Reviews

Are Technetium-99m-Labeled Myocardial Perfusion Agents Adequate for Detection of Myocardial Viability?

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Summary: The noninvasive assessment of myocardial viability in patients with coronary artery disease and depressed left ventricular function has proven clinically useful for identifying those patients with ischemic cardiomyopathy who benefit most from coronary revascularization. Thallium-201 (^{201}Tl) imaging at rest has been the radionuclide imaging technique most often utilized for distinguishing viable myocardium from scar. However, new technetium-99m ($^{99\text{m}}\text{Tc}$) perfusion agents such as $^{99\text{m}}\text{Tc}$ -sestamibi and $^{99\text{m}}\text{Tc}$ -tetrofosmin have emerged as alternatives to ^{201}Tl for imaging of regional myocardial perfusion. Whether these new agents, which have better physical properties for imaging with a gamma camera than ^{201}Tl , are valid for use in assessing myocardial viability is still uncertain. Recent clinical studies have demonstrated that these agents, when imaged using quantitative SPECT, can identify patients with myocardial hibernation who exhibit improved regional systolic function following revascularization. Experimental laboratory studies have shown that the uptake of $^{99\text{m}}\text{Tc}$ -sestamibi and $^{99\text{m}}\text{Tc}$ -tetrofosmin in ischemic myocardium is only slightly lower than the uptake of ^{201}Tl . These $^{99\text{m}}\text{Tc}$ -labeled agents remain bound intracellularly in mitochondria of viable myocytes under conditions of myocardial stunning and short-term hibernation, producing severe myocardial asynergy. With respect to determination of viability, the inferior wall region is at times problematic since attenuation of $^{99\text{m}}\text{Tc}$ -sestamibi and $^{99\text{m}}\text{Tc}$ -tetrofosmin is greatest in this area. Demonstration of preserved systolic thickening on ECG-gated SPECT images is indicative of viability in the instance of decreased regional

$^{99\text{m}}\text{Tc}$ counts due to attenuation and not scar. Administration of nitrates prior to tracer injection improves the sensitivity for identifying viable myocardial segments using rest imaging with $^{99\text{m}}\text{Tc}$ -sestamibi or $^{99\text{m}}\text{Tc}$ -tetrofosmin.

Thus, it appears that the new $^{99\text{m}}\text{Tc}$ perfusion imaging agents can be successfully employed for the determination of myocardial viability in the setting of severe regional dysfunction and chronic coronary artery disease. The greater the myocardial uptake of these agents in the resting state, the greater the probability of improved systolic function after coronary revascularization.

Key words: technetium-99m-sestamibi ($^{99\text{m}}\text{Tc}$), $^{99\text{m}}\text{Tc}$ -tetrofosmin, thallium-201, radionuclide imaging, myocardial perfusion imaging, coronary artery disease, left ventricular dysfunction

Introduction

The topic of myocardial viability has been the subject of intense discussion in the fields of modern cardiology and nuclear medicine.^{1–11} Over the last decade, it has been realized that left ventricular (LV) dysfunction in coronary artery disease (CAD) is not always irreversible, and that a marked improvement in regional and global function can be observed after successful revascularization in some patients. Such patients with reversible LV dysfunction have either hibernating or stunned myocardium. The differentiation of such viable from nonviable myocardium is therefore highly relevant in patients who are being considered for revascularization. It is well known that the cardiac event rate with CAD with LV dysfunction and presence of viability detected by thallium-201 (^{201}Tl) and positron emission tomography (PET) in patients who are treated medically is higher than the event rate in patients with comparable viability who underwent revascularization.^{12, 13} Moreover, many patients who demonstrate viability associated with severe LV dysfunction may still be candidates for revascularization rather than for cardiac transplantation.

To date, several noninvasive approaches have been used to distinguish viable from nonviable myocardium. These include nuclear cardiology techniques [single-photon emission computed tomography (SPECT) and PET], dobutamine echocardiography, and recently magnetic resonance imaging (MRI).

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Received: October 21, 1997

Accepted: October 21, 1997

Nuclear cardiology techniques permit the detection of residual perfusion, cell membrane integrity, and metabolic activity in the myocardium. With dobutamine echocardiography, inotropic reserve in viable myocardium through catecholamine stimulation can be assessed. The standard of reference for detecting the presence of viable but ischemic myocardium in a dysfunctional myocardial region is enhanced myocardial function following revascularization or evidence of preserved glucose uptake by PET or SPECT.^{14, 15} Positron emission tomography is not readily available in most institutions, and postoperative assessment of viability is not helpful for the preoperative decision-making process. For clinical practice, therefore, SPECT has emerged as the most frequently used technique for viability assessment in patients with CAD and reduced LV function. For SPECT imaging, ²⁰¹Tl and technetium-99m (^{99m}Tc)-sestamibi are the most commonly used radiopharmaceuticals. Recently, other ^{99m}Tc-labeled myocardial perfusion agents such as ^{99m}Tc-tetrofosmin, ^{99m}Tc-teboroxime, ^{99m}Tc-furifosmin, and ^{99m}Tc-N-NOET have been introduced to the clinical practice or are under investigation.

The role of ²⁰¹Tl for viability assessment has been intensely studied, and it has gained wide acceptance as a suitable viability agent for use with SPECT or planar imaging.^{16–18} It has a positive value of 70–75% for predicting improvement in regional function after revascularization. Only approximately 20% of segments with < 50% ²⁰¹Tl uptake show improved function after bypass surgery or angioplasty. However, ²⁰¹Tl is far from being an ideal radionuclide imaging agent. Its low energy is suboptimal for gamma camera imaging because of scatter and attenuation problems. Moreover, its long half-life limits the injected dose, which may further reduce the image quality. Therefore, ^{99m}Tc-labeled myocardial perfusion agents are being used increasingly in nuclear cardiology practice. In addition to the better image quality of technetium-labeled agents, the high photon flux of technetium enables us to perform first-pass acquisition as well as gated studies, providing perfusion and functional data at the same time. On the other hand, from the viability point of view, the role of ^{99m}Tc-based myocardial perfusion agents is less defined, and the value of ^{99m}Tc-sestamibi remains controversial. More than ^{99m}Tc-sestamibi, ²⁰¹Tl “redistributes” over time in zones of low flow after a resting injection, resulting in greater uptake in zones of viable myocardium. Some published data indicate that ^{99m}Tc-labeled agents, particularly ^{99m}Tc-sestamibi, significantly underestimate the extent of hypoperfused myocardium, whereas other studies suggest that ^{99m}Tc-sestamibi has a worth comparable to ²⁰¹Tl for viability assessment.^{19–36}

In this review, we address the role of available and emerging ^{99m}Tc-labeled myocardial perfusion agents, particularly ^{99m}Tc-sestamibi, for viability assessment. For clarity of the subsequent review, it is useful to review certain definitions as well as the mechanism of ^{99m}Tc-sestamibi uptake.

Stunned and Hibernating Myocardium

Stunned myocardium is characterized by preserved flow and postischemic dysfunction. Ventricular dysfunction remains de-

pressed although successful reperfusion following a rather short period of severe ischemia has occurred (perfusion-function mismatch). Myocardial dysfunction is usually reversible but may persist several days following reperfusion.^{37, 38}

Hibernating myocardium is characterized by chronic ventricular dysfunction in chronically hypoperfused myocardial areas. Acute hibernation may also occur. Myocardial dysfunction is reversible following restoration of flow (matched perfusion-function reduction).^{39, 40}

Technetium-99m-sestamibi is a synthetic lipophilic cationic myocardial perfusion agent. It has a first-pass myocardial extraction of 65%.⁴¹ Unlike the transport of ²⁰¹Tl, which requires predominantly the Na⁺, K⁺-ATPase active transport system, ^{99m}Tc-sestamibi passively distributes across sarcolemmal and mitochondrial membranes and retains chiefly in mitochondria.⁴² Once ^{99m}Tc-sestamibi binds to mitochondria, it remains relatively fixed and shows negligible redistribution over time.⁴³ A negative mitochondrial charge gradient, which can be maintained only by the persistence of viability, is essential for its accumulation and retention in the myocyte.^{28, 43} Severe metabolic impairment decreases its cellular concentration in cultured myocytes.⁴⁴ An increase in cytosolic calcium ion concentration results in a reduction of its retention, as it occurs after irreversible ischemic injury to the myocardium.

Clinical studies clearly show that ^{99m}Tc-sestamibi and ²⁰¹Tl have similar accuracy for CAD detection when employed with exercise stress.^{45–47} Since the distribution of ^{99m}Tc-sestamibi after injection at rest is proportional to resting blood flow in low-flow regions, the resting uptake of ^{99m}Tc-sestamibi in such areas will be diminished, thereby underestimating the extent of viability. Lack of significant redistribution of ^{99m}Tc-sestamibi over time could result in overestimation of scar, which further potentially limits its value for viability assessment. In such low-flow regions, ²⁰¹Tl is thought to be the most suitable viability agent because of its greater redistribution after a single intravenous injection.

Technetium-99m-Sestamibi and Viability Assessment in Myocardial Stunning

Several experimental^{25, 29} and clinical studies^{30, 33, 48} have been undertaken to evaluate the value of ^{99m}Tc-sestamibi for assessing the risk area during coronary occlusion and the magnitude of salvaged and viable myocardium after reperfusion. It is expected that, in the setting of stunned myocardium, ^{99m}Tc-sestamibi would function well as a viability marker, since flow is restored and the mitochondrial and sarcolemmal processes necessary for viability and for ^{99m}Tc-sestamibi uptake are intact.

In open-chested dogs, Verani *et al.*²⁵ demonstrated that with ^{99m}Tc-sestamibi injection before and after coronary reperfusion, the area of ischemic risk and the amount of myocardium that have been salvaged by reflow could be estimated. Similarly, in a canine myocardial infarction model, Beller *et al.*²⁹ reported that ^{99m}Tc-sestamibi uptake and retention were not

solely dependent on regional blood flow but also on myocardial cell viability. It was also shown that if ^{99m}Tc -sestamibi was administered early after reperfusion and imaging was performed soon afterward, the degree of salvage could be significantly overestimated and infarct size could be underestimated because ^{99m}Tc -sestamibi uptake may be more related to hyperemic flow than to cellular retention.²⁹

Clinical studies are in good agreement with the observations in the experimental laboratory. Gibbons *et al.*³⁰ reported that ^{99m}Tc -sestamibi allows for the quantification of the amount of hypoperfused myocardium at risk in acute myocardial infarction (MI), and the defect size on ^{99m}Tc -sestamibi images taken 6 to 14 days after MI correlated well with the late resting LV ejection fraction. Leavitt *et al.*³³ reported an interesting case in which stunned myocardium was successfully identified by ^{99m}Tc -sestamibi uptake 12 h after thrombolytic therapy in an akinetic region detected on contrast ventriculography. After coronary artery bypass graft (CABG) surgery, follow-up ^{99m}Tc -sestamibi scintigraphy showed normal perfusion and radionuclide ventriculography demonstrated normal LV function, demonstrating that ^{99m}Tc -sestamibi after myocardial reperfusion could detect stunned myocardium and thereby facilitate the decision-making process.

Thus, both experimental and clinical studies have shown the validity of ^{99m}Tc -sestamibi as a viability marker when administered at an appropriate time during the course of evolving ischemic injury in the setting of stunned myocardium.

Technetium-99m-Sestamibi and Viability Assessment in Chronic Coronary Artery Disease

The issue of whether ^{99m}Tc -sestamibi imaging at rest can be accurately employed for assessment of viability in patients with CAD and severe LV dysfunction is not yet entirely resolved. The uptake of ^{99m}Tc -sestamibi at rest after an intravenous injection might be expected to demonstrate a perfusion defect consequent to the low-flow state that does not reflect the amount of viable but underperfused myocardium. Several studies^{19–21, 23, 49} have reported that ^{99m}Tc -sestamibi underestimates myocardial viability in chronic CAD. Using planar scintigraphy in 20 patients with CAD and LV dysfunction, Cuocolo *et al.*¹⁹ compared the results of ^{201}Tl rest/reinjection with those of ^{99m}Tc -sestamibi and concluded that ^{99m}Tc -sestamibi was primarily a perfusion agent and not a viability agent. They did not use quantitative methods to assess ^{99m}Tc -sestamibi uptake; a visual five-point grading system was used instead. Moreover, ^{99m}Tc -sestamibi uptake was compared with that of ^{201}Tl rest/reinjection, and did not correlate directly with the recovery of contractile function. Maurea *et al.*²⁰ reported a case of chronic CAD in which the preoperative ^{201}Tl reinjection study correctly identified the presence of viable myocardium in regions where ^{99m}Tc -sestamibi images showed irreversible perfusion defects; thus, ^{201}Tl but not ^{99m}Tc -sestamibi accurately predicted functional recovery after revascularization. No quantitation for ^{99m}Tc -sestamibi uptake was done and planar scintigraphy was per-

formed for imaging. Maublant *et al.*³¹ reported SPECT ^{99m}Tc -sestamibi results in 25 patients with LV dysfunction and postrevascularization recovery and concluded that as long as some residual ^{99m}Tc -sestamibi uptake was present, viable myocardium was also present. A visual analysis was used for scoring ^{99m}Tc -sestamibi uptake, and the sensitivity and specificity of ^{99m}Tc -sestamibi for viability assessment were 83 and 79%, respectively.

Quantitation of Technetium-99m-Sestamibi Uptake

Previous studies with ^{201}Tl showed that myocardial viability may be related not only to defect reversibility from stress to rest but also to the amount of ^{201}Tl uptake quantitated at redistribution or after reinjection.^{17, 50} Similarly, several studies using quantitation of ^{99m}Tc -sestamibi uptake at rest were performed for viability determination with variable results. Some reports indicate the inability to define a threshold for ^{99m}Tc -sestamibi uptake which could reliably distinguish viable from nonviable myocardium.^{21, 22} In a limited number of patients ($n = 14$), Marzullo *et al.*²¹ compared ^{99m}Tc -sestamibi uptake on planar images with postrevascularization functional recovery and reported that even with quantitative techniques, ^{99m}Tc -sestamibi provided limited information on viability. Technetium-99m-sestamibi sensitivity and specificity in the detection of postvascularization recovery of function were 83 and 71%, respectively. Sawada *et al.*²² compared the results of ^{99m}Tc -sestamibi SPECT with those of PET. It was shown that ^{99m}Tc -sestamibi defects, either moderate (50–59% of peak activity) or severe (<50% of peak activity), frequently had evidence of viability by PET. Moreover, no significant difference was found in mean ^{99m}Tc -sestamibi activity in viable and nonviable myocardium segments. Althoefer *et al.*²⁴ demonstrated that in 80% of severe (<30%), 48% of moderate (31–50%), and 31% of mild (>50%) peak activity, defects shown by ^{99m}Tc -sestamibi were nonviable on the basis of PET.

On the other hand, there are some reports indicating the usefulness of quantitative ^{99m}Tc -sestamibi imaging for viability assessment.^{23, 34, 35, 51} Dilsizian *et al.*²³ reported that ^{99m}Tc -sestamibi significantly underestimated viability on the basis of ^{201}Tl and PET, but the identification of viable myocardium could be greatly enhanced with ^{99m}Tc -sestamibi when the severity of decrease in ^{99m}Tc -sestamibi uptake within irreversible defects was considered, or when an additional redistribution image was acquired 4 h after the rest injection. With an additional redistribution image, the concordance between ^{201}Tl and ^{99m}Tc -sestamibi studies was increased from 70 to 82%. When <50% of normal activity was considered as the evidence for nonviability, then the overall concordance between ^{201}Tl and ^{99m}Tc -sestamibi uptake increased to 93%. Udelson *et al.*³² compared the regional activities of ^{201}Tl and ^{99m}Tc -sestamibi for predicting functional recovery after resting injection in 31 patients. They indicated that regional activities of both agents as assessed by quantitative analysis were similar in reversibly dysfunctional myocardium ($72 \pm 11\%$ vs. $75 \pm 9\%$ of peak activity for ^{201}Tl and ^{99m}Tc -sestamibi, respectively) and both agents comparably predicted postopera-

FIG. 1 Comparison of ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi uptake in patients with normal or mildly reduced viability by ^{201}Tl scintigraphic criteria. Open bars indicate initial rest ^{201}Tl uptake; hatched bars, delayed rest ^{201}Tl uptake; solid bars, $^{99\text{m}}\text{Tc}$ -sestamibi uptake. Reprinted from Ref. No. 35 with permission.

FIG. 2 Comparison of ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi uptake in patients with a severe reduction in viability by ^{201}Tl scintigraphic criteria. Open bars indicate initial rest ^{201}Tl uptake; hatched bars, delayed rest ^{201}Tl uptake; solid bars, $^{99\text{m}}\text{Tc}$ -sestamibi uptake. Reprinted from Ref. No. 35 with permission.

tive functional recovery. If 60% of peak activity was considered as a threshold cutoff point, the positive and negative predictive values for functional recovery after revascularization were 80 and 96%, respectively, for $^{99\text{m}}\text{Tc}$ -sestamibi and 75 and 92%, respectively, for ^{201}Tl . Overextraction of $^{99\text{m}}\text{Tc}$ -sestamibi at low flow rates, redistribution of $^{99\text{m}}\text{Tc}$ -sestamibi (although slight) over time, and better imaging resolution of $^{99\text{m}}\text{Tc}$ -sestamibi related to the superior physical characteristics of $^{99\text{m}}\text{Tc}$ over ^{201}Tl were all proposed as explanations for the comparability of $^{99\text{m}}\text{Tc}$ -sestamibi with ^{201}Tl .

Kauffman *et al.*³⁵ confirmed the findings of Udelson *et al.*³² Using quantitative SPECT in 25 patients with LV dysfunction, rest-delayed ^{201}Tl uptake and rest $^{99\text{m}}\text{Tc}$ -sestamibi uptake were compared. Myocardial segments were classified as either normal, a mild reduction in viability (defined as delayed ^{201}Tl uptake <75% and >50%), or a severe reduction in viability (defined as delayed ^{201}Tl uptake <50%). Mild and se-

vere defects were further classified as fixed or having rest ^{201}Tl redistribution. As shown in Figures 1 and 2, uptake of ^{201}Tl and $^{99\text{m}}\text{Tc}$ -sestamibi were comparable in segments with both mildly and severely reduced viability. Sciagra *et al.*⁵¹ reported similar results indicating the importance of quantitation for viability assessment. They studied 44 patients and pointed out the possibility to identify a cutoff point that differentiates hibernating from fibrotic myocardium. A significant difference was found in percent severity between the defects in territories with postvascularization functional recovery and those in territories with unchanged dysfunction. In a more recent study using quantitative SPECT, Maes *et al.*³⁴ reported that $^{99\text{m}}\text{Tc}$ -sestamibi reflects not only flow but also myocardial viability. A significant inverse linear relationship was found between $^{99\text{m}}\text{Tc}$ -sestamibi uptake and the amount of fibrotic tissue from myocardial biopsy specimens obtained at the time of surgery (Fig. 3). Moreover, significantly higher $^{99\text{m}}\text{Tc}$ -sestamibi values were found in patients with improved ejection fraction at 3 months following revascularization compared with those who did not improve ($76 \pm 13\%$ vs. $53 \pm 22\%$) (Fig. 4). When using postrevascularization recovery as the standard of reference for

FIG. 3 Percent fibrosis detected by biopsy specimens versus $^{99\text{m}}\text{Tc}$ -sestamibi uptake (A) and versus relative myocardial blood flow detected by PET (B). Note the significant inverse linear relationship between $^{99\text{m}}\text{Tc}$ -sestamibi uptake and presence of fibrosis. Reprinted from Ref. No. 34 with permission.

FIG. 4 Technetium- $^{99\text{m}}$ -sestamibi uptake values in patients showing improvement of regional ejection fraction after revascularization and in those without improvement. Reprinted from Ref. No. 34 with permission.

viability, an optimal threshold of 50% for ^{99m}Tc -sestamibi was identified, with positive and negative predictive values of 82 and 78%, respectively.

In an interesting study of 37 patients who underwent revascularization, Soufer *et al.*⁴⁹ specifically addressed the regional distribution of ^{99m}Tc -sestamibi/PET discordance and found that discordant ^{99m}Tc -sestamibi nonviable segments were predominantly in the inferior wall. It was thought that attenuation artifacts were less likely to explain all of the discordance detected in the inferior wall, since all of the defects were severe (<50% of maximal counts) and attenuation artifacts usually cause mild-to-moderate nonreversible ^{99m}Tc -sestamibi defects. On the other hand, since PET images are attenuation-corrected, it would have been worthwhile to compare attenuation-corrected SPECT images with PET images. The same group also reported that ^{99m}Tc -sestamibi images overestimated apical segment viability as assessed by PET.

Late Technetium-99m-Sestamibi Acquisition

Experimental studies showed that there is some delayed ^{99m}Tc -sestamibi redistribution,^{36, 52, 53} and that finding was confirmed by clinical studies.^{23, 54} Sansoy *et al.*³⁶ performed serial imaging at 5 min and 2 h after ^{99m}Tc -sestamibi administration in dogs with chronic reduction in flow, and a small but significant amount of ^{99m}Tc -sestamibi redistribution was detected by in vivo quantitative planar imaging. Clinically, Dilsizian *et al.*²³ detected ^{99m}Tc -sestamibi redistribution in 22% of their patients who underwent initial and 4-h resting ^{99m}Tc -sestamibi SPECT. On the other hand, there are some reports indicating no change in defect size and thus no evidence of redistribution between images taken at 1 h and 4 h after ^{99m}Tc -sestamibi injection.⁵⁵

Assessment of Left Ventricular Function with Technetium-99m-Sestamibi

Due to the high count density of technetium, ^{99m}Tc -sestamibi imaging permits a functional evaluation of the left ventricle by first-pass radionuclide ventriculography⁵⁶ or gated acquisition of the SPECT perfusion images.^{57–61} With a single radiopharmaceutical injection, evaluation of both function and perfusion of myocardium can be accomplished. Functional data obtained from gated ^{99m}Tc -sestamibi images can significantly enhance the ability of ^{99m}Tc -sestamibi to assess myocardial viability consistent with the concept that preserved function (wall motion and thickening) is equivalent to myocardial viability. Recent data show that quantification of systolic LV function can be derived from gated ^{201}Tl perfusion images that appear to provide information as reliable as does ^{99m}Tc -sestamibi-gated SPECT.⁶²

Other Interventions

To enhance the ability of ^{99m}Tc -sestamibi as a viability marker, some modifications or interventions during ^{99m}Tc -sestamibi injection have been introduced, such as prolonged

^{99m}Tc -sestamibi infusion⁶³ or nitrate administration during ^{99m}Tc -sestamibi injection.^{51, 64, 65} Bisi *et al.*⁶⁵ reported that nitrate administration before ^{99m}Tc -sestamibi injection induced a significant decrease in the extent of global defect size only in patients who showed postrevascularization recovery, and that the nitrate-induced changes in the extent of the defect correlated well with postrevascularization changes in ejection fraction. Sciagra *et al.*⁵¹ indicated that nitrate infusion, in combination with analysis of defect severity, clearly improved the value of ^{99m}Tc -sestamibi for the recognition of hibernating myocardium and postrevascularization recovery.

Thus, although theoretically and by interpretation of animal experimental studies ^{99m}Tc -sestamibi underestimates myocardial viability in hibernating myocardium, recent clinical studies using certain "enhancement approaches" such as quantitative analysis of tracer uptake, acquisition of delayed redistribution ^{99m}Tc -sestamibi images, and nitrate administration, have yielded information of value comparable to that of ^{201}Tl for assessment of myocardial viability.

The Role of Other Technetium-99m-Labeled Myocardial Perfusion Agents for Viability Assessment

Technetium-99m-tetrofosmin has sensitivity and specificity similar to those of ^{201}Tl for detection of CAD^{66–68} and chemical characteristics similar to those of ^{99m}Tc -sestamibi. It is easily prepared at room temperature, leading to faster preparation than ^{99m}Tc -sestamibi, which is an important consideration in acute patients. Since, like ^{99m}Tc -sestamibi, it shows little redistribution over time, it was suggested that it may have limitations for viability assessment.⁶⁹ In a low-flow model with profound dysfunction, ^{99m}Tc -tetrofosmin uptake was reported to be quantitatively comparable with initial ^{201}Tl uptake, but it was significantly less than 2-h ^{201}Tl uptake. On the other hand, substantial ^{99m}Tc -tetrofosmin uptake (>50%) reflective of viability was observed in the dysfunctional areas perfused by the stenotic artery.⁷⁰ Recently, Galassi *et al.*⁷¹ reported that the concordance between ^{201}Tl and ^{99m}Tc -tetrofosmin for the assessment of viability (>50% of normal uptake) in patients with LV dysfunction was 91%.

Technetium-99m-teboroxime is a perfusion agent that is chemically different from ^{99m}Tc -sestamibi and is rarely employed in the clinical setting. It has high early myocardial extraction, rapid blood clearance, and rapid myocardial washout. It has been suggested that the differential washout of ^{99m}Tc -teboroxime (more rapid washout from normal area than from ischemic zone) may be helpful in viability detection.^{72–76} Nevertheless, this agent is most suitable for assessment of myocardial flow with dipyridamole or adenosine stress. Technetium-99m-furifosmin and ^{99m}Tc -N-NOET are new agents, and no data on their ability to assess myocardial viability in the clinical setting are available.^{77, 78}

Recently, new high-energy collimators and SPECT gamma cameras with an ability of imaging 511 keV photon of ^{18}F -fluorodeoxyglucose (FDG) have been introduced into clinical practice. It seems quite useful in routine clinical practice to

combine perfusion imaging with ^{99m}Tc -labeled myocardial agents, with metabolic information using FDG SPECT.⁷⁹

Conclusions

Several conclusions can be drawn: First, in the setting of stunned myocardium, ^{99m}Tc -sestamibi functions as a reliable marker for viability assessment; second, in the setting of hibernating myocardium, ^{99m}Tc -sestamibi may underestimate viability when PET and postrevascularization functional recovery are used as standards of reference. There are several limitations to the studies, concluding that ^{99m}Tc -sestamibi was a poor marker for viability assessment in hibernation. These include the fact that (1) the number of patients studied was generally small; (2) planar scintigraphy was used instead of SPECT; (3) quantitation of ^{99m}Tc -sestamibi uptake was seldom used and, instead, visual interpretation was employed; (4) in some studies, the reference standard for myocardial viability assessment, such as postrevascularization functional improvement or PET, was lacking; and (5) no late images of ^{99m}Tc -sestamibi in which some redistribution could have been detected were acquired.

Approaches to maximize the ability of ^{99m}Tc -sestamibi to detect viable myocardium are as follows: (1) quantitation of ^{99m}Tc -sestamibi uptake in the defect regions; (2) administration of nitrate before ^{99m}Tc -sestamibi injection; (3) electrocardiographic gating for determination of residual myocardial thickening; (4) acquisition of additional "redistribution" ^{99m}Tc -sestamibi images after the initial rest image; and (5) correction of ^{99m}Tc -sestamibi images for attenuation to get more accurate measurement of regional activity.

Finally, a major reason to consider ^{99m}Tc -sestamibi over ^{201}Tl for viability determination is its advantage of having technetium as the radiolabel. Based on the better image quality, ^{99m}Tc -sestamibi counts will be more efficient than ^{201}Tl counts among the relatively thinned, poorly contractile hibernating segments. This is particularly true in obese and female patients. Further data derived from a larger number of patients are required for definite determination of whether ^{99m}Tc -sestamibi can, indeed, provide information comparable to ^{201}Tl for distinguishing viable from nonviable myocardium. Similarly, more studies must be performed to determine the worth of some of the new ^{99m}Tc -labeled myocardial imaging agents for viability assessment.

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