

Improved Detection of Viable Myocardium with Thallium-201 Reinjection in Chronic Coronary Artery Disease: Comparison with Technetium-99m-MIBI Imaging

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Exercise-redistribution ^{201}Tl with reinjection at rest and exercise-rest $^{99\text{m}}\text{Tc}$ -methoxy isobutyl isonitrile (MIBI) cardiac imaging was performed in a patient with multivessel chronic coronary artery disease (CAD) and evaluated before and after coronary revascularization. Thallium reinjection showed reversible defects of the inferior and septal walls and irreversible defect of the infero-apical region. Technetium-99m-MIBI scintigraphy demonstrated irreversible defects of the inferior, septal and infero-apical regions. After coronary artery bypass grafts, both thallium reinjection and $^{99\text{m}}\text{Tc}$ -MIBI images showed only irreversible defects of the infero-apical region. Functional recovery of the inferior and septal walls was observed on two-dimensional echocardiography. Thallium reinjection identifies severely ischemic but viable myocardium more accurately than $^{99\text{m}}\text{Tc}$ -MIBI in chronic CAD. Thallium myocardial imaging with reinjection at rest is recommended for evaluating patients with chronic ischemic left ventricular dysfunction to determine if these patients are candidates for revascularization procedures.

Key Words: chronic coronary artery disease; thallium-201; technetium-99m-MIBI

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Exercise-redistribution ^{201}Tl myocardial scintigraphy with reinjection at rest has been shown to accurately differentiate irreversibly fibrotic myocardium from severely hypoperfused but still viable tissue in patients with coronary artery disease (CAD) (1-4). Technetium-99m-methoxy isobutyl isonitrile (MIBI) and thallium imaging have shown excellent agreement in the detection of CAD (5), but the precise role of $^{99\text{m}}\text{Tc}$ -MIBI in the evaluation of myocardial viability in patients with chronic ischemic LV dysfunction is still under investigation (6-10). Previous studies suggested that exercise-redistribution thallium scintigraphy with reinjection at rest provides superior informa-

tion regarding viable myocardium to those offered by exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI cardiac imaging (11,12). The improved detection of viable myocardium with thallium reinjection compared to $^{99\text{m}}\text{Tc}$ -MIBI in a patient with chronic CAD evaluated before and after coronary revascularization is reported.

CASE PRESENTATION

A 54-yr-old man with CAD was initially evaluated in our department in July 1990. The patient had a clinical history of previous myocardial infarction (May 1988) of the postero-inferior wall of the left ventricle and was treated with nitrates, calcium channel blocking agents and platelet aggregation inhibitors. On admission, the patient was asymptomatic, and physical examination revealed a resting heart rate of 79 bpm and blood pressure of 115/80. Baseline ECG showed regular sinus rhythm; Q-waves with associated ST-segment and T-wave abnormalities were present in leads D2, D3 and aVF. Bicycle ECG stress test demonstrated ST-segment depression (>2 mm) in leads V4 and V5, without angina or other symptoms. Echocardiography revealed resting left ventricular ejection fraction (LVEF) of 40%. Analysis of regional LV function on echocardiographic images demonstrated septal, inferior and infero-apical akinesia. Coronary angiography showed three-vessel CAD with a 90% stenosis of the left anterior descending artery and a 75% stenosis of the right coronary vessel and of the obtuse marginal branch of the circumflex coronary artery. On the basis of clinical history and cardiac work-up, the diagnosis of ischemic chronic LV dysfunction was made. Therefore, radionuclide imaging studies were performed to assess myocardial perfusion and viability in order to determine the need for coronary revascularization procedures. Antianginal therapy was withdrawn 3 days before imaging.

Exercise-redistribution ^{201}Tl scintigraphy with reinjection at rest was performed as previously described (11). Five days later, exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI imaging was also performed using a two-day protocol as previously described (11). Hemodynamic parameters recorded under control conditions and during the two exercise tests did not show significant differences.

Thallium and $^{99\text{m}}\text{Tc}$ -MIBI imaging results are illustrated in Figure 1. Each view was normalized to its own maximum. The exercise-redistribution thallium study showed irreversible perfusion defects of the inferior and infero-apical regions and of the distal segment of the interventricular septum. Thallium reinjection

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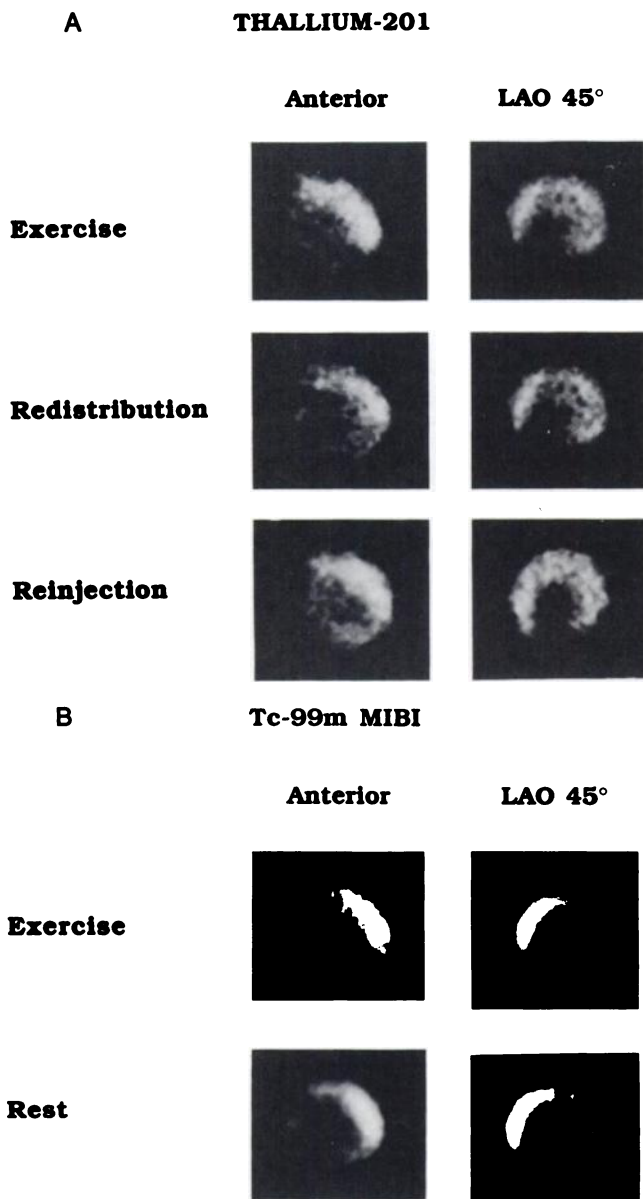


FIGURE 1. (A) Preoperative exercise-redistribution ^{201}Tl cardiac imaging with reinjection at rest. Exercise and redistribution anterior views demonstrate an irreversible perfusion defect involving the inferior region. Thallium reinjection shows enhanced tracer uptake in the inferior region. Exercise and redistribution left anterior oblique (LAO) 45° views demonstrate irreversible perfusion defects involving the infero-apical region and the distal segment of the interventricular septum. Thallium reinjection shows enhanced tracer uptake in the distal segment of the interventricular septum and no significant change in tracer uptake in the infero-apical region. (B) Preoperative exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI cardiac imaging. Exercise and rest anterior views demonstrate an irreversible perfusion defect involving the inferior region. Exercise and rest left anterior oblique (LAO) 45° views demonstrate an irreversible perfusion defect involving the infero-apical region and a moderate irreversible perfusion defect in the distal segment of the interventricular septum.

at rest demonstrated enhanced tracer uptake in the inferior and septal walls. The defect located in the infero-apical region showed no significant change in thallium uptake after reinjection. Exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI scintigraphy showed severe irreversible de-

fects of the inferior and infero-apical myocardial regions. A moderate irreversible defect was also present in the distal segment of the interventricular septum.

On the basis of thallium reinjection results, the presence of severely ischemic but still viable myocardium in the inferior wall and in the distal segment of the interventricular septum was detected. Therefore, the patient was a potential candidate for coronary revascularization. On October 1990, coronary artery bypass graft (CABG) was undertaken, with grafts placed from the aorta to the left anterior descending artery and to the right coronary vessel. The postoperative course was unremarkable.

One year later (November 1991), the patient was re-admitted to our department for postsurgical evaluation. The patient was on treatment with platelet aggregation inhibitors only. Postoperative echocardiography showed an LVEF of 55%. Analysis of regional LV function demonstrated improved wall motion at rest of the septal and inferior wall compared to the preoperative study. Postoperative ^{201}Tl and $^{99\text{m}}\text{Tc}$ -MIBI imaging studies were also performed following the same acquisition and processing protocols used for the preoperative evaluation.

Postoperative thallium and $^{99\text{m}}\text{Tc}$ -MIBI imaging results are illustrated in Figure 2. Exercise-redistribution thallium imaging with reinjection at rest showed an irreversible defect of the infero-apical region. Exercise thallium uptake in the inferior wall and in the distal segment of the interventricular septum was normal. Exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI images showed an irreversible defect of the infero-apical myocardial region. Exercise $^{99\text{m}}\text{Tc}$ -MIBI uptake in the inferior wall and in the distal segment of the interventricular septum was normal. The patient was then discharged from our department and his clinical follow-up was unremarkable.

DISCUSSION

The case illustrated here is a clear starting point for discussing the controversies regarding the comparison between thallium and $^{99\text{m}}\text{Tc}$ -MIBI imaging for identifying viable myocardium in patients with chronic ischemic LV dysfunction (13). In the pre-CABG evaluation of this patient, inferior, apical and septal akinesia were detected on the echocardiography study, and LVEF at rest was 40%. Both standard exercise-redistribution thallium and exercise-rest $^{99\text{m}}\text{Tc}$ -MIBI imaging showed irreversible defects of the inferior and infero-apical myocardial walls and of the distal segment of the interventricular septum, suggesting the presence of necrotic myocardium. However, thallium reinjection at rest showed enhanced tracer uptake in the inferior wall and in the septum, suggesting the presence of severely ischemic but still viable myocardium in these regions and therefore the possibility of obtaining functional recovery of these myocardial segments after revascularization. Conversely, reinjection images showed no change in thallium uptake in the infero-apical region, suggesting the presence of irreversibly scarred tissue in this area.

Preoperative thallium reinjection findings were confirmed by functional evaluation after CABG. Postoperative echocardiography showed improvement of global and regional LV function, with an ejection fraction of 55% and improved wall motion of the inferior and septal regions. Furthermore, inferior and septal myocardial segments had

normal uptake on both postoperative exercise thallium and ^{99m}Tc -MIBI images, while the infero-apical region still showed an irreversible defect. Therefore, the preoperative thallium study with reinjection at rest correctly identified the presence of viable tissue in regions where ^{99m}Tc -MIBI images showed irreversible perfusion defects, and, thus,

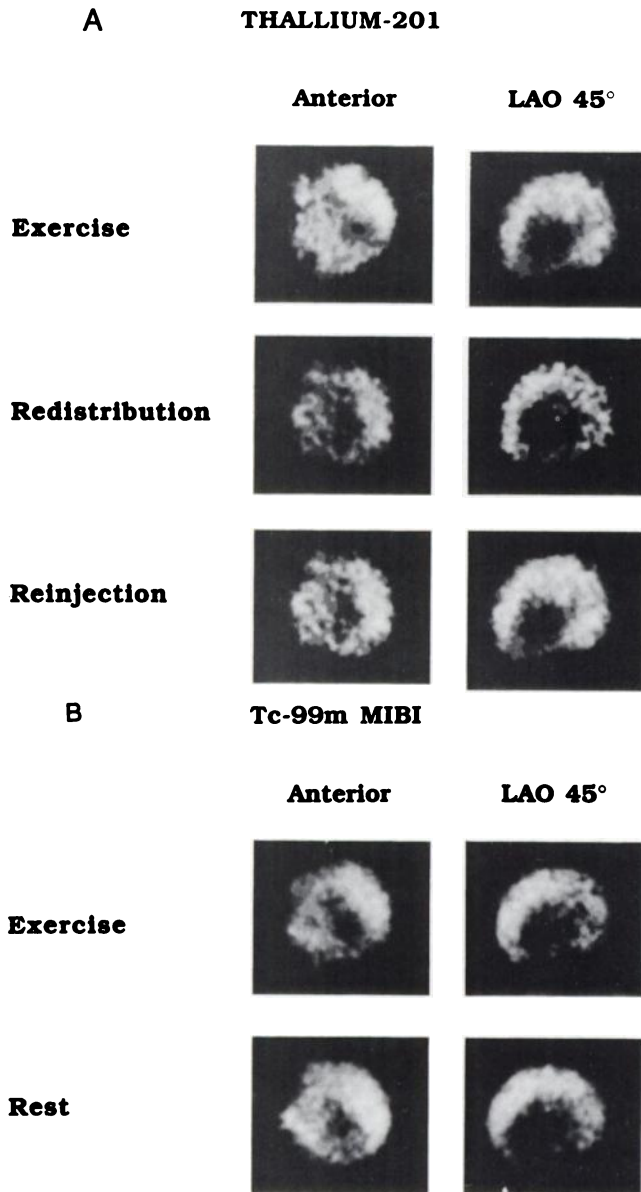


FIGURE 2. (A) Postoperative exercise-redistribution ^{201}Tl cardiac imaging with reinjection at rest. Exercise, redistribution and reinjection anterior views demonstrate normal thallium uptake in the inferior region. Exercise, redistribution and reinjection left anterior oblique (LAO) 45° views demonstrate normal thallium uptake in the distal segment of the interventricular septum and an irreversible perfusion defect involving the infero-apical region. (B) Postoperative exercise-rest ^{99m}Tc -MIBI cardiac imaging. Exercise and rest anterior views demonstrate normal ^{99m}Tc -MIBI uptake in the inferior region. Exercise and rest left anterior oblique (LAO) 45° views demonstrate normal ^{99m}Tc -MIBI uptake in the distal segment of the interventricular septum and an irreversible perfusion defect involving the infero-apical region.

accurately predicted functional recovery after revascularization.

In this report, the discordant results between preoperative thallium and ^{99m}Tc -MIBI imaging may be explained by the different kinetic features of these two tracers. Thallium-201 is a potassium analog which has been developed as a myocardial perfusion tracer reflecting initial tissue uptake in proportion to coronary blood flow delivery (14). However, thallium is also a marker of myocardial viability because only viable cells with an intact membrane retain the tracer, reflecting cell membrane integrity (15). Therefore, severely ischemic but still viable myocardium preserves the capability to take up thallium even though coronary blood flow is extremely reduced. When scarred myocardium is present, thallium is not taken up as in normal or in severely hypoperfused but still viable tissue, because of very low coronary blood flow levels and myocardial cell death. Exercise thallium images reflect the distribution of increased myocardial perfusion during exercise or coronary flow reserve modified by flow-dependent extraction. Redistribution thallium images demonstrate reversibility or irreversibility reflecting a region of decreased coronary flow reserve or an area of reduced flow reserve around an infarction, respectively. Enhanced thallium uptake after reinjection within apparently irreversible thallium defects on redistribution images has been shown to be compatible with the presence of severely hypoperfused but still viable myocardium (1-4). Therefore, although exercise-redistribution thallium images do not reliably predict myocardial viability, thallium reinjection realizes a resting image superimposed on stress images containing viability information.

Technetium-99m-MIBI is a cationic lipophilic myocardial tracer which accumulates linearly in the myocardium according to coronary blood flow as measured by microspheres (16). Recent animal studies demonstrated that the uptake and retention of ^{99m}Tc -MIBI in isolated rat hearts (8) and in the occlusion-reperfusion swine model of acute ischemia in vivo (9) are significantly reduced in necrotic myocardium. Technetium-99m-MIBI uptake in myocardial cells is diffusional and is not dependent on a sodium-potassium-adenosine triphosphatase pump. Previous studies demonstrated that this tracer is sequestered in the cytoplasm and mitochondria in response to electrical potentials across the membrane bilayers (8,17,18). In particular, negative mitochondrial and plasma membrane potentials seem to promote ^{99m}Tc -MIBI uptake, and this mechanism may provide a model to better know the biodistribution of ^{99m}Tc -MIBI in the heart muscle. Of note, cardiac tissue shows negative plasma membrane potentials and is rich in mitochondrial content. Therefore, changes in myocardial metabolism which modify membrane potentials could influence ^{99m}Tc -MIBI tissue uptake as demonstrated by Piwnica-Worms et al. (19). These authors showed that ^{99m}Tc -MIBI net uptake into cultured heart cells approached a plateau level, implying that an equilibrium or steady-state process is involved in net cellular accumula-

tion of the tracer. Their results indicated that myocardial cell net accumulation and uptake kinetics can be affected by pharmacological alterations in membrane transport and metabolic status, respectively (19). These data suggest that ^{99m}Tc -MIBI has properties as a definitely good perfusion agent and a reasonably good viability tracer. However, the precise role of ^{99m}Tc -MIBI for assessing viable myocardium in chronic CAD has not yet been completely clarified, and further experimental and clinical investigations are required (6,9,13).

Moreover, the apparently discordant results of this case and those of other studies in animal models (8,20–22) can be explained by examining the different mechanisms in CAD by which regional LV function may be impaired in the absence of irreversible myocardial damage. Two different states, stunned and hibernated myocardium, may determine the presence of dysfunctional but still viable myocardium (23,24). In both of these situations, LV dysfunction is a potentially reversible process. Recent studies (8,21) suggested that viable but stunned myocardium may take up ^{99m}Tc -MIBI similarly to the retention of thallium. However, in chronic hypoperfused hibernating myocardium, there are some limitations in the use of ^{99m}Tc -MIBI to accurately identify viable tissue (11,12). Therefore, ^{99m}Tc -MIBI seems to be promising as a viability index in the setting of stunned myocardium after reperfusion, but it could be inaccurate in the detection of hibernation when prolonged and sustained reduction of myocardial blood flow occurs.

The patient reported in this study had chronic CAD with LV dysfunction. Thus, the identification of hibernating rather than stunned myocardium was clinically in question. These observations may explain the difference between thallium reinjection and ^{99m}Tc -MIBI findings obtained in preoperative imaging studies. Before CABG, thallium reinjection correctly identified severely ischemic but viable myocardium in regions where ^{99m}Tc -MIBI images suggested the presence of irreversibly necrotic tissue. Postoperative imaging demonstrated restored ventricular function and myocardial perfusion in these regions, as showed by normal wall motion and ^{99m}Tc -MIBI uptake. Therefore, these results confirm that, while thallium reinjection is able to accurately predict functional recovery in hibernating myocardium, ^{99m}Tc -MIBI uptake may underestimate the presence of viable tissue in regions with severely reduced coronary blood flow.

In conclusion, this report shows that thallium reinjection imaging correctly identifies severely ischemic but viable myocardium, while ^{99m}Tc -MIBI seems to be primarily a perfusion agent and not an accurate marker of myocardial viability in patients with chronic CAD and LV dysfunction. When myocardial viability is in question, we recommend thallium cardiac imaging with rest reinjection for potential revascularization candidates with chronic ischemic left ventricular dysfunction.

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