Relationship between segmental thallium-201 uptake and regional myocardial blood flow in patients with coronary artery disease

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ABSTRACT The relationship between the spatial distribution of thallium-201 in myocardial perfusion scintigrams and the distribution of left ventricular regional myocardial blood flow was examined in 25 patients undergoing coronary arteriography. Thallium-201 myocardial scintigrams were obtained after symptom-limited exercise and after a 4 hr delay. Regional myocardial blood flow was measured by the xenon-133 clearance method in patients at rest and during rapid atrial pacing to a double product comparable with that achieved during exercise stress testing. Patterns of regional thallium-201 activity and regional myocardial blood flow, recorded in similar left anterior oblique projections, were compared for left ventricular segments supplied by the left anterior descending (LAD) and left circumflex (CIRC) arteries. In 11 patients without significant lesions of the left coronary artery (group 1), thallium-201 was homogeneously distributed in the LAD and CIRC distributions in scintigrams taken during peak exercise; these scintigrams correspond to homogeneous regional myocardial blood flow in the LAD and CIRC regions during pacing-induced stress. In 14 patients with significant lesions of the left coronary artery (group 2), ratios of regional thallium-201 activity in the LAD and CIRC distributions of exercise scintigrams correlated well ($r = .84$) with ratios of regional myocardial blood flow measured during rapid pacing. Background subtraction altered the relationship between relative thallium-201 uptake and regional myocardial blood flow, causing overestimation of the magnitude of flow reduction on exercise scintigrams. These data indicate that: (1) in patients with normal left coronary arteries, thallium-201 is homogeneously distributed to the left ventricle, reflecting the homogeneous distribution of regional myocardial blood flow over a wide range of mean left ventricular flow rates and (2) in patients with significant lesions of the left coronary artery, the relative spatial distribution of thallium-201 activity in exercise perfusion scintigrams reflects the distribution of regional myocardial blood flow.
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THE BASIS for myocardial perfusion scintigraphy with thallium-201 is the assumption that the initial distribution of thallium-201 in heart muscle after intravenous injection is proportional to the relative distribution of myocardial blood flow. Animal experiments done with the radioactive microsphere technique have supported the validity of this assumption.[1-3] Although extraction of thallium-201 can be influenced by the blood flow rate, by the activity of Na, K-ATPase, and by hypoxia, the predominant determinant of the initial myocardial distribution of the tracer is the distribution of myocardial blood flow.[4-6] Therefore it is assumed clinically that the relative spatial distribution of thallium-201 in perfusion scintigrams reflects the relative distribution of myocardial blood flow.

This assumption was tested in 25 patients who underwent myocardial perfusion scintigraphy with thallium-201 during exercise and who also underwent measurement of regional myocardial blood flow with xenon-133 while at rest and during rapid atrial pacing. Our objective was to determine whether the relative spatial distribution of thallium-201 activity in the exercise myocardial perfusion scintigrams reflected the relative spatial distribution of myocardial blood flow rates measured in patients with a scintillation camera during atrial pacing to a comparable double product.

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Studies in experimental animals[7, 8] and man[9] have indicated that the absolute blood flow rate in heart muscle is a linear function of myocardial oxygen consumption, which is proportional to the product of heart rate and systolic blood pressure.[10, 11] Comparisons were made between the relative uptake of thallium-201 and the relative perfusion rate measured with xenon-133 in patients with and without coronary artery disease.

Methods

Patient selection. Patients undergoing coronary arteriography and thallium-201 scintigraphy during exercise for clinical evaluation of chest pain were considered candidates for the study. Excluded from the study were patients with valvular heart disease, congestive cardiomyopathy, recent myocardial infarction, or patients who had undergone coronary bypass surgery. Informed written consent was obtained from each patient under a protocol approved by the Institutional Review Board and Joint Radioisotope Committee of the Columbia Presbyterian Medical Center.

Twenty-five patients were studied: 20 men and five women with a mean age of 53 years (range 32 to 67, table 1). Patients were separated into two groups on the basis of left coronary anatomy. Group 1 consisted of six patients with normal coronary arteriograms and five patients with lesions of the left anterior descending (LAD) or left circumflex (CIRC) arteries that obstructed less than 70% of the luminal diameter. Group 2 consisted of 14 patients with stenotic lesions greater than 70% of the luminal diameter of the LAD and/or CIRC arteries. Since regional left ventricular myocardial blood flow was measured by injection of xenon-133 into the left coronary artery, the presence of right coronary artery lesions was not used as a criterion for separating patients. Twenty-three of the 25 patients (92%) underwent coronary arteriography and measurements of regional myocardial blood flow within 2 months of thallium-201 scintigraphy taken during exercise. The two other patients (patient 8 of group 1 and patient 2 of group 2) underwent thallium-201 scintigraphy 5 and 8 months, respectively, before myocardial blood flow measurement. None of the patients had clinical or electrocardiographic evidence of myocardial infarction occurring between the time they underwent thallium-201 scintigraphy and coronary arteriography. Furthermore, none of the patients reported a change in chest pain symptoms between the two studies. Cardiac medications were not altered except in two group 1 patients (patients 2 and 7) who were receiving propranolol before undergoing thallium-201 scintigraphy; propranolol was subsequently discontinued.

Exercise stress testing. Each patient underwent symptom-limited treadmill exercise according to the Bruce protocol.[12] Exercise tests were performed after an overnight fast and medications were not altered, except that nitrates and propranolol were omitted on the day of the study. Patients exercised until they experienced anginal pain, severe fatigue, dyspnea, or a fall in systolic blood pressure. The response to exercise testing was considered ischemic if the following changes were present for at least 3 beats in the ECG with a stable baseline taken during exercise: (1) horizontal or down-sloping ST segment depression of 0.1 mV at the J point or (2) ST segment elevation of 0.1 mV in leads without Q waves.

Thallium-201 myocardial imaging. At peak exercise, thallium-201 (thallous chloride in 0.9% saline, 1.2 to 1.7 mCi) was administered intravenously. The patient was encouraged to continue exercise at the same level for another minute before terminating exercise. Myocardial scintigraphy was started within 10 min of the thallium-201 injection.[13] Images were collected in the anterior, 30 and 60 degree left anterior oblique (LAO) projections with a multiple-crystal scintillation camera (System 77; Baird-Atomic, Inc.) equipped with a 2 inch tapered parallel-hole collimator. Scintigrams were recorded with a 50 to 250 keV window for a preset counting time of 480 sec in each view. The scintigrams were flood corrected for heterogeneity of crystal efficiency with a uniform thallium-201 planar source. Repeat images were recorded 4 hr later in the same projections with acquisition intervals of 640 sec.

Quantitative analysis of regional thallium-201 activity. On the thallium-201 scintigrams taken in the 30 degree LAO projection, identical rectangular regions of interest, each consisting of 96 pixels (six crystals $\times$ 16 positions), were chosen over the left ventricular myocardial segments supplied by the LAD and CIRC arteries. Localization of regions was facilitated with count profiling across the image which aided in identification of the center and borders of the scintigram. The counts in each region of interest were summed without background subtraction and the ratio of the counts in the LAD region to the counts in the CIRC region was calculated. To determine the effect of background correction, the same ratio was also calculated for each scintigram after subtraction of background activity. For background determination, a region of interest of identical size was positioned over the left lung field posterior to the left ventricle and the counts in this region were subtracted from LAD and CIRC counts.

Coronary arteriography and left ventriculography. Left ventricular catheterization and coronary arteriography were performed percutaneously by the Judkins technique.[14] Coronary arteriograms were recorded on 35 mm cineangiographic film at 50 frames/sec with a 6 inch, cesium-iodide image intensifier. Films were interpreted independently by a cardiovascular radiologist and a cardiologist, and a consensus interpretation was reached.

Measurement of regional left ventricular blood flow. Regional left ventricular myocardial blood flow was measured by recording regional clearance rates of xenon-133 from the left ventricular myocardium with a multicrystal scintillation camera (System 70; Baird Atomic, Inc.).[15] The array of scintigraphic crystals, which is identical to that of the multicrystal camera used for the thallium-201 studies, was equipped with a 1.5 inch parallel-hole collimator and positioned in the 30 degree LAO projection. Radiopaque-radioactive markers, placed on the chest wall, were filmed during an angiogram of the left coronary artery in the LAO projection and also were recorded with the multicrystal scintillation camera in the same LAO projection.

Approximately 20 mCi of xenon-133 dissolved in 1 to 2 ml of sterile pyrogen-free saline was injected rapidly through the left coronary catheter into the left main coronary artery. The regional clearance of xenon-133 from different areas of the myocardium was recorded for 2 min. The slope (κ) of the initial portion of the myocardial xenon-133 clearance curve recorded by each crystal was calculated by monoexponential analysis of the activity recorded for the first 40 sec after the peak count rate. Regional myocardial flow rates were calculated by the Kety formula[16, 17]: $F = 100 \times \kappa \times \lambda/\rho$, where F is the myocardial capillary blood flow (ml/100g/min), λ is the blood/myocardium partition coefficient (0.72) for xenon determined for normal dog heart,[18] and ρ is the specific gravity of tissue (1.05). Mean left ventricular myocardial blood flow per unit mass measured by the xenon-133 clearance technique has correlated well with blood flow measured by radioactive microsphere technique in anesthetized dogs with heterogeneity of local perfusion induced by partial coronary occlusion.[19]

The pattern of local myocardial blood flow rates measured by individual crystals was then superimposed on a tracing of the left coronary arteriogram filmed in the LAO projection. Correct

TABLE 1
Clinical data, exercise stress testing results, and thallium-201 perfusion scintigraphic findings

Patient/ age/sex	History	Resting ECG	Arteriography LAD	LCX	RCA	Left ventricu-lography	Exercise testing BP × HR	ECG ST segment	Thallium scintigraphy Exercise defect	4-hr defect
Group 1: Control patients										
1/47/M	Atyp	Normal	0	0	0	Normal	23,010	−	None	None
2/60/F	Atyp	Normal	0	0	0	Normal	22,475	+	None	None
3/48/F	Atyp	Normal	0	0	0	Normal	23,800	−	None	None
4/48/M	Atyp	Normal	0	0	0	LVH	14,338	−	Inf, Septal	None
5/48/F	Atyp	Normal	0	0	0	Normal	24,160	+	None	None
6/55/M	Atyp	LVH	0	0	0	Normal	29,240	−	None	None
7/50/M	Atyp	Normal	50	0	50	Diffuse Hypo	14,280	−	Inf	Inf
8/64/M	AP	Normal	0	50	0	Diffuse Hypo	26,520	−	None	None
9/57/M	AP	IMI	0	0	90	Inf Hypo	25,560	−	Inf	None
10/32/M	AP	Normal	40	0	100	Normal	20,544	−	None	None
11/38/M	AP	Normal	50	0	100	Inf Hypo	12,768	−	None	None
Group 2: Patients with left coronary artery disease										
1/67/M	MI	IMI	80	0	100	Inf Akinesis Ant Hypo	8,800	−	Inf, Apical Septal	Inf, Apical
2/63/F	AP	ASMI, IMI	100	30	100	Ant Lat, Apical Inf Akinesis	15,840	+	Ant, Septal Inf	Ant, Septal
3/64/M	AP	ASMI	100	50	0	Ant Apical Akinesis	18,480	−	Inf, Apical Septal	Septal
4/52/M	AP	Normal	0	80	100	Inf Akinesis	10,440	+	None	None
5/63/M	AP	Normal	95	0	100	Normal	16,640	+	Ant, Inf Septal	Inf
6/37/M	MI	PLMI	50	75	80	Inf Hypo	25,800	−	Lat	Lat
7/62/M	AP	Normal	100	0	70	Ant Lat Apical Hypo	16,562	+	Apical, Septal Inf	Inf
8/52/M	AP	Normal	0	80	70	Normal	25,200	−	Post-Lat	Post-Lat
9/56/M	AP	Normal	90	60	80	Ant Hypo	23,760	+	None	None
10/49/M	AP	Normal	90	80	100	Inf, Apical Hypo	23,496	+	Ant, Septal Apical	None
11/67/M	AP	PMI	100	70	99	Inf Hypo	16,168	+	Ant, Apical Septal	None
12/62/F	AP	ST changes	90	95	100	Inf Hypo	15,444	+	Inf, Lat	None
13/42/M	AP	IMI, PMI	60	100	60	Normal	12,882	−	Lat	Lat
14/52/M	Atyp	Normal	0	70	0	Normal	23,100	−	None	None

LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; BP × HR = pressure rate product (blood pressure times heart rate); Atyp = atypical chest pain; AP = angina pectoris; MI = myocardial infarction; IMI = inferior myocardial infarction; ASMI = anterior septal myocardial infarction; Ant = anterior; Inf = inferior; Hypo = hypokinesis; PLMI = posterolateral myocardial infarction; PMI = posterior myocardial infarction; LAT = lateral.

alignment and appropriate magnification were achieved with the radiopaque-radioactive markers. Myocardial blood flow rates measured in a rectangular matrix of six crystals overlying the myocardium supplied by the LAD artery were averaged to obtain a mean LAD myocardial blood flow rate. This matrix of crystals was chosen so that it was identical in shape, size, and number of pixels to the six-crystal matrix region of interest selected over the LAD distribution on the exercise thallium-201 perfusion scintigrams taken in the LAO projection. The mean CIRC myocardial blood flow was also determined in a similar six-crystal matrix overlying myocardium supplied by the CIRC artery, and the ratio of LAD/CIRC myocardial blood flows was calculated. Alignment of corresponding regions of interest in the thallium-201 scintigram and xenon-133 myocardial flow pattern was determined by visual inspection.

Rapid atrial pacing. A bipolar pacing electrode was positioned by fluoroscopy in the coronary sinus. The heart rate was increased in 10 beat increments at 1 min intervals until the patient experienced angina or until a maximal heart rate of 150 beats/min was attained.[20] The tachycardia was sustained for several minutes during electrocardiographic monitoring while myocardial blood flow was measured again after repeat intracoronary injection of xenon-133. The double product of heart rate times systolic blood pressure was used as an index of myocardial oxygen consumption.

Statistical analysis. Group differences were evaluated by Student's t test. Relationships between variables were tested by linear regression.[21]

Results

Clinical, electrocardiographic, and angiographic data for the two patient groups are summarized in table

TABLE 1
(Continued)

Regional activity ratios			
Exercise LAD/CIRC	4 hr scintigram LAD/CIRC	Exercise LAD/CIRC	4 hr scintigram LAD/CIRC
(uncorrected)		(background corrected)	
0.89	0.94	0.83	0.90
0.98	0.99	0.97	0.99
0.99	0.99	0.98	0.98
0.91	0.90	0.85	0.87
1.06	1.07	1.09	1.14
0.97	1.00	0.95	1.00
0.94	0.90	0.87	0.82
0.91	0.90	0.84	0.86
0.91	0.95	0.85	0.91
0.92	1.01	0.88	1.02
0.99	1.02	0.98	1.04
0.75	0.85	0.51	0.71
0.81	0.90	0.63	0.76
0.71	0.80	0.38	0.43
0.92	0.98	0.86	0.96
0.86	0.95	0.78	0.92
1.07	1.08	1.12	1.15
0.74	0.80	0.53	0.65
1.15	1.14	1.32	1.30
0.96	1.00	0.95	1.00
0.67	0.85	0.40	0.75
0.85	0.90	0.74	0.83
1.00	0.97	1.00	0.95
1.13	1.14	1.27	1.29
0.86	0.98	0.73	0.96

1 with results of exercise stress testing and analyses of thallium-201 scintigrams. The two groups did not differ significantly in mean age or distribution of men and women. Six of the patients in group 1 had normal coronary arteriograms and nine had normal electrocardiographic responses to exercise. Three patients in group 1 had stenotic lesions of the right coronary artery greater than 70%, and two of these patients developed inferior wall perfusion defects on exercise thallium-201 scintigrams. The remaining nine patients had normal exercise thallium-201 scintigrams. Thirteen of the patients in group 2 had multivessel coronary artery disease (table 1). Seven of the 14 patients in group 2 had ischemic ST segment responses during both exercise stress testing and rapid atrial pacing. Eleven (80%) developed perfusion defects on exercise thallium-201 scintigrams.

The maximal heart rate–blood pressure product attained in groups 1 and 2 during exercise (mean 19,572 ± 5630 SD) did not differ significantly from that attained during rapid atrial pacing (mean 19,591 ± 3042). Maximal heart rate–blood pressure products measured during peak exercise and during rapid pacing correlated moderately (r = .65) for the 25 patients. Mean left ventricular myocardial blood flow measured in patients at rest and during rapid pacing correlated well with pressure rate product for both group 1 (r = .81) and group 2 (r = .76).

Relationship between relative thallium-201 distribution and regional myocardial blood flow for group 1. Figure 1, *top*, shows the thallium-201 scintigram recorded immediately after exercise and the pattern of regional myocardial blood flow measured during rapid atrial pacing in a representative patient from group 1. In this patient with a normal coronary arteriogram, the exercise thallium-201 scintigram was normal and the counts in the LAD and CIRC regions of interest were nearly identical; the LAD/CIRC count ratio was 0.99. During rapid atrial pacing in this patient, regional myocardial blood flow was 115 ml/100 g/min in the LAD region of interest and 116 ml/100 g/min in the CIRC region of interest; the LAD/CIRC myocardial blood flow ratio was 0.99.

Figure 2 shows the regional myocardial blood flow rates recorded during pacing for patients in group 1. The range of mean myocardial blood flow rates attained during pacing varied from 46 to 130 ml/100 g/min (table 2). Over this wide range of absolute flow rates, the regional flow rates in the LAD and CIRC regions were highly correlated (r = .97), and the mean LAD/CIRC myocardial blood flow ratio was 0.97 ± 0.6. Figure 2 shows the LAD/CIRC ratios of thallium-201 activity in the exercise perfusion scintigrams of the group 1 patients. Thallium-201 activity in the two regions during exercise was highly correlated (r = .98). The mean exercise LAD/CIRC thallium-201 activity ratio was 0.95 ± 0.05, a value not significantly different from the LAD/CIRC myocardial blood flow ratio of these patients during atrial pacing. Thus, the homogeneity of thallium-201 myocardial distribution during exercise corresponded to the homogeneity of regional myocardial blood flow during pacing over a wide range of absolute flow rates.

Relationship between relative thallium-201 distribution and regional myocardial blood flow for group 2. Figure 1, *middle*, shows the thallium-201 exercise scintigram and the regional myocardial blood flow pattern during atrial pacing in a representative patient from group 2. Recorded in the LAO projection, the thallium-201 scintigram of this patient with proximal occlusion of the LAD artery displays a large perfusion defect in the interventricular septum region. The LAD/CIRC ratio of thallium-201 activity in the exercise scintigram was 0.75. During atrial pacing in this patient, regional myocardial blood flow was 89 ml/100 g/min in the LAD region of interest and was 122 ml/100 g/min in the CIRC region of interest; the LAD/CIRC myocardial blood flow ratio was 0.73. In figure 3, LAD/CIRC ratios of thallium-201 activity calculated from exercise scintigrams are plotted against the LAD/CIRC flow ratios during pacing for each patient in group 2. The LAD/CIRC myocardial flow ratios in this group varied from 0.54 to 1.14 (table 2); over this range the LAD/CIRC ratio of thallium-201 activity correlated significantly with the LAD/CIRC myocardial blood ratio (r = .84). The regression line of the two ratios did not differ significantly from the line of identity.

Figure 4 shows the same relationship plotted after correction for background thallium-201 activity. Although the relationship between the LAD/CIRC ratio of the thallium-201 activity and LAD/CIRC flow ratio remained linear, the slope was markedly increased. Thus, background subtraction caused the extent of re-

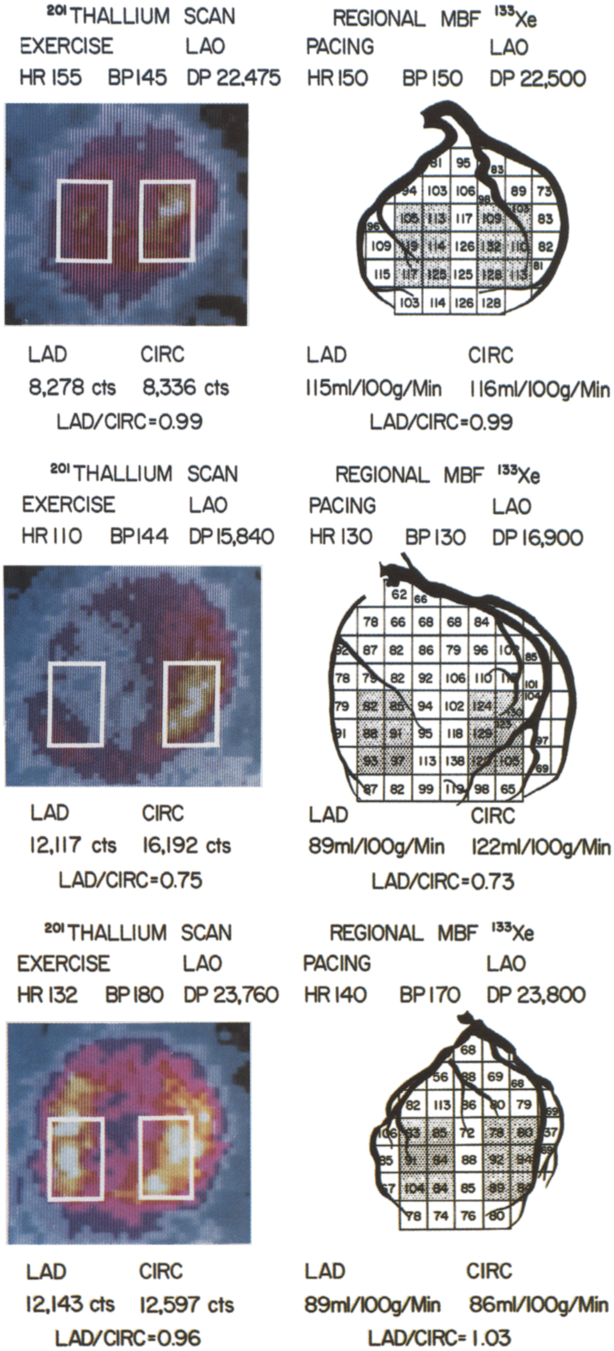

FIGURE 1. *Top*, Thallium-201 exercise scintigram and the pattern of regional myocardial blood flow measured during rapid atrial pacing to a similar pressure-rate product for a patient in group 1. Regional thallium-201 activity was nearly identical for the LAD and CIRC regions delineated by the rectangular regions of interest, and mean regional myocardial blood flow was equivalent for identical LAD and CIRC regions depicted by stippling. *Middle*, Thallium-201 scintigram obtained during exercise and the pattern of regional myocardial blood flow measured during rapid atrial pacing in a patient with proximal occlusion of the LAD and right coronary arteries and extensive anteroseptal and inferior myocardial infarction. A large thallium-201 perfusion defect is evident in the septum and apical-inferior segments with reduced thallium-201 uptake in the LAD region compared with the CIRC region (LAD/CIRC ratio = 0.75). A corresponding reduction in regional myocardial blood flow is evident in the LAD distribution (89 ml/100 g/min) compared with the CIRC distribution (122 ml/100 g/min; LAD/CIRC ratio = 0.73). *Bottom*, Thallium-201 exercise scintigram recorded in the LAO projection and pattern of regional myocardial blood flow measured during rapid pacing in a patient with severe proximal lesions of the LAD and CIRC arteries. Regional myocardial blood flow was nearly equal in the LAD and CIRC regions, and the thallium-201 scintigram appeared normal, which indicated that balanced lesions of the LAD and CIRC arteries may cause diffusely reduced blood flow and homogeneous thallium-201 uptake.

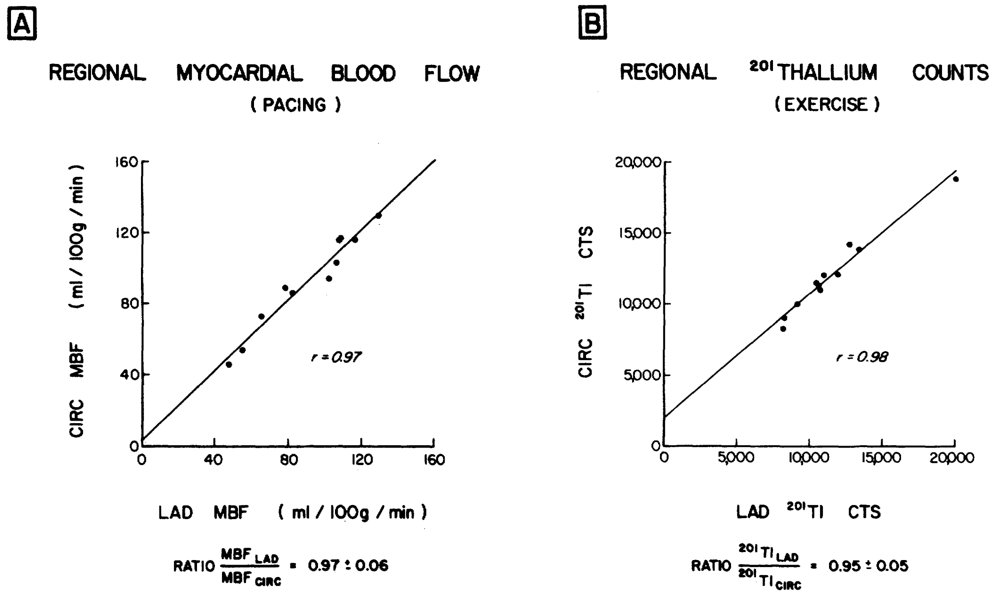

FIGURE 2. *A*, Linear correlation between regional myocardial blood flow measured in the LAD and CIRC distributions during rapid atrial pacing in patients without significant lesions of the left coronary artery (group 1). *B*, Linear correlation between thallium-201 activity recorded in CIRC and LAD distributions from exercise scintigrams for patients in group 1. Patterns of myocardial blood flow and thallium-201 distribution were both homogeneous for group 1 patients.

TABLE 2
Regional left ventricular myocardial blood flow (MBF)

	Regional LV MBF at rest				Rapid atrial pacing		Regional LV MBF during pacing		
	HR × BP	LAD	CX	Ratio LAD/CIRC	Max HR × BP	ST depression	LAD	CIRC	Ratio LAD/CIRC
Group 1: Control patients									
1	8,450	53	57	0.93	20,250	–	78	89	0.88
2	11,560	78	84	0.93	22,500	–	116	116	1.00
3	14,104	74	77	0.96	21,760	+	82	86	0.95
4	6,380	40	44	0.91	14,300	–	55	54	1.02
5	20,400	140	147	0.95	22,500	–	129	130	0.99
6	11,900	73	72	1.01	21,000	–	107	116	0.92
7	4,950	53	53	1.00	11,550	–	65	73	0.89
8	9,045	63	55	1.14	19,500	+	102	94	1.08
9	6,600	50	47	0.94	18,200	+	108	117	0.92
10	10,400	70	70	1.01	19,600	–	105	103	0.97
11	9,660	51	48	1.06	16,250	–	47	46	1.03
Group 2: Left coronary artery disease									
1	8,800	55	59	0.93	15,950	–	98	136	0.72
2	9,045	43	65	0.66	16,900	+	91	119	0.76
3	5,985	42	63	0.67	16,500	–	77	142	0.54
4	7,500	49	47	1.04	18,000	–	71	78	0.91
5	8,775	43	48	0.90	19,600	+	103	116	0.89
6	9,375	63	54	1.17	19,500	–	83	83	1.00
7	6,480	41	45	0.91	15,876	+	65	76	0.86
8	6,600	46	44	1.04	18,200	+	107	104	1.03
9	8,640	49	50	0.98	23,800	–	88	86	1.03
10	9,765	52	56	0.93	22,630	+	82	102	0.80
11	8,520	47	47	1.00	19,610	+	87	109	0.80
12	7,560	50	52	0.95	19,500	+	64	65	0.98
13	5,700	45	41	1.08	13,300	–	73	66	1.09
14	7,695	52	51	1.03	18,000	–	65	69	0.94

For abbreviations see Table 1.

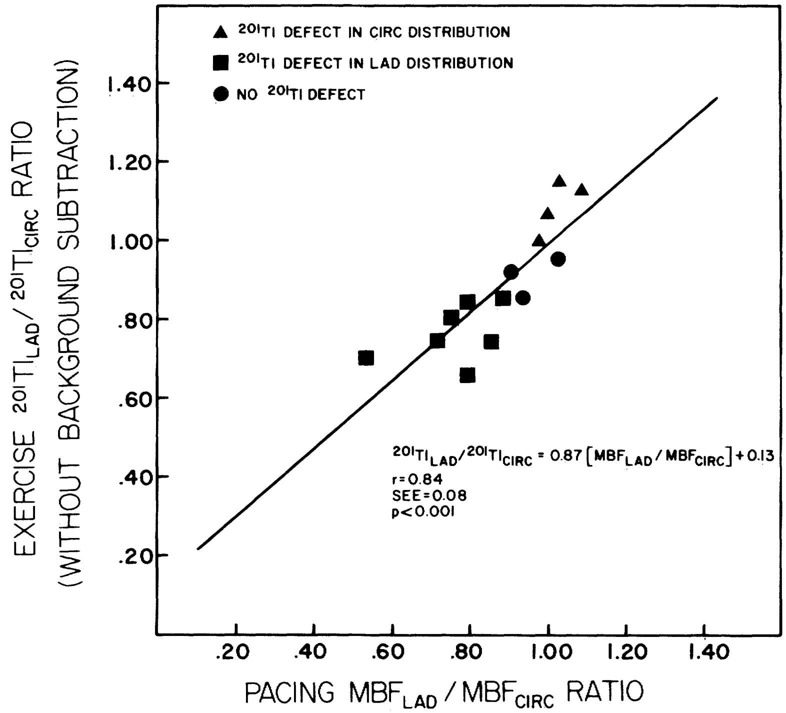

FIGURE 3. Ratios of regional thallium-201 activity recorded from exercise scintigrams correlated with ratios of regional myocardial blood flow measured during rapid pacing for patients with significant lesions of the left coronary artery (group 2). Relative thallium-201 uptake correlates ($r = .84$) with relative myocardial blood flow, which indicates that the distribution of thallium-201 to the left ventricle is determined by the relative distribution of myocardial blood flow. Thallium-201 ratios were calculated from regional thallium-201 activity uncorrected for background activity.

gional blood flow reduction to be overestimated on thallium-201 exercise scintigrams.

Regional LAD/CIRC ratios of thallium-201 activity measured from thallium-201 scintigrams taken 4 hr after exercise also correlated ($r = .68$) with LAD/CIRC ratios of regional myocardial blood flow measured in group 2 patients at rest (figure 5). However, both the slope and intercept of this relationship were altered from that observed in exercise scintigrams and reflected greater thallium-201 activity relative to flow.

In group 2, 11 of the 14 patients (79%) had thallium-201 perfusion defects present on exercise scintigrams. Mean LAD/CIRC ratios for regional thallium-201 activity and regional myocardial blood flow for these patients are shown in table 3. Mean LAD/CIRC ratios for regional thallium-201 activity and myocardial

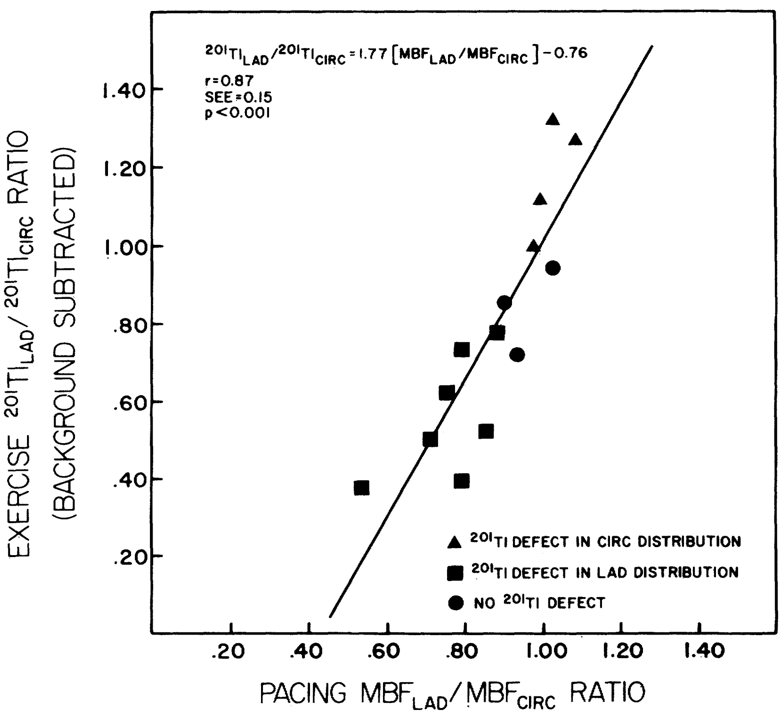

FIGURE 4. Ratios of regional thallium-201 activity recorded from exercise scintigrams correlated with ratios of regional myocardial blood flow measured during rapid pacing for group 2 patients. Thallium-201 ratios were calculated from background corrected thallium-201 activity. Background subtraction altered the slope and intercept of the regression line, causing thallium-201 activity ratios to overestimate flow defects.

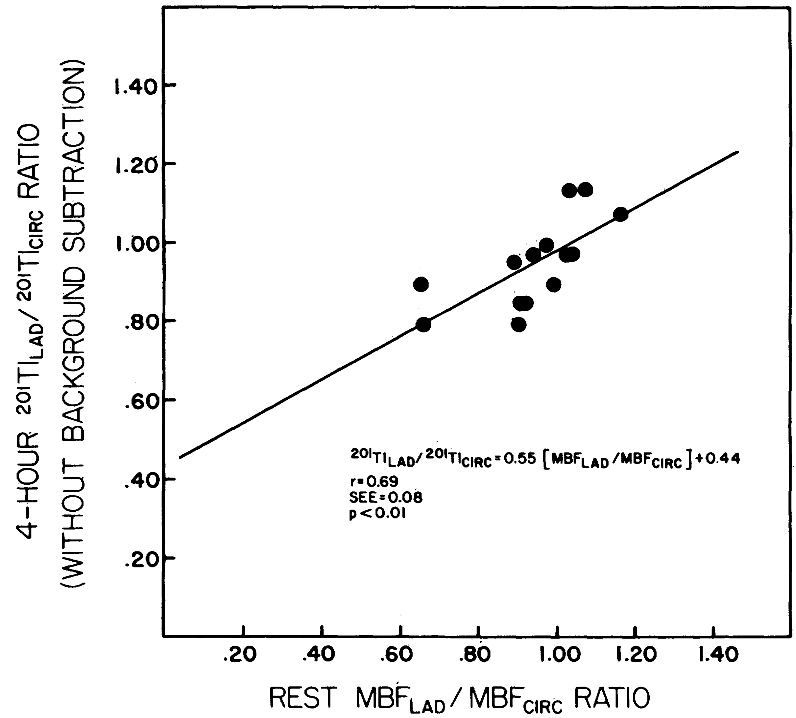

FIGURE 5. Ratios of regional thallium-201 activity recorded from 4 hr delayed thallium-201 scintigrams without background correction correlated with ratios of regional myocardial blood flow measured at rest for group 2 patients. The y intercept of the regression line reflects thallium-201 excess relative to flow in the ischemic zones, consistent with resolution of thallium-201 defects observed clinically on scintigrams taken after a 4 hr delay.

blood flow ratios were less than 1 for the seven patients with defects in the LAD distribution, approached unity for the three patients without perfusion defects, and were greater than 1 for the four patients with CIRC perfusion defects. For these three groups of patients, ratios of regional thallium-201 activity did not differ significantly from ratios of regional myocardial blood flow measured during stress (table 3).

Two of the three group 2 patients (patients 4 and 14) with normal thallium-201 scintigrams taken during exercise had distal CIRC lesions without LAD lesions. Regional myocardial flow was not reduced in the CIRC distribution of these two patients during rapid pacing. The blood flow pattern recorded for the other patient with a normal thallium-201 scintigram taken during exercise is shown in figure 1, *bottom*. Despite significant proximal lesions of the LAD and CIRC arteries, the thallium-201 scintigram was normal and regional thallium-201 uptake was homogeneous. The flow pattern demonstrated that regional myocardial blood flow in the LAD and CIRC distributions was approximately equal.

TABLE 3
LAD/CIRC ratios (mean ± SD) of regional thallium-201 activity and regional myocardial blood flow in group 2 patients

		LAD defect (n = 7)	No defect (n = 3)	CIRC defect (n = 4)
Exercise	^{201}Tl LAD / ^{201}Tl CIRC	0.77±0.07 NS	0.91±0.05 NS	1.07±0.08 NS
Pacing	MBF LAD / MBF CIRC	0.77±0.12	0.96±0.06	1.03±0.05
4 hr	^{201}Tl LAD / ^{201}Tl CIRC	0.86±0.06 NS	0.99±0.01 NS	1.08±0.08 NS
Rest	MBF LAD / MBF CIRC	0.86±0.14	1.02±0.03	1.06±0.09

MBF = myocardial blood flow.

Discussion

In our study, the spatial distribution of thallium-201 activity in LAO exercise scintigrams was compared with the distribution of regional myocardial blood flow rates in LAO myocardial perfusion patterns measured during atrial pacing with intracoronary xenon-133 injection. Thallium-201 scintigrams and regional myocardial blood flow rates were recorded with multicrystal scintillation cameras positioned in similar LAO projections. Use of identical crystal arrays permitted direct comparison of regional thallium-201 activity and regional myocardial blood flow in regions of interest of identical size and configuration in similar positions. Patients with and without significant left coronary obstructions (> 70% luminal diameter) were compared.

Regional myocardial blood flow was measured during rapid atrial pacing because techniques are not currently available for measuring regional myocardial blood flow in patients during upright exercise stress testing. The justification for comparing studies of regional myocardial perfusion during exercise and during pacing was the observation that maximal pressure rate-products were comparable during the two forms of stress for individual patients. The onset of angina pectoris, induced by either exercise or rapid pacing, has been shown to occur reproducibly at similar pressure-rate products in individual patients with coronary artery disease.[22, 23] Since myocardial blood flow has been shown to be proportional to the pressure-rate product in this and other studies,[9, 10] it was assumed that the magnitude of myocardial blood flow was similar during rapid pacing and during exercise.

At rest and during rapid atrial pacing, a wide range of absolute myocardial blood flow rates was observed in patients without significant disease of the left coronary artery (group 1). Studies in animal models have shown that myocardial oxygen consumption and myocardial blood flow are determined primarily by heart rate, myocardial wall stress, and ventricular contractility.[24–26] Studies from this laboratory have demonstrated that left ventricular myocardial blood flow is largely determined by these three hemodynamic variables in patients with multivessel coronary artery disease,[27] congestive cardiomyopathy,[28] aortic stenosis,[29] systemic hypertension,[30] and atypical chest pain.[27, 30] These studies have shown that variations in heart rate, left ventricular cavity size, wall thickness, systolic blood pressure, and ventricular contractility account for the wide range of blood flow rates observed in patients with normal coronary arteriograms. In our study, mean left ventricular myocardial blood flow correlated with pressure rate-product for both patient groups, which reflects the effect of hemodynamic variables on resting flow levels.

Despite the variation in mean left ventricular flow rates among group 1 patients, regional flow rates in the LAD and CIRC distributions were very similar for each patient during rapid pacing ($r = .97$). Regional thallium-201 activity levels in the LAD and CIRC regions were also similar in the exercise thallium-201 scintigrams ($r = .98$). Thus, regardless of whether the absolute mean left ventricular myocardial blood flow was low or high, the relative distribution of thallium-201 activity in the LAD and CIRC regions was homogeneous for individual patients in group 1 and corresponded to the homogeneous distribution of myocardial blood flow in these regions.

In the patients with significant lesions of the left coronary artery (group 2), ratios of regional thallium-201 activity recorded in the LAD and CIRC distributions after exercise correlated closely with ratios of regional myocardial blood flow measured in these distributions during rapid pacing. The resulting regression line approximated the line of identity. This correlation indicates that the relative spatial distribution of thallium-201 activity in exercise perfusion scintigrams accurately reflects the distribution of myocardial blood flow rates in patients with coronary artery disease. These data also support the validity of quantitative analysis of exercise thallium-201 scintigrams with diminished regional thallium-201 uptake expressed as percent normal activity.[31, 32]

The correlation of regional thallium-201 activity ratios with myocardial blood flow ratios was equally good with or without background subtraction ($r = .84$ vs $r = .87$). However, background subtraction significantly altered the slope of this relationship. Without background subtraction, the regression line approximated the line of identity; after background subtraction, ratios of thallium-201 activity overestimated the magnitude of flow reduction. Two possible explanations may account for this discrepancy. First, conventional subtraction of chest activity recorded over the lungs from activity recorded over the myocardium may result in oversubtraction of background, as has been suggested by experiments in animal models.[33, 34] Alternatively, depressed uptake of thallium-201 in ischemic myocardial segments might account for the observed change in the slope and intercept.

The distribution of regional thallium-201 recorded on scintigrams taken after a 4 hr delay after redistribution in the group 2 patients also correlated linearly with relative regional myocardial blood flow measured at rest. However, the correlation was relatively poor and the slope and intercept were changed, which reflects disproportionately greater thallium-201 distribution relative to flow in ischemic regions of the scintigrams taken after a 4 hr delay (figure 5). This observation in patients is consistent with a similar finding in canine experiments reported by Pohost et al.[35] With radioactive microspheres to measure regional myocardial blood flow, they have demonstrated that thallium-201 activity is increased relative to flow in ischemic zones 4 hr after thallium-201 injection. Increased uptake of thallium-201 in ischemic zones, relative to the non-ischemic zones, results in resolution of thallium-201 defects on scintigrams taken after 4 hr. Pohost et al.[35] have also demonstrated that resolution of thallium-201 perfusion defects distal to persistent severe coronary artery stenoses does not require restoration of normal blood flow. Six of the patients with thallium-201 perfusion defects on exercise scintigrams in our study had complete or partial resolution of defects on images taken after a 4 hr delay. In all six of these patients, resting flow was reduced below levels measured in normally perfused zones, which suggests that resolution of thallium-201 defects does not require restoration of normal blood flow.

Although experimental studies in anesthetized dogs have demonstrated a close linear relationship between the thallium-201 uptake and regional myocardial blood flow measured by radioactive microspheres after short-term coronary artery occlusion,[1-3] other studies, reported by Weich et al.[4] and by Gould,[5] have suggested that the distribution of thallium-201 in the myocardium is not linearly related to myocardial perfusion when flow is increased above control values with coronary vasodilators. Conflicting data have been reported by Nielsen et al.,[6] who observed a close linear correlation between thallium-201 uptake and increased regional myocardial blood flow in chronically instrumented dogs during treadmill exercise. In our study, relative thallium uptake during exercise was found to correlate linearly with relative regional blood flow over a moderately wide range of increased flow rates induced by rapid pacing.

In summary, our study demonstrates that the homogeneous distribution of regional thallium-201 in the left ventricle during exercise in patients with normal left coronary arteries corresponds to the homogeneous distribution of regional myocardial flow during atrial pacing over a wide range of left ventricular flow rates, and that relative thallium-201 uptake measured scintigraphically corresponds closely to relative myocardial blood flow in patients with coronary artery disease.

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Erratum

Hull RD et al: The diagnosis of acute recurrent deep-vein thrombosis: a diagnostic challenge. Circulation **67:** 901, 1983.

An error appeared on page 904 under the heading "Comparison of long-term outcome in positive and negative cohorts." Beginning with line six, the article should have read:

> Three of 181 patients negative by impedance plethysmography and leg scanning returned with objectively documented recurrent venous thromboembolism, a frequency of 1.7% (95% confidence interval 0.4% to 4.8%). In contrast, 18 of 89 patients positive by impedance plethysmography or leg scanning returned with objectively documented recurrent venous thromboembolism, a frequency of 20.2% (95% confidence interval 12.5% to 30.1%). The difference between these two groups was statistically significant ($p < .001$).