Technetium Stannous Pyrophosphate Myocardial Scintigrams in Patients with Chest Pain of Varying Etiology

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SUMMARY

Technetium-99m stannous pyrophosphate was utilized for myocardial imaging in 202 patients admitted to the hospital with chest pain of uncertain etiology. One hundred and one patients had clinical and evolved electrocardiographic and enzymatic evidence of acute myocardial infarction. Ninety-six of these 101 patients had increased myocardial uptake of the technetium stannous pyrophosphate and positive myocardial scintigrams; there was nearly precise correlation between the ECG and myocardial imaging localization of the area of infarction for acute transmural myocardial infarctions. In the five patients with negative myocardial images the scintigrams were obtained after seven or more days had elapsed following the myocardial infarction. In the remaining 101 patients no clinical, ECG, or enzymatic evidence of infarction developed; 92 of these patients had negative myocardial scintigrams. Seven of the remaining nine patients were admitted with "unstable angina pectoris" and despite the absence of diagnostic ECG and enzyme evolution each of these patients had faintly and diffusely positive myocardial scintigrams. The remaining two patients had positive myocardial scintigrams but no definite ECG or enzymatic evidence of acute myocardial infarction. Thus the technetium pyrophosphate imaging technique appears safe, inexpensive and to correlate well with ECG and enzyme identification of the presence of infarction and with ECG localization of myocardial infarction. In addition the positive myocardial scintigrams in some patients with "unstable angina" suggest that there may be limited myocardial necrosis that is ordinarily undetected by ECG and enzymes in these patients. The incidence of false positive and false negative scintigrams appears to be small.

Additional Indexing Words:
Myocardial imaging
Acute myocardial infarction

The diagnosis of acute myocardial infarction has traditionally depended on the presence of certain electrocardiographic and enzymatic abnormalities that evolve in an expected manner usually over a period of several days. It is well recognized, however, that precise electrocardiographic documentation of myocardial infarction is difficult if not impossible in patients with subendocardial myocardial infarctions, in those with left bundle branch block, and in some with a previous myocardial infarction. In addition, a few patients with acute myocardial infarction have a very rapid and others a very delayed or occasionally no evolution of their electrocardiogram, again making absolute identification of myocardial infarction sometimes difficult. Cardiac enzyme abnormalities are not so specific for myocardial damage that enzyme elevations in any individual patient might not be due to congestive heart failure, hemolysis, brain or pulmonary damage, intramuscular injections, etc.

Therefore, the development of additional diagnostic techniques capable of identifying the presence of myocardial infarction with near certainty would be of help in caring for patients with chest pain of varying etiology. Furthermore, with the development of new medical and surgical techniques designed to salvage ischemic myocardium, better methods are needed to rapidly determine not only the presence but perhaps even more importantly the loca-
tion and extent of the myocardial damage in order to evaluate the potential effectiveness of physiological and pharmacological interventions designed to limit the extent of myocardial damage occurring during infarction.\textsuperscript{1-4} Accordingly, the present study was performed to evaluate the ability of technetium-99m stannous pyrophosphate (\textsuperscript{99m}Tc-PYP) myocardial scintigrams to identify the presence and location of acute myocardial infarction in patients admitted to a coronary care unit with chest pain of varying etiology. Our initial experience in 23 patients studied with this imaging procedure has previously been reported.\textsuperscript{5}

Material and Methods

Two hundred and two patients admitted to Parkland Memorial Hospital, Dallas, Texas with chest pain of varying etiology were studied. Approximately half of these patients were imaged at their bedside in the coronary care unit utilizing a portable Nuclear Data scintillation camera; the others were done in the Nuclear Medicine Department using a Scare Radiographics Inc. Pho/Gamma HP scintillation camera* with a 16,000-hole "high resolution" collimator. Each patient was imaged in the anterior, lateral, and one or more left anterior oblique projections one hour after the intravenous injection of 15 mCi \textsuperscript{99m}Tc tagged to 5 mg of stannous pyrophosphate (PYP)\# with continuous ECG monitoring. Informed consent was obtained from each patient. No arrhythmia or obvious side effects were observed from either the injection of the radionuclide or from the imaging process itself. The imaging time for 3 to 5 views was approximately 15 min.

The initial myocardial images were obtained from 12 hr to 14 days after the onset of chest pain resulting in admission to the coronary care unit. The scintigrams were graded from zero to 4+, depending on the activity over the myocardium, by one of the authors (RP) without prior knowledge of the clinical diagnosis of the patient. Zero represented no activity and a negative myocardial scintigram (fig. 1A); 1+ was considered to be questionable, but not absolutely definite, activity and was also considered to be a negative scintigram; 2+ was considered to represent definite but faint activity and a positive myocardial scintigram (fig. 1B); 3+ and 4+ represented definite and increased activity within the myocardial image (fig. 1C). In those scintigrams considered to be positive (2+, 3+ and 4+) the area of increased uptake was also described, i.e., anterior, inferior, lateral, or true posterior.

The electrocardiographic diagnosis and location of myocardial infarction was made by one of the authors (JW) without prior knowledge of what the \textsuperscript{99m}Tc-PYP myocardial scintigrams showed. The information regarding ECGs, enzymes and scintigrams was then correlated.

Results

Acute myocardial infarction was recognized in these patients on the basis of clinical history, typical electrocardiographic evolution, and abnormal and evolving cardiac enzymes. Specifically acute transmural myocardial infarction was recognized electrocardiographically by documenting the presence of ST-segment elevation, T wave inversion, and the subsequent development of significant Q waves (0.04 sec) in the ECG leads reflecting the area of damage. Acute subendocardial myocardial infarction was suggested on the electrocardiogram by prominent ST depression and T wave inversion and subsequent return of these abnormalities to baseline.

Two hundred and two patients had technetium-99m stannous pyrophosphate myocardial scintigrams performed. The mean age of these patients was 56 ± 1.1 (se); 140 were males and 62 females. The initial imaging was performed 12 hr to 14 days after the onset of chest pain suggesting myocardial infarction (mean 76 ± 3.7 hr). One hundred and one of these patients had clinical and subsequently evolved electrocardiographic evidence of acute myocardial infarction. Forty-two patients had anterior or anterolateral infarction (mean age 57 ± 2.9 yr; time of myocardial imaging 73 ± 8.4 hr after infarction), 38 had inferior, inferoposterior or inferolateral infarctions (mean age 57 ± 2.4 yr; time of myocardial imaging 78 ± 7.6 hr after infarction), three had true posterior infarctions and 18 had subendocardial (nontransmural) infarctions (mean age 64 ± 3.5 yr; time of myocardial imaging 64 ± 4.3 hr after infarction) (table 1). The myocardial scintigrams were positive in 96 of the 101 patients with myocardial infarction. Each of the initial images in these 96 patients was obtained no sooner than 12 hr and no later than six days after symptoms suggestive of myocardial infarction. Five patients with ECG and enzymatic evidence of myocardial infarction

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\*The scintillation camera is interfaced to a PDP-81 computer with 12 K of core. Images are placed on seven track magnetic tape for later retrieval. The computer processing utilizes image enhancement to help define the lesion.

\#1MP401B (stannous pyrophosphate), Mallinckrodt Chemical Works, St. Louis, Mo.

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Figure 1

Myocardial scintigrams obtained after \textsuperscript{99m}Tc-PYP injection are shown. Panel A is a negative myocardial scintigram; Panel B shows 2+ activity; Panel C demonstrates 4+ myocardial uptake of \textsuperscript{99m}Tc-PYP.
had negative myocardial scintigrams (three with anterior or anterolateral and two with inferior or inferolateral myocardial infarctions); in each of these patients the scintigrams were obtained more than seven days after myocardial infarction (mean 288 hr). The correlation between the ECG and myocardial scintigram localization of infarction is shown in table 1. There was nearly precise correlation between the ECG and scintigram localization of infarction for the transmural infarctions; in fact in only seven instances was there a discrepancy between the area of damage on ECG and that noted on scintigram. However, subendocardial (nontransmural) myocardial infarctions could not always be precisely localized with the scintigram (table 1). Representative scintigraphic examples of each of the different types of myocardial infarction are shown in figure 2. In no instance in this study was it necessary to utilize computer processing of the myocardial scintgram to determine whether the scintigram was positive or negative.

While the $^{99m}$Tc-PYP myocardial scintigrams tended to become positive within 12 hr after myocardial infarction, they generally became increasingly positive over the first 24–48 hr after myocardial infarction (fig. 3). The reason that the $^{99m}$Tc-PYP myocardial scintigrams tend to become increasingly positive over the first two days after infarction is uncertain but several potentially important therapeutic considerations may be involved in the answer to this question. For instance, does the fact that these scintigrams become increasingly positive imply that there is a continual loss of myocardial cells after myocardial infarction for 24 to 48 hr? Alternatively, does the fact that the scintigrams become increasingly more positive over the first two days simply relate to the mechanism of the positive $^{99m}$Tc-PYP myocardial scintigrams in

![Figure 2](http://circ.ahajournals.org/)

**Figure 2**
Representative $^{99m}$Tc-PYP myocardial scintigrams of the different types of transmural myocardial infarction are shown. The panel on the left in each horizontal row is the anteroposterior view; the one in the middle the anterior oblique view; and the one on the right the left lateral view. Panels 1a, 1b, and 1c demonstrate an anterior myocardial infarction; panels 2a, 2b, and 2c show an inferior myocardial infarction; panels 3a, 3b, and 3c show an anterolateral myocardial infarction; and panels 4a, 4b, and 4c show a true posterior myocardial infarction.

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Serial myocardial scintigrams were obtained in 34 patients who had myocardial infarctions. In 20 patients the myocardial scintigrams had become either much less positive or absolutely negative (mean 370 ± 173.1 hr after the initial study). In 13 patients, however, the repeat scintigrams had not changed the intensity of their activity at the time of the second scintigram (mean 203 ± 45.5 hr after the initial one). One patient had a repeat myocardial scintigram that was technically unsatisfactory.

One hundred and one patients did not develop clinical or electrocardiographic evidence of acute myocardial infarction (mean age 55 ± 1.9 yr; time of myocardial imaging 75 ± 4.1 hr after infarction). Ninety-two of these patients had negative myocardial scintigrams. Seven of the remaining nine patients were admitted to the coronary care unit with a clinical diagnosis of “unstable angina pectoris” (mean age 54 ± 1.7 yr; time of imaging 50 ± 12.6 hr after onset of chest pain). Although there was no enzymatic or electrocardiographic evolution suggestive of myocardial infarction, each of these patients had a faintly but definitely positive myocardial scintigram; these scintigrams were typically 2+ in activity and positive diffusely (fig. 4). Six of these patients underwent cardiac catheterization; each had significant coronary artery disease. The seventh patient had suffered a previous inferior myocardial infarction and had been readmitted with “unstable angina pectoris.” He refused cardiac catheterization, however. The remaining two patients were admitted to the coronary care unit with chest pain and each subsequently had a positive myocardial scintigram. Neither had “unstable angina pectoris” however, and neither evolved ECG or enzymatic evidence of myocardial infarction. Whether these two patients had false positive myocardial scintigrams or whether the scintigram was more sensitive in identifying myocardial damage than the ECG or enzymes is presently uncertain.

Two of the 101 patients with clinical, ECG and enzymatic evidence of myocardial infarction with initially-positive myocardial scintigrams developed clinical, ECG, and enzymatic evidence of extension of their infarction 10 to 12 days after the original infarc-

The increase in intensity of the $^{99m}$Tc-PYP myocardial uptake that occurs with time in most patients with acute transmural myocardial infarctions is shown. The top panels demonstrate the faintly positive $^{99m}$Tc-PYP myocardial scintigram approximately ten hours after myocardial infarction, the middle panels the more intensely positive scintigram obtained three days after infarction, and the bottom two panels the marked reduction of $^{99m}$Tc-PYP myocardial uptake seven days after infarction.

The faintly and diffusely positive $^{99m}$Tc-PYP uptake (2+ myocardial scintigram) seen in one-third of the patients with “unstable angina pectoris” and also seen in patients with acute subendocardial myocardial infarction. In this particular patient with “unstable angina” the increased $^{99m}$Tc-PYP uptake is apparent in all three views, but in some other patients the increased uptake is seen in only one view.

the first place? That is, is more calcium deposited intracellularly in irreversibly damaged myocardial cells as a consequence of increased collateral coronary blood flow reaching this area during this time period? These questions need answering in the immediate future.

Figure 3

Figure 4
tion. The repeat myocardial scintigram demonstrated the new area of myocardial damage (fig. 5).

Discussion

The data demonstrate that myocardial scintigrams obtained in patients utilizing $^{99m}$Tc-PYP identify the presence of acute myocardial infarction. The timing of the scintigraphic examination is of crucial importance, however, as the images are positive beginning as early as 12 hours after myocardial infarction and they remain positive at the time of repeat scintigram for at least six days after infarction. Scintigrams obtained prior to 12 hours and/or after six or more days following infarction may be negative. We presume that the reason for the positive myocardial scintigrams after myocardial infarction is that the pyrophosphate combines with hydroxyapatite which is itself deposited near mitochondria in irreversibly damaged myocardial cells.5-6 This formulation suggests that a small area of myocardium without any blood supply at all might not be visualized by the technetium pyrophosphate myocardial scintigram since at least some collateral coronary blood flow will be necessary for intracellular calcium deposition to occur and for $^{99m}$Tc-PYP to reach the area. This hypothesis still remains to be proved, however.

Previous investigations conducted in our laboratory have demonstrated that $^{99m}$Tc-PYP scintigrams are positive in dogs with experimental myocardial infarction.9 In these studies the experimental infarction became visible on the scintigram beginning approximately 12 hours after infarction and from 45 to 60 minutes after the injection of the radionuclide. Localization persisted unchanged at the time of repeat scintigrams for approximately 4–6 days but began to fade thereafter, ordinarily becoming negative by the fourteenth postinfarction day. Thus there is excellent agreement between the results obtained in experimental animals and those obtained in this relatively large number of patients with acute myocardial infarction. It should be pointed out that some patients retain positive $^{99m}$Tc-PYP myocardial scintigrams for a period longer than six days. We are presently trying to determine why some patients' scintigrams become negative at six days or immediately after while others remain faintly positive for longer periods of time.

$^{99m}$Tc-PYP appears to be an ideal agent for the performance of myocardial scintigrams in patients for several reasons. It is given intravenously which is a major advantage over any radionuclide that requires intracoronary injection for myocardial imaging. It appears to be safe, is inexpensive, identifies extension of a myocardial infarction when it occurs and its relatively short half-life (approximately six hours) allows scintigrams to be repeated at 24–48 hour intervals if necessary or desirable. Additionally, these scintigrams are positive relatively early in the course of myocardial infarction thus allowing a precise and early diagnosis of myocardial infarction to be made in patients with chest pain of varying etiology. However, since the scintigrams tend to become increasingly positive over the first 24 to 48 hours after myocardial infarction in patients, any scintigram that is equivocal or negative a few hours after infarction should be repeated 24 to 48 hours later if there is a strong clinical suspicion of myocardial infarction.

$^{99m}$Tc-PYP and other phosphates have been used as bone scanning agents for several years.10,11 The uptake of $^{99m}$Tc-PYP in the skeleton of the chest helps to serve as a reference point for localization of the area of myocardial infarction. In our studies it is anticipated that computer processing will be used to subtract some of the bone uptake in the very rare instances in which it presents a problem of being potentially confused with myocardial uptake, but in the patients reported in this study computer processing was not utilized.

Previously, other agents have been used to obtain myocardial scintigrams in patients and experimental animals with myocardial infarction.12-17 Technetium-99m tetracycline13 has recently been shown to identify the presence of myocardial infarction in a relatively

Figure 5

The $^{99m}$Tc-PYP myocardial scintigrams obtained from a patient whose myocardial infarction extended are shown. The top two panels demonstrate the original small anterior myocardial infarction; the bottom two panels show the extension of the myocardial infarction ten days later.
small number of patients but has the disadvantage of labeling the liver so that diaphragmatic or inferior myocardial infarctions may be difficult to visualize. Additionally, the tetracycline images are apparently not positive until approximately 24 hours after infarction and an additional 24 hours after the injection of \(^{99m}\text{Tc}\)-tetracycline is necessary for optimal imaging concentration in the infarct. Therefore, a longer period of time appears to be required before one can make a scintigraphic diagnosis of myocardial infarction using \(^{99m}\text{Tc}\)-tetracycline than is necessary with \(^{99m}\text{Tc}\)-PYP. Other agents including \(^4\text{K}\), long chain fatty acids, glucoheptonate and \(^67\text{gallium}\), have also been utilized for myocardial imaging but the relatively high cost, the fact that some have less than an ideal abnormal-to-normal myocardial tissue ratio, that some identify normal myocardium leaving abnormal myocardium as a void, and that some require intracoronary injection have thus far limited their clinical usefulness.

It was of interest to find that seven patients in this study with “unstable angina pectoris” had faintly but definitely positive myocardial scintigrams (fig. 4). In these patients the ECG was only nonspecifically abnormal and enzymes were not diagnostically elevated. The exact reason that the scintigrams were positive in these patients is uncertain but several possibilities deserve mention. The positive myocardial scintigrams might have been due to a myocardial infarction in the distant past and the faint \(^{99m}\text{Tc}\)-PYP uptake a reflection of that. Such positive scintigrams also might indicate that there is a continual loss of small diffuse amounts of myocardial tissue in patients with “unstable angina pectoris.” Finally it remains possible that \(^{99m}\text{Tc}\)-PYP myocardial scintigrams may be positive in some patients with severe myocardial ischemia, such as occurs in patients with “unstable angina pectoris.” The lack of histological information in these patients precludes providing a definite answer presently but the data raise the unanswered question of whether this myocardial imaging technique is more sensitive in some instances than the electrocardiogram in identifying the presence of myocardial necrosis.

In summary this study documents that \(^{99m}\text{Tc}\)-PYP scintigrams are positive in patients with acute myocardial infarction when the scintigrams are obtained within 12 hours to six days after myocardial infarction. While the scintigrams tend to become positive within 12 hours after infarction, they tend to become increasingly positive over the first 24 to 48 hours after infarction. The location of the myocardial damage on ECG and \(^{99m}\text{Tc}\)-PYP myocardial scintigram correlates almost precisely for acute transmural myocardial infarctions. The presence of subendocardial myocardial infarction can be identified but its exact location cannot always be precisely determined. On the basis of the data obtained in this study this imaging procedure also appears safe, inexpensive, identifies extension of a recent myocardial infarction and should be of additional help in substantiating the presence or absence of transmural and subendocardial myocardial infarction in patients. Its usefulness in sizing acute myocardial infarction will have to be determined in the future.

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