

Assessment of Jeopardized Myocardium in Patients with One-vessel Disease

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SUMMARY The size of the perfusion defect was assessed from a quantitative analysis of exercise thallium-201 images. Quantitative analysis was determined by measuring the area and the perimeter of the perfusion defect and expressing it as a percentage of the total left ventricular area or perimeter in three projections. Using this technique, we studied 50 patients with one-vessel disease of 50% or greater diameter narrowing. The planimetric and the perimetric methods correlated well ($p < 0.001$, $r = 0.97$). Of the 11 patients with less than 70% diameter narrowing, only one patient had abnormal exercise thallium-201 images. Of the remaining 39 patients with 70% or greater diameter narrowing, 35 had abnormal exercise images. The defects were larger in patients with left anterior descending coronary artery disease ($33 \pm 10\%$; mean \pm SD by perimetry) than in patients with left circumflex coronary artery disease ($19 \pm 14\%$, $p < 0.01$) or right coronary artery disease ($17 \pm 11\%$, $p < 0.01$). There was also significant variation in the sizes of the defects in the three projections in patients with left circumflex and right coronary artery disease, but not in patients with left anterior descending coronary artery disease. Patients with left anterior descending coronary artery disease with collaterals had smaller defects than their counterparts without collaterals ($25 \pm 6\%$ vs $40 \pm 8\%$, $p < 0.001$).

We conclude that in patients with one-vessel disease, the quantitative size of the perfusion defects during exercise is highly variable. Patients with left anterior descending coronary artery disease have larger defects than patients with left circumflex or right coronary artery disease. The significantly lower quantitative thallium scores in patients with left anterior descending coronary artery disease and collaterals suggests that collaterals have a protective role during exercise in these patients.

EXERCISE thallium-201 imaging has received considerable attention recently in the detection of coronary heart disease. It is more sensitive and specific than exercise electrocardiography.¹⁻⁴ It can define the diseased vessel or vessels (the major coronary vessels have corresponding areas of perfusion, which can be identified in the three projections).^{5, 6} It can also assess the viability of the myocardium.^{7, 8}

Image interpretation has been based, for the most part, on qualitative criteria, with reasonable interobserver and intraobserver agreement in the interpretation.⁹ Several quantitative approaches have been used, but not widely;¹⁰⁻¹⁶ some of these techniques have shown results better than those obtained with subjective analysis.¹⁷

The best therapy for patients with one-vessel disease is still controversial.¹⁸⁻²⁰ Several studies suggest that the annual mortality rate of one-vessel disease treated medically is generally higher in patients with left anterior descending coronary artery disease than in patients with right coronary artery disease or left

circumflex disease. Mortality rates undoubtedly depend on left ventricular function: The worse the function, the poorer the prognosis. Therefore, the extent of jeopardized myocardium may have prognostic importance in patients with one-vessel disease; patients with more jeopardized myocardium may be at a higher risk of developing severe left ventricular dysfunction in the event of myocardium infarction.

The purpose of this study was to assess the extent of jeopardized myocardium in patients with one-vessel disease by using quantitative analysis of exercise images, a simple technique that does not require computer manipulation, and to define the factors that affect the size of the defects in these patients.

Materials and Methods

We reviewed our records of exercise thallium-201 imaging and identified 50 patients with one-vessel disease who had undergone exercise perfusion imaging within 3 months of coronary angiography. There were 46 men and four women, ages 32-63 years (mean 52 years). Patients with associated cardiac diseases such as valvular heart disease or idiopathic hypertrophic subaortic stenosis and patients who had had previous bypass surgery were excluded.

All patients were evaluated for symptoms of angina pectoris. No patient had unstable angina or historic or electrocardiographic evidence of myocardial infarction. Left- and right-heart catheterization, left ventriculography and coronary arteriography were per-

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formed with standard techniques. Each coronary vessel was visualized in multiple projections, including the sagittal oblique projection. Each patient had at least 50% diameter narrowing of one coronary artery. The lesion in the left anterior descending artery was classified as either proximal or distal to the first septal perforator and diagonal branches. In each patient with left circumflex artery disease, the lesion was before or involved the major posterolateral branch. In each patient with right coronary artery disease, the lesion was before the crux. The coronary circulation was right-dominant in patients with left circumflex or right coronary artery disease. The remaining vessels were either free of disease or had only slight luminal irregularities.

Collaterals were considered present and significant if the collateral flow partially or completely opacified the diseased vessel beyond the site of occlusion or narrowing. The left ventriculograms, which were assessed qualitatively for wall-motion abnormalities, showed that none of these patients had akinetic or dyskinetic segments. The angiograms were reviewed by two experienced angiographers, and the consensus of both reviewers was used in the final interpretation.

Exercise treadmill testing was performed according to the Bruce protocol. The end points of exercise were ≥ 2 mm of horizontal or downsloping ST depression (with or without angina), excessive fatigue or leg weakness, hypotension, frequent ventricular premature complexes, or attainment of at least 85% of the predicted maximal heart rate. Three electrocardiographic leads (V_1 , V_6 and aV_F) were continuously monitored; lead V_6 was used for interpretation. Blood pressure was obtained by the cuff method every 2 minutes.

At peak exercise, 2 mCi of thallium-201 were injected intravenously and flushed with dextrose and water. The patient continued to exercise for 1 more minute. Within 10 minutes after injection, images were obtained in the anterior, left anterior oblique and left lateral projections by means of a commercially available scintillation camera (Baird Atomic System-77) equipped with a high-resolution, parallel-hole, 1 1/2-inch-thick collimator. Redistribution images were obtained 4 hours after exercise in the projections that showed the perfusion abnormalities. All patients in the study with initial abnormal images showed partial or complete redistribution in the delayed images.

Our method for obtaining the exercise thallium-201 scintigrams has been described.^{4, 5, 8, 21-24} In brief, images were accumulated for a preset count (750,000 to 1,250,000 total counts), which required 8-12 minutes per projection. All images were corrected for background and for detector nonuniformity. Images were displayed on a television screen on a scale of 16 gray shades or 16 colors. The highest count displayed represents 100% on the scale and all other counts are digitally normalized to the maximum. Each of the 16 shades or colors represents a 6.25% increment in counts within the image. Depending on the visual inspection of the background contribution, 20-30%

background subtraction is used and the 16 colors are displayed over the remaining count range. In addition, the images were processed using an algorithm that weighs and spatially averages five adjacent data points in the matrix. The net result is a color-coded isocount contour display of the myocardial thallium-201 distribution. Polaroid pictures were obtained of the computer-smoothed images.

We and others^{7, 25} have found that the color-coded display of the images improve the interpretation. Segments of the myocardium showing 25% decrease in counts (four-color shift) are considered abnormal. The borders of the defects are outlined by two independent observers and minor disagreements were settled by arbitration between the two observers.

Quantitative analysis was done by two methods. In the first method, the size of the thallium-201 defect was determined by the method of Niess et al.²⁶ with a computerized planimetry system (Hewlett-Packard 982A calculator and digitizer). This method expresses the size of thallium-201 perfusion defects as a percentage of total potential thallium uptake. The size of the defect was computed in each projection and expressed as a percentage of the total area of the myocardium, excluding the left ventricular cavity and the region of the valves. The average of the three projections was also determined (fig. 1).

In the second method, the perimeter of the defect was measured and expressed as a percentage of the total left ventricular perimeter in each projection (fig. 1). The region of the valves was excluded. This method is similar to that used by Field et al.²⁷ to assess the extent of akinetic-dyskinetic segments by means of contrast left ventriculograms. The percentage of the average abnormal perimeter was determined from the three projections. The interobserver variability in sizing the defect was 4 ± 4 (mean \pm SD). The maximal difference was 13% in a patient with a large defect. Reproducibility of the quantitative analysis was good. Ten patients with abnormal images were analyzed on two occasions; the mean difference was $3 \pm 3\%$.

Statistical analysis was performed using the *t* test or the analysis of variance when appropriate.

Results

Eleven patients had less than 70% (but greater than 50%) diameter narrowing of one vessel. Five of these patients had left anterior descending coronary artery disease, three had left circumflex coronary artery disease, and three had right coronary artery disease. All but one patient had normal exercise perfusion scan images. The only patient with abnormal exercise images had 60% narrowing of the left anterior descending artery.

The remaining 39 patients had $\geq 70\%$ diameter narrowing of one vessel. All 16 patients with left anterior descending disease, 10 of 12 patients with left circumflex disease, and nine of 11 patients with right coronary artery disease had abnormal exercise perfusion scan images. The 4-hour delayed images were normal in 26 of the 35 patients, but showed small

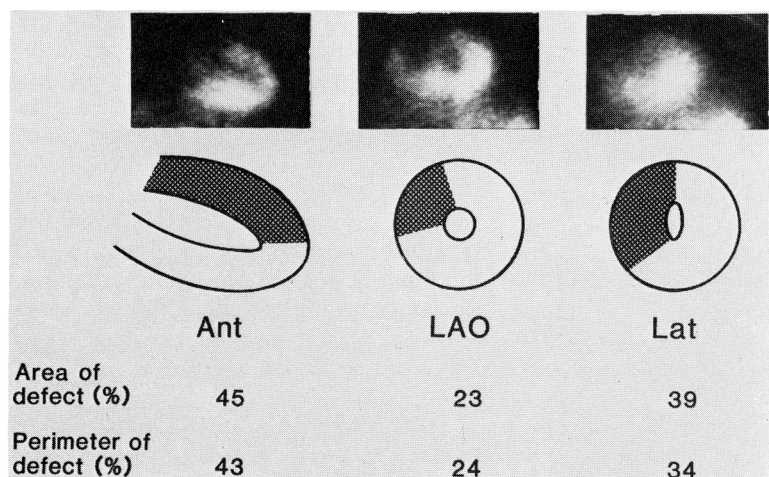


FIGURE 1. Exercise thallium-201 in three projections in a patient with severe disease of the left anterior descending coronary artery. Schematic presentation of the methods used for measuring the size of the defect. Ant = anterior; LAO = left anterior oblique; Lat = lateral.

residual defects in nine patients. These residual defects may be due to scar tissue or to a slow process of filling in; i.e., given enough time after the exercise, or a separate rest study, the images may have shown normalization of the perfusion in these segments.⁸

There was excellent correlation between the two methods (area and perimeter) in measuring the size of the perfusion defect ($r = 0.97$, $p < 0.001$) (fig. 2).

The exercise was stopped because of a positive ECG in 15 patients, angina in five patients, and fatigue or shortness of breath in 17 patients.

The size of the defect varied widely among patients with one-vessel disease, but in general the defect was larger in patients with left anterior descending coronary artery disease than in patients with left circumflex disease or right coronary artery disease ($p < 0.01$) (table 1, fig. 3). The size of the defect did not correlate with the degree of narrowing (fig. 4), with the

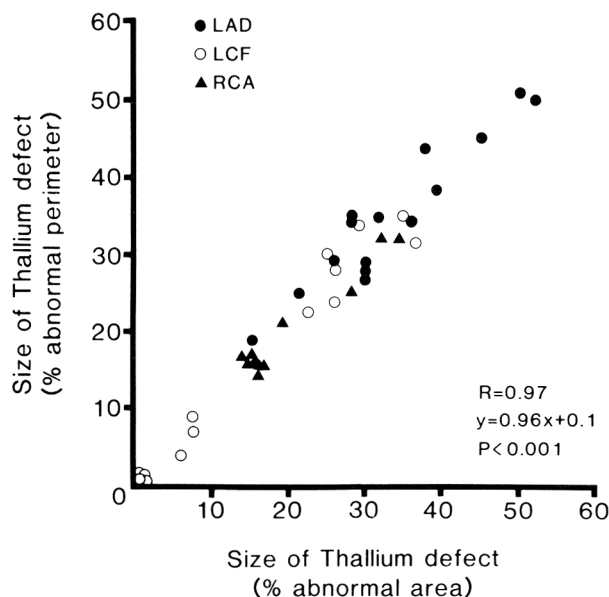


FIGURE 2. Correlation between the average size of the perfusion defect from three projections measured with planimetry vs perimeter in patients with one-vessel disease. LAD = left anterior descending coronary artery; LCF = left circumflex coronary artery; RCA = right coronary artery.

site of narrowing (nine of the patients with left anterior descending disease had stenosis proximal to any major branch), or with the maximal heart rate attained during exercise (fig. 5). The size of the defect varied considerably in the three projections in patients with left circumflex or right coronary artery disease, but not in patients with left anterior descending coronary artery disease (fig. 3).

Effects of Collaterals on the Size of the Perfusion Defects

Seven of the 16 patients with left anterior descending coronary artery disease had collaterals. In these patients the size of the defect ($25 \pm 16\%$ by planimetry) was smaller than in patients without collaterals ($40 \pm 9\%$, $p < 0.001$) (fig. 6).

Four of the 12 patients with left circumflex disease and nine patients with right coronary artery disease had collaterals. Although the number of these patients is small for statistical analysis, we found that in the combined group of 39 patients with one-vessel disease, the size of the defect was smaller in patients with collaterals (20 patients) than in those without collaterals (19 patients) ($19 \pm 11\%$ vs $30 \pm 13\%$, $p < 0.01$). The effect of collaterals on the size of the defect was unrelated to the heart rate or to the degree of obstruction; in fact, the narrowing in patients with collaterals is usually more severe.

Discussion

The results of this study suggest that patients with less than 70% narrowing of one vessel generally have normal exercise images. Only one of 11 patients had abnormal exercise images. However, 35 of 39 patients with ≥ 70 percent narrowing of one vessel had abnormal exercise images.

Quantitative analysis of the thallium images shows that the sizes of the defects in patients with one-vessel disease vary considerably (fig. 3). The size of the defect was larger in patients with left anterior descending coronary artery disease than in patients with left circumflex or right coronary artery disease. Moreover, in patients with left anterior descending disease, the size of the defect in the three standard projections (anterior, left anterior oblique, and left lateral) was approximately the same. However, in patients with

TABLE 1. Results in Patients with One-vessel Disease

| | LAD disease | LCF disease | RCA disease |
|----------------------|-------------|-------------|-------------|
| % Abnormal perimeter | 33 ± 10 | 19 ± 14 | 17 ± 11 |
| % Abnormal area | 32 ± 17 | 18 ± 14 | 17 ± 11 |
| | p < 0.01 | | NS |
| | p < 0.01 | | |

Abbreviations: LAD = left anterior descending coronary artery; LCF = left circumflex artery; RCA = right coronary artery.

left circumflex artery disease, the lateral projection showed larger defects than in the other two projections, whereas the largest defect in patients with right coronary artery disease was in the anterior projection (fig. 3).

These results are not unexpected; the distribution of the left anterior descending artery includes a large portion of the left ventricular myocardium, which is well visualized in all three projections. However, the posterior surface, the area of distribution of the left circumflex artery, is visualized best in the lateral projection. The inferior surface, which is the area of distribution of the right coronary artery, is visualized in its longest axis in the anterior projection.

The sizes of the defects did not correlate with the maximal heart rate during exercise (fig. 5) or with the degree of narrowing of the coronary artery (fig. 4). Because all of our patients had proximal disease, the effect of the site of disease on the size of the defect could not be answered from this study. However, in patients with left anterior descending artery disease, the sizes of the defects did not correlate with the location of the disease with regard to its first septal and diagonal branches.

In this study, patients with left anterior descending coronary artery disease and angiographically demonstrable collaterals had smaller defects than those without collaterals (fig. 6). The functional role of collaterals has been controversial.^{8, 28, 29} Our earlier study⁸ showed that perfusion abnormalities are as fre-

quent in patients with as in those without collaterals.

This conclusion appears to be corroborated by the present study if subjective analysis is used for image interpretation, because it required quantitative analysis to show that the size of the defect is actually smaller in the presence of collaterals. Therefore, although collaterals may not completely protect against ischemia during exercise, they may limit the extent of ischemia in the myocardium during exercise. (There were too few patients with left circumflex or right coronary artery disease with or without collaterals for adequate statistical analysis.) In the 39 patients with one-vessel disease, those with collaterals had smaller defects than those without collaterals.

Our quantitative analysis is simple, can be performed in any laboratory and does not require the computerization described by other investigators.¹¹⁻¹⁶ Our data indicate that the perimetric and planimetric techniques provide excellent correlation in quantitating the sizes of the defects (fig. 2). Because the perimetric method is easier to perform, it may be the method of choice. Superimposition of various segments of the myocardium in the three projections makes even this approach at best semiquantitative. The kinetics of thallium-201, in particular the filling in of ischemic myocardium and the washout from normal myocardium, may affect the size of the defect. Occasionally, the redistribution of thallium-201 may occur early postexercise and thus some filling in may have occurred in the lateral projection images, which

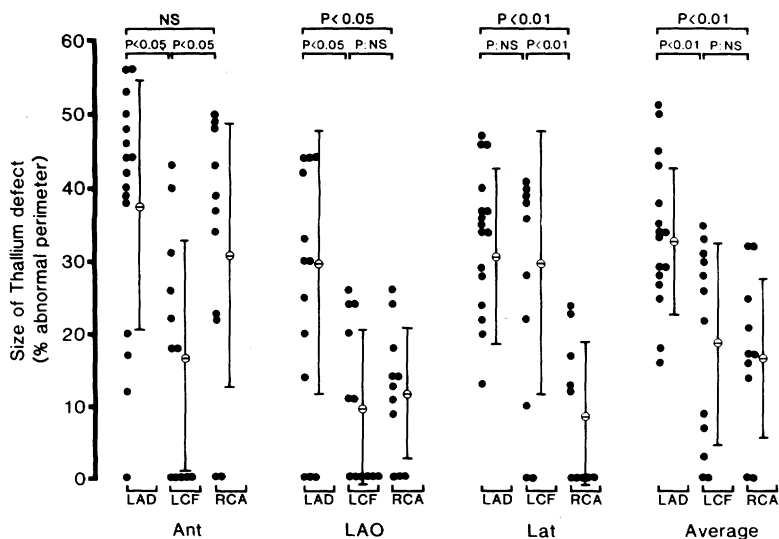


FIGURE 3. The size of the defect measured by perimetry in three projections in patients with one-vessel disease. Abbreviations as in figures 1 and 2.

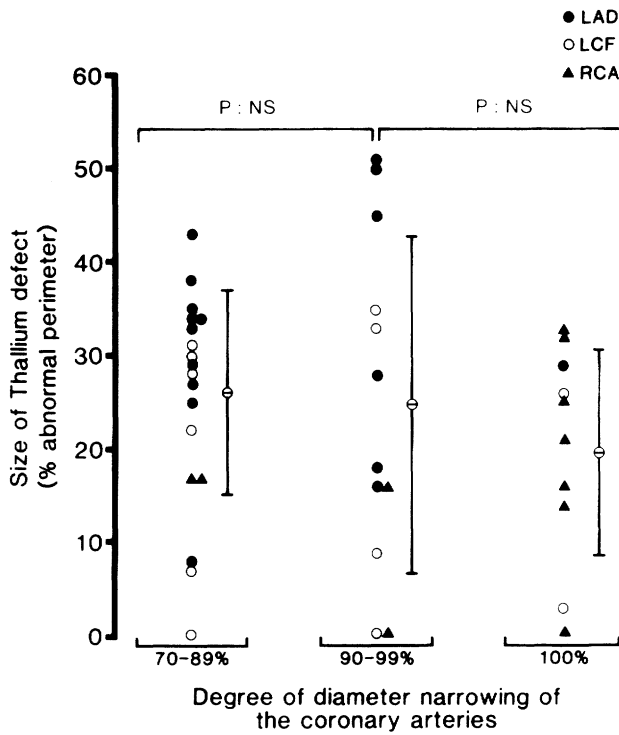


FIGURE 4. Correlation of the size of the defect with degree of coronary narrowing. Abbreviations as in figure 2.

are generally the last to be obtained in our laboratory; because we obtained the images in the same sequence in each patient and analyzed only the post-exercise images, this effect alone could not have accounted for the marked variation in the size of the defects in our patients.

Clinical Implications

Our results indicate that patients with one-vessel disease form a heterogeneous group, regardless of

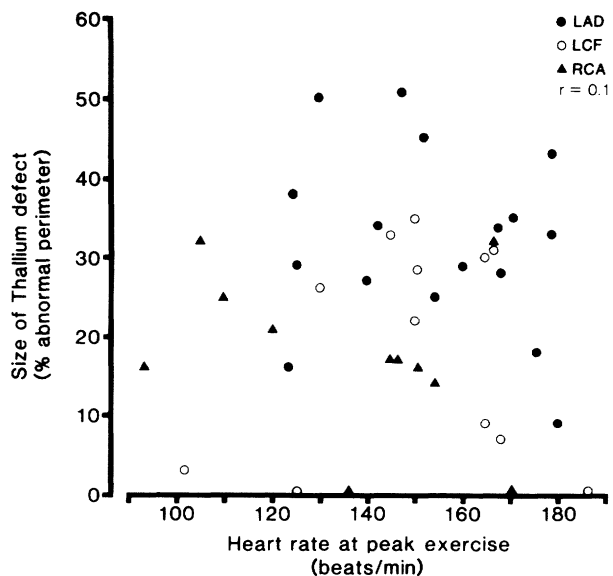


FIGURE 5. Effect of maximal heart rate during exercise on the size of the defect. Abbreviations as in figure 2.

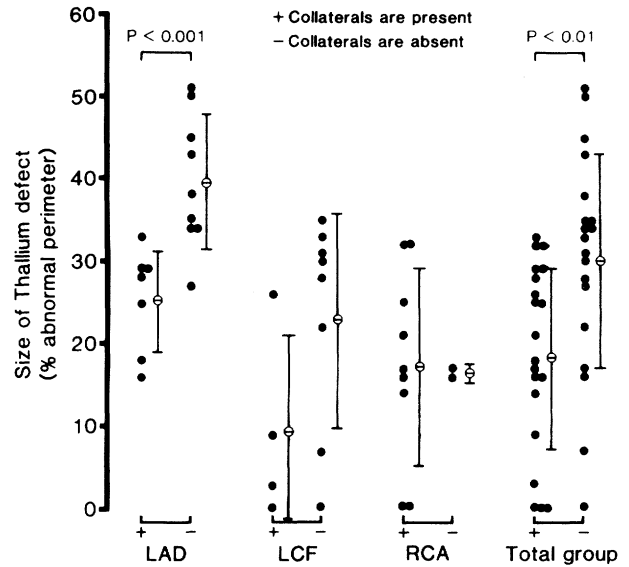


FIGURE 6. Effect of collaterals on the size of the defect. Abbreviations as in figure 2.

which vessel is diseased. The exact correlation between the size of the perfusion defect measured from exercise perfusion images and the subsequent size of scar tissue after infarction is not yet clear. Using both subjective and objective computer-derived scoring systems of rest thallium-201 images, Silverman et al.¹⁶ found a wide variability in the scores in patients during acute infarction. They also found that the high scores heralded a poor prognosis. If their conclusions can be applied to our data, patients with larger defects are at higher risk of developing large infarctions and more severe left ventricular decompensation than patients with smaller defects.

If the objectives of myocardial revascularization procedures are to preserve left ventricular function and to lessen symptoms, patients with large defects may have a better prognosis with surgical therapy. This assumption needs further study, particularly to correlate the prognosis with the size of the exercise-induced defect. The follow-up period in our patients is still very short, and most of our patients with left anterior descending coronary artery disease had coronary artery bypass surgery.

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