Continuing Education

Evaluation and Management of Patients in the Acute Phase of Myocardial Infarction— The Role of Nuclear Medicine in the Coronary Care Unit

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This is the third article in a four-part continuing education series relating to patient care and management. After completing the article, the reader should be able to: 1) understand the application, potential, and problems of nuclear cardiology in the coronary care unit; 2) recognize the utilization of nuclear cardiology in acute coronary care management; and 3) appreciate the important role of nuclear cardiology in cardiac patient care.

The predominant application of radionuclide techniques in the cardiac intensive care unit is in the assessment of the patient with an acute myocardial infarction. In general, these patients require admission to the intensive care unit to be monitored for life-threatening disturbances of cardiac rhythm and signs of deteriorating left ventricular performance; hence in the initial period of time, imaging must be performed at the bedside using a portable scintillation camera. Additionally, the acquisition of nuclear medicine studies must be coordinated with the members of the clinical care team so that the delivery of therapy directed at reducing the patient's discomfort, or more importantly, reducing the size of the patient's myocardial infarction, is not disturbed. It is in the evaluation of therapy directed at reducing the size of the patient's myocardial infarction that radionuclide techniques have their greatest potential.

Present therapy for patients who are hospitalized within a short time (less than 6 hr) from the onset of their myocardial infarction involves the use of thrombolytic therapy. Intravenous streptokinase (*1*) or tissue plasminogen activator (*2*) are directed at dissolution of the occlusive coronary thrombus which causes severe myocardial ischemia. If ischemia persists, this results in an acute myocardial infarction (regional myocardial cell necrosis). The extent of necrosis is predictive of the severity of left ventricular dysfunction and ultimately patient outcome. If the infarct is large, severe left ventricular failure ensues, and there is a high early in-hospital mortality. This increased mortality persists into the post-hospital discharge phase. If the infarct is moderate in size, in-hospital mortality is significantly less; however, these patients often develop significant symptoms of chronic heart failure. The goal, then, of thrombolytic therapy is to dissolve the occlusive coronary thrombus, thus re-establishing coronary blood flow, reversing ischemia, and limiting myocardial damage. This must all occur in a timely fashion. It has been clearly shown (*3*) that the benefits of thrombolytic therapy are greatest when initiated within 2 hr of the onset of coronary occlusion. However, myocardial salvage has been demonstrated if therapy is instituted within 6 hr of the onset of coronary occlusion.

There are several important questions that need to be answered in patients who have sustained an acute myocardial infarction in whom thrombolytic therapy has been given or is being contemplated:

1. What is the extent of myocardial necrosis?
2. What is the size of the region in jeopardy?
3. Has thrombolytic therapy been successful?
4. What has been the effect of therapy on global and regional myocardial function?

The radionuclide imaging techniques most relevant to these questions are: infarct avid scintigraphy using technetium-99m (^{99m}Tc) pyrophosphate, thallium-201 (^{201}Tl) scintigraphy, and either equilibrium or first-pass radionuclide ventriculography. In this article, the utility of each of these techniques and applications in a cardiac intensive care unit setting will be reviewed. Specifically, the history and clinical importance of each technique will be discussed, methodology will be reviewed, and potential pitfalls will be highlighted.

INFARCT-AVID IMAGING WITH TECHNETIUM-99m-PYROPHOSPHATE

In 1974, infarct avid imaging (*4*) was introduced as a method to diagnose acute myocardial infarction. Technetium-99m

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pyrophosphate is the radiopharmaceutical most commonly used. Over 50% of the injected dose is extracted by bone and the rest is excreted by the kidney. After an hour and a half, less than 5% of the injected dose remains in the blood. Myocardial uptake (*5*) of ^{99m}Tc pyrophosphate is related to four important factors: 1) intracellular myocardial calcium; 2) extent of irreversible tissue damage; 3) regional myocardial blood flow (the radiopharmaceutical must be delivered to the site of infarction); and 4) the time after infarction. In the clinical setting, images generally have their highest diagnostic utility at 72 hr and usually do not become positive until 24–48 hr after myocardial infarction. This time lag is explained in part by the flow dependence of the delivery of tracer to necrotic tissues. Maximal uptake occurs when flow is reduced by only 30%–40%. In the setting of a no flow or low flow state, such as is present during an acute myocardial infarction, the time course of uptake of this radiopharmaceutical is prolonged. Because the time course of accumulation of the radiopharmaceutical is so long, the technique is viewed as having minimal clinical relevance as a diagnostic test. However, Wheelan (*6*) explored the time course of uptake as a marker for patients who had successfully reperfused after initiation of therapy with intravenous streptokinase. In patients who had received intravenous streptokinase and were imaged 7 $\pm$ 2 hr after the onset of chest pain, early markedly positive pyrophosphate images were associated with angiographically patent coronary arteries. This was not the case in patients with unsuccessful streptokinase therapy. This may provide a simple means of predicting successful reperfusion. One study (*7*) has shown that infarct-avid imaging when combined with perfusion imaging may allow definition of risk zones and extent of myocardial necrosis. These techniques will need to be evaluated in larger groups of patients to assess their benefit in the management of patients during the acute phase of myocardial infarction. Their potential, however, is great.

Imaging Technique

Imaging should begin 4 hr after injection of 20–25 mCi of ^{99m}Tc stannous pyrophosphate. Scans acquired less than 2 hr post injection result in false-positive scans. A high resolution, low energy parallel hole collimator should be used. Images should be obtained in multiple projections to improve accurate localization of activity and to allow separation from overlying bone. Standard projections include the left anterior oblique, anterior, and left lateral positions. Images are obtained for at least 400,000 counts per projection. It is important to realize that in the patient with a myocardial infarction, significant chest pain may be present while the imaging is being attempted. Coordination with the medical team taking care of the patient is important and imaging can be timed to occur in conjunction with the administration of analgesics and therapy directed at improving the patient's comfort. Additionally, creative patient positioning may be necessary to effect maximal comfort. In some centers, early images are obtained which include the cardiac blood pool. These can be displayed with the delayed images to enhance recognition of focal myocardial uptake (*8*). The normal image shows uptake of the ^{99m}Tc pyrophosphate by the sternum, ribs, and spine. There will be no discrete uptake by the heart muscle (Fig. 1). Positive scans are visually graded in five increments by the amount of uptake present in the myocardium. These grades (*9*) are determined by comparing uptake in the region of the heart with that in the ribs over the left hemithorax. These grades are: no uptake, mild diffuse, moderate diffuse, focal, and massive uptake (Table 1). The latter two grades correlate with a high probability of the presence of myocardial necrosis (Fig. 2).

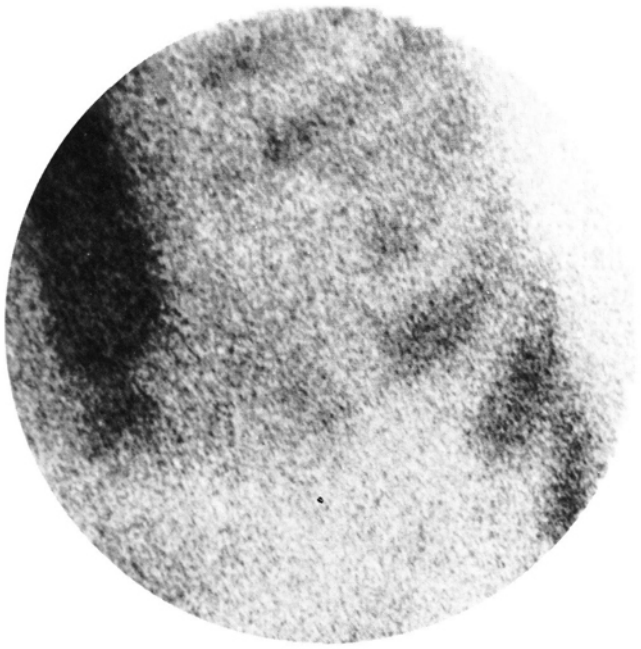

FIG. 1. Anterior projection of a normal planar ^{99m}Tc pyrophosphate myocardial scintigram showing no myocardial uptake.

TABLE 1. Grading System for Technetium Pyrophosphate Infarction Scans*

Scan Appearance	Grade	Diagnosis
No myocardial activity	Normal	No infarction
Activity less than ribs	Mild diffuse	Low probability of infection
Activity equal to ribs less than sternum	Moderate diffuse	Indeterminant
Discrete myocardial uptake	Focal	High probability of infarction
Activity in at least 50% of the cardiac silhouette, greater than or equal to sternum	Massive	High probability of infarction

*See Ref. 9.

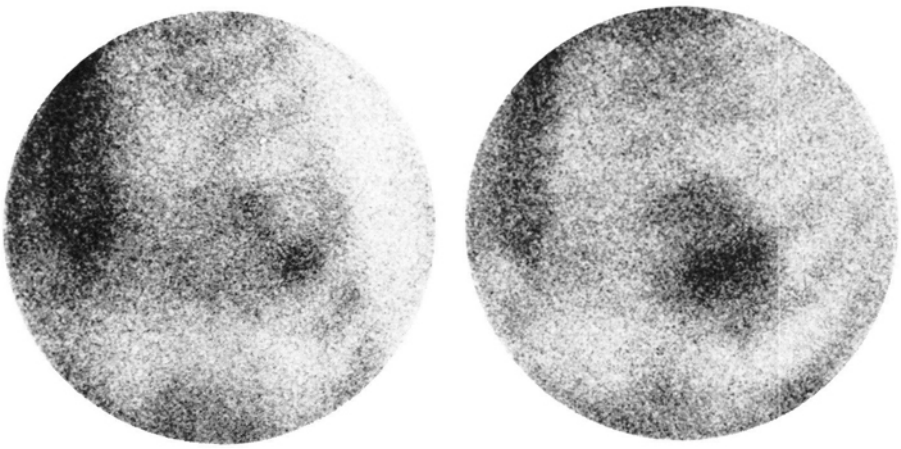

FIG. 2. Anterior and left anterior oblique projections of planar ^{99m}Tc pyrophosphate myocardial scintigrams, demonstrating acute anterolateral, apical, and septal infarction.

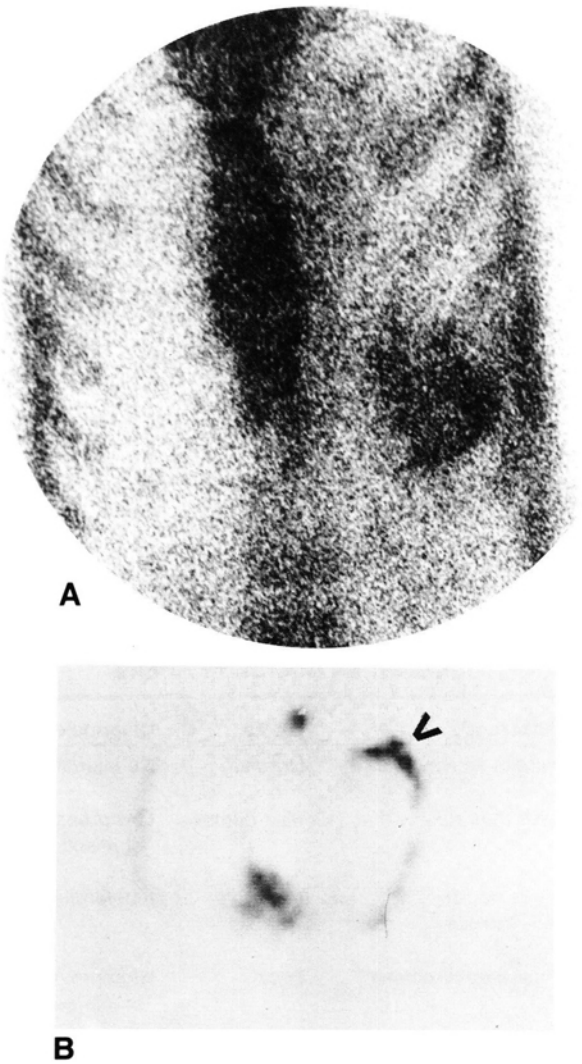

FIG. 3. False-positive technetium pyrophosphate myocardial scintigram probably secondary to cardioversion. (A) Focal technetium uptake in the region of the heart. (B) Transaxial tomography demonstrates the activity to be localized to the chest wall (arrow).

Pitfalls and Problems with Infarct-Avid Imaging

The major problems with infarct-avid imaging are conditions that affect the sensitivity and specificity of the test. There are certain conditions (*10*) associated with false-positive studies. These are: repeated high-energy direct current cardioversion, a frequent occurrence in the first few hours after myocardial infarction; severe heart valve calcification; myocardial contusion; pericarditis; myocardial calcification; ventricular aneurysm; and metastatic carcinoma to the heart (Fig. 3).

THALLIUM-201 SCINTIGRAPHY IN THE INTENSIVE CARE UNIT

Thallium-201 imaging would be the logical choice as an important radiotracer in assessment of reperfusion therapy. Since its introduction in 1976, it has been clear that this agent can be used to delineate regions of decreased perfusion in the presence of acute myocardial infarction (*11*). Additionally, delayed imaging may be used to assess regional myocardial viability by its ability to detect regional redistribution of thallium. This is especially pertinent in the assessment of successful clot lysis with thrombolytic therapy. Also, in the management of patients with atypical chest pain, ^{201}Tl imaging can help differentiate pain caused by decreased coronary blood flow from other noncardiac causes of chest pain. Although, most commonly, ^{201}Tl imaging is performed in conjunction with exercise or pharmacologic stress, in the intensive care unit rest imaging followed by reperfusion imaging would be performed. Rapid initiation of thrombolytic therapy is the most important factor that determines the extent of myocardial salvage. Since routine three-view thallium imaging takes at least 24 min without inclusion of the time required for camera and/or patient positioning, it is unlikely that baseline data will be obtained prior to the institution of thrombolytic therapy. If baseline data are to be obtained, then modification of the imaging protocol might be necessary. Usually the presumed site of myocardial infarction can be localized from the electrocardiogram. It would be acceptable to image in the projec-

tion that best evaluates the myocardial perfusion territory at risk.

The clinical utility of thallium imaging following thrombolytic therapy has been evaluated by De Coster (*12*) and Reduto et al. (*13*). In De Coster's study, sequential thallium images were obtained in 44 patients on admission to the intensive care unit and at 4 hr, 4 days, and 6 wk after thrombolytic therapy. Thallium scores were determined to evaluate the size of perfusion deficit at each of these times after therapy. In both control and successfully reperfused patients, the thallium score decreased over time but this decrease was significantly greater in patients with successful clot lysis. There is, however, controversy regarding the ability of thallium imaging to measure successful reperfusion or tissue viability. There is concern that initial thallium distribution is a function of improved flow and is not a reflection of myocardial viability (*14*). In an animal study (*15*), it has been shown that in the presence of reperfusion, increased amounts of tracer are present in the reperfused area and regions of myocardial necrosis are masked. Finally, another factor that might contribute to misinterpretation is the phenomenon of "reverse redistribution" caused by rapid washout of thallium activity in reperfused areas. Thus the timing of the injection of thallium in relationship to therapy will be one of the most important factors in this application of thallium imaging and will need to be varied depending on the clinical questions to be answered: successful reperfusion?, amount of viable myocardium?, and size of region at risk? Whether successful reperfusion has occurred may require early administration of the thallium. Extent of myocardial salvage may require imaging in the convalescent phase of the illness.

Imaging Technique

If initial and delayed images are to be obtained, scan acquisition should begin 10–15 min after injection of 2–3 mCi of ^{201}Tl. Standard planar imaging would involve acquisition of images in the anterior, left anterior oblique, and left lateral views using a low energy, all purpose parallel hole collimator. However, positioning of the acutely ill patient may be difficult and certain views may need to be omitted. Additionally, if initial and delayed images are to be acquired, the technologist should pay careful attention to patient landmarks during the initial scan so that images in the delayed scans can be acquired in the same views. Each scan should be acquired for 8 min. If delayed imaging is performed, images should be acquired 4 hr after cessation of thrombolytic therapy, an adequate time interval to detect successful reperfusion. These images should also be acquired for 8 min. Analysis of images to compare size of defects initially and on the delayed images should be quantitative. Several of these algorithms exist (*16,17*), and they usually involve interpolative background subtraction and an assessment of regional thallium counts.

Pitfalls and Problems with Thallium-201 Scintigraphy

One of the major problems in applying thallium imaging in the cardiac intensive care unit is the availability of the radionuclide. Most hospitals do not have a ready supply of thallium for injection. With the recent development of a new class of radiopharmaceuticals, the technetium-isonitriles (*18,19*), the availability may become less of an issue. Secondly, as has been previously stated, more must be learned about the most appropriate time to inject thallium in relation to the institution of thrombolytic therapy to answer the important clinical questions of successful myocardial reperfusion and tissue viability. Finally, the first 4 hr of hospitalization after a myocardial infarction are often the busiest with regard to institution of therapy, assessment of clinical parameters, and maintenance of patient comfort. In these circumstances, efficient imaging may prove to be a formidable task.

ASSESSMENT OF LEFT VENTRICULAR PERFORMANCE

Assessment of left ventricular performance in the patient who has suffered a myocardial infarction is extremely important in determining the patient's in-hospital and long term mortality. Equilibrium and first pass radionuclide ventriculography have been shown to be accurate in assessing global left ventricular ejection fraction and regional wall motion. The portability of the nuclear cardiac probe (*20*), a nonimaging device, makes it useful for assessment of global left ventricular ejection fraction on a beat to beat basis. There is a direct relationship between left ventricular ejection fraction after a myocardial infarction and ultimate prognosis. In the Multicenter Post Infarction Research Group (*21*) study of 799 patients, those with ejection fractions > 50% had a 1-yr mortality of < 5%; those with ejection fractions < 20% had a 1-yr mortality of nearly 50% (Table 2). Additionally, it has been shown that in some patients in whom thrombolytic therapy is successful, left ventricular ejection fraction will improve significantly. In discussing the role of the radionuclide assessment of left ventricular function in the intensive care unit, several important points must be emphasized. First, in the early hours of an acute myocardial infarction there is substantial variability in resting left ventricular ejection fraction in the absence of thrombolytic therapy. This measurement is extremely sensitive to changes in "loading conditions" of the heart. For instance, the patient may experience wide fluctuations in systemic blood pressure resulting in significant fluctuations of left ventricular ejection fraction. Additionally, spontaneous clot lysis can occur, resulting in reperfusion. This may result in significant improvement in the left ventricular ejection fraction. Global ejection fraction, then, is not the most sensitive indicator of myocardial salvage. Quantitative measurement of regional function, i.e.,

TABLE 2. Risk Stratification Post Myocardial Infarction Based on Left Ventricular Ejection Fraction*

One-Year Mortality	Ejection Fraction
2%	≥ 60%
4%	40–59%
12%	20–39%
47%	< 20%

*Adapted from the Multicenter Post Infarction Research Group (*21*).

wall motion or regional ejection fraction, is more relevant in assessment of thrombolytic therapy since regional hyperfunction and hypofunction may be present. If, after therapy, regionally hypofunctioning segments improve and regionally hyperfunctioning segments return to normal, there may be no apparent change in measured global ejection fraction. This has been demonstrated to occur in the setting of an acute myocardial infarction (*22*). In fact, most studies evaluating the effects of thrombolyltic therapy on left ventricular function have concentrated on quantitative assessment of regional function. Thus, although the nuclear cardiac probe would be an attractive instrument to use because of its portability, only measurements of global ejection fraction can be obtained. Hence, its usefulness in this setting may be limited. Finally, mention must be made of the concept of "stunned myocardium." When myocardial segments are made ischemic for a prolonged period of time prior to restitution of coronary blood flow, recovery of regional myocardial function may not occur for hours to days. Thus the appropriate timing for assessment of left ventricular function is not clear. If only one study is to be obtained, the literature (*23*) suggests that performing the study just prior to the patient's discharge from the hospital will allow the effects of stunning to wear off.

In summary, the application of radionuclide ventriculography in the setting of an acute myocardial infarction requires an understanding of the factors which affect measures of global and regional ejection fraction. Serial studies of regional ventricular function give the most information about the effectiveness of therapy. The cost-benefit ratio of such imaging needs to be evaluated in future studies.

FUTURE DIRECTIONS

The development of technetium-based perfusion imaging agents will advance the usefulness of scintillation camera imaging in the cardiac intensive care unit, specifically in the assessment of patients who have received thrombolytic therapy. The use of technetium-based agents would allow these radiopharmaceuticals to be readily available. The class of agents that seem to have the most promise in this regard is the technetium-isonitriles. Studies with technetium-99m-hexakis-2-methoxy--2-methylpropyl isonitrile (RP-30) have indicated that this tracer accumulates in direct proportion to regional myocardial blood flow and does not redistribute like ^{201}Tl. Theoretically, this characteristic of RP-30 would allow injection at the time of initiation of thrombolytic therapy. Imaging could then be performed 3–4 hr later when the patient is presumably more stable and easier to image. This initial image would then define the extent of myocardium in jeopardy. Imaging could be repeated in 3–4 days after a second injection of RP-30 to define the extent of myocardium that was salvaged by comparison to the initial images. Certainly, more studies of these agents will be necessary before they can be applied in this setting. The radiolabeled monoclonal antibody antimyosin is presently available as an infarct-avid imaging agent. In the routine infarction (*24*), this agent has been shown to be able to quantitate the size of infarcts quite accurately. Thus far, there have been no reported studies evaluating these agents in acute thrombolytic therapy.

SUMMARY

In this article, we have reviewed the potential applications of nuclear medicine studies in the cardiac intensive care unit in the evaluation of the patient with an acute myocardial infarction who is being considered for or has received thrombolytic therapy. The clinically relevant questions that would affect further management decisions in these patients have been defined. These are: size of myocardial region at risk, success of reperfusion, and extent of irreversibly damaged myocardium after therapy. Presently, these questions are answered imperfectly with available radiopharmaceuticals. However, in selected individuals, important information may be gained. Timing of studies is critical to the particular clinical question that is being posed, and this will direct the selection of the radiopharmaceutical and its application. In the future, technetium-labeled isonitriles have great potential to expand the use of nuclear medicine in the acute care setting.

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