Thallium-201/Technetium-99m-RP-30A Disparity in the Course of Myocardial Infarction After Attempted Reperfusion

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Recent reports have established that ^{201}Tl may be taken up in areas of recent myocardial infarction after myocardial blood flow is re-established. In addition, there is accelerated ^{201}Tl "washout" from these regions producing a pattern of "reverse redistribution." We present a case in which these phenomena may have contributed to a disparity of findings between a ^{201}Tl stress imaging study and a repeat stress imaging study performed with a [^{99m}Tc] isonitrile (^{99m}Tc-RP-30A).

J Nucl Med 29:1283–1286, 1988

While thallium-201 (^{201}Tl) has been used for the detection and sizing of myocardial infarction, with the advent of routine thrombolysis certain details of the kinetics of thallium uptake and washout which have previously received limited consideration have become clinically important. For example, ^{201}Tl uptake by irreversibly damaged myocardium has now been reported by several investigators (*1–4*). This has only rarely caused misleading results in the detection of myocardial infarction in the past, as infarction has been associated with continuing coronary occlusion and, therefore, compromised perfusion in the infarct zone ensured a myocardial perfusion defect on ^{201}Tl scintigraphy. However, in the present era of cardiac care, in which acute reperfusion by pharmacologic lysis or interventional means is standard practice, not only is it likely that this important property of ^{201}Tl kinetics will produce misleading results regarding the presence or absence of infarction, but more importantly it may adversely affect the accuracy of ^{201}Tl scintigraphic evaluation of underlying ischemia in the early postreperfusion period. The new generation of technetium-99m- (^{99m}Tc) labeled isonitrile radiopharmaceuticals may offer a reliable alternative to ^{201}Tl in this setting.

PATIENT STUDY

A 39-yr-old white man with no previous cardiac history presented to an emergency room with severe left-sided chest, shoulder, and arm pain accompanied by diaphoresis, pallor, nausea, dizziness, and 12 mm ST elevation in chest leads V2-V5. The patient subsequently developed ventricular tachycardia requiring cardioversion twice for hemodynamic instability. One million units of streptokinase was administered intravenously ~4 hr following the onset of pain. The patient was then transferred to the coronary intensive care unit of a large teaching hospital. On arrival the patient's electrocardiogram revealed 1.5 mm ST elevation in V1-V2, loss of R wave amplitude in V1-V6, abnormal septal Q waves, and T wave inversion in V4-V6. The findings were consistent with an acute anterior myocardial infarction. Serum creatine kinase subsequently peaked at 2,750 IU/ml (CPK MB 8%). The patient was maintained on intravenous heparin anticoagulation.

Two days following admission, the patient underwent cardiac catheterization including contrast ventriculography and coronary angiography. Resting hemodynamics were normal. The ventriculogram demonstrated an ejection fraction of 63% but abnormal regional wall motion, with hypokinesis of the antero-lateral and septal regions of the left ventricle. The coronary angiogram revealed a 30% stenosis of the proximal left anterior descending coronary artery and a 20% stenosis of this vessel distal to its first diagonal branch. The first diagonal demonstrated an 80% proximal stenosis. There was no other significant coronary disease.

Nine days following admission, the patient underwent a stress ^{201}Tl imaging study. The patient was exercised on a modified Naughton protocol for 13 min to a heart rate of 110. The study was terminated because of the development of an additional 1 mm of horizontal ST depression. One minute prior to the completion of the stress test the patient received an intravenous tracer dose of ^{201}Tl. Approximately 6 min

Received Aug. 6, 1987; revision accepted Feb. 23, 1988.

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following the completion of the stress routine a single photon emission computerized tomography (SPECT) ^{201}Tl acquisition of the heart was initiated. This acquisition consisted of 64 angles through 180° (LPO to RAO) and was completed within 22 min. Short axis and horizontal long axis reconstructions obtained from the first image set (Fig. 1) demonstrated a small perfusion defect in the proximal anterior wall region as confirmed by quantitative radial profile analysis. However, the redistribution reconstruction images obtained 4 hr following the initial injection of ^{201}Tl demonstrated extensive high grade defects in the anterior wall and septum. This distribution of defects coincided with the wall motion abnormality noted on contrast ventriculography. There was accelerated washout, both absolutely and relatively, in the antero-septal region compared with regions known to be free of disease.

On the following day, the patient underwent a repeat stress test in conjunction with a ^{99m}Tc isonitrile (^{99m}Tc-RP-30A) (DuPont Company, No. Billerica, MA) imaging study. This study was performed in accordance with an experimental protocol approved by the Institutional Committee on the Conduct of Human Research, and written informed consent was obtained from the patient. The patient duplicated the exercise protocol of the previous day, exercising for 13 min to a heart rate of 110. The patient again had a "positive" ECG exercise test with 2 mm of additional ST depression. One-minute prior to the completion of this exercise study the patient received 22 mCi of ^{99m}Tc-RP-30A. One hour following the administration of radiotracer a SPECT acquisition of the heart was obtained. The imaging protocol was the same as that for the ^{201}Tl study except for the necessary change in energy settings. Short axis and long axis reconstructions revealed significant perfusion defects in the antero-septal regions which corresponded in location and extent to the defects noted on the ^{201}Tl redistribution study (Fig. 2).

The following day the patient received a second intravenous injection of 22 mCi of ^{99m}Tc-RP-30A at rest and was imaged one hour later on the same SPECT system. Short axis and long axis reconstructions from this resting RP-30A acquisition (Fig. 2) revealed a persistent proximal anterior wall defect; however, there was significant improvement in the septal uptake of tracer. The findings on this study, in conjunction with the stress test, were interpreted as being consistent with the presence of a mixture of scar and reversibly ischemic tissue.

DISCUSSION

Although ^{201}Tl has been frequently described as a potassium (K^+) analog, there are important differences in the dynamics of distribution of ^{201}Tl as compared with K^+ (*5*). This raises questions as to the validity of assumptions regarding thallium distribution under conditions of anoxia and ischemia which are based on the behavior of K^+ and the Na^+/K^+ ATPase pump under the same conditions.

This dissociation of ^{201}Tl behavior from that of K^+ has not adversely affected the clinical utilization of ^{201}Tl scintigraphy for the evaluation of coronary artery disease. The successful utilization of ^{201}Tl imaging (*6–9*) has rather been founded on its ability to accurately map regional myocardial blood flow (*10–13*).

However, there are potential clinical difficulties caused by the fundamental flow dependence of ^{201}Tl distribution (i.e., its relative independence of myocardial viability) as emphasized by Melin et al. (*1*), who concluded that ^{201}Tl may be an unreliable marker of cell injury. In addition, to further complicate the interpretation of ^{201}Tl images, there have been several reports, including both in vivo and in vitro studies, which describe accelerated ^{201}Tl efflux from infarcted myocardium (*2,3,14,15*).

While in previous clinical applications this has not been a major problem because regional myocardial perfusion is usually significantly depressed in the presence of acute myocardial infarction, this frequently will not be the case with the widespread clinical use of thrombolysis for acute myocardial infarction. The first clinical study to address this problem was reported by Weiss et al. (*16*). These investigators demonstrated a pattern of "reverse redistribution" in 75% of the pa-

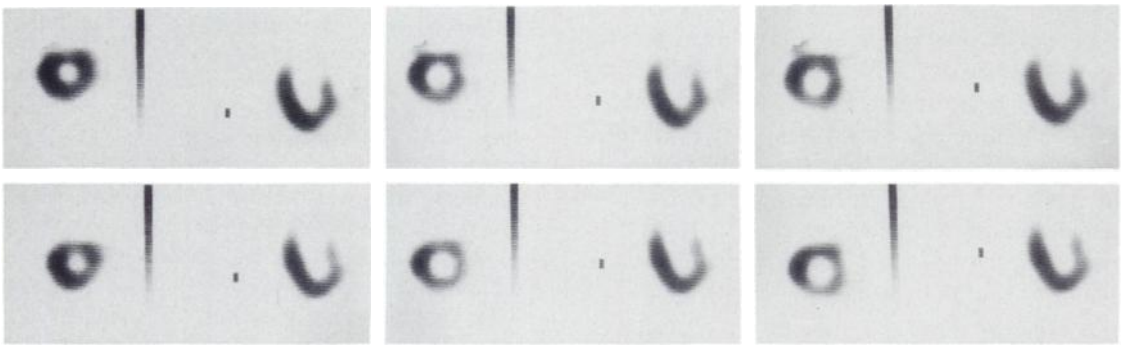

FIGURE 1
Long axis (left) and corresponding short axis (right) tomographic images of the heart immediately following stress (top) and on redistribution (bottom) delayed 4 hr following injection of ^{201}Tl. Stress images demonstrate a small anterior wall perfusion defect seen on the most proximal (basilar) short axis slice. Redistribution images demonstrate an extensive region of "reverse redistribution" involving the entire antero-septal region.

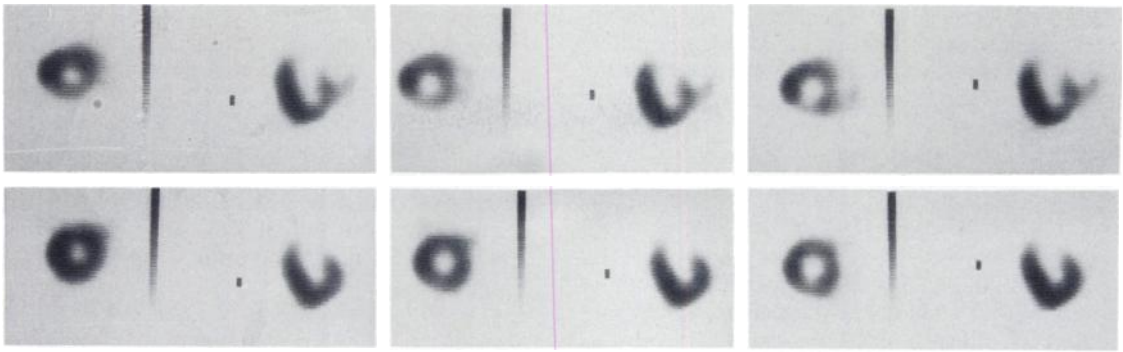

FIGURE 2
Long axis (left) and corresponding short axis (right) tomographic images of the heart obtained following ^{99m}Tc-RP-30A administration at stress (top) and rest images obtained following ^{99m}Tc-RP-30A injection at rest (bottom). Stress images demonstrate an extensive antero-septal perfusion defect. Rest images continue to demonstrate a small proximal anterior wall defect however there is significant improvement in the antero-septal region.

tients undergoing ^{201}Tl imaging within 10 days of thrombolytic therapy for acute myocardial infarction.

In the case reported here, the pattern of ^{201}Tl uptake and washout in the reperfused zone was that of initially normal uptake with accelerated washout (i.e., "reverse redistribution") as described by Weiss et al. in patients with successful reperfusion therapy of acute myocardial infarction. The area of decreased activity on the ^{201}Tl redistribution imaging study was comparable in location and extent to the region of wall motion abnormality noted at contrast ventriculography.

Our patient was referred for the assessment of possible postinfarction ischemia and for evaluation of the extent of myocardium in jeopardy. The ^{201}Tl scintigraphic results did not provide classical evidence of ischemia (i.e., a region with a reversible perfusion defect or prolonged washout). The ECG portion of the stress test, however, was "positive" by standard electrocardiographic criteria. In contrast, the results of the stress/rest imaging study utilizing technetium(I)-99m hexakis 2-methoxy 2-methylpropyl isonitrile (RP-30A) indicated the presence of an area of infarction (defect seen on both the resting and exercise images) as well as an area of ischemia (defect only seen on exercise images). Unlike ^{201}Tl, ^{99m}Tc-RP-30A does not redistribute, and the distribution of ^{99m}Tc-RP-30A on a delayed study correlates with the distribution of simultaneously administered microspheres. Although this lack of redistribution is important, the reported differences in the uptake of ^{99m}Tc-RP-30A as compared to ^{201}Tl may be paramount. While ^{99m}Tc-RP-30 has been shown to depict regional blood flow (and thus initial thallium distribution) in normal control animals, the metabolic handling of this cationic complex differs from that of ^{201}Tl (*17*). Although the kinetics of RP-30A have not been fully investigated, it is known that while RP-30A distributes in relation to regional myocardial blood flow, extraction may be altered by hypoxia or ischemia. Mousa et al. (*18*) demonstrated significant depression of ^{99m}Tc-RP-30 uptake in regions of infarction but normal blood flow, while concurrent experiments with ^{201}Tl did not reveal similar alterations in uptake.

Thus, ^{201}Tl stress/redistribution imaging possess a "blind spot" to ischemia in areas of overlapping or mixed necrotic, ischemic or normal myocardium because of offsetting differences in ^{201}Tl uptake and washout. Technetium-99m-RP-30A may provide advantages relative to ^{201}Tl in the evaluation of reperfused myocardium. In general terms, this case suggests that using a tracer whose initial uptake reflects primarily blood flow to assess the potential for ischemia in an area of reperfused infarction may be problematic in this era of aggressive thrombolytic therapy.

REFERENCES

1. Melin JA, Becker LC, Bulkley BH. Differences in thallium-201 uptake in reperfused and nonreperfused myocardial infarction. *Circ Res* 1983; 53:414–419.
2. Okada RD. Kinetics of thallium-201 in reperfused canine myocardium after coronary artery occlusion. *JACC* 1984; 3:1245–1251.
3. Krivokapich J, Watanabe CR, Shine KI. Effects of anoxia and ischemia on thallium exchange in rabbit myocardium. *Am J Physiol* 1985; 249 (*Heart Circ Physiol* 18):H620–H628.
4. Sochor H, Schwaiger M, Schelbert HR, et al. Relationship between Tl-201, Tc-99m(Sn) pyrophosphate and F-18 2-deoxyglucose uptake in ischemically injured dog myocardium. *Am Heart J* 1987; 114:1066–1077.
5. Krivokapich J, Shine KI. Effects of hyperkalemia and glycoside on thallium exchange in rabbit ventricle. *Am J Physiol* 1981; 240 (*Heart Circ Physiol* 9):H612–H610.
6. Bailey IK, Griffith LS, Rouleau J, Strauss HW, Pitt B. Thallium-201 myocardial perfusion imaging at rest and during exercise: comparative sensitivity to electrocardiography in coronary artery disease. *Circulation* 1977; 55:79–87.
7. McLaughlin PR, Martin RP, Doherty P, et al. Reproducibility of thallium-201 myocardial imaging. *Circulation* 1977; 55:497–503.

8. Ritchie JL, Trobaugh GB, Hamilton GW, et al. Myocardial imaging with thallium-201 at rest and during exercise: comparison with coronary arteriography and resting and stress electrocardiography. *Circulation* 1977; 56:66–71.
9. Wackers FJ, Sokole EB, Samson G, et al. Value and limitations of thallium-201 scintigraphy in the acute phase of myocardial infarction. *N Eng J Med* 1976; 295:1–5.
10. Strauss HW, Harrison K, Langan JK, Lebowitz E, Pitt B. Thallium-201 for myocardial imaging: relation of thallium-201 to regional myocardial perfusion. *Circulation* 1975; 51:641–645.
11. Weich HF, Strauss HW, Pitt B. The extraction of thallium-201 by the myocardium. *Circulation* 1977; 56:188–191.
12. Nielsen AP, Morris KG, Murdock R, Bruno FP, Cobb FR. Linear relationship between the distribution of thallium-201 and blood flow in ischemic and nonischemic myocardium during exercise. *Circulation* 1980; 61:797–801.
13. Chu A, Murdock RH, Cobb FR. Relation between regional distribution of thallium-201 and myocardial blood flow in normal, acutely ischemic, and infarcted myocardium. *Am J Cardiol* 1982; 50:1141–1144.
14. Goldhaber SZ, Newell JB, Alpert NM, Andrews E, Pohost GM, Ingwall JS. Effects of ischemic-like insult on myocardial thallium-201 accumulation. *Circulation* 1983; 67:778–785.
15. Okada RD, Boucher CA. Differentiation of viable and nonviable myocardium after acute reperfusion using serial thallium-201 imaging. *Am Heart J* 1987; 113:241–250.
16. Weiss AT, Maddahi J, Lew AS, et al. Reverse redistribution of thallium-201: a sign of nontransmural myocardial infarction with patency of the infarct-related coronary artery. *JACC* 1986; 7:61–67.
17. Mousa SA, Maina M, Williams SJ. Myocardial uptake and retention of Tc-99m-RP-30: evidence for specificity. *Circulation* 1986; 74:II–513.
18. Mousa SA, Cooney JM, Williams SJ. Regional myocardial distribution of RP-30 in animal models of myocardial ischemia and reperfusion. *J Nucl Med* 1987; 28:A620.