Demonstration of Reperfusion After Thrombolysis with Technetium-99m Isonitrile Myocardial Imaging

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Technetium-99m isonitrile myocardial perfusion imaging was employed in a patient undergoing thrombolytic therapy with recombinant tissue plasminogen activator for acute anteroseptal myocardial infarction. Technetium-99m isonitrile does not demonstrate significant myocardial redistribution after intravenous injection. The imaging agent was administered in the emergency room, prior to the initiation of thrombolytic therapy. The initial area at risk for infarction was visualized on images obtained after the patient had been effectively treated. Imaging performed 5 days later, after repeat injection of [^{99m}Tc]isonitrile, showed a smaller myocardial perfusion defect indicating salvage of myocardium. Thus, this technique offers promise as a noninvasive means of assessing the area at risk, the success of reperfusion, and the presence of salvaged myocardium, early in the course of acute myocardial infarction.

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Demonstration of successful salvage of jeopardized myocardium following thrombolytic therapy for acute myocardial infarction is clinically important, but difficult with current imaging modalities. Ideally, it requires an imaging technique which assesses both myocardial perfusion and viability prior to and after the intervention. Initial myocardial perfusion images would visualize total myocardium at risk, and later images (after thrombolysis) the ultimate extent of infarction. The difference between the two images would indicate salvaged myocardium. Imaging with thallium-201 (^{201}Tl) before and after thrombolysis has been proposed for this purpose (*1,2*). However, this approach significantly delays the initiation of therapy when myocardial imaging is performed first, and is therefore impractical. Moreover, significant hyperemia after reflow and disproportionate accumulation of ^{201}Tl may overestimate the amount of salvaged myocardium immediately after thrombolysis (*3,4*).

Recently, a new class of radiopharmaceuticals for myocardial imaging, technetium-99m- (^{99m}Tc) labeled isonitriles, has been developed (*5,6*). Technetium-99m isonitrile (Hexakis-methoxy-isobutyl isonitrile), the prototype of these isonitriles, accumulates in the myocardium in proportion to the distribution of coronary blood flow, but unlike ^{201}Tl is not subject to significant subsequent myocardial redistribution. We utilized these characteristics of [^{99m}Tc]isonitrile to demonstrate noninvasively salvage of myocardium by thrombolytic therapy in a patient with acute myocardial infarction.

CASE REPORT

A 49-yr-old black male presented to the emergency room with 100 mins of acute sustained chest pain. The admission ECG showed 2-3 mm ST segment elevation in leads V_{1-2}, and 5-6 mm ST segment elevation in leads V_{3-4} consistent with acute anteroseptal myocardial infarction. In order to assess myocardial perfusion prior to thrombolytic therapy, 25 mCi of [^{99m}Tc]isonitrile (hexakis-methoxy-isobutyl isonitrile) was administered immediately before i.v. administration of the thrombolytic agent recombinant tissue plasminogen activator (rt-PA) and heparin. This did not delay or interfere with the initiation of thrombolytic therapy. Seventy five min after the beginning of rt-PA infusion, the patient's chest pain subsided dramatically and at that time multiple premature ventricular contractions were noted. The subsequent clinical course was unremarkable. The patient was treated initially with topical

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nitrates; a calcium channel blocker was begun on Day 3 and changed to a beta blocker at Day 6, at which time the nitrates were discontinued. The patient's hemodynamic status was unchanged during his hospitalization. Peak serum creatinine kinase was 3,170 IU/l (9.7% MB) 8 hr after the onset of thrombolytic therapy.

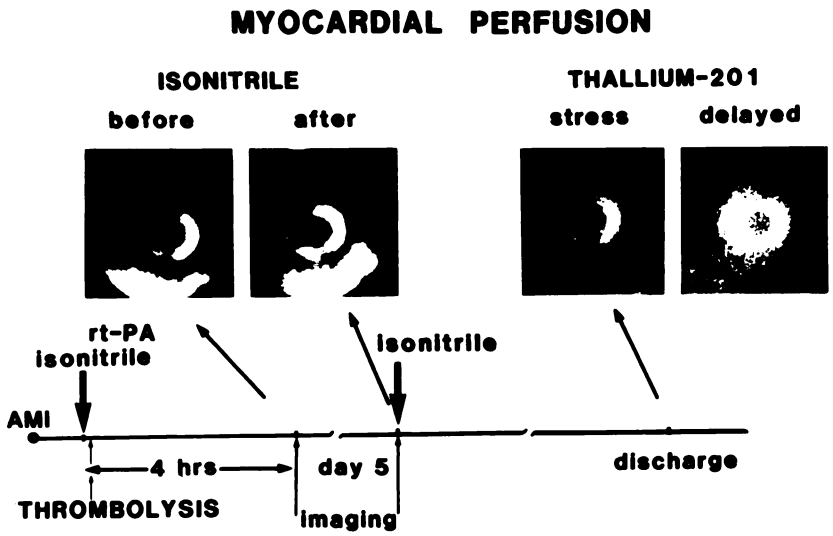
Myocardial perfusion imaging was performed in the coronary care unit, 4 hr after the administration of [^{99m}Tc]isonitrile. These images (Figure 1; "before") showed a large anteroseptal and apical myocardial perfusion defect. Repeat imaging was performed 5 days later following a second injection of [^{99m}Tc]isonitrile (Fig. 1, "after") and showed improved visualization of the septum and anterolateral wall, although a defect was still present. Predischarge (Day 10) ^{201}Tl stress imaging showed a partially reversible septal and a fixed anteroapical defect (Fig. 1, ^{201}Tl). The defect in the septum appears more clearly defined with [^{99m}Tc]isonitrile imaging than by ^{201}Tl. This may in part be due to the imaging characteristics of ^{99m}Tc compared to ^{201}Tl resulting in poorer structural definition of the myocardium. Equilibrium radionuclide angiocardiography performed at hospital discharge demonstrated anteroseptal and apical hypokinesis with a global left ventricular ejection fraction of 35%. Follow-up study performed 6 wk later showed improvement in global ejection fraction to 49% with some improvement in regional wall motion.

DISCUSSION

This new radiopharmaceutical for myocardial perfusion imaging, [^{99m}Tc]isonitrile, accumulates in the myocardium in proportion to myocardial blood flow and remains bound to cytosolic proteins (*7*). Therefore the first set of [^{99m}Tc]isonitrile images showed the extent of impaired myocardial perfusion (risk zone) at the time before thrombolysis, while the second set of images showed the presumed final extent of myocardial infarction. We hypothesize that the improved regional myocardial perfusion demonstrated in the septum and anterolateral wall reflects salvage of viable tissue. Although in this case imaging was performed early and at Day 5, an additional study performed one day after thrombolysis might provide earlier information on reperfusion status. However, the effects of edema might obscure improvement in perfusion occurring during this time period. The temporal sequence of imaging will require further study. Thallium-201 stress imaging 10 days later showed evidence of exercise induced ischemia in viable myocardium of the septum, supporting this hypothesis. The improvement in global ejection fraction and regional wall motion from hospital discharge to 6 wk follow-up further suggests the presence of reversibly dysfunctional myocardium at the time of hospital discharge. Thus, perfusion imaging indicated that a region of dysfunctional myocardium was still viable and possibly stunned; the subsequent improvement in ejection fraction supports this concept. These results suggest a possible role in this type of study in defining the presence of stunned myocardium.

This case report demonstrates the unique potential of [^{99m}Tc]isonitrile imaging for noninvasive assessment of myocardial perfusion before and after thrombolysis. Administration of [^{99m}Tc]isonitrile in the emergency room does not induce an undesirable delay in the administration of thrombolytic therapy. Currently, the isonitrile is supplied in a kit which requires 15 min for preparation. A new kit is prepared each morning and is available for immediate use during that day. Since no significant myocardial redistribution occurs, the timing of imaging after injection is not critical and can be performed hours later when the patient is clinically

FIGURE 1
Myocardial perfusion imaging with [^{99m}Tc]isonitrile and ^{201}Tl in left anterior oblique view. Technetium-99m isonitrile was administered 150 mins after the onset of acute myocardial infarction (AMI) immediately prior to the initiation of thrombolytic therapy. The first image ("before") visualizes myocardial perfusion with [^{99m}Tc] isonitrile prior to thrombolytic therapy. A septal defect is present with normal perfusion of the left ventricular lateral wall and right ventricle. The second image ("after") shows partial visualization of the septum after a second injection of [^{99m}Tc]isonitrile 5 days later. The improved visualization of the septum indicates reperfusion of the infarct artery. Thallium-201 imaging performed at hospital discharge shows a partially reversible septal defect (images on right).



stable and effectively treated. The approach presented in this brief report appears to be promising in answering clinically relevant questions concerning the success of reperfusion and the presence of viable or jeopardized myocardium early in the course of myocardial infarction. At the present time, these questions are being evaluated prospectively in a multicenter study involving patients with acute myocardial infarction using [^{99m}Tc] isonitrile imaging.

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REFERENCES

1. Markis JE, Malagold M, Parker JA, et al. Myocardial salvage after intracoronary thrombolysis with streptokinase in acute myocardial infarction. Assessment by intracoronary thallium-201. *N Engl J Med* 1981; 305:777–782.
2. De Coster PM, Melin JA, Detry JMR, Brasseur LA, Beckers C, Col J. Coronary artery reperfusion in acute myocardial infarction: assessment by pre- and postintervention thallium-201 myocardial perfusion imaging. *Am J Cardiol* 1985; 55:889–895.
3. Melin JA, Becker LC, Bulkley BH. Differences in thallium-201 uptake in reperfused and non reperfused myocardial infarction. *Circ Res* 1983; 53:414–419.
4. Granato JE, Watson DD, Flanagan TL, Gascho JA, Beller GA. Myocardial thallium-201 kinetics during coronary occlusion and reperfusion: influence of method of reflow and timing of thallium-201 administration. *Circulation* 1986; 73:150–160.
5. Holman BL, Sporn V, Jones AG, et al. Myocardial imaging with technetium-99m CPI: initial experience in the human. *J Nucl Med* 1987; 28:13–18.
6. Okada R, Williams S, Glover D, Crowley K, Garneau J. Myocardial kinetics of technetium-99m-hexakis-2-methoxy-2-methylpropyl-isonitrile [Abstract]. *J Am Coll Cardiol* 1987; 9 (suppl A):26A.
7. Mousa SA, Maina M, Brown BA, Williams SJ. Retention of RP-30 in the heart may be due to binding to a cytosolic protein [Abstract]. *J Nucl Med* 1987; 28:619.