The Pacing Stress Test: Thallium-201 Myocardial Imaging After Atrial Pacing. Diagnostic Value in Detecting Coronary Artery Disease Compared With Exercise Testing

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Many patients suspected of having coronary artery disease are unable to undergo adequate exercise testing. An alternate stress, pacing tachycardia, has been shown to produce electrocardiographic changes that are as sensitive and specific as those observed during exercise testing. To compare thallium-201 imaging after atrial pacing stress with thallium imaging after exercise stress, 22 patients undergoing cardiac catheterization were studied with both standard exercise thallium imaging and pacing thallium imaging.

Positive ischemic electrocardiographic changes (> 1 mm ST segment depression) were noted in 11 of 16 patients with coronary artery disease during exercise, and in 15 of the 16 patients during atrial pacing. One of six patients with normal or trivial coronary artery disease had a positive electrocardiogram with each test. Exercise thallium imaging was positive in 13 of 16 patients with coronary artery disease compared with 15 of 16 patients during atrial pacing. Three of six patients without coronary artery disease had a positive scan with exercise testing, and two of these same patients developed a positive scan with atrial pacing. Of those patients with coronary artery disease and an abnormal scan, 85% showed redistribution with exercise testing compared with 87%during atrial pacing. Segment by segment comparison of thallium imaging after either atrial pacing or exercise showed that there was a good correlation of the location and severity of the thallium defects (r = 0.83, p = 0.0001, Spearman rank correlation).

It is concluded that the location and presence of both fixed and transient thallium defects after atrial pacing are closely correlated with the findings after exercise testing. Thus, atrial pacing may be used as a stress for myocardial perfusion scintigraphy in patients unable to complete a satisfactory exercise test.

Graded exercise testing is a well established method for the evaluation of myocardial ischemia (1-4), and the use of thallium-201 myocardial scintigraphy in conjunction with electrocardiography has enhanced the usefulness of exercise

testing for the detection and quantification of coronary artery disease (5-14). Thallium scintigraphy has been particularly useful in evaluating patients with ventricular conduction defects that interfere with the electrocardiographic interpretation of the test (10). However, adequate exercise testing is not always possible in patients in whom the diagnosis of coronary artery disease is suspected, since some patients are physically incapable of an adequate level of exercise because of pulmonary or peripheral vascular disease or musculoskeletal abnormalities. In addition, beta-receptor blocking agents may interfere with the chronotropic effect of exercise and prevent some patients from reaching a sufficient level of tachycardia.

Graded tachycardia using atrial pacing has been suggested as an alternative to exercise testing for the assessment of myocardial ischemia, but earlier studies have reported a

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lower sensitivity and specificity when compared with exercise testing (15-19). As a result, atrial pacing with thallium-201 imaging has not been fully investigated (20). However, these investigations were completed before the routine use of multichannel electrocardiographic monitoring (21-23)and in many cases were not based on attainment of predictive heart rates.

Because of the need for alternatives to exercise testing, we tested the hypothesis that thallium-201 imaging with pacing-induced tachycardia produces the same results as thallium imaging with exercise testing in the same patients. Improvement of the thallium image between the stress and delayed images has been associated with transient reduction of blood flow at the time of exercise-induced stress and, therefore, is consistent with ischemia (8–12). The ability to induce transient thallium defects must also be demonstrated for thallium imaging with atrial pacing to be useful as a diagnostic test (20).

Methods

Subjects. Twenty-two patients referred to the Beth Israel Hospital for diagnostic coronary cineangiography participated in the study. They were referred to one of the authors because of unacceptable symptoms despite medical therapy or for diagnosis of chest pain. Patients with other cardiac disease such as valvular disorders or cardiomyopathies were excluded from the study. All medications were continued throughout the catheterization and stress tests (exercise and pacing). The protocol was approved by the Beth Israel Hospital Human Investigation Committee. Informed written consent was obtained and there were no complications as a result of this investigation.

Patient groups. Five patients without demonstrable coronary artery disease and one with less than 25% diameter reduction in two coronary vessels constituted the control group (Group I). None of these patients had other underlying cardiac disease or wall motion abnormalities by contrast ventriculography. The remaining 16 patients (Group II) had significant stenosis (50% or greater luminal diameter reduction in two angiographic views) in at least one coronary artery or major branch. There was no significant difference between the mean age in the two groups (Group I, 49 \pm 11 years; Group II, 56 \pm 9 years).

Exercise testing. Each patient performed multistage exercise testing by bicycle ergometry (1) in the fasting state. Exercise testing was performed within 3 days of the atrial pacing test in 18 patients, within 2 weeks in 1 patient and within 1 month in the remaining 3 patients. After a 12 lead electrocardiogram at rest, patients were exercised using a bicycle ergometer in the upright position. Speed was held constant while resistance was uniformly increased in 3 minute intervals beginning at a work load of 25 to 30 watts. Exercise was continued until the patient developed char-

acteristic chest discomfort, severe fatigue, profound ST segment depressions (>3 mm), a decrease in systolic blood pressure, serious arrhythmias or 85% of predicted maximal heart rate. Blood pressure was measured intermittently throughout the test. The electrocardiogram was monitored using a Hewlett-Packard multichannel recorder (model 1514D, Hewlett-Packard). Three electrocardiographic channels (II, V₁ and V₅) were monitored continuously, while 12 lead electrocardiograms were recorded at 1 minute intervals during exercise, peak exercise, immediately after cessation of exercise and after exercise until chest pain or electrocardiographic changes, or both, resolved. At least 1 minute before cessation of exercise, thallium-201 was injected. Imaging was begun within 5 minutes of injection.

Selective coronary cineangiography. Coronary cineangiography was performed using standard techniques. Multiple projections of each coronary artery were obtained with good visualization of the entire coronary circulation in each patient. The degree of coronary stenosis was evaluated subjectively and independently by at least two of the authors, and was estimated using the greatest degree of diameter narrowing in any projection. Differences in evaluation were resolved by consensus. Coronary artery stenosis was classified on the basis of the most severe narrowing of each of the coronary arteries or major branches (left main, left anterior descending, major diagonal branches, circumflex, major marginal branches and right coronary arteries). Patients with at least 50% narrowing of one of these branches in two views were considered to have hemodynamically significant disease and, therefore, a positive angiogram.

Atrial pacing test. Right atrial pacing was performed at the completion of coronary arteriography. A bipolar flared pacing catheter was placed within the right atrium (Atri-Pace I, Mansfield Scientific) using the percutaneous femoral approach. No dislodgment occurred during pacing with this pacing catheter. When a satisfactory pacing position had been achieved, the pacing rate was then increased rapidly until 85% of age-predicted maximal heart rate or atrioventricular (AV) block occurred. If the patient developed AV block at a rate that was less than 85% of the age-predicted maximal rate, 1 mg of atropine was administered intravenously. This was done in advance to ensure an adequate level of pacing-induced tachycardia during the pacing stress test. Atropine was administered if AV block occurred (90%).

Systemic arterial pressure was monitored using a percutaneous radial or femoral artery cannula. A rest electrocardiogram was obtained using a multichannel recorder. Pacing was initiated at a rate of 80 beats/min, with progressive 15 beats/min increases of heart rate at 2 minute intervals. At the peak heart rate, pacing was continued for 5 minutes if well tolerated. Leads II, V₁ and V₅ were monitored continuously during pacing. A 12 lead electrocardiogram was obtained during the last minute at each pacing level, immediately after cessation of pacing and at 1 minute intervals until any chest symptoms or electrocardiographic changes resolved. At each pacing rate, the presence, intensity and character of chest discomfort were recorded. Pacing was discontinued when the patient had developed either typical and progressive chest symptoms with significant electrocardiographic changes, or when a pacing rate had been achieved that was at least 85% of the age-predicted maximal rate.

Myocardial imaging. *Protocol.* Patients fasted for a minimum of 4 hours before pacing or exercise testing to reduce splanchnic concentrations of thallium. Thallium-201 was administered intravenously at peak stress (either pacing or exercise) in a dose of 55 to 75 megabecquerels (1.5 to 2 mCi). To ensure adequate myocardial distribution of thallium during pacing-induced ischemia, pacing was continued for 5 minutes after the thallium injection. This procedure was not associated with any complication. There was prompt resolution of chest pain and electrocardiographic changes after termination of pacing.

Myocardial imaging was begun within 5 minutes of tracer administration. Images in the anterior, 40° modified left anterior oblique and 70° left anterior oblique projections were obtained with the patient in the supine position. The anterior view was repeated at the completion of the other views to assess early changes in myocardial size and lung uptake. Redistribution images were obtained approximately 4 hours after cessation of stress.

Imaging was performed with a 37 photomultiplier tube Anger-type scintillation camera (Technicare 410) using a 20% window centered on the mercury X-ray images produced after thallium decay (69 to 80 keV). A slant-hole collimator was used to collect all of the images. The anterior view was performed with the head of the collimator in a 30° left anterior oblique position with the hole pointed to the left. The modified left anterior oblique view was performed with the camera in the 40° left anterior oblique position with the holes pointed down. The 70° left anterior oblique was performed with the camera in the 40° left anterior oblique position with the holes pointed to the right. Each of the images was collected for a total of 6 minutes. Images were displayed and stored using a Technicare VIP computer system with flexible disk storage media.

Imaging analysis. Without prior knowledge of the results of stress testing or coronary cineangiography, three of us interpreted all images by consensus. The uptake of thallium in the three images was scored on a 4 point system (0 = normal, 1 = slightly decreased, 2 = markedly decreased, 3 = absent) in each of five segments (Fig. 1). The scoring was compressed to a binary evaluation (normal or abnormal) for some phases of the interpretation.

Thallium images were considered positive for the presence of coronary artery disease if one or more segments unequivocally showed less uptake of the radionuclide than surrounding areas. These criteria included patients with prior



Figure 1. Illustration of analysis of thallium-201 scans. Each view was divided into 5 segments, for a total of 15 segments. Each segment was graded: 0 = normal; 1 = slight photon deficiency; 2 = marked photon deficiency; 3 = absent activity, same as background. LAO = left anterior oblique; MLAO = modified left anterior oblique.

myocardial infarction and those with reversible ischemia (5,6). Thallium imaging was considered consistent with ischemia if there was improvement of the delayed scans when compared with the peak stress scans (8,11). The imaging techniques used could not distinguish between delayed reperfusion (occurring after 4 hours) and prior myocardial infarction.

Arterial thallium distribution. To determine the time course of thallium distribution during pacing, arterial blood samples were collected in seven patients starting at the time of intravenous injection. Samples were obtained at 1, 2, 3, 5, 10, 15 and 20 minutes after injection. Activities determined by well counting were expressed as a fraction of injected dose.

Interpretation of the electrocardiogram. The electrocardiogram (both exercise and pacing) was regarded as positive if any lead demonstrated 1 mm or greater horizontal or downsloping ST segment depression for 0.06 second or longer from the J point, using the PR segment as the baseline. Slow upsloping ST segments were considered positive if 1.5 mm or more ST segment depression was present 0.08 second from the J point (4). The changes must have been observed on three consecutive beats with a steady baseline. All electrocardiograms were interpreted independently by two of the authors who did not have prior knowledge of the patients' coronary anatomy or the results of the other stress test.

Statistical methods. Mean values ± 1 standard deviation were calculated. The Wilcoxon signed rank test was used to compare data. For comparison between exercise and atrial pacing tests, sensitivity (Positive test/Positive angiogram $\times 100$) and specificity (Negative test/Negative angiogram $\times 100$) were calculated. The myocardial perfusion scores with exercise testing and pacing were tabulated for the anterior, modified left anterior oblique and 70° left anterior oblique views. The number of segments with exact agreement or with one, two or three category differences was calculated. The chance probability (p) of obtaining one, two or three category disagreement given the row and column frequency was also calculated. The Spearman rank correlation coefficient was used to compare results on a segment to segment basis (24).

Results

Arterial thallium distribution. The results of activity collected from arterial samples during and after cessation of atrial pacing are shown in Figure 2. Pacing was continued for the first 5 minutes of the sample collections. Counts of the blood from all seven patients demonstrated a similar peak and disappearance of thallium from the arterial blood. The arterial activity was highest during the first minute after injection and decreased to approximately one-tenth of the peak level within 5 minutes. However, moderate activity did remain for at least 3 minutes after injection. Thus, the highest blood activity of thallium occurred well within the pacing period (first 5 minutes).

Exercise testing versus pacing. The heart rate-blood pressure product at peak stress was the same with both atrial pacing-induced tachycardia and exercise. Results for Group I with regard to symptoms, electrocardiographic findings

Figure 2. Fraction of injected dose of thallium-201 in the arterial blood as a function of time after injection.



and thallium scans are shown in Table 1. Chest pain occurred in two of six patients with normal coronary arteries during pacing tachycardia alone, in one patient during exercise alone and in one patient during both procedures. One patient in Group I had ischemic electrocardiographic changes during exercise and pacing. Thallium imaging was considered positive for coronary artery disease if one or more segments showed less uptake of the radionuclide than the surrounding areas. Because our purpose was to determine the presence or absence of coronary artery disease, a scan with either a fixed or reversible defect was classified as positive. Thallium scintigraphy was positive in three of six patients in Group I during exercise testing. During atrial pacing, two patients in Group I had a positive scan, both of whom also had positive scans during exercise.

Comparison of exercise testing and atrial pacing in patients with documented coronary artery disease (Group II) is shown in Table 2. Nine of 16 patients developed chest pain during both exercise and pacing tachycardia. In all patients who developed symptoms, the chest pain was present during both forms of stress. The electrocardiogram was positive in 11 of 16 patients during exercise and in 15 of 16 during atrial pacing tachycardia. Thallium scintigraphy was positive for coronary artery disease in 13 of 16 patients with exercise and 15 of 16 patients with pacing.

An example of thallium imaging with exercise and pacing in the same patient is shown in Figure 3. During both procedures, the patient was subjected to stress to the point of progressive chest pain and significant ischemic electrocardiographic changes. Both scans at peak stress revealed photon-deficient areas in the apex and posterolateral and inferior walls. Delayed scans (4 hours later) demonstrated partial redistribution in the same areas. Coronary cineangiography of this patient documented severe three vessel disease.

The ability of pacing tachycardia to induce reversible thallium defects compatible with ischemia was also evaluated. Comparisons were made between the peak stress and delayed images obtained after both atrial pacing and exercise testing in the same patients (Table 3). Any reduction in score was considered compatible with redistribution. Redistribution was classified as either partial or complete, depending on whether the region returned to normal thallium activity. Of the 15 patients with abnormal thallium imaging during atrial pacing, 87% showed either partial (10 patients) or complete (2 patients) redistribution. Three patients had persistent defects consistent with previous infarction. Exercise testing resulted in similar findings. Of 13 patients with positive scans, 85% showed either partial (9 patients) or complete (2 patients) redistribution.

Segmental analysis of thallium abnormalities. To determine whether the same areas were affected by the two methods of stress, a statistical comparison of regional perfusion defects was performed. Scans obtained at peak stress were

	Presenting					Thallium Defect Score‡			
		Chest Pain*		ECG ⁺		Exercise		Pacing	
Case	Symptoms	Exercise	Pacing	Exercise	Pacing	Stress	Delay	Stress	Delay
1	Α	+				7	3	0	0
2	А	_	+	-	_	2	2	4	2
3	А	-		+	+	0	0	0	0
4	А	+	+	_	_	2	2	1	0
5	А	_	-	-		0	0	0	0
6	А			_	_	0	0	0	0

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*Positive test indicates stress-related chest pain; \dagger positive test if 1 mm or greater ST segment depression; \ddagger thallium defects based on 0 to 45 scale on which 0 = normal. A = atypical angina.

compared with regard to agreement or disagreement on a segment by segment basis. Each peak stress comparison was determined on the basis of three views divided into 5 segments each, or 15 segments per study. Results are shown in Table 4. The total number of segments analyzed was 325. Total agreement was found in 263 segments (81%), disagreements of one category in 59 segments (18%), disagreements of two categories in 3 segments (1%) and disagreements of three categories in none. The chance occurrence of disagreements of zero, one, two and three categories would have been 60, 30, 9 and 1%, respectively. Spearman rank correlation coefficient demonstrated a highly significant correlation (r = 0.81, p = 0.0001). Therefore, these data demonstrate a close correlation between segmental analysis of thallium abnormalities induced by pacing and exercise.

Discussion

The purpose of the present study was to assess the value of thallium-201 imaging during graded atrial pacing tachycardia for the detection of coronary artery disease. We compared the results of immediate and delayed imaging obtained with atrial pacing tachycardia and those obtained by standard exercise testing in patients with known coronary artery anatomy. There were similar electrocardiographic and thallium image patterns with both forms of stress. In addition, segment by segment analysis revealed similar findings with regard to location of thallium defects in both atrial pacing and exercise stress testing. Thus, we found the pacingthallium stress test to be comparable with exercise-thallium testing in the diagnosis of coronary artery disease.

Case	Presenting Symptoms	ng Coronary					Thallium Defect Score‡			
			Chest Pain*		ECG ⁺		Exercise		Pacing	
		Anatomy	Exercise	Pacing	Exercise	Pacing	Stress	Delay	Stress	Delay
7	Т	3V	+	+	+	+	4	1	4	0
8	Т	LAD,RCA	+	+		+	8	4	12	10
9	Т	RCA	+	+	+	+	0	0	0	0
10	Т	LAD,LCx	+	+	+	+	9	3	5	2
11	Т	RCA	_	-	+	+	7	1	6	1
12	Α	3V	+	+	_	+	0	0	4	0
13	Т	3V	_	_	_	_	10	9	16	11
14	А	LAD,RCA		-	+	+	1	0	3	1
15	Т	3V	+	+	+	+	16	4	15	5
16	А	3V		_	+	+	2	2	5	1
17	Т	3V	+	+	+	+	12	7	7	4
18	Т	LCx	_	_	_	+	5	4	6	6
19	Т	3V	+	+	+	+	8	2	9	2
20	Т	RCA	+	+	+	+	8	7	8	8
21	Т	RCA,LCx	-	_	+	+	0	0	2	0
22	Å	3V	_	_	_	+	8	0	13	6

 Table 2. Comparison of Exercise Testing With Atrial Pacing in Patients With Significant Coronary Artery Disease (Group II)

*Positive test indicates exercise- or pacing-related chest pain; \dagger positive test if 1 mm or greater ST segment depression; \ddagger thallium defects based on 0 to 45 scale on which 0 = normal. A = atypical angina; LAD = left anterior descending artery or diagonal coronary artery, or both; LCx = left circumflex artery or marginal coronary artery, or both; RCA = right coronary artery; T = typical angina; 3V = three vessel coronary artery disease.



Figure 3. Case 15. Comparison of thallium-201 imaging at peak exercise and atrial pacing. A patient with three vessel coronary artery disease was subjected to stress until chest pain and electrocardiographic changes appeared with both tests. Thallium imaging revealed apical, posterolateral and inferior photon-deficient areas that showed marked improvement in delayed views. The same defects were obtained during pacing and exercise stress.

Analysis of the study patients. The patients studied were referred for coronary angiography because of severe symptoms. Most of the patients had symptoms of typical angina pectoris and clinical data strongly suggestive of coronary artery disease, while others had atypical symptoms but noninvasive data suggesting the presence of coronary artery disease. In the latter category, despite atypical symptoms, a number of patients had positive electrocardiographic or thallium exercise tests. It would be expected that a significant percent of those patients would have normal or minimal coronary artery disease (25). Because of patient selection, the present study was not designed to evaluate the sensitivity or specificity of atrial pacing stress as an isolated test for the diagnosis of coronary artery disease, but rather to compare atrial pacing with exercise testing in the same patients.

Thallium distribution during pacing. There are several theoretical reasons why thallium distribution after atrial pacing might be different from thallium distribution after

Atrial Pacing or Exercise Stress	ind Delayed Views Alter
	Thallium Imaging

Table 3 Comparison of Peak Stress and Delayed Views After

	Patients		Redistrib	Persistent		
	(no.)	Normal	Complete	Partial	Defect	
Normal patients						
Atrial pacing	6	4	1	1	0	
Exercise testing	6	3	0	1	2	
Patients with						
Atrial pacing	16	15	3	10	2	
Exercise testing	16	13	2	9	2	

*Transient defects demonstrated by a change between the peak stress views and 4 hour delay scans. CAD = coronary artery disease.

exercise. During pacing, coronary flow is increased without an increase in cardiac output and, therefore, the percent flow to the heart is increased. The increased percent of flow to the heart could enhance the quality of thallium images during pacing (26). In contrast, splanchnic flow is reduced during exercise, but it is not affected by pacing. This factor could reduce the quality of imaging during pacing. In our study, we obtained images of comparable quality during both pacing and exercise, suggesting that these two factors either tended to cancel each other or were not of sufficient magnitude to affect image quality.

Another difference between exercise and pacing is the duration of stress-induced ischemia. When exercise is discontinued, tachycardia persists for several minutes, allowing continued but gradually lessening ischemia. When atrial pacing is discontinued, the heart rate immediately returns to prepacing levels, and ischemia decreases rapidly. For thallium imaging to be useful during atrial pacing, thallium must reach the myocardium while the tissue is ischemic. We determined the optimal duration of pacing after injection of thallium by observing the arterial activity time curve (Fig. 2). The curve shows that the thallium activity approaches equilibrium within 5 minutes. Because we continued pacing for 5 minutes after injection, thallium distribution occurred at the time of increased coronary blood flow. Furthermore, the high percent of transient defects (87%) suggests that the thallium is distributed while the tissue is ischemic (8,11).

 Table 4.
 Segment by Segment Comparison of Exercise vs.

 Pacing Defects During Thallium-201 Scintigraphy

	Atrial Pacing						
Exercise	Normal	Slight Decrease	Marked Decrease	Absent			
Normal	225	24	1	0			
Slight decrease	20	30	6	1			
Marked decrease	1	6	8	3			
Absent	0	0	0	0			

Alternate methods of inducing ischemia. The use of radionuclide imaging with exercise has resulted in a resurgence of interest in the noninvasive diagnosis and prognosis of coronary artery disease (13,14). Recently, attention has been focused on a group of patients in which standard maximal exercise testing is not possible. Included in this group are patients with physical impairments such as musculoskeletal disorders, peripheral vascular disease or unstable angina and those undergoing treatment with beta-receptor blocking agents.

The use of intravenous dipyridamole in conjunction with thallium-201 scanning has been proposed as a method for evaluating patients with limited exercise tolerance. Gould et al. and others (27-31) have shown that this procedure can reliably detect coronary artery disease. Utilizing delayed imaging, transient defects have also been demonstrated (31). Although the dipyridamole test can demonstrate ischemia by thallium imaging without the need to exercise the patient, two potential disadvantages exist. First, the administration of dipyridamole has potentially serious side effects, including prolonged chest pain and ischemia (31). Although the ischemic effects are reversible with aminophylline, dipyridamole stress may be less useful in evaluation of patients with unstable angina or after myocardial infarction. On the other hand, atrial pacing has been used successfully to study patients shortly after myocardial infarction (32). Second, the electrocardiogram is not of diagnostic usefulness during the dipyridamole test and, therefore, this marker of ischemia is lost.

Cold temperature stimulation (33-36) is another method which has been suggested as an alternative method to exercise. The cold pressor test has been used with both radionuclide ventriculography (33,34) and thallium imaging (35). A recent study (36) reported unfavorable results using the cold pressor test and, as with dipyridamole, the electrocardiogram could not be utilized. The choice between pacing, dipyridamole or cold pressor as a stress in patients who cannot exercise needs to be evaluated further. Each method may have special advantages in specific situations.

Pacing thallium-201 imaging for the detection of significant coronary artery disease. Thallium imaging after pacing-induced tachycardia has not been widely used for the diagnosis of coronary artery disease. This lack of interest may be a result of the earlier studies (15–19) of atrial pacing without imaging, which report poor sensitivity and specificity of the electrocardiographic changes when compared with exercise testing. However, we demonstrated that comparison between exercise testing and atrial pacing can be improved by the use of a number of modifications of the pacing test. These include the use of a multichannel electrocardiogram and utilization of electrocardiographic changes or 85% maximally predicted heart rate as end points, rather than the first onset of chest pain or excessively high heart rates in patients without pain.

Numerous studies (5-14) demonstrated that the addition of thallium-201 imaging to exercise testing improves the detection of coronary artery disease. In addition to diagnosis, it has also been found that differences between peak stress and delayed images can identify areas of reversible ischemic myocardium (8-12). Identification of ischemic but viable myocardium is a major benefit to be obtained from a comparison of the exercise and rest thallium scan. Therefore, any test that serves as an alternative to exercise must also be able to induce reversible changes (30). With atrial pacing tachycardia, one recent study (20) using thallium imaging has suggested that the ability to detect ischemic defects is less than 10%. This study has demonstrated reversible thallium defects in 11 (85%) of 13 patients with known coronary artery disease and abnormal scans. These data compare favorably with our results with exercise testing, which produced reversible defects in 69% of the same patients. In previous reports, reversible thallium defects occurred in 75% of patients given dipyridamole (30) and in 56% of patients with exercise testing (5).

In our patients, myocardial imaging with thallium-201 during atrial pacing correlated well with imaging during exercise testing. Our series of patients was relatively small and highly selected. Therefore, it was not possible to determine the sensitivity and specificity of the pacing thallium test. However, the similar location of both transient and fixed thallium defects with pacing and exercise testing provides additional support for the comparability of the pacing and exercise stress test.

Implications. We conclude that the atrial pacing thallium test is a safe and reliable test for the diagnosis of ischemic heart disease. This technique may be especially useful in the study of patients unable to perform a standard exercise test or in whom the interpretation of the exercise test is difficult because of beta-receptor blockade.

References

 Ellestad MH, Cooke BM Jr, Greenberg PS. Stress testing: clinical application and predictive capacity. Prog Cardiovasc Dis 1979;21:431– 60.

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- Diamond GA, Forrester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. N Engl J Med 1979;300:135–58.
- Zohman LR, Kattus AA. Exercise testing in the diagnosis of coronary heart disease: a perspective. Am J Cardiol 1977;40:243–50.
- Ellestad MH. Stress Testing: Principles and Practice. 2nd ed. Philadelphia: FA Davis, 1980:210.
- Bailey IK, Griffith LSC, Rouleau J, Strauss HW, Pitt B. Thallium-201 myocardial perfusion imaging at rest and during exercise. Circulation 1976;55:79–87.
- Ritchie JL, Trobaugh GB, Hamilton GW, et al. Myocardial imaging with thallium-201 at rest and during exercise. Circulation 1977;56:66– 71.
- Ritchie JL, Zaret BL, Strauss HW, et al. Myocardial imaging with thallium-201: a multicenter study in patients with angina pectoris or acute myocardial infarction. Am J Cardiol 1978;42:345–50.
- Turner DA, Battle WE, Deshmukh H, et al. The predictive value of myocardial perfusion scintigraphy after stress in patients without previous infarction. J Nucl Med 1978;19:249–55.
- 9. Melin JA, Piret LJ, Vanbutsele RJM, et al. Diagnostic value of exercise electrocardiography and thallium myocardial scintigraphy in patients without previous myocardial infarction: a Bayesian approach. Circulation 1981;63:1019–24.
- Botvinick EH, Taradash MR, Shames DM, Parmley WW. Thallium-201 myocardial perfusion scintigraphy for the clinical clarification of normal, abnormal and equivocal electrocardiographic stress tests. Am J Cardiol 1978;41:43-51.
- Pohost GM, Zir LM, Moore LH, McKusick KA, Guiney TE, Beller GA. Differentiation of transiently ischemic from infarcted myocardium by serial imaging after a single dose of thallium-201. Circulation 1977;55:294–302.
- Leppo J, Yipintsoi T, Blankenstein R, et al. Thallium-201 myocardial scintigraphy in patients with triple vessel disease and ischemic exercise stress tests. Circulation 1979;59:714–21.
- Rehn T, Griffith LS, Achuff SC, et al. Exercise thallium-201 myocardial imaging in left main coronary artery disease: sensitive but not specific. Am J Cardiol 1981;48:217–23.
- Iskandrian AS, Segal BL, Haaz W, Kane SA. Effects of coronary artery narrowing, collaterals, and left ventricular function on the pattern of myocardial perfusion. Cathet Cardiovasc Diagn 1980;6:159– 68.
- Helfant RH, Forrester JS, Hampton JR, Haft JI, Kemp HG, Gorlin R. Coronary heart disease: differential hemodynamic, metabolic and electrocardiographic effects in subjects with and without angina pectoris during atrial pacing. Circulation 1970;42:601–10.
- 16 Linhart JW. Atrial pacing in coronary artery disease, including preinfarction angina and postoperative studies. Am J Cardiol 1972;30:603– 10.
- Kelemen MH, Gillilan RE, Bouchard RJ, Heppner RL, Warbasse JR. Diagnosis of obstructive coronary artery disease by maximal exercise and atrial pacing. Circulation 1973;48:1227–33.
- Piessens J, Van Mieghem W, Kesteloot H, De Geest H. Diagnostic value of clinical history, exercise testing and atrial pacing in patients with chest pain. Am J Cardiol 1974;33:351-6.
- 19. Robson RH, Pridie R, Fluck DC. Evaluation of rapid atrial pacing in

diagnosis of coronary artery disease. Evaluation of atrial pacing test. Br Heart J 1976;38:986-9.

- Vrobel TR, Madison JD, Schwartz JS, Forstrom L, Jorgensen CR. Insensitivity of thallium 201 imaging in detecting pacing-induced myocardial ischemia (abstr). Circulation 1979;59 (suppl II):II-172.
- Chaitman BR, Bourassa MG, Wagniart P, Corbara F, Ferguson RJ. Improved efficiency of treadmill exercise testing using a multiple lead ECG system and basic hemodynamic exercise response. Circulation 1978;61:44–50.
- Chaitman BR, Waters DD, Bourassa MG, Tubau JF, Wagniart P, Ferguson RJ. The importance of clinical subsets in interpreting maximal treadmill exercise test results: the role of multiple lead ECG systems. Circulation 1979;59:560-70.
- Tubau JF, Chaitman BR, Bourassa MG, Waters DD. Detection of multivessel coronary disease after myocardial infarction using exercise stress testing and multiple ECG lead systems. Circulation 1980;61:44– 50.
- Siegel S. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill, 1956:202.
- Bungo MW, Leland OS. Discordance of exercise thallium testing with coronary arteriography in patients with atypical presentations. Chest 1983;83:112-6.
- Slutsky R. Response of the left ventricle to stress: effects of exercise, atrial pacing, afterload stress and drugs. Am J Cardiol 1981;47:357– 64.
- Gould KL. Noninvasive assessment of coronary stenosis by myocardial imaging during pharmacologic coronary vasodilation. I. Physiologic basis and experimental validation. Am J Cardiol 1978;41:267– 78.
- Gould KL, Westcott RJ, Albro PC, Hamilton GW. Noninvasive assessment of coronary stenoses by myocardial imaging during pharmacologic coronary vasodilation. II. Clnical methodology and feasibility. Am J Cardiol 1978;41:279–87.
- Albro PC, Gould KL, Westcott RJ. Noninvasive assessment of coronary artery stenoses with myocardial perfusion imaging during pharmacological coronary vasodilation. III. Clinical trial. Am J Cardiol 1978;42:751-60.
- Wilde P, Walker P, Watt I, Rees JR, Davies ER. Thallium myocardial imaging: recent experience using a coronary vasodilator. Clin Radiol 1982;49:43–9.
- Leppo J, Boucher CA, Okada RD, Newell JB, Strauss HW, Pohost GM. Serial thallium-201 myocardial imaging after dipryridamole infusion: diagnostic utility in detecting coronary stenoses and relationship to regional wall motion. Circulation 1982;66:649-57.
- Tzivoni D, Keren A, Gottlieb S, et al. Right atrial pacing soon after myocardial infarction. Circulation 1982;53:330–5.
- Verani MS, Zacca NM, DeBauche TL, Miller RR, Chahine RA. Comparison of cold pressor and exercise radionuclide angiocardiography in coronary artery disease. J Nucl Med 1982;23:770-6.
- Ahmad M, Dubiel JP, Haibach H. Cold pressor thallium-201 myocardial scintigraphy in the diagnosis of coronary artery disease. Am J Cardiol 1982;50:1253-7.
- Jordan LJ, Borer JS, Zullo M, et al. Exercise versus cold temperature stimulation during radionuclide cineangiography: diagnostic accuracy in coronary artery disease. Am J Cardiol 1983;51:1091–102.
- Wasserman AG, Reiss L, Katz RJ, et al. Insensitivity of the cold pressor test for the diagnosis of coronary artery disease (abstr). J Am Coll Cardiol 1983;1:624.