+d

TABLE 3
Pretest Probability 10%

	CAD present	CAD absent	
Test +	70	180	250
Test −	30	720	750
	100	900	1000

CAD = coronary artery disease.

Here, the positive predictive value = 28%, giving a post-test probability of disease with a positive test of 28%, an 18% increase from pretest probability. The negative predictive value = 96%, giving a post-test probability of disease with a negative test of (1−NPV) = 4%, a 6% decrease from pretest probability. In Table 4, the positive predictive value = 78%, a 28% increase from pretest probability. (1−NPV) = 27%, a 23% decrease from pretest probability. In Table 5, the positive predictive value = 97%, a 7% increase from pretest probability. (1−NPV) = 77%, a 13% decrease from pretest probability.

One can see from this analysis that a test is most useful in discriminating between disease and its absence in the middle pretest probability range, usually 40%–60%, and is least useful at the extremes of pretest probability, i.e., near 0% and 100% (*7,8*). In the three examples illustrated, the difference between the likelihoods of disease presence or absence is 51% for a pretest probability of 50%, 24% for a pretest probability of 10% and 20% for a pretest probability of 90%. Although other values of pretest prob-

TABLE 4
Pretest Probability 50%

	CAD present	CAD absent	
Test +	350	100	450
Test −	150	400	550
	500	500	1000

CAD = coronary artery disease.

TABLE 5
Pretest Probability 90%

	CAD present	CAD absent	
Test +	630	20	650
Test −	270	80	350
	900	100	1000

CAD = coronary artery disease.

ability are not illustrated, the discriminant ability of the test rises as the pretest probability rises from 0% and falls from 100% toward the middle range. This analysis may also be displayed on a graph of pretest versus post-test probability (Fig. 5). When applied to dipyridamole-thallium testing, this means that the test is most valuable in a population with an intermediate probability of coronary artery disease (*6*). In one study, Albro et al. (*9*) found a peak discrminant function for thallium detection of coronary artery disease at a pretest probability of about 40%. The test patient described in their case report probably had an intermediate pretest probability: for although he had multiple risk factors for coronary occlusive disease, the chest pain was atypical for angina.

Current Applications of Dipyridamole-Thallium Imaging

Detection of Coronary Artery Disease. Dipyridamole-thallium imaging is used for both detection of coronary artery disease and for risk stratification in patients with suspected coronary artery disease, following myocardial infarction, and patients undergoing noncardiac surgery. The sensitivity of dipyridamole-thallium imaging in the detection of coronary artery disease has been reported between 70%–95%. The reported specificity is between 60%–100% (*1*). These are comparable to results with exercise-thallium imaging, although dipyridamole produces angina, ST changes and an elevation in the heart rate-blood pressure product less often than exercise. Leppo et al. (*10*) found a sensitivity of 93% and a specificity of 80% using intravenous dipyridamole with thallium in 60 patients with angiographically documented coronary diameter stenoses of 50% or greater. Josephson et al. (*11*) found a sensitivity of 85% and specificity of 64% in 33 patients for the detection of 50% or greater coronary stenoses. Of interest, the sensitivities for detection of one-, two- and three-vessel disease were similar, 84%, 88%, and 83%, respectively. Albro et al. (*9*) found a sensitivity of 67% and specificity of 91% in 51 patients undergoing dipyridamole and exercise-thallium imaging as well as coronary arteriography. In a study of 170 patients with unstable angina, sensitivity was 91% and specificity was 79% in comparison to angiography (*12*).

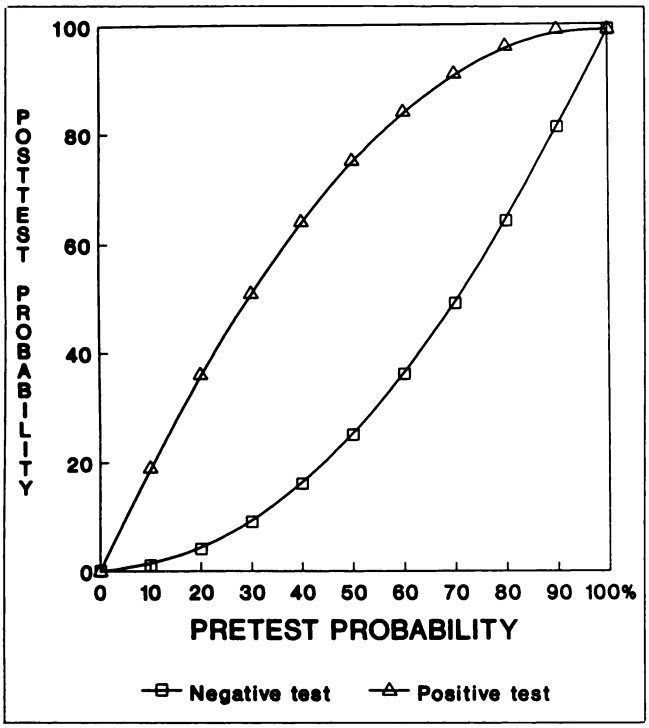

FIGURE 5. Discriminant function of a hypothetical test with a given sensitivity and specificity demonstrates the variation in post-test probability following both a "positive" and a "negative" test at a given pretest probability of disease.

Risk Stratification in Populations with Suspected Coronary Artery Disease. In multiple dipyridamole and exercise-thallium studies published for risk stratification in coronary artery disease, the strongest and most frequent independent predictor of future cardiac events is the existence of reversible thallium perfusion defects (*13*). There are fewer published studies regarding risk stratification using dipyridamole-thallium imaging than with exercise-thallium imaging, but several large series have been performed which are applicable to the test patient in this report. Younis et al. (*14*) analyzed clinical, scintigraphic and angiographic variables in 107 asymptomatic patients undergoing dipyridamole-thallium imaging for reasons of peripheral vascular disease, stroke, poor exercise tolerance or preoperative screening. The presence of reversible or combined (defined as both reversible and fixed defects in different regions) thallium defects conferred a poorer prognosis than either a normal scan or one with fixed defects only. The risk of death or nonfatal myocardial infarction in a 2-yr follow-up period was 0%, 7%, 35% and 42% for normal, fixed, reversible and combined thallium patterns, respectively. The risk of any cardiac event, defined as unstable angina, bypass surgery, angioplasty, class III or IV angina, death or myocardial infarction, was 7%, 33%, 79% and 56%, respectively. By using logistic regression analysis, a reversible defect was the only significant independent predictor of adverse outcomes.

Hendel et al. (*15*) followed 504 patients with chest pain, peripheral vascular disease or postrevascularization for a mean of 21 mo and found that while a history of diabetes, infarction or congestive heart failure was predictive of death or myocardial infarction, the only independent predictor of adverse events was an abnormal thallium scan, 12% and 6%, respectively, of patients with an abnormal scan of any type had an infarction or cardiac death in the follow-up period, compared to 3% and 1%, respectively, of patients with normal scans.

One question generated by this report is with what degree of certainty does a normal dipyridamole-thallium study rule out coronary artery disease (i.e., what is the negative predictive value of the test?). Negative predictive accuracies were 96% in Hendel's study (*15*) and 100% in Younis's study (*14*) for prediction of myocardial infarction and cardiac death in the follow-up period. The yearly rates

of death or myocardial infarction were 0% (*14*) and 2% (*15*). Therefore, a normal dipyridamole-thallium study, even in the presence of angiographically documented coronary disease, confers a good prognosis, with typical cardiac event rates of 1% per year for death or infarction (*13*). This identifies a very low risk group of patients and in most circumstances should suggest that no additional diagnostic testing, i.e., angiography, is necessary.

Risk Stratification for Noncardiac Surgery. A major use of dipyridamole-thallium scanning has been in risk stratification for patients undergoing vascular or other major noncardiac surgery, since these patients tend to be less able to perform a full exercise tolerance test than a nonselected population. Many investigators have found that an abnormal study significantly predicts adverse events in both the perioperative and follow-up period. Leppo et al. (*16*) tested 89 patients prior to vascular surgery, 69 of whom also had exercise thallium tests, and found that among multiple clinical, exercise and scintigraphic variables only groups with either reversible thallium defects or all abnormal thallium scans combined were significant predictors of postoperative myocardial infarction or death. Two percent of patients with scans without reversible defects and 33% of patients with reversible defects had either one of these adverse events. Eagle et al. (*17*) found that of 111 patients stratified before vascular surgery, 38% of those with reversible thallium perfusion defects and 3% of those without, had postoperative ischemic events. Lette et al. (*18*) found that among patients tested before noncardiac surgery 0% of 39 patients with either no or only fixed defects on thallium scans had occurrence of either cardiac death or nonfatal infarction, whereas 43% of patients with either reversible or combined fixed and reversible defects had postoperative events.

Younis et al., in a separate study (*19*), tested 131 patients with dipyridamole, 111 of whom underwent vascular surgery. An abnormal scan, total number of fixed and reversible thallium defects, a history of angina and angina during dipyridamole infusion predicted perioperative cardiac events, whereas only reversible defects predicted later events in an 18-mo follow-up. Of 51 surgical patients with normal scans, none had perioperative infarction or cardiac death, compared with 10%, 17% and 12% of patients with fixed, reversible and combined defects, respectively. Of 63 total patients with normal scans, only 6% had similar events in the follow-up period, compared with 18%, 36% and 29% of patients with fixed, reversible and combined defects. Boucher et al. (*20*) studied 54 patients before vascular surgery with dipyridamole and thallium. Of 16 patients with reversible defects preoperatively, 8 had either infarction, death, angina or ST-segment changes in the immediate postoperative period. Of 32 patients with normal scans or fixed defects only, none had cardiac events. In addition, clinical assessment in this study was not predictive of cardiac events. Therefore, dipyridamole-thallium testing is a powerful predictor of adverse events in populations undergoing major noncardiac surgery.

Risk Stratification Following Acute Myocardial Events. Another use of dipyridamole-thallium scanning has been used for risk stratification following myocardial infarction. Younis et al. (*21*), in a separate study of 33 patients after acute myocardial infarction and 44 patients with unstable angina over a mean follow-up of 12 mo, found that univariate predictors of cardiac death or infarction were the presence of a reversible thallium defect, angiographic extent of coronary artery disease and angiographic left ventricular ejection fraction. The risk of death or infarction was 0%, 12%, 19% and 25%, respectively, for normal, fixed, reversible and combined defects. When angina and revascularization procedures were added as endpoints, the respective risks were 7%, 47%, 85% and 82%. Again, a normal dipyridamole-thallium scan was a strong predictor of a benign outcome. Leppo et al. (*22*) found that only reversible thallium defects predicted future cardiac events over a mean follow-up period of 19 mo in 51 patients recovering from acute infarction. The occurrence of death, reinfarction or of admission with angina was not predicted by history, clinical variables or fixed thallium defects. As in risk stratification in patients with suspected coronary artery disease or patients undergoing noncardiac surgery, transient perfusion defects are the most important prognostic indicators (*13*).

Comparison of Dipyridamole-Thallium with Exercise-Thallium Imaging

Sensitivity and Specificity in Detection of Coronary Artery Disease. The sensitivity and specificity of exercise-thallium testing for detection of coronary artery disease are equal to dipyridamole-thallium imaging. A large review of exercise-thallium scintigraphy (*23*) places the sensitivity for exercise studies from 68% to 96% (mean 84%) and specificity from 65% to 100% (mean 87%). This is based on detection of coronary artery disease with 50%–70% diameter narrowing of at least one vessel, but does not differentiate between fixed and reversible perfusion defects and number of vessels involved. In the same analysis, the sensitivity and specificity of dipyridamole-thallium imaging were the same, 67%–98% (mean 85%), and 78%–91% (mean 82%), respectively (*23*). In individual studies, Albro et al. (*9*) compared 62 patients who underwent exercise-thallium imaging, dipyridamole-thallium imaging and coronary angiography. For the detection of coronary stenoses of 50% or greater, both thallium techniques had sensitivities of 67% and specificities of 91%. In Josephson's study of 33 patients undergoing both exercise- and dipyridamole-thallium imaging, the sensitivities for detection of 50% stenoses were 84% and 85%, respectively, with subgroup sensitivities based on number of stenotic vessels between 82% and 88% for all three subgroups in both the dipyridamole and exercise groups. The respective specificities for exercise and dipyridamole were 68% and 64% (*11*). Therefore, sensitivity and specificity are equal whether dipyridamole or exercise is used to increase coronary blood flow for thallium perfusion imaging.

Use of Exercise-Thallium in Risk Stratification. Exercise-thallium imaging, like dipyridamole-thallium imaging, carries significant prognostic information in populations with chest pain, suspected coronary artery disease and myocardial infarction. Koss et al. (*24*) evaluated 515 patients with suspected coronary artery disease with exercise thallium studies and followed them for a mean of three years. Of 206 patients with abnormal scans, 7% had death or nonfatal myocardial infarction. Of 309 patients with normal thallium scans, only 2% had death or infarction. They also followed 299 patients with chest pain of 4–8 yr duration who had both exercise thallium tests and coronary angiography (*25*). Independent predictors of all cardiac events, defined as death, infarction and revascularization, were number of diseased vessels and number of myocardial segments with thallium redistribution. The latter, however, was the best predictor of myocardial infarction. Brown et al. (*26*) followed 139 patients with chest pain, all of whom had exercise thallium tests and angiography. Of the 100 patients without previous infarction, the only independent predictor of infarction or death was the number of reversible thallium defects. Iskandrian et al. (*27*), in a study of 743 patients, found the total number of thallium perfusion defects, both fixed and reversible, to be the only independent predictor of myocardial infarction and death.

A normal exercise-thallium study, like a normal dipyridamole-thallium study, carries an excellent prognosis. In the Koss study (*24*), the annual death and infarction rate was 0.5% per year. In another study Pamelia et al. followed 345 patients with a normal exercise-thallium test over a mean of 34 months (*28*). The cardiac death rate was 0.5%, the nonfatal infarction rate 0.6% and the bypass surgery rate 0.4% per year. This is comparable to the negative predictive value of an arteriogram without significant coronary stenoses (*28*). Wackers et al. (*29*) followed 95 patients with chest pain but normal exercise thallium studies for a mean of 22 mo. There were no deaths, two nonfatal infarctions and one coronary angioplasty in the study group. The overall event rate of 1% per year indicated that even in a group with moderate to high pretest probability of coronary artery disease, a normal thallium study confers a good prognosis.

Patients with Myocardial Bridging

Anatomic and Pathologic Correlations. Myocardial bridging is defined angiographically as systolic compression of an intramyocardial segment of a normally epicardial coronary artery. The artery is of normal caliber during diastole, but during systole becomes compressed, or "milked." Anatomically, bridging is defined as "a coronary artery that becomes engulfed, for a limited segment, by myocardial fibers" (*30*). Bridged coronary arteries are normal in rodents, in which the entire coronary tree is intramyocardial, occasional in man, dogs, cats, goats and sheep, and never found in horses, cows or pigs.

Pathologic studies have reported myocardial bridging in 5%–86% of human hearts (*30,31*). All major epicardial coronary arteries have been involved, with incidence at autopsy being 5%–60% of the LAD, 6%–51% diagonals, 12%–43% circumflex, 0.4%–52% circumflex marginals and 0.4%–41% of the RCAs (*33*). Angiographic studies in humans, however, have a much lower reported incidence of myocardial bridging. Bridging has been reported in 0.5%–12% of human angiograms, almost always confined to the left anterior descending artery (*6,31,32*). The degree of systolic compression is increased by isoproterenol, epinephrine and nitroglycerin and is either unchanged or reduced by pacing, ergonovine and phenylephrine (*30*).

Clinical Significance of Bridging. Historically, bridging has been thought to be without hemodynamic significance, since most coronary blood flow occurs during diastole, but it has been reported to cause ischemia in a few cases (*6*). Kramer et al. (*33*) found systolic bridging in 12% of 658 angiograms, all in the LAD. Of the 26 patients with less than 30% maximal narrowing, 10 of 10 had normal exercise tests. Of the 55 patients with 30%–50% narrowing, 2 of the 12 who were stress tested had EKG changes with exercise. Of the 11 patients with greater than 50% bridging, 1 of 3 had ischemic EKG changes with exercise. The 5-yr survival was 98%, with one death from aortic dissection but none from other cardiovascular causes. These investigators concluded that bridging could cause ischemia but in general was a benign condition. Various case reports have described bridging as a benign anomaly, including one patient with anomalous origin of the left coronary artery from the right sinus of Valsalva (*34*). In this patient, the LAD tunneled intramyocardially through the septum over 5.5 cm, but had never caused symptoms for 71 yr.

Other investigators, however, have disagreed with the assertion that all bridging is benign. Noble et al. (*32*) found an incidence of LAD bridging in 0.5% of 5,250 patients undergoing angiography. The 11 patients with bridging but without other coronary abnormalities on angiography were studied with both pacing and exercise. Of the five patients with greater than 75% systolic narrowing, four had ST-segment depression and increased coronary sinus lactate production with pacing at 150 bpm, three had angina with pacing at 150 bpm and two had exertional angina on treadmill testing. Of the four patients with 50%–75% systolic narrowing, two had angina and ST depression with pacing at 150 bpm. Of the two patients with less than 50% bridging, none had EKG changes, lactate production or symptoms with either pacing or exercise. None of the patients in any group demonstrated ST changes, angina, or coronary sinus lactate production with pacing at 120 bpm. The authors concluded that myocardial bridging was indeed capable of provoking ischemia, possibly via preferential shortening of diastole with increased heart rate and consequently diminished coronary blood flow. In a single patient with LAD bridging (*35*), Pichard and colleagues reported that pacing at 140 bpm caused angina, ST depression and reduced flow in the great cardiac vein,

which drains the LAD territory, although the overall coronary sinus flow increased. There also have been case reports linking myocardial bridging with acute infarction (*36,37*), remote infarction (*38*), paroxysmal supraventricular tachycardia (*36*), angina (*36,39*) and ventricular tachycardia (*39*). Only one report of thallium imaging in patients with myocardial bridging could be found in the English language literature. In seven patients with chest pain and with 60%–80% LAD bridging, Greenspan et al. (*40*) reported that all seven exercise thallium studies were normal.

Symptoms, including both typical and atypical angina, which have been attributed to myocardial bridging have been improved by myotomy and bypass surgery, but it is not clear if this is the result of denervation, placebo effect or actual relief of ischemia (*30*). The relationship between systolic compression and ischemia is still debated, since only 5%–30% of coronary blood flow occurs during systole. No controlled follow-up studies exist in the literature, so the issue of whether bridging causes ischemia, morbidity or mortality is still unresolved.

SUMMARY

Both dipyridamole and exercise-^{201}Tl imaging are sensitive, specific and of prognostic value in patients with suspected coronary artery disease, following myocardial infarction, and undergoing major noncardiac surgery. Though reported sensitivities and specificities vary widely from 60% to 100%, the consensus is that both are between 80% and 90% for both dipyridamole and exercise studies (*23*). Moreover, when compared directly in the same study populations, the two have equal sensitivities and specificities (*9,11,13,23*). Transient thallium perfusion abnormalities are the most consistent predictors of adverse cardiac events and have more predictive power than clinical and angiographic parameters. Thallium reversibility may be a better predictor of adverse cardiac events than angiography since it represents more of a physiologic rather than a purely anatomic evaluation of the heart. It is difficult to make an exact comparison of some of the studies in the literature because they use different patient populations, sometimes define coronary stenosis in different ways, may have different cardiac endpoints and may not differentiate between reversible and fixed thallium perfusion defects. Exercise has the advantage of a graded examination and more experience historically and is of importance in a detailed study of cardiopulmonary hemodynamics, as in cardiac transplantation. Dipyridamole is more useful in patients who cannot achieve symptom-limited, submaximal exercise. It may also be more useful for patients who are bedridden or have peripheral vascular disease. Angina occurs less frequently with dipyridamole. Dipyridamole has superior sensitivity, specificity and predictive value, when compared with exercise testing, in the patient who cannot achieve the 85% maximal predicted heart rate or is limited by cardiac symptoms.

Once a test for making the diagnosis of coronary artery disease has been selected and performed, the result must be interpreted with respect to epidemiologic principles. In this patient, the normal dipyridamole-thallium study diminishes the post-test probability of disease. The post-test probability is not zero, as neither the specificity nor negative predictive value is 100% for thallium testing. However, the patient's prognosis is excellent regardless of angiography results, because several studies have demonstrated a 1% or less risk of infarction or death per year in patients with normal dipyridamole or exercise-thallium studies (*14,15,24,28,29*). It would have been reasonable and perhaps advisable not to proceed to angiography in view of the thallium result.

The conflicting reports of the clinical implications of myocardial bridging, unlike the consensus from thallium imaging, do not enable accurate prediction of an outcome based on the angiographic findings alone for the patient presented here. Also, the literature contains no controlled follow-up studies of patients with bridging. Thus, based on the angiographic findings alone, a recommendation for prognosis or therapy cannot be made for this patient. However, the studies of dipyridamole-thallium imaging performed in other populations suggest that even in the presence of an abnormal coronary arteriogram, a normal thallium study confers a good prognosis. The patient presented here most likely has a good prognosis, for there is only moderate bridging of the left anterior descending artery and the dipyridamole-thallium study was normal.

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