Thallium-201 Scintigraphic Quantitation of Regional Flow Disparity and Subsequent Redistribution in Dogs

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Although quantitative analysis of postexercise thallium-201 (^{201}Tl) scintigrams has been employed clinically for the diagnosis of coronary disease, the precise relationship of the quantitated defects to microsphere determined blood flow has not been determined. Accordingly, ^{201}Tl was injected during exercise in 12 control dogs and seven with left circumflex (LCf) artery stenosis. Gamma camera scanning was started 10 min after ^{201}Tl injection and continued for 3 hr. In the control animals, scintigraphic ^{201}Tl activities in left anterior descending (LAD) and LCf perfusion territories were equal 10 min after ^{201}Tl injection and the loss of ^{201}Tl activity over 3 hr was 54.3 ± 3.4% and 57.0 ± 3.6% (mean ± s.e.e.) of initial LAD and LCf activity, respectively (p = N.S.). In the experimental group, LCf activity 10–14 min after ^{201}Tl injection averaged 67.4 ± 5.9% of LAD activity in the same heart ($p < 0.001$). Furthermore, LCf activity in the experimental animals was significantly lower than LCf activity in the control dogs ($p < 0.005$), while LAD activities were not different in the two groups. The ratio of LCf/LAD scintigraphic ^{201}Tl activity immediately after exercise was linearly related to, but higher than, the ratio of regional blood flows at peak exercise ($r = 0.88$, $p < 0.001$) as determined by microsphere injection. Scintigraphic redistribution was also correlated with directly measured redistribution determined by well counter analysis ($r = 0.83$, $p < 0.025$). Thus, in this exercise model, quantitative ^{201}Tl scintigraphy accurately assessed the initial postexercise flow disparity and subsequent redistribution.

J Nucl Med 27:75–83, 1986

Numerous experimental studies have demonstrated that immediately after injection of thallium-201 (^{201}Tl) isotope distribution to the myocardium is proportional to blood flow (*1–5*). With time however, ^{201}Tl "redistributes," and the isotope content and distribution in the left ventricular wall are then determined by the mass of viable myocardium (*1–5*). These properties have been exploited in clinical practice as qualitative analysis of exercise ^{201}Tl scintigrams has become a useful method for the detection of coronary artery obstructive disease and differentiation of potentially ischemic from infarcted myocardium (*6–8*).

Recently, postexercise quantitative ^{201}Tl scintigraphy has been introduced. Reduction in quantitative ^{201}Tl regional myocardial activity immediately after exercise and/or delayed ^{201}Tl washout over time is associated with significant obstructive coronary artery disease (*9–11*). However, there are few data available regarding the feasibility of employing such scintigraphic techniques to quantitate the magnitude of the relative flow reduction associated with exercise. We therefore compared quantitative scintigraphic measurements with those obtained by well counter analysis of myocardial flow in a dog model of exercise-induced regional flow disparity.

Received Apr. 1, 1985; revision accepted Aug. 30, 1985.

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* Presented in part at the National Meeting of the American Federation for Clinical Research, Washington, DC, May 2, 1983.

MATERIALS AND METHODS

Experimental Preparation

Large mongrel dogs (20–25 kg) were initially sedated with i.v. morphine sulfate (1 mg/kg) and then anes-

thetized with intravenous sodium pentobarbital (25 mg/kg). Through a left thoracotomy the left circumflex (LCf) coronary artery was isolated proximal to the first major marginal branch. After placement of a balloon occluder around the artery, the LCf was critically stenosed by tying a ligature around the artery and an interposed 18 or 19 g needle. The latter was then removed. This stenosis was considered satisfactory if the peak reactive hyperemic response to a 15-sec LCf occlusion measured with a proximal encircling electromagnetic flow probe was diminished by 50–80% when compared with the hyperemic response seen prior to narrowing of the coronary artery. In four animals, a small branch of the LCf immediately distal to the balloon occluder and region of vessel narrowing could be isolated for insertion of a 16-g polyethylene catheter which was advanced in retrograde fashion until its tip was at the junction of the branch with the main vessel. The catheter was securely tied in place so that it could not migrate into the lumen of the main LCf. Postmortem examination confirmed proper positioning in all animals.

Polyvinyl chloride catheters (15 g) were inserted into the left atrial appendage for pressure monitoring and microsphere injections and the descending thoracic aorta for pressure measurements and blood sampling. A third catheter was inserted through the right atrial appendage and advanced into the atrial cavity for injection of thallium-201. The ends of the catheters were exteriorized near the dog's spine. The edges of the pericardium were approximated and the chest closed in layers. Each dog received an antibiotic injection following the completion of the surgical procedure. The animals were studied 4–8 days later after recovery from surgery. No studies were performed unless it was evident that the animal was willing and able to cooperate with minimal discomfort.

Treadmill Exercise and Blood Flow Measurement

Pressure catheters were attached to Statham P23 Db fluid-filled transducers. The electrocardiogram recorded with adhesive electrodes applied to the external thoracic wall and left atrial and aortic pressures were continuously monitored with a multichannel oscillographic recorder. A withdrawal pump was connected to the aortic catheter for timed collection of microspheres in arterial blood. Interposed in the withdrawal line was a densitometer for indocyanine green cardiac output determinations.

Myocardial blood flow was determined with 15 ± 1-μm microspheres labeled with scandium-46(^{46}Sc) and either strontium-85(^{85}Sr) or tin-113 (^{113}Sn). Four to 7 $\times 10^6$ microspheres suspended in 10 ml of 6% dextran to which two drops of Tween 80 had been added were injected into the left atrium over 10–15 sec for each flow determination. Prior to injection, the suspension was ultrasonicated for 10–20 min to prevent clumping.

On the day of the study while the dog was resting quietly on a treadmill baseline heart rate, left atrial and aortic pressures and cardiac output were recorded. After completion of these measurements, the treadmill was started and speed and incline were increased until the heart rate either reached 220 beats/min or the animal began pulling on the leash as the work stage was increased. These endpoints were chosen as a compromise to adequately stress the coronary circulation while allowing the animals to run long enough to complete the exercise measurements and thallium injection. Exercise hemodynamic recordings were made. Subsequently, the arterial withdrawal pump was started, and after 5–10 sec ^{46}Sc-labeled microspheres were injected into the left atrium. After completion of the microsphere injection, 0.5 ml indocyanine green was injected into the left atrium for cardiac output determination. Left atrial pressure was then monitored. After 70 sec, the withdrawal pump was stopped and arterial pressure recorded. Immediately after termination of the blood collection, 2 mCi of ^{201}Tl were injected into the right atrium. The animal continued running for one additional minute at this exercise level. The treadmill was slowed in stages over ~30 sec and then stopped. The dog was anesthetized 2–3 min after exercise with sodium pentobarbital in small incremental doses designed to produce light anesthesia.

Twelve control animals also underwent exercise thallium scintigraphy. A polyethylene catheter was inserted percutaneously into a superficial vein in a hind limb. The animals were monitored electrocardiographically during treadmill running using the same exercise protocol as described above. Thallium-201 was injected during exercise, and the animals continued running at this level for 1 min. After a brief cool-down period, the animals were anesthetized with sodium pentobarbital. The scan acquisition and analysis protocols were thereafter identical for the experimental and control groups.

Thallium Scintigraphy

The anesthetized animals were placed right side down on an imaging table. A gamma camera equipped with an all-purpose collimator was positioned parallel to and just above the chest wall with the heart in the center of the field. A 15% energy window centered at 77 keV was used to collect ^{201}Tl scintigraphic data. Data were acquired in a 64 × 64 pixel matrix on a dedicated minicomputer. Scanning was begun 10 min after ^{201}Tl injection and continued for 36 5-min frames with the camera-animal relationship held constant. The initial 5-min frame contained a minimum of 450,000 counts, with at least 75,000 counts in the region of the left ventricle.

To determine the scintigraphic perfusion territory of the circumflex artery, 0.1 mCi of ^{201}Tl was injected

through the small polyethylene catheter in a branch of the LCf in four resting animals at least 1 wk prior to the experimental study described above. The animals were then positioned under the gamma camera as previously described, and a 10-min acquisition was begun on the minicomputer. In this way, the LCf (active) and left anterior descending (LAD) (inactive) territories were clearly and reproducibly circumscribed. The animals were scanned again prior to the exercise protocol to ensure complete absence of residual myocardial ^{201}Tl activity.

For processing of the postexercise scintigrams, a region of interest was manually drawn around the perimeter of the left ventricle with the operator designating that pixel of the circumference corresponding to the left ventricular apex (Fig. 1). The operator also designated a rectangular background region of interest situated 4 pixels from the edge of the heart. A computer algorithm then determined the centroid of the left ventricle and generated 24 radials, at 15° increments, from this centroid to pixels on the circumference. That point on the circumference opposite the apex was designated radius 1 with numbering proceeding in a clockwise fashion around the ventricle. Guided by the results of the intracoronary ^{201}Tl injections that helped to demarcate the perfusion territory of the distal LCf, average counts within radials 3–11 (30–150°) were designated as LCf activity, while counts from radials 14–18 (195–255°) were designated as LAD activity. The apex (165–180°) and the central and eight surrounding pixels were excluded from the analysis since LAD and LCf distributions overlap in these regions (Fig. 1).

Background subtraction was accomplished using a modification (*10*) of the bilinear interpolation algorithm first described by Goris et al. (*12*). Since the gamma camera-animal relationships were not changed over the 3 hr of scanning, the same regions of interest selected for the first frame were then employed to analyze each of the ensuing 35 frames, with background determinations made on a frame by frame basis. Scans were not decay corrected since physical decay of the isotope would account for a less than 3% loss of activity over 3 hr.

For analysis of LAD and LCf count activity in the initial 5-min frame, count data were expressed as a percentage of the highest activity in the heart. For analysis of ^{201}Tl "washout" within the LAD and LCf distributions, data from each dog were expressed as a percentage of the heart's average LAD ^{201}Tl activity in the initial 5-min frame. Washout was calculated as the difference in activity between frames 1 and 36. To determine intra- and interobserver variabilities for these methods, scans from nine different animals were processed several months apart by a single observer, and independently by a second observer. The difference in the repeated determinations of initial thallium activity within the LCf and LAD distributions was 0.60 ± 0.8% (mean ± s.e.e.) for a single observer, and 1.03 ± 2.0% for two observers. For washout rates, the differences in repeated determinations within and between observers were 1.3 ± 0.6% and 0.9 ± 0.5%, respectively.

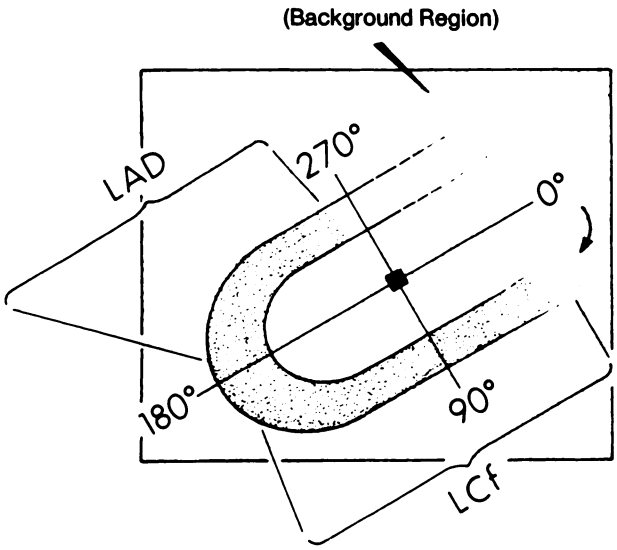

FIGURE 1
Artist's drawing of a frame from a ^{201}Tl scintigram demonstrating a left ventricular silhouette. Background region of interest is shown by stippled area. After operator outlined left ventricle and designated that pixel on circumference corresponding to left ventricular apex, computer algorithm generated 24 radials in 15° increments. By convention, that radius opposite apex was designated radius 1 (0 degrees) with numbering proceeding in clockwise direction

Resting Blood Flow Determination

Immediately after completion of the 3-hr scan in the experimental group, hemodynamics were again recorded and a second myocardial blood flow determination was made with a left atrial injection of microspheres labeled with either ^{85}Sr or ^{113}Sn. These dogs were killed by injection of 20 ml saturated KCl solution into the left atrium.

Myocardial Sample Preparation

To demarcate the myocardial area perfused by the LCf beyond the stenosis (stenosis territory), 3 ml of a concentrated aqueous solution of Evans blue dye were injected through a needle inserted in the LCf or the LCf branch catheter coincident with the administration of the KCl solution. To prevent retrograde flow of the dye into the proximal LCf, the balloon occluder was inflated just before the dye injection. Postmortem examination revealed the LCf to be stenosed but patent in six of the seven dogs. The LCf was completely occluded in one animal, but there was no gross evidence of infarcted tissue.

The ventricular chambers of the extirpated heart

TABLE 1
Hemodynamics at Rest, During Exercise, and 3 hr After Exercise in Dogs with Coronary Stenoses

	HR (bpm)	$\overline{AoP}$ (mmHg)	$\overline{LAP}$ (mmHg)	CO (l/min)
Rest	125.7 ± 4.3*	104.9 ± 3.8	10.2 ± 1.4	3.8 ± 0.3
Exercise	208.6 ± 5.5†	114.6 ± 3.1†	12.6 ± 3.0	8.5 ± 0.5†
3 hr after exercise	149.3 ± 12.0	112.1 ± 4.7	7.4 ± 1.5	2.9 ± 0.1‡

* Mean ± s.e.e.

† $p < 0.001$, Statistical significance of paired comparison between rest and exercise or postexercise state.

‡ $p < 0.05$.

Abbreviations: $\overline{AoP}$ = mean aortic pressure; CO = cardiac output; HR = heart rate; $\overline{LAP}$ = mean left atrial pressure.

were distended with gauze and frozen and stored for at least 1 wk to allow for decay of ^{201}Tl. The left ventricle was then serially sectioned from apex to base into 0.5 cm thick slices. The rings were carefully subdivided into nonstained or normal and Evans blue stained or "stenosis" myocardial regions and cut into wedges. Each wedge was subdivided into inner and outer halves weighing 0.3 to 0.6g. Isotope activity (microsphere labels and ^{201}Tl) of all weighed tissue and reference blood samples was counted in a gamma spectrometer. Net counts/minute (cpm) for each isotope was determined by correcting the raw count data for isotope decay during the period of counting and overlap of isotope energies in the respective energy windows used for counting. A computer was used to solve the multiple mathematical expressions. The cpm for each myocardial piece was normalized for the weight of that piece to obtain cpm/g.

Data Analysis

Myocardial microsphere blood flow (ml/min/g) to each piece was calculated as $(cpm/g)_i \times (f_r/cpm_r)$ where $(cpm/g)_i$ represents the net cpm/g for the ith piece, and f_r and cpm_r represent reference pump collection rate and total counts of the pump sample, respectively. Average flows to the entire stained and unstained myocardial regions were obtained by summing the cpm and the net weight of all pieces within the region of interest and then expressing the results as ml/min/g. Absolute ^{201}Tl myocardial flows could not be calculated. Instead stenosis/normal (LCf/LAD) territory ^{201}Tl myocardial ratios at 3 hr were determined. Since ^{201}Tl distribution to the myocardium immediately after injection during exercise has been shown to be proportional to blood flow (*5*), the microsphere stenosis/normal myocardial blood flow ratio measured at peak exercise was considered to be equivalent to the initial ^{201}Tl ratio. Therefore, the change from the stenosis/normal myocardial blood flow ratio at peak exercise to the directly measured stenosis/normal myocardial ^{201}Tl ratio at 3 hr after exercise was used as a measure of the magnitude of ^{201}Tl redistribution.

Statistical Analysis

All results are expressed as mean ± 1 s.e.e. The significance of differences in flows, flow ratios, in vitro ^{201}Tl ratios and scan parameters between myocardial regions was determined by a paired Student's t-test (*13*). Relationships between variables were tested with linear regression and the significance of these relationships was tested by one-way analysis of variance (*13*). A p value of <0.05 was considered significant.

RESULTS

Exercise Hemodynamics and Blood Flow

During exercise the average heart rate in the 12 control dogs rose to 223 ± 7.3 bpm while they ran at 5.5 ± 0.2 mph and 10.7 ± 1.0% incline. The seven experimental animals ran at 4.7 ± 0.4 mph and 9.1 ± 1.3% incline (both p = N.S.). The control dog exercise heart rates were marginally higher than for experimental animals (223 compared with 209 bpm, $p < 0.05$). Experimental animal hemodynamics before, during exercise, and 3 hr later are presented in Table 1. During exercise, heart rate, mean arterial pressure and cardiac

TABLE 2
Well Counter Analysis

	Stenosis territory (% LV)	Normal territory MBF (ml/min/g)	Stenosis territory MBF (ml/min/g)	Stenosis / Normal MBF	Stenosis / Normal ^{201}Tl
Exercise	40.3 ± 1.7*	2.73 ± 0.22	1.02 ± 0.16	0.37 ± 0.05	
3 hr after exercise		1.74 ± 0.13†	0.76 ± 0.17†	0.44 ± 0.08‡	0.54 ± 0.08§

* Mean ± s.e.m.

† $p < 0.01$, Statistical significance of paired comparison between exercise and postexercise state.

‡ $p < 0.05$.

§ Significantly different ($p < 0.01$) from exercise stenosis/normal MBF.

Abbreviations: LV = left ventricle; MBF = myocardial blood flow.

output were all significantly greater than resting values. Left atrial pressure did not change significantly with exercise. At rest 3 hr later, heart rate and mean arterial pressure had returned to baseline. Cardiac output was lower than control, probably because the animals were anesthetized when these final measurements were made. Left atrial pressure remained relatively constant.

Table 2 details the results of well counter analysis. The LCf stenosis region averaged 40.3 ± 1.7% of total left ventricular mass. At peak exercise, the ratio of stenosis to normal myocardial blood flow was 0.37 ± 0.05, indicating a severe flow deficit to the stenosis territory ($p < 0.001$). At rest 3 hr later, the stenosis to normal flow ratio was 0.44 ± 0.08. Importantly, the stenosis to normal ^{201}Tl ratio at 3 hr was 0.54 ± 0.08, significantly greater than the myocardial blood flow ratio and therefore greater than the thallium distribution ratio at peak exercise ($p < 0.01$).

Scintigraphic Assessment of Peak Exercise Regional Blood Flow

Figure 2 illustrates the average radial distribution of ^{201}Tl activity recorded in the first 5-min frame of the 3-hr scan (from 10 through 14 min following isotope injection) for control and experimental animals expressed as a percentage of the highest radial activity in the heart. There is an obvious separation between LCf activities in control animals and dogs with LCf stenoses, whereas LAD activities are virtually superimposed. When the activities in all radials representing the two (LAD and LCf) myocardial regions of interest were compared, the ^{201}Tl activity in the LCf distribution of the control animals averaged 73.9 ± 1.5%, while LAD ^{201}Tl activity was similar (76.6 ± 2.2%, p = N.S.). In the experimental group initial LAD radial activity averaged 77.5 ± 4.3%, not different from LAD activity in the control animals. However, experimental group LCf ^{201}Tl activity averaged only 52.5 ± 6.0%, significantly lower than LAD activity in the same hearts ($p < 0.001$) and LCf activity in the control dogs ($p < 0.005$). Furthermore, in the experimental group, the ratio of scintigraphic LCf/LAD ^{201}Tl activity in this first frame was higher than, but linearly related to the ratio of stenosis/normal blood flow at peak exercise as determined by microsphere injection ($r = 0.88$, $p < 0.001$) (Fig. 3).

Scintigraphic Assessment of Regional ^{201}Tl Washout

A comparison of the scintigraphic LAD and LCf ^{201}Tl activities over 3 hr is shown in Figs. 4A and B, with the data from each heart normalized to the initial LAD ^{201}Tl activity. In the control animals (Fig. 4A), LAD and LCf activities are nearly superimposed for the entire 3 hr observation period. Thallium-201 loss from the LAD myocardium during the 3-hr scanning period was 54.3 ± 3.4% of the initial activity, while ^{201}Tl loss from the LCf perfusion territory was 57.0 ± 3.6% (p = N.S.). The data from the experimental group are presented in Fig. 4B. As already noted above, LCf activity was initially lower than LAD activity. However, the rate of ^{201}Tl loss from the LAD territory was faster than that from the LCf territory. Consequently, the residual ^{201}Tl activity in the two myocardial regions became nearly equal after 2.5 hr. The eventual equalization of ^{201}Tl activity in the two myocardial regions in the experimental group was caused by a significant increase ($p < 0.001$) in the rate of ^{201}Tl washout from the LAD territory (80.2 ± 2.5% over 3 hr) and a decrease (although not statistically significant) in the rate of washout from the LCf territory (49.1 ± 5% over 3 hrs) when compared to the respective washout rates in the control animals.

This difference between LAD and LCf washout rates

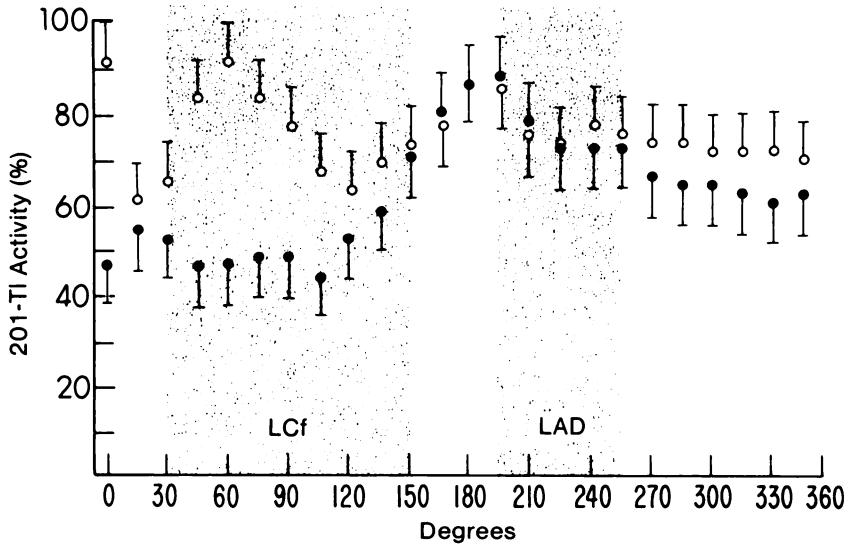

FIGURE 2
Left ventricular ^{201}Tl activity expressed as percentage of highest radial activity within heart (mean ± s.e.e.) measured in 24 radials in control (O) dogs and experimental (●) animals following left circumflex (LCf) stenosis. These data were obtained by scanning during tenth to fourteenth minutes after ^{201}Tl injection. Isotope was injected while the dogs were running on treadmill. Experimental animal LCf ^{201}Tl activity is significantly lower than either control LCf or experimental left anterior descending (LAD) activity ($p < 0.005$). LAD activities in control and experimental animals are not different. ⊥ s.e.m.

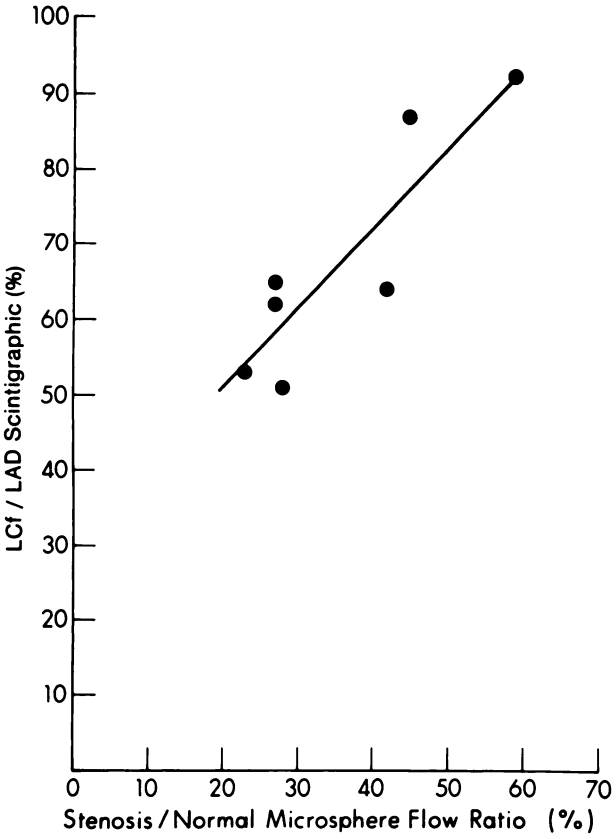

FIGURE 3
Relationship between stenosis/normal (LCf/LAD) myocardial blood flow ratio measured with radioactive microspheres during exercise and LCf/LAD scintigraphic ^{201}Tl activity 10–14 min after ^{201}Tl injection. Straight line relationship (r = 0.88) exists, although flow disparity as assessed by microsphere injection is underestimated by scintigraphic data. y = 1.05X + 29.9; r = 0.88; p < 0.001

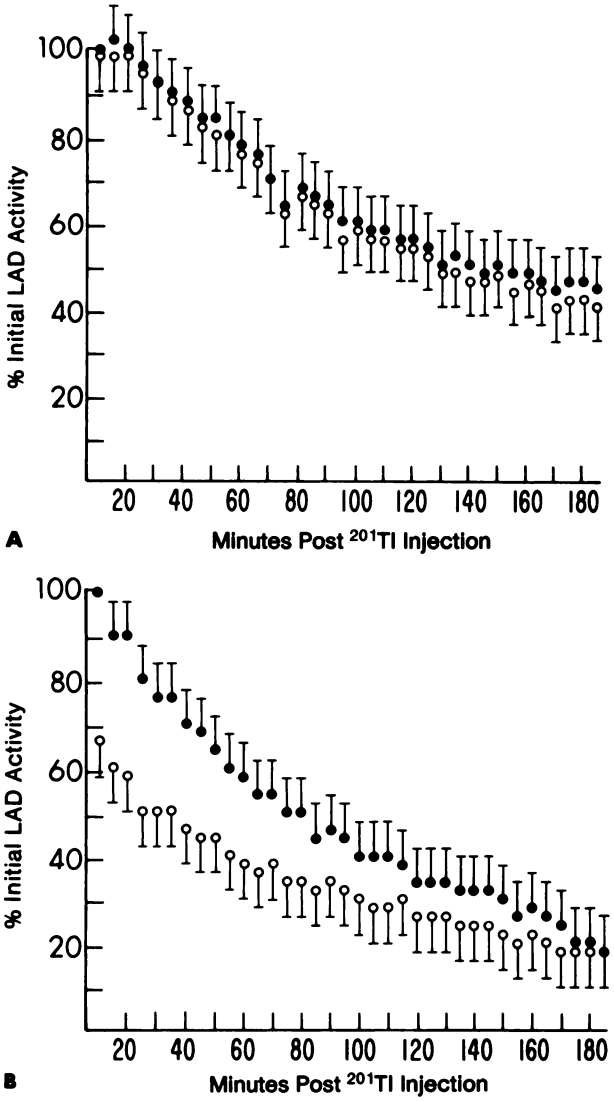

FIGURE 4
Scintigraphic LAD (●) and LCf (○) ^{201}Tl activities starting 10 min after ^{201}Tl injection and continuing over 3-hr scanning interval. One frame consists of counts recorded for 5 min. LAD activity in first frame from each dog was set at 100% and all other activities were normalized in this value. A: Control dogs: LAD and LCf activities are similar to each of 36 frames. B: Experimental animals: LCf activity initially averaged 67% of LAD activity, but two curves converged and nearly superimposed after 2.5 hr. ⊥ s.e.m.

within a heart was a useful scintigraphic measure of redistribution as validated by direct tissue counting. In Fig. 5 well counter ^{201}Tl redistribution is plotted on the abscissa, and is expressed as the difference between the peak exercise stenosis/normal flow ratio and the stenosis/normal ^{201}Tl ratio after 3 hr divided by the peak exercise stenosis/normal flow ratio. The difference between scintigraphic LAD and LCf ^{201}Tl loss over 3 hr is represented on the ordinate. These data are expressed as a percentage of initial LAD activity. There was an excellent linear correlation between scintigraphic and directly measured ^{201}Tl redistribution over the 3-hr observation period ($r = 0.83$, $p < 0.025$). In contrast, no relationship was apparent between the individual scintigraphic LCf ($r = -0.082$) or LAD ($r = 0.03$) washout rates and redistribution as determined by direct well counter tissue measurements.

DISCUSSION

In this model, critical coronary stenoses were surgically created so as to blunt the reactive hyperemic response, yet maintain normal resting flow. The substantial resting LCf flow deficit seen several days later most likely reflects variable progression of the surgically created stenoses. Pathological examination revealed no gross evidence of infarction. Microsphere determined blood flow during exercise also confirmed the flow limitation imposed by the stenosis. At 3 hr after ^{201}Tl injection, the myocardial stenosis/normal ^{201}Tl ratio was significantly greater than the initial blood flow ratio, and therefore greater than the ^{201}Tl distribution ratio during exercise (*5*), an indication that redis-

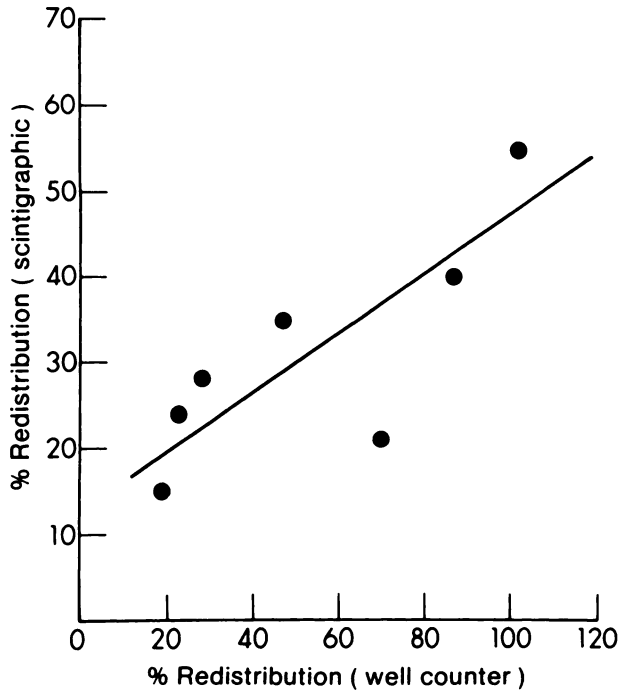

FIGURE 5
Relationship between redistribution determined by well counter and scintigraphic methods. Scintigraphic activity from within LAD and LCf distributions was expressed as percentage of heart's LAD activity in initial 5-min frame. LAD and LCf washout was calculated as difference in activity between frames 1 and 36. Difference between washout of LAD and LCf ^{201}Tl activity (ordinate) was highly correlated (r = 0.83) with redistribution determined by well counter (abscissa). y = 0.35X + 12.6; r = 0.83; p < 0.001

tribution had occurred over the 3-hr scanning interval. The results demonstrate that under these experimental conditions, ^{201}Tl scintigraphy can be employed to quantitate the severity of exercise-related regional flow disparity and the magnitude of redistribution over the ensuing 3 hr. Computer analysis of ^{201}Tl scintigrams has been employed in an attempt to improve the ability to detect coronary disease and grade its severity (*7,8,14,15*). To date computer methods have not been employed to quantitate the magnitude of regional flow reduction during exercise. Quantitative methods employ either circumferential profiles (*11*) or profile slices (*9*) across the ventricle. Most investigators advocate the use of background correction and employ the interpolated background subtraction method originally developed by Goris et al. (*12*) and later modified by Watson et al. (*10*). Importantly, these quantitative methods detect not only an initial defect, but also determine the rate of ^{201}Tl loss from normal, infarcted, and ischemic regions (*16*).

In the present investigation the ratio of LCf to LAD ^{201}Tl activity by quantitative gamma camera scintigraphy 10–14 min after injection was substantially higher than the stenosis to normal myocardial blood flow ratio as determined by microsphere injection during exercise (Fig. 3). This underestimation of the flow deficit by quantitative scintigraphy can be explained by overlap of normal and ischemic myocardium within the solid angle of the camera field. Gamma camera analysis is also limited by inhomogenous background, tissue attenuation, and subject and cardiac motion (*17–23*). The latter three factors pose even greater problems in clinical imaging. In the present study imaging was performed while the animals were anesthetized to prevent motion under the gamma camera. It is therefore important to examine whether pentobarbital anesthesia could influence ^{201}Tl distribution and redistribution. Pentobarbital induced anesthesia was not accomplished until 2 to 2.5 min after ^{201}Tl injection allowing for distribution to the heart during exercise and exponential decay from the blood for at least an additional minute under physiological conditions. Further, pentobarbital was administered in small incremental doses to minimize the hypotensive effects. Three hours after ^{201}Tl injection, while the dogs were anesthetized, the blood pressure was equivalent to that in the resting state, but the cardiac output was somewhat lower. Thallium-201 redistribution has been shown to be highly resistant to even major changes in coronary perfusion (*24*). It is therefore unlikely that pentobarbital anesthesia had a major impact on scintigraphic distribution or redistribution. However, scintigraphic imaging was begun 10 min after ^{201}Tl injection to allow for proper positioning and to produce a more favorable target to background relationship (*17*). This delay may have resulted in some redistribution of ^{201}Tl, contributing to the underestimation of the peak exercise flow disparity. Despite these limitations, the linear relationship (y = 1.05x + 29.9) between scintigraphic and gamma spectrometer measurements establishes the ability of quantitative planar scintigraphy to predict the exercise induced flow deficit, and thus provides important physiologic information.

There is abundant experimental evidence from in vitro measurements indicating that the pattern of thallium distribution varies with the time from injection. Although distribution of this potassium analog is initially flow limited, the final pattern of distribution is proportional to the mass of viable myocardium (*3*). Thus, regardless of differing tissue flows, areas of similar viable myocardial mass will have similar thallium contents. The process that leads to this equalization is complex and somewhat controversial. It is likely that equalization of activity results from both a more rapid loss of thallium from normal zones and a slower loss or frank increase of thallium in the ischemic zone when compared with control washout rates (*1,25–31*). In the present investigation, neither the washout of thallium from the LAD nor from the LCf territory alone correlated with redistribution measured by well counter.

Scintigraphic redistribution analysis is complicated by the above mentioned limitations of planar imaging, diminishing myocardial thallium content and target to background ratios over time, as well as potential changes in ventricular geometry as the ischemic insult of exercise subsides (*23*). Only by using the differences in the washout rates of the two territories within a heart and thus amplifying the differences from the control state did scintigraphic redistribution correlate with well counter determinations. This scintigraphic analysis is then dependent on the altered temporal behavior of myocardial thallium activity in both the normal and reduced flow territories. These considerations may limit its utility as a quantitative measure of regional blood flow in the face of multivessel coronary disease.

In conclusion, in this experimental model, quantitative scintigraphic measurements were highly correlated with both the initial postexercise flow disparity and subsequent redistribution as determined by well counter analysis. This methodology has great potential for the analysis of interventions designed to alter the inhomogeneity of coronary blood flow during exercise.

ACKNOWLEDGMENTS

The authors thank Ann DeVita, Dominick Moreschi, and Robert Bontemps for technical assistance; Ari Rabinowitz for programming support; and Lori Fields for help in preparing this manuscript.

This study was supported in part by National Heart, Lung and Blood Institute Grant HL-17809. Dr. Cohen is the recipient of a National Heart, Lung and Blood Institute Research Career Development Award HL-00281.

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