Relationship Between Reverse Redistribution on Planar Thallium Scintigraphy and Regional Myocardial Viability: A Correlative PET Study

Robert Soufer, Holley M. Dey, Andrew J. Lawson, Frans J.Th. Wackers and Barry L. Zaret

Departments of Radiology and Internal Medicine, Cardiology Section, Yale University School of Medicine, New Haven, Connecticut, Yale University-VA Positron Emission Tomography Center, Department of Veterans Affairs Medical Center, West Haven, Connecticut

The purpose of this study was to assess myocardial metabolic activity in the area of reverse redistribution and determine the prognostic value of reverse redistribution and PET imaging. Reverse redistribution is thought to be a manifestation of reperfusion therapy and associated with a favorable clinical outcome. Preliminary observations from the Thrombolysis and Myocardial Infarction (TIMI) trial suggest that reverse redistribution is associated with higher incidence of future cardiac events. **Methods:** Thirty-two patients with chronic coronary artery disease and reverse redistribution on planar thallium scintigraphy had PET $^{13}NH_3/^{18}FDG$ imaging. Radionuclide angiocardiography was performed in 23 patients. **Results:** Fifty segments showed reverse redistribution on planar thallium images; 19 segments had normal $^{13}NH_3$ and ^{18}FDG uptake and 17 were ischemic by PET criteria. Thus, a total of 72% (36 of 50) of reverse redistribution segments were PET viable. Sixty-one percent of segments with abnormal regional wall motion and reverse redistribution were PET scar. On follow-up, 31% (10/32) had a cardiac event (nine unstable angina and one myocardial infarction). Fifty percent of patients (5/10) with cardiac events had severe reverse redistribution and PET viability versus 9% (2/22) without cardiac events ($p = 0.01$). **Conclusions:** The majority of thallium reverse redistribution segments was PET viable as judged by ^{18}FDG uptake. Viability in areas of reverse redistribution is not inferred by regional wall motion analysis. Regional PET viability identifies patients with reverse redistribution with a higher likelihood of future cardiovascular events. PET viability assessment may be helpful with the impact of reverse redistribution on planar thallium scintigraphy.

Key Words: coronary artery disease; prognosis; imaging; metabolism

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Reverse redistribution is defined as a new or larger defect seen on thallium-201 redistribution perfusion imaging following stress. This phenomenon has been noted on planar and SPECT (*1–9*). It is observed most often in patients with prior myocardial infarction, usually in the setting of thrombolysis or revascularization (*1*). This finding was initially thought to be a manifestation of effective reperfusion therapy (*2*). However, preliminary observations in a large group of patients in the Thrombolysis in Myocardial Infarction (TIMI) trial indicate that reverse redistribution following thrombolysis is associated with a higher incidence of future cardiac events with substantial regional and global left ventricular dysfunction (*10*). The incidence of reverse redistribution in patients with chronic coronary artery disease and previous myocardial infarction, undergoing planar thallium stress scintigraphy and cardiac catheterization for the evaluation of chest pain, has been reported to be as high as 18% (*3*). The description of reverse redistribution of chronic stable coronary artery disease is limited to a few reports (*5,9*).

PET has been a useful technique for the characterization of myocardial flow and metabolism (*11,12*). Consequently, application of this approach to patients with reverse redistribution may provide additional insight into its pathophysiology. The interaction of reverse redistribution with PET data was related to long-term outcome.

MATERIALS AND METHODS

For this study, reverse redistribution was defined as a defect either first appearing on redistribution imaging as compared to stress studies or appearing larger at redistribution. Thallium defect patterns met the criteria for reverse redistribution only if they were visually apparent on unprocessed images and were also quantifiable by circumferential profile analysis of processed images. To avoid inclusion of artifacturally derived findings, defects that were apparent only on background subtracted images were not included. The severity of reverse redistribution was calculated by the decrement in counts observed in the defect on the redistribution image in comparison to the poststress image. The degree of redistribution was defined by quantitative count-based criteria. A decrement of 10%–19% within the reverse redistribution segment was defined as mild, 20%–24% moderate and ≥25% severe.

Study Population

Thirty-two patients with chronic coronary artery disease demonstrated reverse redistribution on a clinical stress thallium study

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For correspondence or reprints contact: Robert Soufer, MD, Yale University-VA PET Center, 950 Campbell Avenue/115A, West Haven, CT 06516.

(West Haven Veterans Affairs Medical Center) from June 1991 to March 1992. Patients were prospectively indexed into the study based on the presence of reverse redistribution alone. Cardiac catheterization was not requested, but was available in 11 patients within 1 mo of the studies. A radionuclide angiocardiogram was requested of all patients, of whom 23 consented and 9 refused. Requests for a stress thallium test included atypical angina (n = 12), evaluation for cardiac rehabilitation program (n = 12), and routine follow-up (n = 8). Twenty-one of 32 had a standard exercise treadmill stress performed according to the Bruce protocol, and 11 out of 32 patients had intravenous dipyridamole pharmacological stress. Their mean age was 66 ± 8 yr. All patients had chronic coronary artery disease based on these criteria: 24 out of 32 had a history of previous myocardial infarction documented by history, enzymatic criteria or presence of q waves (n = 21). The remaining patients had coronary artery disease on angiography and/or angina with a regional wall motion abnormality or myocardial ischemia on thallium.

All patients had quantitative planar thallium scintigraphy and ^{13}N-ammonia, ^{18}F-deoxyglucose ^{18}FDG PET studies were performed. Twenty-three also had a 4-view (left anterior oblique, anterior, left lateral and left posterior oblique) radionuclide angiocardiogram performed for analysis of regional wall motion. The radionuclide angiocardiogram, ^{201}Tl and PET studies were all performed within a month, and each was independently read by two observers blinded to clinical history and other imaging results. Coronary arteriography was performed in 11 patients within 1 mo of the radionuclide studies. Three patients had previous percutaneous transluminal coronary angioplasty a mean of 4 yr (range 3 to 5 yr) and 7 patients had coronary artery bypass graft a mean of 6 yr (range 3 to 8 yr) before entry into the study. There were no patients with a revascularization procedure within 3 yr of entry into this study. During the study time frame all patients were maintained on existing medication, which included beta blockers (n = 9), Ca^{++} channel blockers (n = 11), nitrates (n = 5) and digoxin (n = 7).

Planar Thallium Imaging

Stress involved either standard treadmill exercise according to the Bruce protocol (n = 21) or intravenous dipyridamole pharmacological stress [0.568 mg/kg intravenously over 4 min (n = 11)]. Thallium-201 (2.50 mCi) was injected either 4 min after the end of dipyridamole infusion or at peak exercise in those undergoing treadmill stress. Image acquisition was performed 5 min after radionuclide injection in patients receiving dipyridamole, and 5 to 10 min in those who performed treadmill exercise. Acquisition was obtained for a minimum of 500,000 counts in the left anterior oblique, anterior and left lateral views. Redistribution imaging was performed 2–3 hr following the poststress acquisition (*13*).

Thallium Quantification in Perfusion Defects

Planar images were analyzed quantitatively according to previously described techniques (*13*). All images were subjected to interpolative background subtraction. The left ventricle was divided into 36 segments, each segment with an angle of 10°. The mean activity in each segment was normalized to maximum segmental activity within that image. Profiles were generated for both poststress and redistribution image sets, and compared to those derived from a normal database. All perfusion defects in all views (inclusive of redistribution images) were identified quantitatively when at least 5° adjacent 10° sectors (total angle 50°) of the circumferential profile fell below the lower limit of the normal (>2 standard deviations below the mean counts derived from a normal database) myocardial distribution of ^{201}Tl for that view.

Radionuclide Angiocardiogram

Equilibrium blood-pool labeling was achieved using a modified in vivo technique. Imaging was obtained with a small field of view cardiac camera and data were acquired in frame mode with a 20–50 msec interval, depending on the heart rate. Images were acquired in the anterior, left anterior oblique, left lateral and left posterior oblique views. Global left ventricular ejection fraction was measured by standardized count based techniques. Wall motion was visually graded on a 4 point scale (normal, hypokinetic, severely hypokinetic and akinetic).

Resting ^{18}FDG/^{13}N-ammonia PET

Patients were studied under basal conditions and a random plasma glucose measurement was performed prior to scanning. If plasma glucose was within normal limits, the patient received 50 gr of oral dextrose and imaging was performed 45 min thereafter. If plasma glucose was elevated, intravenous insulin was administered and the plasma glucose was serially monitored until ≤120 μg/dl. The patient was subsequently positioned for imaging. At the time of imaging plasma glucose was <120 μg/dl in all patients. Oral dextrose was withheld in patients with elevated plasma glucose.

Patients were positioned within the camera gantry (Posicam 6.5, Positron Corp., Houston, TX) for myocardial imaging, using careful physical examination of the chest and cardiac auscultation. Confirmation of cardiac positioning was accomplished by a preview image following intravenous administration of 4 mCi of ^{13}N-ammonia. Following rapid reconstruction of the acquired data, images were inspected for proper positioning of the heart within the field-of-view. Any necessary adjustments to patient positioning were then made.

A 15-min transmission scan was subsequently performed using a rotating 3 mCi ^{68}Ge rod source. The acquired data transmission was used to correct emission images for body attenuation. Upon completion of the attenuation scan, the patient received 15 mCi of ^{13}N-ammonia intravenously. After a 5-min delay (to allow pulmonary background activity to clear) resting myocardial perfusion imaging was performed over 5 min. Following completion of the perfusion scan, the patient received 5 mCi intravenously of ^{18}FDG. Forty-five min were allowed for cardiac uptake of the ^{18}FDG. Images of glucose utilization were acquired over 20 min.

When imaging was completed, both the ^{13}N-ammonia and ^{18}FDG image data underwent computerized attenuation correction and filtered back projection reconstruction. PET images were displayed in short-axis, vertical axis and horizontal long-axis views using a graded color display. Quantitative criteria were used to define uptake patterns.

Definition of Viability

The ^{18}FDG and ^{13}N-ammonia images were quantified and compared to maximal counts within a reference region and a normal database. Segmental activity within respective image sets was normalized to reference regions that exhibited the top 5% of maximal counts, which also had normal wall motion and/or normal resting blood flow. Fluorine-18-FDG and ^{13}N-ammonia image sets were also compared to a normal database of healthy volunteers with a low likelihood of coronary artery disease. Normal resting blood flow was defined as >80% of activity in the reference region and within two standard deviations of the mean counts observed in the corresponding region for normal volun-

TABLE 1
Correlation Between PET and Planar Thallium Images

	Planar	PET
Anterior	LL	SA, HLA
Inferior	LL	SA, HLA
Septum	LAO	SA, VLA
Lateral	LAO	SA, VLA
Apex	ANT, LL, LAO HLA	

ANT = anterior; HLA = horizontal long-axis; LAO = left anterior oblique; LL = left lateral; SA = short-axis; VLA = vertical long-axis.

teers. Moderately reduced blood flow was activity within 50%–79% of reference counts. Severely reduced and/or absent blood flow included counts that were reduced <50% of reference counts and >2 standard deviations below the corresponding region measured by the normal database.

The presentations of viability were regions with normal ^{18}FDG and ^{13}N-ammonia, ^{18}FDG/^{13}N-ammonia mismatch and moderate reduction of ^{18}FDG and ^{13}N-ammonia. The ^{18}FDG activity was graded into three categories: normal and viable (≥80% of activity in the normal reference region), reduced and viable (50%–79% of normal reference activity) representing an admixture of viable and nonviable myocardium and absent (<50% of normal reference activity). The 50% of normal reference activity serves as a threshold below which nonviability is considered consistent with most recent reports (*9,14–19*). In addition to the latter criteria for nonviability, we required FDG nonviable segments to be reduced >2 standard deviations below the mean data sets compared to a normal database. Therefore, a nonviable segment had FDG metabolic activity and blood flow less than 50% of normal reference activity and counts reduced greater than two standard deviations below the mean data set of a normal database. FDG/^{13}N-ammonia mismatch the PET scintigraphic criterion for ischemia was defined as a region with severely reduced blood flow with a relative increase of FDG that was greater than 50% of activity in the reference region and within two standard deviations of reference mean values for that segment as defined by a normal database.

Correlation of Planar with Tomographic Images

Careful anatomic correlation of planar thallium PET images was performed as follows. For both planar and tomographic image sets, the left ventricle was divided into five anatomical areas (segments): anterior, inferior, lateral, septum and apex. The appropriate segments were identified on planar images in the left anterior oblique, left lateral and anterior views according to standard convention. PET segments were also localized regionally according to standard techniques. The apex was identified on PET images using a computer-selected horizontal long axis slice through the mid ventricle. Reverse redistribution in segments, seen on planar thallium imaging, were then correlated with the corresponding segment noted on the PET image displays (Table 1, Fig. 1). The five anatomical areas in each particular tomographic orientation were inspected by two observers. If more than two contiguous slices (within each tomographic display) met the criteria for viable, ischemia or scar, it was noted. Correlation between the radionuclide angiocardiogram and PET data was performed in the same manner.

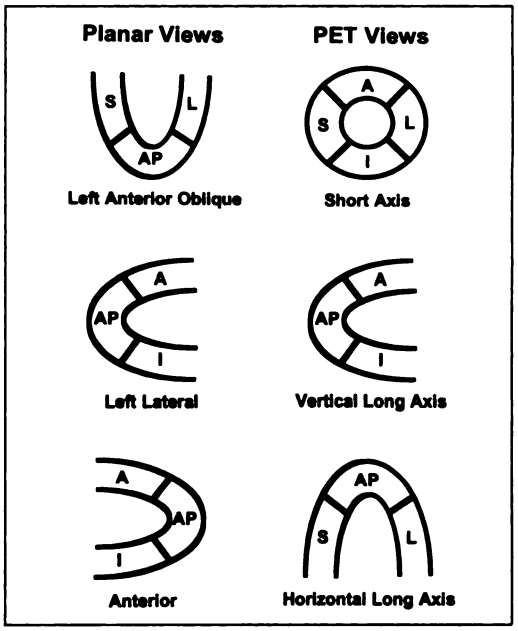

FIGURE 1. Schematic diagram outlining the planar thallium views (left column) and the PET views (right column) which were used for anatomic correlation. A = anterior; AP = apex; I = inferior; L = lateral wall; S = septum.

Frequency of Reverse Redistribution

To assess the frequency of reverse redistribution in our patient populations, clinical reviews were performed on all thallium-201 studies in a 3-mo period (from April to June 1992). This represents a separate population than those involved in this study, but with the similar clinical characteristics of chronic coronary artery disease and absence of a revascularization procedure within 3 yr of the thallium study.

Cardiovascular Morbidity and Mortality at Follow Up

Patients were contacted at a mean of 14 mo (range 9–19 mo) from entry into the study. In addition to patient interviews, patient charts were reviewed and physicians contacted. The endpoints recorded were: death, recurrent infarction, unstable angina or congestive heart failure requiring hospitalization.

Data Analysis

Data are expressed as mean ± standard deviation and percent total observations. The Chi square test was used to assess the frequency of phenomena in subgroups. All values less than $p < .05$ were significant.

RESULTS

A total of 50 segments with reverse redistribution were seen in the 32 patients. There were 18 patients with reverse redistribution seen in more than one view and 16 seen in one view. However, all defects met strict quantifiable criteria. Of the 50 reverse redistribution segments, 44 were initially normal on the postexercise image and showed defects at redistribution. The regional distribution of the 50 reverse redistribution segments were: 11 inferior, 11 lateral, 16 apical and 12 anterior. Reverse redistribution was quantified as mild in 5 segments, moderate in 28 and severe in 17.

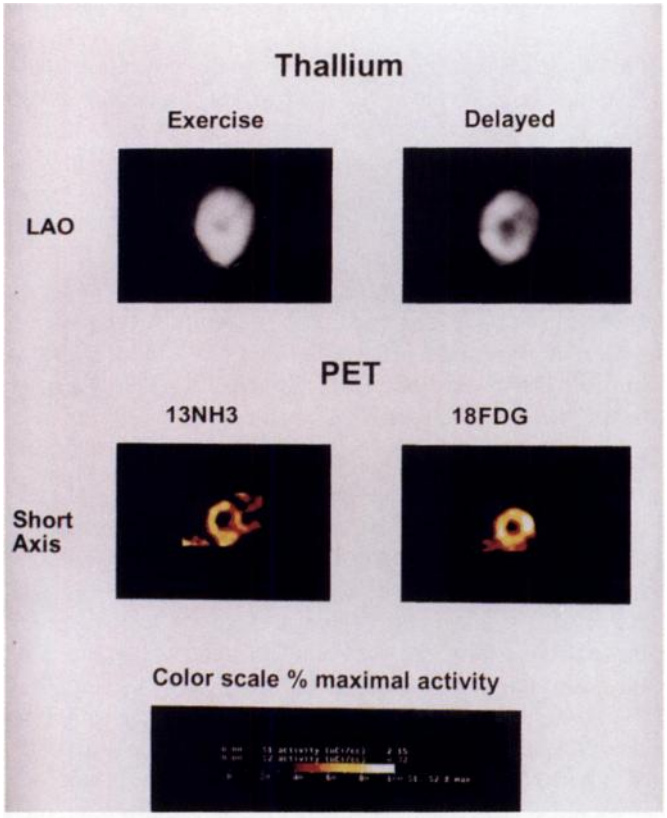

FIGURE 2. Study of a 71-yr-old white male with an infero lateral MI in 1991, who was referred after adjustment of his medical therapy. The thallium left anterior oblique view images (upper panel) are representative of short axis left anterior oblique ^{13}N-ammonia flow and ^{18}FDG studies are also shown (lower panel). The lateral wall on the thallium left anterior oblique view reveals a defect on the 2.5 hr delayed images. The corresponding PET images below show decreased perfusion of the lateral wall on the ^{13}N-ammonia image with augmented ^{18}FDG in the corresponding segment. The lateral wall is considered viable (ischemic) in this example.

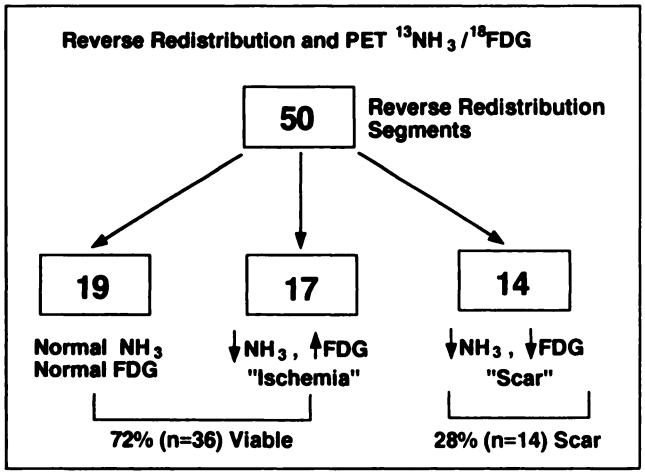

FIGURE 3. The distribution of the 50 reverse redistribution segments on planar thallium scintigraphy characterized by PET blood flow and glucose metabolism (shown above). Seventy-two percent of these reverse redistribution segments were PET viable. PET viability includes the subset of normal homogeneous uptake of blood flow and metabolism, and an ischemic subset which comprised 34% (17 segments) of the total reverse redistribution segments. Twenty-eight percent of the total reverse redistribution segments were characterized as scar by PET criteria.

Of the 50 reverse redistribution segments, 19 (38%) were normal by PET criteria, with homogeneous uptake of ^{13}N-ammonia and ^{18}FDG. Seventeen segments (34%) were considered ischemic by PET criteria (Fig. 2). Thus, 36 (19 normal, 17 ischemic) reverse redistribution segments were viable (72% normal or ischemic) when correlated with PET (Fig. 3). The remaining 14 segments (28%) exhibited scar on PET imaging (Fig. 4).

The relationship between the degree of reverse redistribution and corresponding PET characterization was as follows. In the five segments exhibiting mild reverse redistribution, four were normal and one demonstrated scar. Of the 28 moderate reverse redistribution segments, 17 (61%) were viable (8 ischemic, 9 normal) and 11 (39%) were scar. Of the 17 severe reverse redistribution segments, 15 (88%) were viable (9 ischemic, 6 normal), and 2 (12%) were scar.

Regional Wall Motion

Radionuclide angiocardiography data were available for direct correlation in 35 of the 50 segments with reverse redistribution. Eighteen segments exhibited a wall motion abnormality (3 akinetic, 5 severe hypokinetic and 10 hy-

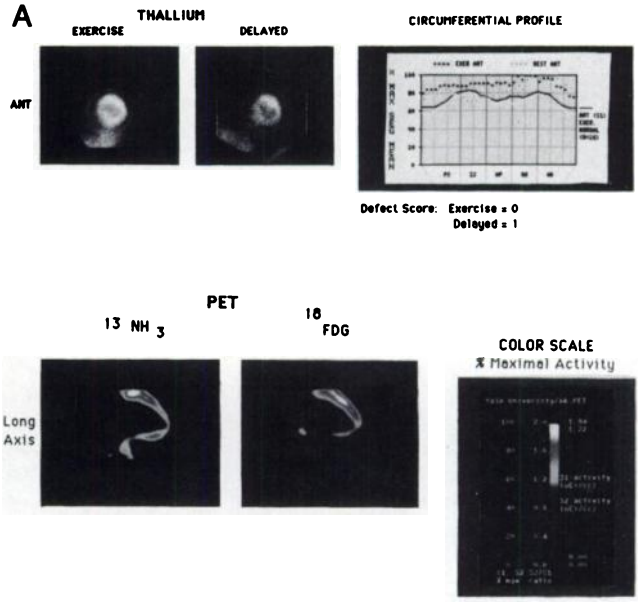

FIGURE 4. (A) Analog planar thallium images (left) and quantitative circumferential profile (right). There is a visual and quantifiable area of reverse redistribution seen on the delayed images in the inferior wall. A defect in this area on the post exercise image is not visually apparent or quantifiable. (B) The corresponding PET image of the planar thallium described in (A). Both PET images are in the long-axis orientation, with the ^{13}N-ammonia flow image (left), the ^{18}FDG (middle) and the color scale (right). This PET study shows a concordant reduction in blood flow (measured with ^{13}N-ammonia) and of metabolism (measured by ^{18}FDG) in the mid-inferior to posterobasal segmental. This is an example of PET scar in an area of reverse redistribution in the inferior wall.

pokinetic) (Fig. 5). Of these, 18 segments showed wall motion abnormalities, 7 were viable by PET (1 severe hypokinetic, 6 hypokinetic) and 11 were scar (2 akinetic, 4 severe hypokinetic and 5 hypokinetic). Of the 17 segments with normal wall motion, all but one were confirmed as viable by PET analysis. The frequency of viability was highly different in the groups with and without abnormal wall motion (7/18 versus 16/17, $p < 0.0001$). Thus, a segment with reverse redistribution and normal wall motion is PET viable. In contrast, a reverse redistribution segment with abnormal wall motion cannot reliably be predicted as viable or nonviable.

Coronary Arteriography

Coronary arteriography was performed in 11 patients and revealed critical stenosis (≥70%) in the artery supplying the myocardial segment exhibiting reverse redistribution in all but one patient, who had angiographically subcritical coronary artery disease. Of the ten patients, two had single-vessel disease, five had double-vessel disease and three had triple-vessel disease. Accounting for overlap, seven patients had critical stenosis in the left anterior descending, four patients in the circumflex distribution and eight patients in the right coronary artery. The patient with subcritical disease had an antero-septal infarct with hypokinesis on radionuclide angiocardiography and q waves in V_1 and V_2. The PET study showed an absence of ^{18}FDG in the anterior wall consistent with scar.

Follow-Up

A mean 14-mo follow-up was performed in 100% of the patients. Thirty-one percent (10/32) had a cardiac event that included hospitalization for unstable angina (n = 9) and myocardial infarction (n = 1). There were no deaths. In those patients with a cardiac event, 50% (5/10) had severe reverse redistribution and PET viability versus 9% (2/22) without an event ($p = 0.001$). Mild and moderate reverse redistribution did not significantly distinguish those patients with a cardiac event. In order to assess the potential impact of PET findings (viable vs. scar) on future cardiac events in severe reverse redistribution, we analyzed only those patients (n = 13) with severe reverse redistribution demonstrating scar and viable myocardium. In these 13 patients, those who had PET viability all had a cardiac event, compared to those who had PET scar of whom none had an event ($p < 0.03$). The impact of PET ischemia (as a subset of viability) to a cardiac event vs. PET scar was also analyzed. PET ischemia in the patients with reverse redistribution was three times more frequent in those with a cardiac event than those without one ($p = 0.01$).

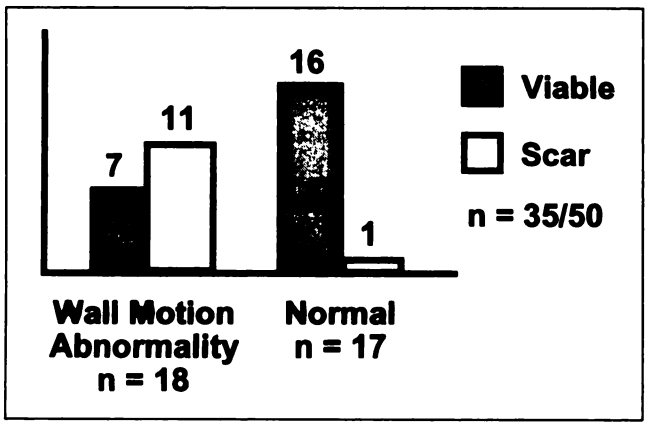

FIGURE 5. Thirty-five segments with reverse redistribution were analyzed with respect to their wall motion. The white bars represent viable segments and the cross-hatch bars represent segments which were scar by PET criteria.

Other Predictors of Outcome

Of the 21 patients who had treadmill exercise, the endpoints were: fatigue (10), chest pain (4), ECG changes (3) and attainment of maximum heart rate (4). Lung-to-heart ratio was below 0.5 in all but two patients who were at the 0.5 level; there was no evidence of cavity dilatation. Of those patients who had a radionuclide ventriculogram, only three had left ventricular ejection fractions less than 40%.

In order to determine whether additional information on the ^{201}Tl studies had an impact on prognosis, the frequency of adjacent myocardial ischemia was assessed. Adjacent myocardial ischemia alone did not predict a poor outcome. Irrespective of the severity of reverse redistribution, there were ten patients with adjacent quantifiable myocardial ischemia, of whom two had an event and eight were event free (p = ns).

The other standard predictors of outcome such as exercise time, ECG changes or chest pain did not predict outcome. Left ventricular cavity dilatation was not observed. Mild and moderate reverse redistribution did not distinguish these patients with regard to future outcome.

Frequency of Reverse Redistribution

In an attempt to assess the frequency of reverse redistribution in our population, we identified reverse redistribution in 15% of 177 sequential thallium studies (n = 27) during a 3-mo period (April–June 1992).

DISCUSSION

This study indicates that 72% of segments with reverse redistribution on planar thallium scintigraphy are viable by PET. Of the 36 segments which were viable by PET, 47% (17 of 36) met PET criteria for ischemia. Twenty-eight percent (14 of 50) of reverse redistribution segments on planar thallium scintigraphy met PET criteria for scar. The presence of a wall motion abnormality in a reverse redistribution segment did not predict whether a segment was viable or scar as judged by PET criteria.

Our data indicate that of those segments with the most severe reverse redistribution, 88% were viable by PET. With respect to outcome, PET viability and ischemia were both associated with an increased frequency of cardiac events in patients with severe reverse redistribution. These data underscore the potential value of PET metabolic data in this patient population. Specific PET findings in areas of

reverse redistribution may identify a subset of patients with a higher likelihood of cardiac events and therefore require closer follow-up. The potential value of PET data in this patient population is also underscored by the findings that myocardial segments, which on thallium scintigraphy showed ischemia adjacent to reverse redistribution segments, did not identify those patients with a higher likelihood of cardiac events.

Accelerated thallium clearance has been reported in experimental canine model studies of regional hyperemia and coronary reperfusion (*20,21*). Reverse redistribution has been clinically noted in several thallium-201 images obtained following injection at rest of patients undergoing streptokinase therapy for acute myocardial infarction (*2*). In the latter study, 50 patients demonstrated reverse redistribution solely in the region of the reperfused myocardium. Reverse redistribution was associated with patency of the infarct related artery and quantitative improvement in the resting thallium defect size on a 10 day follow-up study. Improvement to normal or near-normal wall motion on the 10 day radionuclide angiocardiogram reinforced the view that viable myocardium constituted a major proportion of reverse redistribution segments. In comparison, the nonreversible defects were associated with significantly lower frequencies of patency of the infarct vessel and improvement in defect size and normal wall motion.

Our study consisted of patients with chronic coronary artery disease and old previous myocardial infarction, rather than patients with acute myocardial infarction receiving thrombolytic therapy. In contrast to the prior study (*2*), only 34% of the myocardial segments with reverse redistribution in this study exhibited normal wall motion.

The pathophysiology of reverse redistribution is multivariate and may depend upon the clinical presentation. Immediately following reperfusion and thrombolytic therapy of acute infarction, a higher than normal blood flow to the noninfarcted tissue in the reperfused zone could explain the rapid ^{201}Tl washout and near normalization of the 10-day ^{201}Tl pattern with normal wall motion (*2*). Initial ^{201}Tl myocardial uptake is proportional to regional myocardial blood flow (*22*). The reperfused zone represents an admixture of viable and nonviable myocardium. Establishment of flow to a jeopardized zone results in a higher than expected concentration of ^{201}Tl, which may significantly mask a decrease in ^{201}Tl uptake in the necrotic portion of the reperfused zone (*2,21,23–25*). The regional washout of thallium-201 also is proportional to the initial ^{201}Tl concentration (*23*). Therefore, the washout rate of ^{201}Tl in the reperfused viable myocardium zone with initially higher flow would exceed that in normal myocardium. This leads to worsening of a defect on delayed imaging, resulting in the pattern of reverse redistribution.

The mechanism of reverse redistribution, in a population with chronic coronary artery disease, without reperfusion therapy is not well understood. The majority of our patients had previous myocardial infarction. An admixture of viable myocardium within the infarct zone is presumed in those patients who exhibited ischemia on their corresponding PET study. It may be hypothesized that these same areas exhibited reverse redistribution due to an accelerated washout from the infarct zone (*26*).

The mechanism that explains reverse redistribution in areas that are nonviable by PET is similar. Significant uptake of ^{201}Tl by nonviable myocardium, the interstitial compartment or both has been described (*23,27*). The washout rate of ^{201}Tl from the interstitial compartment or the necrotic zone may be higher than adjacent normal myocardium. This may result in a defect that is apparent only on redistribution imaging. There were 12 reverse redistribution segments in our study that exhibited scar by PET, where regional wall motion analysis was also available. Of these 12 segments, 11 had regional wall motion abnormalities. Accelerated washout from areas of well-established infarct may explain reverse redistribution in coronary artery disease patients with previous myocardial infarction. More investigation concerning this issue is required to provide further clarification.

In a study of patients with previous myocardial infarction, the accelerated washout in areas of reverse redistribution was also related to the severity of the initial perfusion defect as well as to a potential artifact of background subtraction (*3*). This potential technical explanation did not apply to our patients since a criterion for reverse redistribution was visualization on the unsubtracted analogue images.

Seventeen of fifty segments with reverse redistribution demonstrated ischemia by PET. In several of these segments, the postexercise thallium image appeared normal and the corresponding resting flow by PET was low. Thallium uptake on the postexercise image may be in the interstitial space and not the myocardium in regions that are ischemic and dysfunctional. Subsequently, it is in these regions that thallium clearance is faster and thus appears as a defect on redistribution imaging (*27*). Marin-Netto et al. studied a subset of patients (n = 16) with PET and reverse redistribution (9). In review of their data, there were three patients with an FDG/flow pattern of mismatch and abnormal PET blood flow with corresponding normalized thallium activity on the poststress image exceeding ≥85% (*9*). They explain these findings as a function of normalization to a reference region that itself had impairment of blood flow on exercise. In their study, the reference region in 15 patients was supplied by native arteries with significant stenosis, and bypass grafts in 10 patients. In the remaining patients with normal arteries to the reference zone, these vessels supplied collaterals to other myocardial regions.

The potential limitations of this study relate to the comparison of planar and tomographic data. However, the intent of this study was not to compare planar ^{201}Tl and PET diagnostically. Instead, the goal was to characterize with PET those myocardial segments which show reverse redistribution on planar thallium imaging. The heterogeneity and admixture of viable and nonviable segments within the myocardium is likely to contribute to the presentation

of reverse redistribution in patients with previous myocardial infarction assessed on planar scintigraphy. PET is appropriate to address this issue since FDG imaging has characteristics distinct from thallium and as such is an additional independent metabolic marker. The correlation of planar and tomographic images was performed by experienced nuclear cardiologists in our institution. The reliability of comparing corresponding anatomical territories between the two techniques was maximized by applying standard, widely accepted anatomical criteria. One advantage in making the comparison of reverse redistribution to planar thallium scintigraphy is that it may address issues relating to the concept that reverse redistribution on SPECT may be artifactual due to poor count statistics (*28*). Nonetheless, the results in this study with planar imaging are similar and confirm data of a recently published article addressing reverse redistribution on SPECT thallium scintigraphy (*9*).

It is relevant to compare thallium reinjection and PET with regard to viability in areas of reverse redistribution. Although PET ischemia correlates with reinjection thallium scintigraphy a high percentage of the time in defects less than 50% of maximum on the initial poststress image, intermediate density defects have a 25% discordant rate with respect to PET ischemia (*12*). This has also been confirmed by Tamaki et al. where the thallium defects score was not segregated according to the magnitude of the defect, but an overall discordance rate was 25% (*29*). The findings here are similar to a published report comparing reverse redistribution in a chronic coronary artery disease population with thallium reinjection and a subset who were compared additionally with PET imaging (*9*). The majority of the segments analyzed in this report were viable (82%) by thallium reinjection and 18% were persistent defects associated with Q waves, regional wall motion abnormalities and reduced 18-FDG uptake. Collateral circulation was observed with much higher frequency in those patients with viability in reverse redistribution segments than in scar. This supports the hypothesis that these regions may be associated with a higher resting flow rate and attendant faster thallium washout rates.

This paper's findings describe a subset of patients with chronic coronary artery disease, previous myocardial infarction and reverse redistribution on planar thallium scintigraphy. Occurrence of reverse redistribution in similar populations has been noted in the distribution of critically diseased vessels and a high percentage has been associated with abnormal regional wall motion, suggesting that reverse redistribution is a marker of significant coronary artery disease (*6,9*). We have characterized the myocardial segments that exhibit reverse redistribution on planar thallium scintigraphy using paired metabolic flow imaging with PET. A significant finding is the relationship of PET viability in the area of severe reverse redistribution. These patients were more likely to have a subsequent cardiac event requiring hospitalization. Furthermore, our data support that viability in areas of reverse redistribution cannot be inferred by regional wall motion analysis. A regional wall motion abnormality in an area of reverse redistribution may be viable or nonviable. PET assessment of viability in patients with reverse redistribution may be helpful in indexing patient subgroups which require closer follow-up. The role of PET in these patients will require additional studies.

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