Variability of Normal Coronary Anatomy: Implications for the Interpretation of Thallium-SPECT Myocardial Perfusion Images in Single-Vessel Disease

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Standard criteria for assigning perfusion defects to a specific vascular territory often result in mistaken identification of the affected coronary artery due to the normal variability of coronary anatomy. A retrospective study was performed to determine the frequency of this type of error and to identify the most common perfusion patterns associated with specific coronary lesions. **Methods:** Records were reviewed of all patients with single-vessel coronary artery disease (CAD) who had exercise or dipyridamole thallium SPECT myocardial perfusion studies since 1987. Patients with coronary artery bypass grafts and an interval between the two studies greater than 6 wk or interval change in medical status were excluded. Ninety-three studies were available for review. The size, severity and location of all perfusion defects were noted by three observers who had no knowledge of the angiographic data. Significant CAD was defined as luminal diameter stenosis greater than 50%. **Results:** The diseased vessel was correctly identified in 85% of positive studies. Thallium SPECT, however, mistakenly predicted additional vessel involvement in 29% of those studies. Another 15% correctly predicted single-vessel disease but identified the wrong artery. Using standard criteria, thallium SPECT correctly predicted the arteriogram findings in only 56% of studies. Most of these findings could be correlated with variations in individual coronary anatomy. **Conclusion:** The accurate localization of coronary stenoses by thallium SPECT imaging requires close correlation with arteriography owing to the significant variability in normal coronary anatomy.

Key Words: thallium; single-photon emission computed tomography; coronary artery disease

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Normal coronary anatomy is highly variable. The typical right dominant pattern where the right coronary artery gives rise to the posterior descending artery and posterolateral left ventricular branches is only found in 71% of hearts. Numerous other variations exist.

Previous reports have focused on the sensitivity and specificity of SPECT myocardial perfusion studies using standard criteria (*1–6*). Standard criteria are needed when a technique is being evaluated for comparative accuracy. They are also convenient to use in daily practice. Standard criteria, however, introduces systematic error in the localization of coronary artery disease (CAD) because they do not take into account the normal variability of coronary anatomy.

The precise localization of CAD is not important when scintigraphy is used as a screening test before beginning anti-anginal medication or deciding whether coronary arteriography is indicated in a patient with chest pain. Scintigraphy, however, is frequently performed after angiography to evaluate the hemodynamic significance of noncritical stenoses. At the Palo Alto Department of Veterans Affairs Medical Center, scintigraphy was performed *after* angiography to evaluate equivocal lesions in 47% of patients who had both studies within a 6-wk interval since 1987. Because therapeutic decisions are often based on the results from scintigraphy, it is vitally important to be familiar with the normal variations in coronary anatomy and the effect this has on the size and location of perfusion defects in this situation.

We retrospectively reviewed all the thallium-SPECT studies performed in patients with single-vessel CAD since 1987 to examine the variability in size and location of perfusion defects associated with specific coronary lesions, and to determine the frequency of incorrect localization of coronary stenoses when standard criteria are used.

MATERIALS AND METHODS

Patients

The medical records of all patients referred for a thallium SPECT myocardial perfusion study at the Palo Alto Department of Veterans Affairs Medical Center since 1987 were reviewed.

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There were 3553 studies performed during this period. Patients who also had a coronary arteriogram within 6 wk of the thallium study were identified. There were 542 patients in this group. The results of coronary arteriography could not be found in 64 patients. Another 112 patients had coronary bypass surgery and were excluded from further analysis. Seventy-three patients had three-vessel disease, 140 had two-vessel disease and 102 had one-vessel disease. Fifty-one did not have any significant disease. Thallium studies in patients with one-vessel CAD form the basis of this report. The thallium studies of 13 patients could not be located, therefore, there were 89 patients in the study group.

Eighty-seven patients were male and two were female. The average age was 60 ± 9 yr. Thirty-eight patients (43%) had a history of myocardial infarction. The clinical history of one patient was unavailable. Twelve patients (13%) had Q-waves on the electrocardiogram. The electrocardiograms of another 13 patients were not available for review. Four patients had a myocardial perfusion study and coronary arteriography on two separate occasions.

Exercise and Dipyridamole Protocols

Seventy-three studies were performed following symptom-limited treadmill exercise using the Bruce or Naughton protocol. Patients were given dipyridamole if they were unable to exercise. Dipyridamole was administered orally (375 mg) in six studies and intravenously (0.56 mg/kg) in 14 studies. Three millicuries of ^{201}Tl-Cl were administered intravenously at peak stress. Patients were imaged 5–10 min later.

SPECT Acquisition and Processing Parameters

Sixty-four studies were performed with patients lying prone and 17 were performed supine. Patient position could not be ascertained in 12 studies. Patients were imaged with a single-head rotating large field of view camera fitted with a low-energy, medium-resolution, medium-sensitivity collimator. Fifteen percent windows centered on the 70-keV and 167-keV photo peaks were used. A 180° elliptical orbit starting at the 45° right anterior oblique position was used for all studies regardless of patient position. Sixty images were acquired in a 64 × 64 pixel matrix using step-and-shoot mode at a framing rate of 25 sec per image.

Projection images were preprocessed with a Butterworth filter having a cutoff frequency of 0.35 cycles/pixel, order 5. Six-millimeter thick transaxial images were reconstructed by backprojection using a ramp filter. The transaxial images were smoothed using a three-point filter before generating 6 mm thick vertical long-, horizontal long- and short-axes slices. Images were recorded on x-ray film.

Image Interpretation

Images were read by three independent reviewers experienced in the interpretation of myocardial perfusion studies. Agreement was reached by consensus. Reviewers did not know the clinical history, details about the stress protocol or results of angiography. Circumferential profiles and polar maps were not used. Perfusion defects were recorded on a diagram which included the mid-ventricular slice from the vertical long-, horizontal long- and short-axes projections. Each slice was divided into 6–12 segments, as shown in Figure 1. Only moderate to severe defects (<75% of peak activity) were recorded. Mild defects (>75% of peak activity) were not included in order to maximize specificity. Reviewers were also asked to indicate whether there were any significant stenoses in the left anterior descending, left circumflex and/or right coronary arteries based on their interpretation of the thallium study. Standard criteria were used for assignment of vessel territory: left anterior descending artery for anterior wall, septum and/or apex; left circumflex artery for lateral wall, and right coronary artery for inferior wall. Specific vessel territories were not assigned to watershed areas a priori.

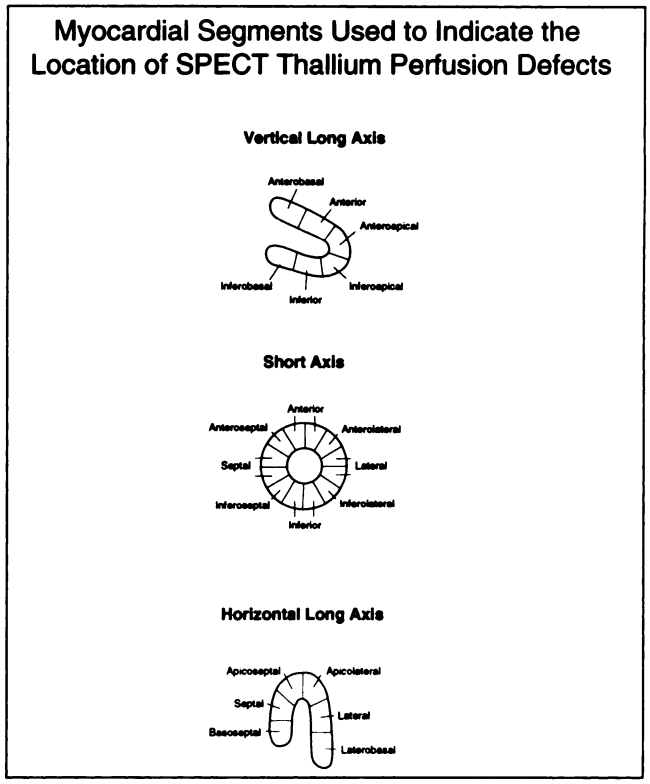

FIGURE 1. Midventricular slice from the three orthogonal projections. Perfusion defects for each patient were indicated by shading the appropriate myocardial segments. The short-axis slice was divided into 12 segments in order to accurately represent the scan findings, whereas six segments were adequate for the vertical long- and horizontal long-axes.

Coronary Arteriography

Coronary arteriograms were performed and interpreted by the patient's attending cardiologist who was sometimes aware of the results of the thallium study. The original report was used in all cases. Percent luminal diameter stenosis of the major epicardial arteries and their main branches was estimated visually from multiple projections. The most severe stenosis in any projection was taken as the data point for that vessel. Stenoses equal to or greater than 50% were considered significant.

Scintigraphy was performed before angiography in 46% and after angiography in 54% in patients with single-vessel disease. These percentages are similar to the values of 53% and 47%, respectively, for all patients who had both studies.

RESULTS

Thallium SPECT was abnormal in 59% (55/93) of studies in patients with single-vessel disease. Table 1 shows the predicted vessel involvement based on the SPECT findings using standard criteria versus the actual location of disease.

Thallium SPECT findings in the 55 positive studies are

TABLE 1
Correlation between Thallium SPECT and Coronary Angiography in 93 Paired Studies

	Angiography		
SPECT	LCX (n = 12)	RCA (n = 27)	LAD (n = 54)
LCX	5 (42%)	5 (19%)	0
RCA	1 (8%)	6 (22%)	2 (4%)
LAD	0	0	20 (37%)
LCX + RCA	0	0	0
LCX + LAD	0	0	2 (4%)
RCA + LAD	0	3 (11%)	9 (17%)
LCX + RCA + LAD	0	0	2 (4%)

TABLE 2
Correlation between Angiographic Stenosis Severity and the Occurrence of Perfusion Defects in 91 Paired Studies*

Angiography				Thallium	
% stenosis	LCX	RCA	LAD	Normal	Abnormal
90%–100%	5	12	21	10	28
80%–90%	2	2	3	3	4
70%–80%	0	5	10	9	6
60%–70%	2	3	8	5	8
50%–60%	3	4	11	9	9

*Stenosis severity unavailable in two studies.

shown in Figure 2. The diseased vessel was correctly identified in 85% (47/55) of positive studies. Thallium SPECT, however, mistakenly predicted additional vessel involvement in 29% (16/55) of those studies. Another 15% (8/55) correctly predicted single-vessel disease but identified the wrong artery. Using standard criteria, thallium SPECT correctly predicted the arteriogram findings in only 56% (31/55) of studies.

Table 2 correlates stenosis severity and perfusion findings according to the diseased vessel. The findings in each group of patients with single-vessel disease is presented below in greater detail.

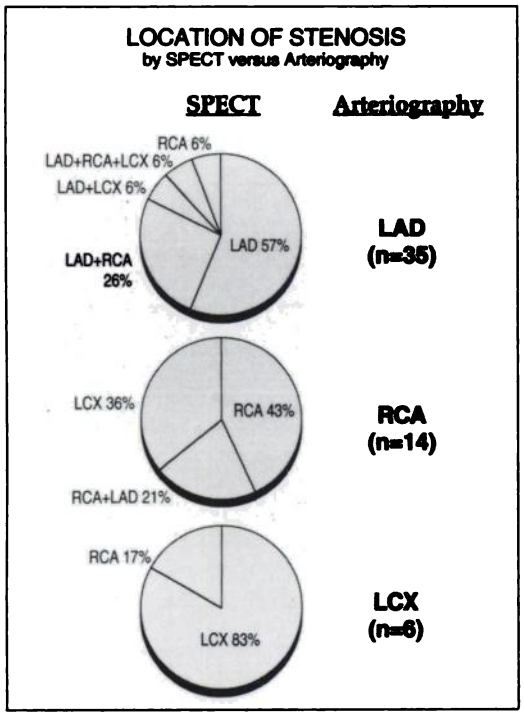

FIGURE 2. Identification of the diseased vessel(s) according to the scan findings versus the actual location of disease. Although the vessel was correctly identified in 85% of studies, the scan was incorrectly interpreted as showing multivessel involvement in 29%. Fifteen percent correctly indicated single-vessel disease, but identified the wrong artery. LAD = left anterior descending artery; RCA = right coronary artery; LCX = left circumflex artery.

Left Circumflex Artery Group

There were 12 patients in this group. The anatomy was right dominant in six patients (50%), left dominant in three (25%) and codominant in three (25%). Six patients (50%) had abnormal thallium-SPECT studies. Although the left circumflex artery supplies a larger area of the left ventricle in patients with left or codominant circulation, four of the six (67%) patients with an abnormal study had right dominant circulation. The location of the perfusion abnormalities in these six studies is shown in Figure 3. Perfusion defects were seen most frequently in the inferior, inferolateral and lateral segments on the short-axis view, the inferior segment on the vertical long-axis view and the lateral segment on the horizontal long-axis view. An inferior defect or inferior extension of a lateral defect was seen in four patients even though only one patient's coronary

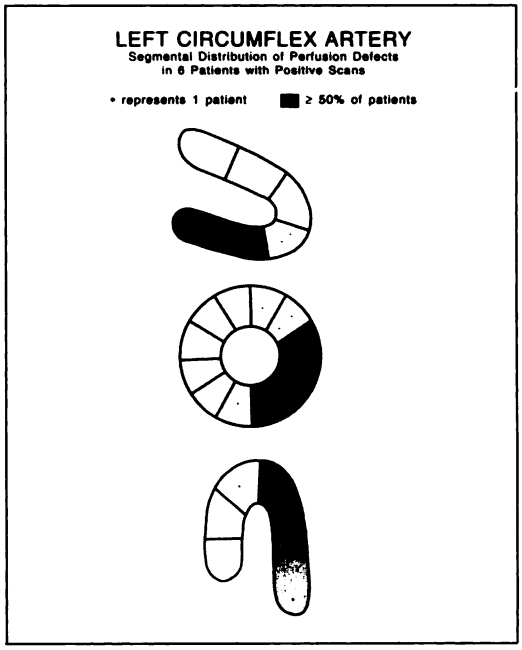

FIGURE 3. Segmental distribution of perfusion defects in patients with left circumflex artery disease. Perfusion defects extend to the inferior wall in the majority of patients. Comparison with Figure 6 shows a significant overlap in perfusion territories of the left circumflex and right coronary arteries.

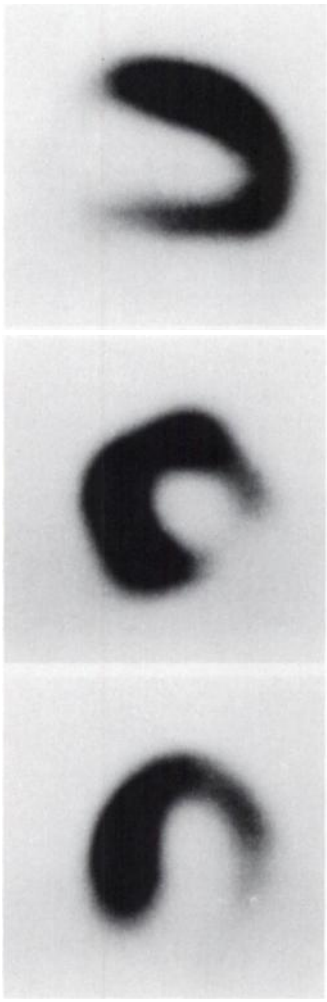

FIGURE 4. Dipyridamole thallium myocardial perfusion study of a 54-yr-old man with a normal dominant right coronary artery, normal left anterior descending artery and 50%–70% stenosis in the left circumflex artery proximal to the first obtuse marginal branch. Midventricular slices from the vertical long- (top), short- (middle) and horizontal long- (bottom) axis views show a severe lateral wall defect which extends to the mid-inferior wall (6 o'clock position on the short-axis view).

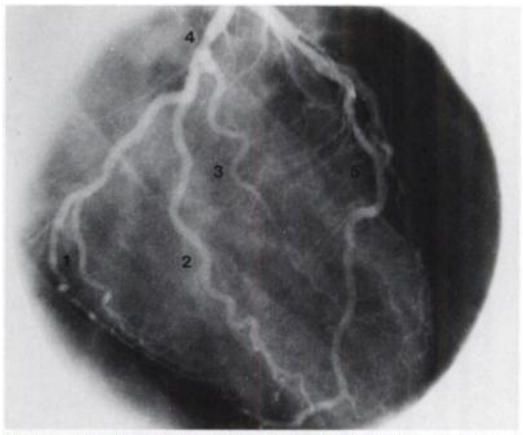

FIGURE 5. Right anterior oblique projection from the coronary arteriogram of the subject in Figure 4. The arteriogram demonstrates large posterior branches of the left circumflex artery supplying the inferior wall. 1 = posterior branches of the left circumflex artery; 2 and 3 = obtuse marginal branches of the left circumflex artery; 4 = left circumflex artery; 5 = left anterior descending artery.

anatomy was left dominant (Fig. 4). The arteriograms of three of the four patients with right dominant anatomy and inferior wall involvement were available for review. All three patients had large circumflex arteries with extensive posterolateral branches supplying the inferior wall (Fig. 5).

Right Coronary Artery Group

There were 26 patients in this group. One patient was studied twice for a total of 27 studies. The anatomy in all of these patients was right dominant. Thallium SPECT was abnormal in 14 studies (52%). The location of the perfusion abnormalities in these 14 studies is shown in Figure 6. The inferobasal segment on the vertical long-axis view was abnormal in every study but one. Apical involvement, however, was seen only in one study. Extension of the inferior defect to the mid-lateral wall was seen in four studies (Fig. 7), and extension to the mid-septum was seen in one study (Fig. 8). The arteriograms of four of these five patients were available for review. Three patients with lateral wall involvement had large posterolateral branches which reached the lateral wall (Fig. 9). The single patient with septal involvement had a big acute marginal branch which supplied the septum (Fig. 10). Septal branches from the left anterior descending artery were small and did not supply much collateral flow.

Left Anterior Descending Artery Group

There were 51 patients in this group. Three patients were studied twice for a total of 54 studies. The anatomy was right dominant in 38 patients, left dominant in 8 patients and codominant in 4 patients. The posterior descending artery was absent in one patient. It was replaced by the left anterior descending artery which wrapped around the apex and continued all the way up the interventricular sulcus. Thallium SPECT was abnormal in 35 studies (65%). The location of the perfusion abnormalities in these 35 studies is

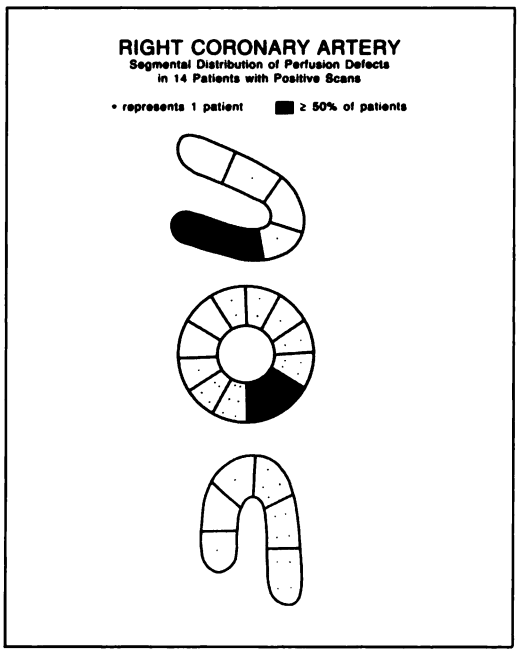

FIGURE 6. Segmental distribution of perfusion defects in patients with right coronary artery disease. Perfusion defects are seen in the inferolateral region in the majority of patients which can lead to the erroneous conclusion of left circumflex artery stenosis.

FIGURE 7. Dipyridamole thallium myocardial perfusion study of a 64-yr-old man with a normal left anterior descending artery, normal left circumflex artery, tandem 50% stenoses in a dominant right coronary artery and 80% stenosis in a posterior branch. Midventricular slices from the vertical long- (top), short- (middle), and horizontal long- (bottom) axis views show a severe inferior wall defect which extends to the mid-lateral wall (3 o'clock position on the short-axis view).

FIGURE 8. Dipyridamole thallium myocardial perfusion study of a 44-yr-old man with a normal left anterior descending artery, normal left circumflex artery and subtotal occlusion of a dominant right coronary artery. Midventricular slices from the vertical long- (top), short- (middle), and horizontal long- (bottom) axis views show a severe inferior wall defect which extends to the mid-septum (9 o'clock position on the short-axis view).

shown in Figure 11. Perfusion defects were seen most often in the anteroapical segment on the vertical long-axis view and apicoseptal segment on the horizontal long-axis view (86% of positive studies). The perfusion defect wrapped around the apex to involve the inferoapical segment in 23 (66%) positive studies. In addition, perfusion of the inferior segment on the vertical long-axis view was abnormal in 10 (29%) positive studies, and perfusion of the inferobasal segment was abnormal in 6 of these studies (Fig. 12). The arteriograms of 9 of these 10 patients were available for review. The left anterior descending artery wrapped around the apex in 8 patients and extended to the mid-inferior wall in five patients (Fig. 13). Inferior wall involvement could not be explained by coronary anatomy in 4 patients.

DISCUSSION

Segmental analysis of myocardial perfusion studies is based on certain assumptions regarding coronary anatomy. The nearly universal approach is to assign the anterior wall and septum to the left anterior descending artery, the lateral wall to the left circumflex artery and the inferior wall to the right coronary artery. There is no consensus, however, on the exact borders of each vascular territory as evidenced by the significant variation in quantitative polar maps (*1,4–6*). These differences may be explained by the normal variability in coronary anatomy.

The most frequent variation is the origin of the posterior

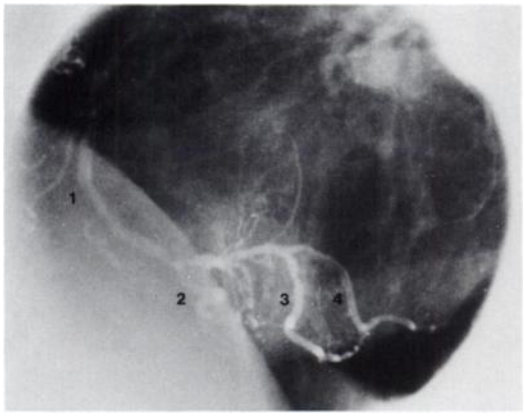

FIGURE 9. Left anterior oblique view from the coronary arteriogram of the man whose thallium myocardial perfusion study is shown in Figure 7. The arteriogram demonstrates large posterior branches of the right coronary artery reaching the lateral wall. 1 = right coronary artery, 2 = posterior descending artery, 3 and 4 = posterior branches of the right coronary artery.

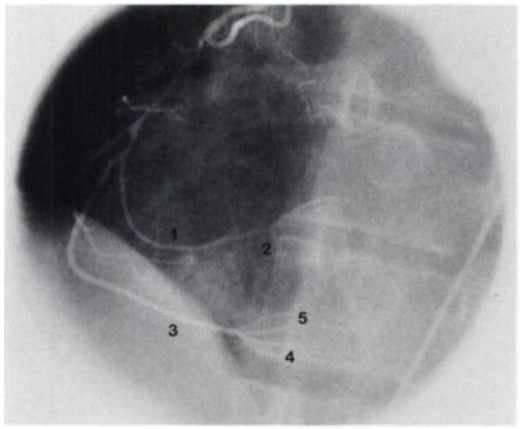

FIGURE 10. Left anterior oblique cranial view from the coronary arteriogram of the man whose thallium myocardial perfusion study is shown in Figure 8. The arteriogram demonstrates a large acute marginal branch of the right coronary artery which supplies a distal posterior descending artery and large septal branches. Key: 1 = right coronary artery, 2 = proximal posterior descending artery, 3 = acute marginal branch of the right coronary artery, 4 = distal posterior descending artery, 5 = septal branches.

FIGURE 12. Dipyridamole thallium myocardial perfusion study of a 74-yr-old man with a normal dominant large left circumflex artery, small right coronary artery and 70% stenosis of the proximal left anterior descending artery. Midventricular slices from the vertical long- (top), short- (middle), and horizontal long- (bottom) axis views show a severe anteroseptal, apical and inferior perfusion defect.

descending artery. This artery is a terminal branch of the right coronary artery in 88%–90% of hearts and a terminal branch of the left circumflex artery in the remainder (*7,8*). The posterior descending artery begins at the crux where it makes a deep turn and travels a variable distance down the posterior interventricular sulcus to supply the inferior wall adjacent to the septum. Other terminal branches of the right coronary artery and left circumflex artery, called posterolateral branches, supply a variable amount of the inferior wall. The artery which gives rise to the posterior descending artery and one or more posterolateral branches is called dominant (*9,10*). The right coronary artery is dominant in only 71% of hearts (*8*). Furthermore, the term dominance is misleading because it implies that the vessel supplies to a large amount of myocardium. In fact, a dominant right coronary artery may supply less than 5% of the inferior wall of the left ventricle. In a series of 71 autopsy specimens with right dominant anatomy, the percentage of the inferior wall supplied by the right coronary artery was less than 20% in 21 specimens, between 20%–80% in 43 specimens and greater than 80% in 7 specimens (*8*).

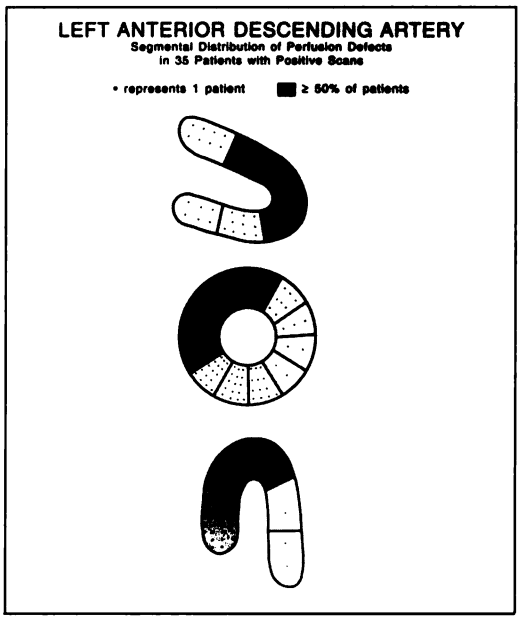

FIGURE 11. Segmental distribution of perfusion defects in patients with left anterior descending artery disease. Perfusion defects wrap around the apex to involve the inferoapical region in the majority of patients. Extension of the perfusion defect to the inferior wall frequently leads to the erroneous conclusion that the right coronary artery is also involved.

The right coronary artery occasionally terminates as the posterior descending artery without giving rise to any other posterolateral branches. The posterolateral branches are all supplied by the left circumflex artery in this case. The terms balanced or codominant circulation are used to describe this pattern which is encountered in 17% of hearts (*8–10*). Disregarding dominance, the right coronary artery supplies less than one-half of the area between the posterior interventricular sulcus and the obtuse margin in 64% of hearts (*7*).

The great variability in blood supply to the inferior and lateral walls is reflected in the findings of this study. Four

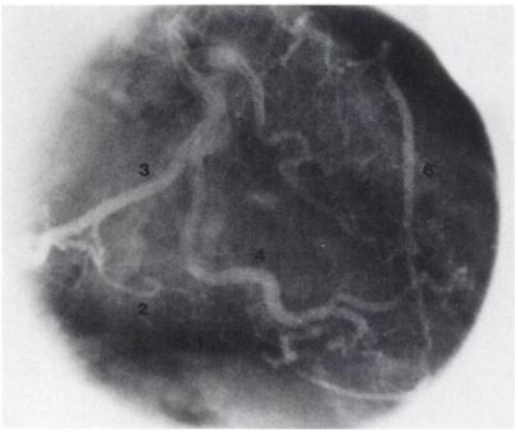

FIGURE 13. Right anterior oblique caudal view from the coronary arteriogram of the man whose thallium myocardial perfusion study is shown in Figure 12. The arteriogram demonstrates a long left anterior descending artery which wraps around the apex and extends far up the inferior wall. 1 = terminal segment of the left anterior descending artery; 2 = posterior descending artery; 3 = left circumflex artery; 4 and 5 = obtuse marginal branches of the left circumflex artery; 6 = left anterior descending artery.

of the 6 (67%) patients in this series with single-vessel left circumflex artery disease and an abnormal thallium scan showed extension of the lateral wall perfusion defect to the mid-inferior wall. The anatomy of one patient was left dominant whereas three others had extensive posterolateral branches reaching towards the posterior interventricular sulcus. Similarly, 4 of 14 patients (29%) with single-vessel right CAD (all right dominant) and an abnormal thallium scan showed extension of the inferior perfusion defect to the mid-lateral wall. This observation is similar to the finding that the right coronary artery terminates at the obtuse margin in 18% of hearts (7).

The finding of an inferior perfusion defect extending to the mid-septum in a patient with right CAD is more unusual. Although the septum is supplied by branches from both the left anterior descending artery and posterior descending artery, the posterior septal branches are usually less than 15 mm in length whereas the anterior septal branches are typically 70–80 mm long (7). The apical portion is almost exclusively supplied by branches from the left anterior descending artery. The relative contributions, however, of the two arteries can be quite variable, as demonstrated by one patient in this series.

Another significant source of variability is the length and termination point of the left anterior descending artery. The termination point is the anteroapical segment in 17%, the inferoapical segment in 23%, from 2 to 5 cm up the posterior interventricular sulcus in 42% and more than 5 cm up the posterior interventricular sulcus in 18% (7). Since the length of the average left ventricle is approximately 10 cm, the left anterior descending artery perfuses the inferoapical and inferior segments in the majority of hearts. This data is consistent with our observation that perfusion defects in patients with stenosis of the left anterior descending artery involved the inferoapical segment in 66%, extended to the inferior segment in 29% and extended to the inferobasal segment in 17% of studies. It must be pointed out, however, that inferior wall involvement could not be explained on the basis of coronary anatomy in four patients.

The apex is one of the most variable regions in regards to blood supply. Branches of all three major arteries may reach the apex. Apical perfusion defects, therefore, are generally considered nonspecific, although sometimes this region is assigned to the territory of the left anterior descending artery. There is generally a reciprocal relationship between the length of the left anterior descending artery and the posterior descending artery. A certain degree of overlap, however, exists because pathologic studies have shown that the left anterior descending artery and the posterior descending artery reach the inferior apex in 82% and 31% of hearts, respectively (7). We observed inferoapical perfusion defects in 66% of positive studies in patients with left anterior descending artery disease, in 33% of positive studies in patients with left circumflex disease and in 7% of positive studies in patients with right CAD. Eighty-eight percent of all inferoapical perfusion defects, however, occurred in patients with stenosis of the left anterior descending artery since this was the most prevalent form of single-vessel disease in this series.

Certain limitations of this study should be acknowledged. Most of the patients in this study were male. There may be gender differences in coronary anatomy, particularly in regards to the blood supply of the inferior wall because left dominant anatomy may be more prevalent in males (7).

The threshold for CAD was set at 50% luminal diameter stenosis. Thirty-five percent of our patients with abnormal thallium studies had a second vessel with 30%–40% stenosis. This degree of stenosis has been previously associated with perfusion defects (*11*). Mild perfusion defects were excluded from the analysis in order to minimize the possible contribution of nonsignificantly diseased vessels to the perfusion image. The exclusion of mild perfusion defects, however, may have caused us to underestimate the size of the vascular perfusion beds of individual coronary arteries.

Scintigraphy was performed before arteriography in 53% of studies. Post-test referral bias may have resulted in patients with extensive perfusion defects being referred more frequently for coronary arteriography. The ordering of the tests might especially have affected the findings of patients with left anterior descending artery disease, the anatomical subgroup most frequently mistaken to have multivessel disease. Forty-one percent of perfusion studies in patients with left anterior descending artery disease were performed before angiography. Fifty-four percent of the 13 studies mistakenly suggesting multivessel disease were seen in this subgroup.

It is important to note that this study was not designed to measure the sensitivity of thallium SPECT for detecting single-vessel CAD. We did not include mild perfusion defects, use circumferential profiles or polar maps, analyze

related stress test results or use quantitative angiographic techniques which might influence test sensitivity. We sought only to relate the distribution of obvious perfusion defects to the related anatomy. Post-test referral bias undoubtedly contributed to the low overall sensitivity of 59%. Accurate measurement of sensitivity (and specificity) requires that all patients in a cohort have both tests. This was not the case in this study where the decision to perform angiography was influenced by the thallium scan and vice versa. The thallium scan is expected to be more sensitive in patients subsequently referred for arteriography because patients with normal perfusion scans are unlikely to be catheterized. The sensitivity of thallium imaging was 74% in the 43 studies performed before arteriography, versus only 46% in the 50 studies performed after arteriography for equivocal lesions. Sensitivity was also affected by stenosis severity. Sensitivity was 74% in patients with 90%–100% stenoses versus 50% in patients with 50%–60% stenoses.

It is possible that some of the perfusion defects were due to artifact rather than CAD. Artifacts due to attenuation, motion, creep and other causes have been well documented (*12*). Images were routinely examined for motion and creep. Equivocal evidence for motion was found in only 1 patient with left anterior descending artery disease. Furthermore, we have previously reported that false-positive inferior wall findings due to diaphragmatic attenuation are minimized by prone positioning (*13*). Inferior wall perfusion defects could be explained on the basis of coronary anatomy in 3/3 patients with left circumflex artery disease and 5/9 patients with left anterior descending artery disease. There were only 4 patients with left anterior descending artery disease in whom inferior wall involvement could not be explained on the basis of coronary anatomy. The defects were fixed in two studies and reversible in two studies.

CONCLUSION

Most physicians interpreting perfusion studies are aware of the normal variability in coronary anatomy only in a general sense. This limited knowledge is adequate when perfusion imaging is used as a screening test for CAD. Specific knowledge of coronary anatomy becomes important when the demonstration of perfusion defects in a single versus multivessel distribution makes a difference in further diagnostic evaluation, therapeutic intervention or assessment of prognosis. In these situations, accurate interpretation of the perfusion study requires correlation with the arteriogram because of the great variability in normal coronary anatomy.

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