Comparison of Fluorine-18-FDG with Rest-Redistribution Thallium-201 SPECT to Delineate Viable Myocardium and Predict Functional Recovery After Revascularization

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Recently, the use of ^{18}F-fluorodeoxyglucose (FDG) with SPECT has been proposed to identify viable myocardium. Thallium-201 rest-redistribution SPECT is frequently used for this purpose. The aim of this study was to compare the relative merits of the two techniques to predict improvement of regional left ventricular function after revascularization. **Methods:** Twenty-four patients scheduled for revascularization were studied. Regional contractile function was evaluated with echocardiography before and 3 mo after revascularization. The patients underwent ^{201}Tl rest-redistribution SPECT and FDG SPECT on the same day; the early ^{201}Tl image obtained in the rest-redistribution protocol was also used as a perfusion study for comparison with FDG SPECT. The SPECT data were analyzed semiquantitatively using polar maps. For analysis of echo and SPECT data, a 13-segment model was used. Dysfunctional segments were classified as viable on FDG SPECT if normal perfusion or mismatch pattern (increased FDG uptake in perfusion defects) was seen. For ^{201}Tl rest-redistribution SPECT, criteria for viability included the percentage of ^{201}Tl uptake and reversibility of defects. **Results:** On echocardiography, 106 segments were dysfunctional. Recovery of function was observed in 36 segments, whereas function did not improve in 70. FDG SPECT showed a sensitivity of 89% [95% confidence interval (CI) 79%–99%] and a specificity of 81% (95% CI 72%–90%). Thallium-201 rest-redistribution SPECT had a sensitivity of 67% (95% CI 52%–82%) and a specificity of 77% (95% CI 67%–87%). **Conclusion:** Our data show that the diagnostic accuracies (to predict improvement of contractile function after revascularization) of both techniques were not significantly different, indicating that both imaging modalities may provide comparable information concerning prediction of improvement of function.

Key Words: fluorine-18-fluorodeoxyglucose; SPECT; thallium-201; rest-redistribution; myocardial viability

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Regional left ventricular (LV) dysfunction may not necessarily represent irreversibly damaged myocardium. Both hibernation and (repetitive) stunning may lead to regional myocardial dysfunction in the presence of viable myocardium, and complete or partial recovery of function may occur after revascularization (*1*). Moreover, if a substantial amount of dysfunctional but viable myocardium is present, improvement of global LV function may occur after revascularization (*2,3*). Thus, the differentiation between dysfunctional but viable versus necrotic myocardium may allow a more adequate selection of patients with coronary artery disease, who may benefit from a revascularization procedure. Metabolic imaging using ^{18}F-fluorodeoxyglucose (FDG) and PET has been shown to differentiate viable from necrotic myocardium (*2,4–9*). FDG may also be used in combination with SPECT (*10–15*). SPECT cameras are widely available and may allow more widespread use of FDG.

To further validate the use of this approach, we studied 24 patients undergoing revascularization with FDG SPECT and ^{201}Tl rest-redistribution SPECT, which is frequently used to assess viability (*3,16–21*), and compared the results with improvement of function after revascularization.

MATERIALS AND METHODS

Patients and Study Protocol

We prospectively studied 24 patients with regional wall motion abnormalities on echocardiography who were scheduled for revascularization. All had chronic coronary artery disease and were studied > 1 mo after infarction. All patients were clinically stable during the study period. Seventeen patients underwent coronary artery bypass grafting and 7 underwent percutaneous transluminal coronary angioplasty (PTCA). Referral for revascularization was based on clinical and angiographic data, whereas the scintigraphic data did not influence patient management. After an overnight fast, ^{201}Tl rest-redistribution SPECT was performed, with the initial image reflecting myocardial perfusion and the late image representing viability (*18*). On the same day, FDG SPECT was performed during hyperinsulinemic euglycemic clamping. To compare myocardial FDG uptake with regional perfusion, the early image of the ^{201}Tl rest-redistribution study was used. Regional wall motion and thickening were analyzed by echocardiography before and 3 mo after revascularization. Each patient gave informed consent to the study protocol, which was approved by the ethical committees of the participating hospitals.

Thallium-201 Rest-Redistribution SPECT

The ^{201}Tl rest-redistribution study was performed as described previously (*3,16–21*). In short, images were obtained 10–15 min after injection of 111 MBq Tl-chloride. A late (redistribution) image was acquired 4 hr after tracer injection. A dual-head gamma camera system (ADAC Laboratories, Milpitas, CA) was used, and data acquisition was performed over 360°. Transaxial slices (1 pixel, 6-mm thickness) were obtained by filtered backprojection; slices were not corrected for attenuation. Further reconstruction yielded long- and short-axis projections perpendicular to the heart axis. Circumferential count profiles (60 radii, highest pixel activity/

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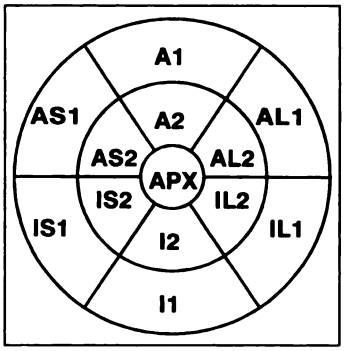

FIGURE 1. Schematic presentation of the 13-segment model used for echocardiographic and scintigraphic studies. A = anterior; AL = anterolateral; APX = apex; AS = anteroseptal; I = inferior; IL = inferolateral; IS = inferoseptal; 1 = basal; 2 = distal.

radius) from the early and late ^{201}Tl short-axis slices were generated and displayed in a polar map format. To compare the polar map data with the echo data, the polar maps were divided into 13 segments (Fig. 1), aligning the 13 echo segments (see below).

A region of normal perfusion (defined as the segment with the highest ^{201}Tl uptake) was selected from the early ^{201}Tl polar map. The activity of this segment was normalized to the activity of the same segment of a normal database (*11*), and all other segments were adjusted correspondingly. For example, if the patient's ^{201}Tl activity was 70% in the selected normal region, and the corresponding activity in the normal database was 90%, then all other activities on the patient's polar map were adjusted by a factor of 90/70.

The region of normal perfusion was projected on the late ^{201}Tl polar map, and the same normalization procedure was followed. Segments were considered to have a perfusion defect when the ^{201}Tl activity on the early polar map was > 2 s.d. below the normal reference value. The early and late segmental ^{201}Tl activities were expressed as percentage of the corresponding normal reference values. A segment was considered viable if significant redistribution occurred in a perfusion defect or if the segmental ^{201}Tl activity on the late image exceeded a threshold (*3,18*). The optimal cutoff levels for ^{201}Tl redistribution and activity were defined by receiver operating characteristic (ROC) curve analysis (see statistical analysis).

FDG SPECT

Subjects underwent a hyperinsulinemic glucose clamp as described previously (*22*) to standardize metabolic conditions throughout FDG SPECT. FDG (185 MBq) was injected after 60 min of clamping; another 45 min were allowed for myocardial FDG uptake (*23*). Data acquisition was performed with the same camera system as described for ^{201}Tl. Specially designed collimators were used to detect 511-keV photons (van Mullekom; Nuclear Fields, Boxmeer, The Netherlands) (*24*). Reconstruction and analysis of data were identical to that of the ^{201}Tl data.

On FDG SPECT, a segment was considered viable if perfusion was normal or if FDG uptake was increased >7% in a perfusion defect. The cutoff level of 7% increased FDG uptake in perfusion defects has been established using ROC analysis on the level of increased FDG uptake in perfusion defects in 44 patients undergoing revascularization (*25*).

Two-Dimensional Echocardiography

The echocardiographic images were recorded on videotape, digitized on optical disk (PreVue III; NovaMicrosonics,) and displayed side by side to facilitate comparison of pre- and post-revascularization images. The data were reviewed off-line and consensus was achieved by two observers blinded to the SPECT data. A 13-segment model was used, matching the SPECT segments (*12*). Both wall motion and wall thickening were analyzed.

TABLE 1
Clinical Characteristics of the Study Population

Characteristic	Number
Patients	24
Sex (M/F)	21/3
Age (yr)	65 ± 8
Previous infarction	21 (88%)
Q wave on electrocardiogram	14 (78%)
Coronary anatomy	
One-vessel disease	3 (12%)
Two-vessel disease	9 (38%)
Three-vessel disease	12 (50%)
LVEF	45% ± 14%

LVEF = left ventricular ejection fraction.

Each segment was assigned a wall motion score ranging from 0–3: normal = 0, hypokinetic = 1 (decreased endocardial excursion and systolic wall thickening), akinetic = 2 (absence of endocardial excursion and systolic wall thickening) or dyskinetic = 3 (paradoxical outward movement in systole). Wall thickening was primarily used for the classification of septal wall motion, thereby preventing the problem of paradoxical septal motion after coronary artery bypass graft (CABG) (*26*). Improvement of regional wall motion after revascularization was considered if systolic thickening (hypo- or normokinesia) was seen in a segment that was akinetic or dyskinetic at baseline or if normal wall motion was seen in segments that were hypokinetic at baseline. Only segments that were succesfully revascularized were analyzed; revascularization was based on a review of the CABG and PTCA reports.

Statistical Analysis

All results were expressed as mean ± s.d. Patient data were compared using the Student's t-test for paired and unpaired data when appropriate. A $p < 0.05$ was considered significant. ROC analysis was performed to determine the optimal cutoff levels for percentage ^{201}Tl redistribution and activity on the late image to predict functional improvement after revascularization. The optimal cutoff values chosen were defined as those providing the maximal sum of sensitivity and specificity. Sensitivity and specificity are based on their standard definitions and presented with their 95% confidence intervals (CIs). Statistically significant ($p < 0.05$) differences between techniques are present whenever 95% CIs do not overlap.

RESULTS

Patient Characteristics

The characteristics of the study population are given in Table 1. Twenty-one patients had a previous infarction > 1 mo before the study. Patients had on average 2.2 ± 2.8 stenosed coronary arteries.

Baseline Characteristics and Functional Outcome

In the 24 patients, 312 segments were analyzed by echocardiography, showing normal wall motion in 199 (64%) segments and abnormal wall motion in 113 (36%) segments. Seven segments were excluded from the analysis because of inadequate revascularization (by review of the surgical and PTCA reports). Of the remaining 106 dysfunctional segments, 56 (53%) were hypokinetic and 50 (47%) were akinetic or dyskinetic. After revascularization, 36 (34%) segments had improved function, including 20 akinetic and 16 hypokinetic segments. Seventy (66%) segments demonstrated no improvement after revascularization, including 2 dyskinetic, 28 akinetic and 40 hypokinetic segments.

TABLE 2
Comparison Between Characteristics of Segments After Revascularization

	Group I* (n = 36)	Group II† (n = 70)	p
Segmental WMS before	1.58 ± 0.50	1.52 ± 0.56	NS
Segmental WMS after	0.37 ± 0.48	1.58 ± 0.56	<0.001
Thallium activity on late image (%)	81.7 ± 15.5	74.7 ± 13.4	<0.05
Redistribution on late image (%)	5.1 ± 7.5	0.4 ± 5.1	<0.01
FDG activity (%)	92.6 ± 13.9	73.6 ± 16.3	<0.01
Increased FDG uptake in perfusion defects	19.3 ± 15.1	−0.8 ± 10.2	<0.01

*With improved function after revascularization.
†Without improvement of function after revascularization.
NS = not significant; WMS = wall motion score.

TABLE 3
Sensitivity and Specificity of FDG SPECT and Thallium-201 Rest-Redistribution SPECT to Predict Improvement of Function After Revascularization

	Sensitivity (95% CI)	Specificity (95% CI)
FDG SPECT	89% (79%–99%)	81% (72%–90%)
^{201}Tl RR RED	67% (52%–82%)	77% (67%–87%)
^{201}Tl RR ACT	78% (64%–92%)	59% (47%–71%)*
^{201}Tl RR COMB	78% (64%–92%)	59% (47%–71%)*

*$p < 0.05$ vs. FDG SPECT.
ACT = ^{201}Tl activity on late image; CI = confidence interval; COMB = combination of RED and ACT; RED = percentage redistribution; RR = rest redistribution.

Scintigraphic Characteristics of the Segments With Versus Without Improvement

The differences between segments with and without functional improvement after revascularization are listed in Table 2. The severity of wall motion abnormalities before revascularization was comparable between both groups.

The segments with improvement had increased FDG uptake relative to ^{201}Tl uptake, indicating metabolism-perfusion mismatch in these segments. Also, these segments showed significant redistribution on ^{201}Tl rest-redistribution imaging. Finally, the ^{201}Tl activity on the late image was significantly higher in segments with improvement compared with those without improvement in function.

Prediction of Functional Outcome

FDG SPECT. FDG SPECT classified 32 of 36 segments that improved after revascularization as viable, including 10 segments with normal perfusion and 22 segments with a perfusion defect and increased FDG uptake. Conversely, FDG SPECT classified 57 of 70 segments that did not improve as nonviable. Hence, FDG SPECT had a sensitivity of 89% (95% CI 79%–99%) and a specificity of 81% (95% CI 72%–90%) to predict functional recovery after revascularization.

Thallium-201 Rest-Redistribution SPECT. The cutoff level for ^{201}Tl activity on the late image, discriminating best between segments with and without improvement, was 75%. Using this criterion alone, a sensitivity of 78% (95% CI 64%–92%) and a specificity of 59% (95% CI 47%–71%) were reached. The cutoff value for the percentage redistribution, discriminating best between segments with and without improvement, was 5%. Applying this criterion yielded a sensitivity of 67% (95% CI 52%–82%) and a specificity of 77% (95% CI 67%–87%). When both criteria were combined, a sensitivity of 78% (95% CI 64%–92%) and a specificity of 59% (95% CI 47%–71%) were found.

Comparison Between FDG SPECT and Thallium-201 Rest-Redistribution SPECT. The sensitivities and specificities of both tests were not significantly different when percentage redistribution was used as the only determinant of viability on ^{201}Tl rest-redistribution images (Table 3). When ^{201}Tl activity on the late image or the combination of ^{201}Tl activity and percentage redistribution were used as criteria for viability, FDG SPECT showed a higher specificity than ^{201}Tl rest-redistribution SPECT. An example of a patient with improvement of function after revascularization and concordant FDG SPECT and ^{201}Tl rest-redistribution results is shown in Figure 2.

Influence of Segment Location on Prediction of Functional Outcome. Because ^{201}Tl and FDG have different photon energies, possibly leading to differences in attenuation (particularly in the inferoseptal region), the accuracy of FDG SPECT (and also of ^{201}Tl rest-redistribution imaging) was determined in the different regions (anterior, lateral and apical versus inferior and septal). Of the 36 segments with recovery after revascularization, 19 were located in the anterior, lateral or apical regions and 17 were located in the inferior or septal regions. Of the 70 segments without recovery, 35 were located in the anterior, lateral or apical regions and 35 in the inferior or septal regions. The sensitivity and specificity of FDG SPECT in the anterior, lateral and apical regions were 89% (95% CI 75%–100%) and 77% (95% CI 63%–91%), respectively. In the inferior and septal regions, these values were 88% (95% CI 73%–100%) and 86% (95% CI 74%–98%), respectively. For ^{201}Tl rest-redistribution imaging, the sensitivity and specificity in the anterior, lateral and apical segments were 68% (95% CI 47%–89%) and 60% (95% CI 44%–76%), respectively. For the inferior and septal regions, these values were 82% (95% CI 64%–100%) and 54% (95% CI 37%–71%), respectively.

DISCUSSION

The findings in this study show that FDG SPECT can accurately detect dysfunctional but viable myocardium in patients with coronary artery disease. FDG SPECT was both a

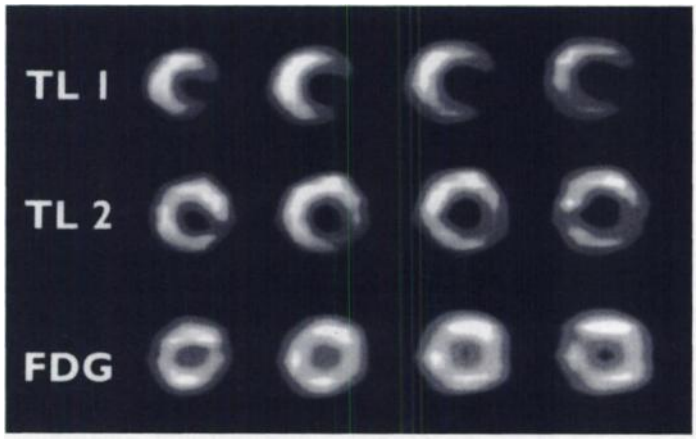

FIGURE 2. Corresponding series of ^{201}Tl rest-redistribution SPECT and FDG SPECT short-axis slices. The early ^{201}Tl slices (top) show a defect in the lateral wall, with redistribution on late ^{201}Tl images (middle). FDG slices (bottom) show increased uptake in the lateral wall compared with early ^{201}Tl images. Lateral wall was akinetic on resting echocardiography and improved in function after revascularization.

sensitive and specific predictor of improvement of regional contractile function after revascularization. Thallium-201 rest-redistribution SPECT showed a comparable sensitivity and specificity, when only percentage redistribution was used as an indicator of viability. When the activity on the late ^{201}Tl image was also used as an indicator of viability, the specificity of ^{201}Tl rest-redistribution SPECT was lowered significantly.

Pathophysiology of Chronic Dysfunctional but Viable Myocardium

Under physiological circumstances, myocardial perfusion is closely matched with the energy requirements of the myocardium; myocardial energy production is used mainly for maintainance of myocardial contraction. In the presence of a significant coronary artery stenosis, however, myocardial ischemia and regional dysfunction occurs because of the reduced supply of metabolic substrates and oxygen (*27*). It has been suggested that a chronic reduction in perfusion may result in contractile downregulation of the cell as a mechanism of reducing energy requirements, resulting in a new situation of perfusion-contraction matching (*28*). Rahimtoola (*29*) popularized the term hibernation, describing a reduction in contractile function secondary to chronic hypoperfusion, which may be reversed after revascularization. Recently, several studies have challenged this hypothesis by showing a lack of reduction in resting perfusion in dysfunctional segments that had improved function after revascularization (*30–33*). Alternatively, it has been shown that these segments have significantly reduced flow reserve, and Vanoverschelde et al. (*30*) suggested that repeated episodes of ischemia have resulted in chronic dysfunction.

Regardless of the underlying mechanism, numerous studies have recently focused on the identification of viable myocardium and the prediction of functional recovery after revascularization (*2–9,19–21,30–37*). Several characteristics of chronic dysfunctional but viable myocardium have been used for its identification, including preserved metabolic activity, cell membrane integrity and contractile reserve. Many studies with FDG and PET have demonstrated that the presence of preserved glucose utilization can predict improvement of function after revascularization (*4–9*). Subsequent studies have used ^{201}Tl as a marker of cell membrane integrity to identify hibernating myocardium (*3,16–21*), and more recently the infusion of low-dose dobutamine to assess contractile reserve has been proposed to unmask viable myocardium (*34–38*).

FDG SPECT and Viability

In this study, we showed that hypoperfused, dysfunctional myocardium with residual metabolic activity, as evidenced by increased FDG uptake, was to improve contractile function after revascularization. Our findings confirm those reported in many FDG PET studies (*2,4–9*). Those studies demonstrated that dysfunctional myocardium with decreased perfusion but relatively increased FDG uptake (mismatch pattern) were able to improve contractile function after revascularization. These segments may have contained hibernating myocardium. On the other hand, it should also be emphasized that "increased FDG signal" is not very specific for hibernation, because increased FDG uptake has also been observed during ongoing ischemia (*39*) or postischemic stunning (*40*).

In addition, a substantial number of segments that had improved function after revascularization had normal perfusion, as indicated by normal ^{201}Tl uptake immediately after tracer injection. These findings confirm the data reported by Vanoverschelde et al. (*30*).

In this study, FDG SPECT showed a sensitivity of 89% and a specificity of 81%. These values are in line with data obtained with FDG PET (*41*). Moreover, several studies have emphasized the good agreement between FDG PET and FDG SPECT (*12,13,15*). Martin et al. (*13*) studied nine patients with FDG PET and SPECT, showing that in all nine patients the detection of viable myocardium was equivalent by both techniques. Another study compared FDG PET and SPECT data with resting wall motion, as assessed by two-dimensional echocardiography (*12*). In the segments with abnormal wall motion an agreement of 76% was found between FDG PET and FDG SPECT.

Thallium-201 Rest-Redistribution SPECT and Viability

Thallium-201 Redistribution. Thallium-201 rest-redistribution imaging was initially proposed by Gewirtz et al. (*17*), demonstrating that a substantial number of segments with a perfusion defect on the early ^{201}Tl image showed redistribution on the late image. After intravenous administration, the initial uptake of ^{201}Tl by the myocardium reflects perfusion (*42*). After the initial myocardial uptake, there is a continous exchange of ^{201}Tl between the blood pool and the myocardium (*43*). Initial ^{201}Tl defects can represent either necrotic myocardium or hypoperfused but viable (hibernating) myocardium. The delayed uptake and retention of ^{201}Tl depends on cell membrane intergrity and hence viability. Redistribution and delayed defect resolution can therefore occur only when hibernating myocardium is present. In this study, we found a sensitivity of 67% and a specificity of 77% for the prediction of functional recovery after revascularization. The level of redistribution was determined using ROC analysis and was set at 5%, which is in line with data presented by Sansoy et al. (*44*)

Thallium-201 Activity on Late Image. Another marker of viability that can be extracted from ^{201}Tl studies is the percentage of ^{201}Tl activity on the late image. Considering that delayed myocardial retention of ^{201}Tl represents cell membrane integrity, it is likely that the percentage activity on the late image reflects the amount of viable myocardium in a certain segment. Traditionally, a cutoff level of 50% is used to classify a segment as viable (*18*). It should be kept in mind, however, that the 50% cutoff level has never been rigorously tested in patients undergoing revascularization to establish whether it can predict improvement of function. It is possible that a segment with mildly reduced tracer uptake (^{201}Tl activity on the late image $> 50\%$) represents a mixture of scar tissue and normal myocardium. Indeed, Zimmerman et al. (*45*) have demonstrated that the ^{201}Tl activity corresponded very well with the amount of fibrosis. In a more recent study, it was demonstrated that many segments with $> 50\%$ ^{201}Tl activity showed fibrosis in the inner endocardial half of the cardiac wall, with preserved morphostructure of the outer myocardial layer (*46*). Although classified as viable, these segments will never have improved function after revascularization. In this study, we found that the optimal cutoff level of ^{201}Tl activity was 75% to predict improvement of function after revascularization. This finding may implicate that more viable (and less necrotic tissue) is necessary to result in improved function after revascularization.

Methodological Considerations

For FDG SPECT, the criterion for viability was either normal perfusion or increased FDG uptake in ^{201}Tl perfusion defects. Thallium-201 has a lower photon energy than FDG, and no attenuation correction was used, possibly leading to differences in attenuation, especially in the inferoseptal region of the myocardium. However, we have previously shown in normal subjects that no differences between tracer activities occurred in the different regions of the myocardium (*11*). Moreover, the comparison with normal references for ^{201}Tl and FDG reduces

the effects of attenuation. Finally, the sensitivity and specificity of the technique were comparable for the anterior, lateral and apical regions compared with the inferior and septal regions, suggesting that differences in photon energy did not influence diagnostic accuracy significantly. Other factors possibly influencing attenuation (and diagnostic accuracy) are patient sex and body habitus. Because of the relatively small number of patients in our study, we were not able to evaluate the influence of these factors.

In this study, we used 360° SPECT imaging. The issue of 360° versus 180° imaging remains a matter of debate, in particular with ^{201}Tl imaging. Although Tamaki et al. (*47*) demonstrated increased defect contrast with 180° ^{201}Tl imaging, Go et al. (*48*) reported a higher prevalence of false-positive ^{201}Tl defects and image distortions with 180° imaging compared with 360° imaging.

Study Limitations

Several limitations need to be addressed. First, the study population consisted of 24 patients with a mean left ventricular ejection fraction (LVEF) of 45%. However, myocardial viability is crucial in patients with severely depressed LV function, because these patients have an increased surgical risk (*49*) but favorable long-term survival after revascularization (*50,51*). It remains unclear whether similar results will be obtained in a study with patients with a more severely reduced LVEF. A larger study population with more severely depressed LV function needs to be studied with FDG SPECT. Moreover, in patients with preserved LV function, stress-induced ischemia may occur more frequently than hibernation. However, we were not able to distinguish between these two syndromes, because some form of stress testing (with stress-perfusion imaging) was not performed.

Second, improvement of regional myocardial function after revascularization was used as the gold standard of viable myocardium in this study. Although revascularization reports were reviewed, lack of adequate revascularization may have reduced diagnostic accuracy of both imaging techniques. Furthermore, graft or vessel patency was not evaluated by coronary angiography after the revascularization. In addition, functional recovery may not have been complete by the time of follow-up echocardiography. All these potential limitations, however, would affect both techniques equally.

Next, aside from nuclear imaging with either ^{201}Tl or FDG, dobutamine stress echocardiography is frequently used to assess myocardial viability (*34–38*). Unfortunately, we did not have the opportunity to perform dobutamine stress echocardiography.

Finally, improvement of LVEF, instead of regional LV function, may be more important in the clinical setting; however, LVEF was not measured after revascularization.

CONCLUSION

The results of this study indicate that FDG SPECT can predict improvement of regional function after revascularization. Moreover, the results are comparable with those obtained with ^{201}Tl rest-redistribution SPECT when redistribution was used as an indicator of viability. Finally, the results indicate that ^{201}Tl activity on the late image may be less accurate in predicting functional recovery after revascularization.

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Direct Evidence of Impaired Cardiac Sympathetic Innervation in Essential Hypertensive Patients with Left Ventricular Hypertrophy

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Increased sympathetic nervous activity has been proposed as one of the causes of left ventricular hypertrophy (LVH) associated with hypertension. However, the precise relationship is not fully understood. **Methods:** To elucidate the relationship between myocardial sympathetic nervous activity and LVH in patients with essential hypertension (EHT), we performed ^{123}I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy in 49 patients with EHT and 17 normotensive control subjects. Sympathetic innervation of the left ventricle was evaluated using SPECT, and the whole heart uptake of the tracer was quantitatively assessed as the heart-to-mediastinum uptake ratio on both the early (15-min) and delayed (5-hr) images. Myocardial washout rate (MWR) of the tracer from 15 min to 5 hr after the isotope administration was also calculated. The left ventricular mass index (LVMI) was determined echocardiographically. **Results:** In 49 hypertensive patients, there was a negative correlation between LVMI and heart-to-mediastinum uptake ratio on both the early and delayed images ($r = -0.55$, $p < 0.0001$; $r = -0.63$, $p < 0.0001$, respectively). In addition, there was a positive correlation between the LVMI and MWR of ^{123}I-MIBG in these hypertensive patients ($r = 0.59$, $p < 0.0001$). As for the regional uptake of the tracer, there was no significant difference between control subjects and hypertensive patients without cardiac hypertrophy, but a significant decrease of the uptake in the inferior and lateral regions was observed in hypertensive patients with cardiac hypertrophy. **Conclusion:** Patients with EHT had decreased accumulation and increased MWR of ^{123}I-MIBG in proportion to the degree of LVH. Hypertensive patients with cardiac hypertrophy had impaired sympathetic innervation in the inferior and lateral regions of the left ventricle.

Key Words: sympathetic nervous system; norepinephrine; left ventricular hypertrophy; iodine radioisotope; hypertension

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Essential hypertension (EHT) is a major risk factor for the progression of cardiovascular damage in such organs as the brain, heart and kidney. Left ventricular hypertrophy (LVH), one of the types of end-organ damage associated with hypertension, is recognized as an independent risk factor for cardiovascular events (*1*), including cardiac sudden death (*2*). It is recognized that not only mechanical factors, but also humoral factors, are related to LVH in hypertension. Increased sympathetic nervous activity has been proposed as one of the influential factors on LVH (*3–5*), based on the observations that catecholamine administration induces LVH (*3*) and that sympatholytic intervention diminishes myocardial hypertrophy (*4*). In addition, alpha-1 adrenergic agonists were found to be potent stimuli for the hypertrophy of fetal cardiac myocytes (*5*). However, some experimental studies reported that chemical or surgical sympathectomy failed to block the development of LVH induced by hypoxia or hypertension (*6,7*). Moreover, Cooper et al. (*8*) postulated that mechanical load itself, rather than catecholamines, was directly responsible for cardiac hypertrophy. Thus, the role of sympathetic nervous activity in the genesis of LVH, especially in humans, has not been fully elucidated.

Iodine-123-labeled metaiodobenzylguanidine (MIBG) is a norepinephrine analog that is taken up by sympathetic nerve

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