

Comparison of Rest Thallium-201 Imaging and Rest Technetium-99m Sestamibi Imaging for Assessment of Myocardial Viability in Patients With Coronary Artery Disease and Severe Left Ventricular Dysfunction

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Objectives. We prospectively compared myocardial uptake of thallium-201 (^{201}Tl) at rest with rest technetium-99m ($^{99\text{m}}\text{Tc}$) sestamibi uptake in the same patients, using quantitative single-photon emission computed tomography (SPECT).

Background. Because of only slightly delayed redistribution, $^{99\text{m}}\text{Tc}$ -sestamibi uptake at rest may be less than ^{201}Tl uptake, thereby underestimating the extent of viability.

Methods. Twenty patients (2.25 stenoses per patient) with a mean left ventricular ejection fraction of $33 \pm 2\%$ underwent early and 3-h delayed rest ^{201}Tl SPECT, rest $^{99\text{m}}\text{Tc}$ -sestamibi SPECT and two-dimensional echocardiography.

Results. The 280 scan segments were classified as either a normal, mild reduction in viability, defined as delayed ^{201}Tl uptake $\leq 75\%$ and $\geq 5\%$, or a severe reduction in viability, defined as delayed ^{201}Tl uptake $< 50\%$. Mild and severe defects were further classified as fixed or having rest ^{201}Tl redistribution. Comparisons by patients were made using repeated measures analysis of variance and Dunnett's multiple comparisons test to compare $^{99\text{m}}\text{Tc}$ -sestamibi with initial rest ^{201}Tl and delayed ^{201}Tl uptake. Twenty patients had at least one mild fixed defect (95 total segments). The average percent uptake in these defects for initial ^{201}Tl , delayed ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi was $62.5 \pm 2.7\%$, $63.1 \pm 7.1\%$ and $67.3 \pm 9.7\%$, respectively ($p = \text{NS}$). Twelve patients (27

segments) had mild redistribution defects on serial rest ^{201}Tl imaging. The average percent uptake was $61.6 \pm 5.2\%$ for initial ^{201}Tl , $67.0 \pm 9.1\%$ for delayed ^{201}Tl and $67.7 \pm 12.4\%$ for $^{99\text{m}}\text{Tc}$ -sestamibi defects. Technetium-99m sestamibi uptake was not significantly different than that for delayed ^{201}Tl but was significantly greater than initial ^{201}Tl uptake. Seventeen patients (52 segments) had severe fixed ^{201}Tl defects. The average percent uptake was $38.9 \pm 7.3\%$ for initial ^{201}Tl , $38.3 \pm 12.2\%$ for delayed ^{201}Tl and $42.7 \pm 14.2\%$ for $^{99\text{m}}\text{Tc}$ -sestamibi defects in these patients ($p = \text{NS}$). Ten patients (19 segments) had severe redistribution defects on rest ^{201}Tl imaging. The average percent uptake was $37.0 \pm 8.5\%$ for initial ^{201}Tl , $42.9 \pm 8.6\%$ for delayed ^{201}Tl and $44.5 \pm 11.3\%$ for $^{99\text{m}}\text{Tc}$ -sestamibi defects. As was seen for mild ^{201}Tl redistribution defects, $^{99\text{m}}\text{Tc}$ -sestamibi uptake was significantly higher than initial ^{201}Tl uptake, but not significantly different than delayed ^{201}Tl uptake in these severe defects.

Conclusions. Technetium-99m sestamibi uptake after injection at rest is comparable to ^{201}Tl uptake after injection at rest in patients with severe coronary artery disease and left ventricular dysfunction, suggesting comparable worth for viability assessment.

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Thallium-201 (^{201}Tl) imaging performed solely in the rest state has been proved clinically useful for predicting which asynergic myocardial segments will demonstrate improved regional systolic function after coronary revascularization in patients with severe coronary artery disease (1-4). It has been shown that the greater the extent of ^{201}Tl uptake on delayed rest images, the greater the extent of preserved myocardial viability (2).

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New technetium-99m ($^{99\text{m}}\text{Tc}$)-labeled myocardial perfusion agents have emerged as alternatives to ^{201}Tl for the assessment of regional myocardial blood flow and myocardial cellular viability (5-10). These technetium-labeled radionuclides, such as $^{99\text{m}}\text{Tc}$ -sestamibi, are superior to ^{201}Tl because they have better physical characteristics. The 140-keV photon energy peak of $^{99\text{m}}\text{Tc}$ is optimal for imaging with a camera and produces higher quality images than those produced by ^{201}Tl . The relatively short half-life of $^{99\text{m}}\text{Tc}$ allows one to administer doses 10 to 15 times larger than those for ^{201}Tl , permitting higher photon yield suitable for generation of gated tomographic perfusion images.

Despite its good results as a flow tracer for detecting stress-induced ischemia, $^{99\text{m}}\text{Tc}$ -sestamibi remains controversial insofar as its ability to detect myocardial viability (7). Although some recent experimental and clinical data have

indicated that ^{99m}Tc -sestamibi may be a valid imaging agent for detection of myocardial cellular viability (11-20), other reports suggest that ^{99m}Tc -sestamibi may underestimate the extent of viable myocardium (21-24), perhaps because of its negligible delayed redistribution over time (25,26). Accordingly, the purpose of the present study was to prospectively compare myocardial uptake of ^{201}Tl at rest with rest ^{99m}Tc -sestamibi uptake in the same myocardial scan segments, employing quantitative single-photon emission computed tomography (SPECT) in a group of patients with chronic coronary artery disease and regional left ventricular dysfunction.

Methods

Patient entry criteria. The study's entry criteria included patients with chronic stable coronary artery disease and at least one area of significant left ventricular asynergy. No patients with unstable angina or acute myocardial infarction within 8 weeks of enrollment were included. All patients had to have undergone previous cardiac catheterization. Each patient had to be able to undergo rest ^{201}Tl SPECT and rest ^{99m}Tc -sestamibi SPECT, as well as two-dimensional echocardiography, without a change in clinical status during the periods between tests. Echocardiograms were obtained on the same day that the ^{99m}Tc -sestamibi SPECT scans were acquired.

Radionuclide imaging protocols. Each patient was injected intravenously with 3.0 mCi of ^{201}Tl in the rest state. Ten minutes later, SPECT acquisition was performed on a Sopha DS-7 gamma camera (Sopha Medical), with 180° contoured acquisition centered on the heart, using 32 steps of 40 s each in a 25% window centered on the 80-keV x-ray peak of ^{201}Tl . Three hours after injection, a delayed ^{201}Tl SPECT acquisition was performed with the same parameters.

For the ^{99m}Tc -sestamibi imaging protocol, each patient was first injected with 25.0 mCi of ^{99m}Tc -sestamibi in the rest state. One hour later, a SPECT study was acquired employing 32 steps of 25 s each in a 20% window centered on the 140-keV gamma-ray peak of ^{99m}Tc -sestamibi. As undertaken for ^{201}Tl imaging, the ^{99m}Tc -sestamibi SPECT study was acquired over 180° using contouring centered on the heart. There was a mean of 3.4 days between ^{201}Tl and ^{99m}Tc -sestamibi SPECT studies.

SPECT reconstruction and quantitative analysis. Both ^{201}Tl and ^{99m}Tc SPECT studies were processed identically using the same filters. Studies were aligned with each other and the same reorientation was used. The quantitation uses a conventional bull's-eye map generated by searching along radii across the myocardium for the maximal pixel value as the radius crosses the myocardial wall. This method is not dependent on endocardial and epicardial edge detection. Search limits are set to confine the search to within the myocardium. The resulting bull's-eye maps are partitioned into segments, and the average of all values within a segment is used as the quantitative parameter. We used the average value of the segment rather than the nadir to reduce the Poisson noise. The bull's-eye maps were partitioned into 14 segments: 6 proximal short-axis, 6 distal short-axis and 2 apical segments identified



Figure 1. Distal and proximal short-axis and vertical long-axis tomograms are diagrammatically displayed with the location of the 14 scan segments analyzed shown.

on the vertical long-axis tomograms. The segment with the highest average maxima was set to 100%, and all other segments were normalized to that segment. The values for each segment represent the percent maximal uptake of the tracer.

Figure 1 depicts the distal short-axis, proximal short-axis and vertical long-axis tomograms with the location of the 14 scan segments analyzed shown. Each scan segment was scored, by two independent observers in blinded manner, from 0 to 4 based on the assessment of relative tracer activity: 0 = normal activity; 1 = slightly reduced activity; 2 = moderately reduced activity; 3 = severely reduced activity; 4 = absent activity. Then, each segment was classified as normal, a fixed defect, a partially reversible defect or a totally reversible defect. Indication of total redistribution was reflected by a change in score from 0 to 2 or from 1 to 2. Partial redistribution was designated when a score changed from 0 to 1. This classification was undertaken by comparison of the early and delayed rest ^{201}Tl images.

Echocardiographic analysis. Figure 2 depicts the comparable tomographic views acquired for scoring of echocardiographic segmental wall motion. Segments were scored by two observers by consensus as follows: 1 = normal function; 2 = mild hypokinesia; 3 = severe hypokinesia; 4 = akinesia; or 5 = dyskinesia.

Statistical analysis. Patients were used as the unit for statistical analysis because of the question of statistical independence of multiple samples. For this purpose, when there were multiple samples in a given category for a patient, the average value was computed and treated as a single measurement. The ^{99m}Tc -sestamibi, initial ^{201}Tl and delayed ^{201}Tl uptakes were then compared by patient using repeated measures analysis of variance. Dunnnett's multiple comparisons test

Figure 2. Tomographic views of scan segments analyzed for echocardiographic segmental wall motion on single-photon emission computed tomographic images.



Table 1. Clinical Characteristics of 20 Patients With Coronary Artery Disease

| | |
|---|-----------|
| Gender | |
| Male | 13 (65%) |
| Female | 7 (35%) |
| Age (yr) | 56 ± 2 |
| Cardiac history | |
| Prior myocardial infarction | 20 (100%) |
| Congestive heart failure | 16 (80%) |
| Angina pectoris | 13 (65%) |
| Prior coronary artery bypass surgery | 5 (25%) |
| Prior coronary angioplasty | 5 (25%) |
| Medications | |
| Angiotensin-converting enzyme inhibitors | 13 (65%) |
| Nitrates | 15 (75%) |
| Digoxin | 7 (35%) |
| Beta-blockers | 4 (20%) |
| Calcium channel blockers | 6 (30%) |
| Diuretic drugs | 13 (65%) |
| Electrocardiographic Q waves/patient | 3.4 ± 2 |
| Cardiac catheterization | |
| Left ventricular ejection fraction (%) | 33 ± 2 |
| No. stenotic vessels/patient | 2.3 ± 0.2 |

Data presented are mean value ± SD or number (%) of patients.

was used to compare ^{99m}Tc -sestamibi with initial rest ^{201}Tl and ^{99m}Tc -sestamibi with delayed ^{201}Tl uptake. Comparisons of viability classification were made using McNemar's test. The kappa statistic was used to test concordancy.

Results

Patients. Twenty patients with chronic coronary artery disease and left ventricular dysfunction comprised the study group. Table 1 summarizes the clinical characteristics of these 20 patients (13 [65%] men, mean age 56 ± 2 years). All 20 patients had a history of a myocardial infarction; 16 (80%) had symptomatic heart failure at the time of study entry. There were 3.4 Q waves on the 12-lead electrocardiogram per patient. On cardiac catheterization, the mean left ventricular ejection fraction was 33 ± 2%, and the group had 2.25 stenotic (≥50%) vessels per patient.

Imaging results. Figure 3 depicts the percent uptake of ^{201}Tl and ^{99m}Tc -sestamibi in regions classified as normal or mildly reduced viability by ^{201}Tl criteria. Normal viability was defined as >75% initial ^{201}Tl uptake, as determined by the quantitative analysis using the maxima or bull's-eye maps. Mildly reduced viability was defined as ≥50% but ≤75% of initial ^{201}Tl uptake. The vertical axis represents the percent uptake of each radionuclide normalized to the segment with maximal uptake, which is represented as 100% on this scale. Patients with abnormal segments were divided into those demonstrating redistribution on serial ^{201}Tl images and those showing no redistribution and identified as persistent ^{201}Tl defects on serial rest images. The corresponding rest ^{99m}Tc -sestamibi uptake is depicted in the bars set adjacent to the bars depicting the delayed ^{201}Tl uptake.

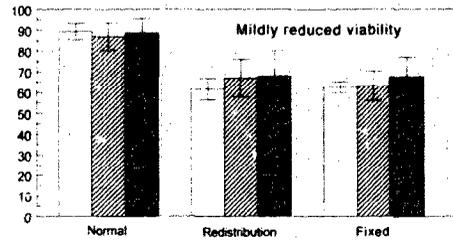


Figure 3. Percent uptake of thallium-201 (^{201}Tl) and technetium-99m (^{99m}Tc) sestamibi in patients with normal or mildly reduced viability by ^{201}Tl scintigraphic criteria. Normal viability was defined as >75% initial ^{201}Tl uptake. Mildly reduced viability was defined as ≥50% but ≤75% of initial ^{201}Tl uptake. Vertical axis represents the percent uptake of each radionuclide normalized to 100%. Note the comparable uptake of ^{201}Tl and ^{99m}Tc -sestamibi. Open bars = initial rest ^{201}Tl uptake; hatched bars = delayed rest ^{201}Tl uptake; solid bars = ^{99m}Tc -sestamibi uptake.

Figure 4 shows the same comparison for patients with segments classified as showing a severe reduction in viability. Table 2 summarizes the patient averages and standard deviations for all patients with segments in each classification. The bar graphs and table show close agreement between initial rest ^{201}Tl , delayed ^{201}Tl and ^{99m}Tc -sestamibi for normal segments and for fixed defects. In patients having segments showing rest ^{201}Tl redistribution, ^{99m}Tc -sestamibi uptake was closer to the delayed ^{201}Tl uptake. The amount of redistribution was small, as would be expected from rest injections in this group of patients.

Table 3 shows the results of statistical comparisons when patients were used as the unit of analysis. When multiple samples were obtained within a category for an individual patient, the average value was used. This was done to address the problem of statistical dependence of multiple samples from an individual. Repeated measures analysis of variance and Dunnett's multiple comparisons test were used to compare ^{99m}Tc -sestamibi with initial rest ^{201}Tl and delayed ^{201}Tl uptake. There were no significant differences when comparing

Figure 4. Rest thallium-201 (^{201}Tl) and technetium-99m (^{99m}Tc) sestamibi uptake values in patients with a severe reduction in viability (initial ^{201}Tl uptake <50% of peak). Note that percent uptake of ^{99m}Tc -sestamibi is comparable to the delayed ^{201}Tl uptake in patients showing rest ^{201}Tl redistribution and in patients with a persistent, severe reduction in ^{201}Tl activity. Symbols as in Figure 3.

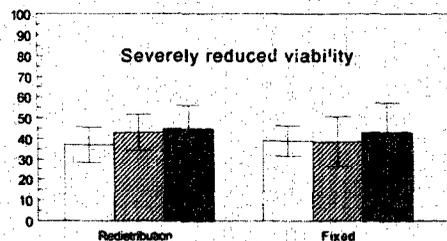


Table 2. Comparison of Thallium-201 and Technetium-99m Sestamibi Uptake by Analysis of Patients Who Underwent Both Imaging Procedures

| Group Definition | No. of Pts | Initial ²⁰¹ Tl (%) | Delayed ²⁰¹ Tl (%) | ^{99m} Tc-Sestamibi (%) |
|--|------------|-------------------------------|-------------------------------|---------------------------------|
| Normal (initial ²⁰¹ Tl >75%) | 20 | 89.6 ± 3.9 | 86.9 ± 6.6 | 88.5 ± 7.0 |
| Mild (initial ²⁰¹ Tl ≥50% and ≤75%) | | | | |
| With redistribution | 12 | 61.6 ± 5.2 | 66.9 ± 9.1 | 67.7 ± 12.4 |
| Fixed defects | 20 | 62.5 ± 2.7 | 63.1 ± 7.1 | 67.3 ± 9.7 |
| Severe (initial ²⁰¹ Tl <50%) | | | | |
| With redistribution | 10 | 37.0 ± 8.5 | 42.9 ± 8.6 | 44.5 ± 11.3 |
| Fixed defects | 17 | 38.9 ± 7.3 | 38.3 ± 12.2 | 42.7 ± 14.2 |

Data presented are mean value ± SD. Pts = patients; ^{99m}Tc = technetium-99m; ²⁰¹Tl = thallium-201.

^{99m}Tc-sestamibi with delayed ²⁰¹Tl uptake. Technetium-99m sestamibi uptake was significantly greater than initial rest ²⁰¹Tl uptake in both mild and severe groups with redistribution. There was a marginal difference (p = 0.051) when comparing ^{99m}Tc-sestamibi with initial rest ²⁰¹Tl for mild, fixed defects.

Concordance between ²⁰¹Tl and ^{99m}Tc-sestamibi uptake. Figure 5 demonstrates the concordance between ^{99m}Tc-sestamibi and delayed ²⁰¹Tl uptake based on ^{99m}Tc-sestamibi uptake criteria for viability. Less than 50% uptake compared with normal uptake of ^{99m}Tc-sestamibi was defined as a severe reduction in viability. Fifty percent or greater uptake in a segment was defined as demonstrating a mild reduction or normal viability. The concordance rate between ^{99m}Tc-sestamibi uptake and delayed ²⁰¹Tl uptake was 88% (kappa value 0.66). Note, no significant difference in the number of discordant segments for each group existed (p = 0.18).

Radionuclide uptake patterns in zones of severe myocardial asynergy. Figure 6 depicts initial ²⁰¹Tl uptake, delayed ²⁰¹Tl uptake and ^{99m}Tc-sestamibi uptake in myocardial segments classified as demonstrating severe hypokinesia or akinesia by two-dimensional echocardiographic analysis in all 20 patients. Note that in these 156 segments, some of which corresponded to scan segments showing reversible ²⁰¹Tl defects and some showing persistent defects, percent ^{99m}Tc-sestamibi uptake was comparable to percent delayed ²⁰¹Tl uptake (60 ± 22% vs. 59 ± 21%, p = 0.68).

Table 3. Comparison of Initial and Delayed Rest Thallium-201 and Technetium-99m Sestamibi Uptake Using Repeated Measures Analysis of Variance

| Group Definition | Initial ²⁰¹ Tl Uptake vs. ^{99m} Tc-Sestamibi (p value)* | Delayed ²⁰¹ Tl Uptake vs. ^{99m} Tc-Sestamibi (p value)* |
|--|---|---|
| Normal (initial ²⁰¹ Tl >75%) | NS | NS |
| Mild (initial ²⁰¹ Tl ≥50% and ≤75%) | | |
| With redistribution | < 0.05 | NS |
| Fixed defects | 0.05 | NS |
| Severe (initial ²⁰¹ Tl <50%) | | |
| With redistribution | < 0.05 | NS |
| Fixed defects | NS | NS |

*Dunnnett's multiple comparisons test. Abbreviations as in Table 2.

Discussion

The results of the present study indicate that rest ^{99m}Tc-sestamibi uptake is comparable to rest ²⁰¹Tl uptake in myocardial zones of asynergy, as identified by rest two-dimensional echocardiography. Defect magnitude, as quantitated on SPECT scans, was similar for ²⁰¹Tl and ^{99m}Tc-sestamibi in regions of both mild and severe reduction in tracer uptake, as defined using a 50% cutoff with respect to quantitative criteria.

Comparison of ²⁰¹Tl and ^{99m}Tc-sestamibi uptake. Our findings confirm those reported by Udelson et al. (11), who also compared rest redistribution ²⁰¹Tl imaging with rest ^{99m}Tc-sestamibi imaging using quantitative SPECT techniques. Their study also showed a high concordancy (87%) in defect severity between ^{99m}Tc-sestamibi activity and delayed ²⁰¹Tl activity. Udelson et al. (11) demonstrated that in segments determined to be normal or demonstrating mild, moderate or severe defects, ^{99m}Tc-sestamibi uptake was comparable to delayed ²⁰¹Tl uptake. No difference was found in that study between the two imaging agents for predicting enhanced regional systolic function after revascularization. Althoefer et al. (12) showed good concordance between myocardial uptake of ^{99m}Tc-sestamibi and ¹⁸F-fluorodeoxyglucose uptake, as assessed by positron emission tomography (PET) in 111 patients with coronary artery disease and rest wall motion abnormalities. Marzullo et al. (14) reported that the sensitivity and specificity of ^{99m}Tc-sestamibi imaging for prediction of post-revascularization recovery of function by echocardiography were 83% and 71%, respectively. In a subsequent study by Marzullo et al. (27), ^{99m}Tc-sestamibi activity and delayed ²⁰¹Tl activity (percent of peak) were found to be comparable (60%

Figure 5. Concordance between technetium-99m (^{99m}Tc) sestamibi and delayed thallium-201 (²⁰¹Tl) uptake based on ^{99m}Tc-sestamibi uptake criteria for viability. Concordance rate between ^{99m}Tc-sestamibi uptake and delayed ²⁰¹Tl uptake was 88% (kappa 0.66). *McNemar's paired test, p = 0.18.

| | | Sestamibi | |
|---------------------------|-------|-----------|-------|
| | | < 50% | ≥ 50% |
| Delayed ²⁰¹ Tl | < 50% | 48 | 22 |
| | ≥ 50% | 13 | 194 |

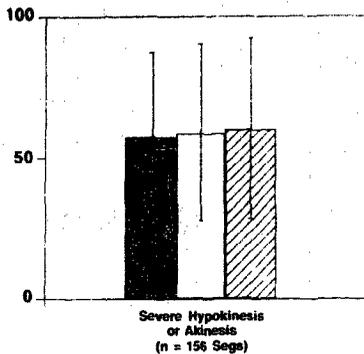


Figure 6. Initial thallium-201 (^{201}Tl) uptake (solid bars), delayed ^{201}Tl uptake (open bars) and technetium-99m ($^{99\text{m}}\text{Tc}$) sestamibi uptake (percent normal) (hatched bars) in segments (Segs) classified as demonstrating severe hypokinesia or akinesia by two dimensional echocardiographic analysis. Percent $^{99\text{m}}\text{Tc}$ -sestamibi uptake was comparable to percent delayed ^{201}Tl uptake in these asynergic segments. Results are mean value \pm SD.

vs. 59%) in asynergic myocardial regions supplied by severely stenotic coronary arteries (mean cross-sectional area of stenosis 93%).

Other investigators have evaluated $^{99\text{m}}\text{Tc}$ -sestamibi imaging for detection of myocardial viability in various patient populations. Cuocolo et al. (22), using exercise scintigraphy, reported that ^{201}Tl reinjection imaging was superior to rest and stress $^{99\text{m}}\text{Tc}$ -sestamibi imaging for detection of defect reversibility. Dilsizian et al. (21) also compared results of stress redistribution reinjection ^{201}Tl SPECT with $^{99\text{m}}\text{Tc}$ -sestamibi SPECT and found a 93% concordancy rate between ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi studies when using >50% uptake of $^{99\text{m}}\text{Tc}$ -sestamibi as the definition of viability, as undertaken in our study. However, more reversibility of defects was seen with ^{201}Tl reinjection. Maurea et al. (13) reported that rest ^{201}Tl uptake was higher than $^{99\text{m}}\text{Tc}$ -sestamibi uptake in myocardial segments supplied by a totally occluded artery; however, uptake of ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi was comparable in segments supplied by vessels with 50% to 99% stenosis. Sawada et al. (24) compared rest $^{99\text{m}}\text{Tc}$ -sestamibi SPECT results with positron emission tomography. Rest $^{99\text{m}}\text{Tc}$ -sestamibi imaging was undertaken with a dose of only 8 to 10 mCi. Viability by positron emission tomographic criteria was evident in 50% of segments demonstrating 40% or less uptake of $^{99\text{m}}\text{Tc}$ -sestamibi. Most of the segments in which viability was underestimated using $^{99\text{m}}\text{Tc}$ -sestamibi were confined to the inferior or posterior segments. This may be related to the known attenuation of $^{99\text{m}}\text{Tc}$ -labeled tracers in the posterior wall. Interestingly, this study also showed substantial $^{99\text{m}}\text{Tc}$ -sestamibi uptake in 37% of segments with severe reduction in ^{18}F -fluorodeoxyglucose uptake. Thus, discordance was seen in both directions. Thus, data from the clinical research studies cited above, as well as the results of the present study, suggest that $^{99\text{m}}\text{Tc}$ -sestamibi

imaging can provide information comparable, or nearly comparable, to information provided by ^{201}Tl scintigraphy.

Experimental validation. Experimental studies in animal models have shown that $^{99\text{m}}\text{Tc}$ -sestamibi may provide substantial information pertaining to myocardial viability (17-20). When sarcolemmal membrane or mitochondrial membrane potentials are depolarized as with severe ischemic injury, inhibition of uptake and failure of retention of $^{99\text{m}}\text{Tc}$ -sestamibi are demonstrated (15,16). Metabolic insults mimicking myocardial ischemia or hypoxia result in impaired $^{99\text{m}}\text{Tc}$ -sestamibi uptake that is independent of flow. Technetium-99m sestamibi uptake is preserved in stunned myocardium (17), as has been shown for ^{201}Tl (17,28), but uptake and retention are impaired in myocardium that has been irreversibly injured by prolonged occlusion and reperfusion (18). Technetium-99m sestamibi defect size correlates well with histologic infarct size in these animal models (19,20). Work from our laboratory by Sansoy et al. (26) showed only 5% lower $^{99\text{m}}\text{Tc}$ -sestamibi uptake compared with 2-h delayed ^{201}Tl uptake in an animal model of sustained low flow causing severe regional asynergy. However, ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi activities were comparable in dogs with a previous subendocardial infarction and persistently reduced perfusion distal to a severe coronary stenosis.

Technetium-99m sestamibi redistribution. Several experimental and clinical studies have shown some slight delayed $^{99\text{m}}\text{Tc}$ -sestamibi redistribution over 2 to 3 h after tracer injection in the rest state (21,25,26,29). In a canine model of sustained low flow, $^{99\text{m}}\text{Tc}$ -sestamibi defect magnitude improved from 49% to 52% of nonischemic uptake on images obtained serially over 2 h (26). Dilsizian et al. (21) detected some $^{99\text{m}}\text{Tc}$ -sestamibi redistribution in 22% of patients who underwent initial and 4-h rest $^{99\text{m}}\text{Tc}$ -sestamibi SPECT. In the present study, $^{99\text{m}}\text{Tc}$ -sestamibi images were acquired 1 h after tracer injection. This would have permitted at least some slight delayed redistribution, although perhaps not as much had we waited 3 to 4 h to acquire the $^{99\text{m}}\text{Tc}$ -sestamibi images. Despite absence of redistribution $^{99\text{m}}\text{Tc}$ -sestamibi images, uptake of the tracer was comparable to delayed ^{201}Tl uptake employing the protocol as described.

Study limitations. One limitation of the present study that deserves mention is that no reference standard for myocardial viability could be employed. Neither positron emission tomographic nor postrevascularization assessment of improved function was undertaken. The use of the 50% cutoff for severe versus mild to moderate reduction in viability has been validated previously (2). As seen in Figure 5, however, there were a substantial number of segments where there is discord relative to the 50% cutoff. This appears to be largely the result of measurement uncertainty in the amount of uptake in a single myocardial segment. We have no way of knowing the viability of a segment that has, for example, 51% ^{201}Tl uptake and 46% $^{99\text{m}}\text{Tc}$ -sestamibi uptake. With respect to the 50% cutoff, these are discordant. In fact, both values are within the range of 50% uptake and clinically would have to be considered as borderline in consideration of the sizable error in measuring a single segment in a single individual.

Clinical implications. The major clinical implication of this study is that ^{99m}Tc -sestamibi SPECT at rest can be successfully used for the determination of myocardial viability in patients with extensive coronary artery disease and left ventricular dysfunction indicative of hibernating myocardium. Technetium-99m-sestamibi imaging for viability assessment may have a greater advantage to ^{201}Tl in obese patients or in women, in whom breast attenuation artifacts may yield suboptimal ^{201}Tl images. One possible explanation for why ^{99m}Tc -sestamibi uptake in patient imaging protocols is comparable to ^{201}Tl uptake, despite a lack of substantial ^{99m}Tc -sestamibi redistribution, is the superior image quality with a ^{99m}Tc -labeled agent yielding less attenuation.

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