Acute Subendocardial Myocardial Infarction in Patients
Its Detection by Technetium 99-m Stannous Pyrophosphate Myocardial Scintigrams

By James T. Willerson, M.D., Robert W. Parkey, M.D., Frederick J. Bonte, M.D., Steven L. Meyer, M.D., and Ernest M. Stokely, Ph.D.

SUMMARY
Eighty-eight patients admitted to a coronary care unit with chest pain of varying etiology but without ECG evidence of an acute transmural myocardial infarction had myocardial scintigrams using technetium-99m stannous pyrophosphate (\textsuperscript{99m}Tc-PYP). Seventeen of these patients had ECG and enzymatic evidence suggestive of acute subendocardial myocardial infarction. In each of these the scintigrams were positive demonstrating increased \textsuperscript{99m}Tc-PYP uptake either in a faintly but diffusely positive pattern or in a well-localized strongly positive one. The remaining 71 patients did not evolve ECG or enzymatic evidence of acute myocardial infarction. In each of these patients the myocardial scintigram was negative. Thus \textsuperscript{99m}Tc-PYP myocardial scintigrams are capable of identifying the presence of acute subendocardial myocardial infarction in patients. The absolute frequency with which subendocardial myocardial infarction can be recognized utilizing this technique will have to be established in a larger number of patients in the future.

Additional Indexing Words:
Myocardial infarction Myocardial scintigrams Subendocardial infarction

ON STRICTLY CLINICAL GROUNDS it is difficult to make a positive identification of acute subendocardial myocardial infarction in patients. The diagnosis from the electrocardiographic point of view depends on the presence of deep ST-segment depression and inverted T waves, but these ECG abnormalities, even when present, are not necessarily specific for subendocardial infarction. The only evolution of this abnormal pattern is for the depressed ST-segment to return to baseline and the T waves to become upright over a period of days to weeks after infarction. Cardiac enzymes are depended upon to substantiate the diagnosis of subendocardial infarction but even when elevated their elevation does not necessarily reflect cardiac damage. Since the subendocardial portion of the heart is the area most vulnerable to myocardial ischemia in experimental animals,\textsuperscript{1,2} it seems possible that subendocardial infarction might be a relatively common type of infarction in patients. However, because of the difficulty in recognizing subendocardial infarctions clinically it is probable that some patients with subendocardial infarction have gone undetected in the past and others without infarction have been falsely identified as having had one.

Thus the development of diagnostic methods capable of identifying the presence of subendocardial infarction with greater certainty than is presently possible would be of additional clinical help. Accordingly we have utilized technetium-99m stannous pyrophosphate (\textsuperscript{99m}Tc-PYP) to obtain myocardial scintigrams in 88 patients admitted to the coronary care unit\textsuperscript{*} with chest pain of varying etiology in whom the initial electrocardiograms did not reveal evidence of acute transmural myocardial infarction. The purpose of this study was to identify the value of \textsuperscript{99m}Tc-PYP myocardial scintigrams in recognizing the presence of acute subendocardial infarction in patients.

\textsuperscript{*}Parkland Memorial Hospital, Dallas, Texas.
Materials and Methods

Each of these 88 patients was admitted to the coronary care unit at Parkland Memorial Hospital with chest pain suggestive of the possibility of myocardial infarction. The patients were studied at their bedside in the coronary care unit utilizing a portable Nuclear Data scintillation camera within the first few days after admission. Some patients also had myocardial scintigrams performed in the nuclear medicine department using a Searle Radiographics Inc. Pho/Gamma HP scintillation camera with a 16,000 hole "high resolution" collimator. This scintillation camera is interfaced to a PDP-8 I computer with 12 K of core. Images are placed on 7 track magnetic tape for later retrieval. The computer processing utilizes image enhancement to help to precisely define the lesion. Each patient was imaged in the anterior, lateral, and one or more left anterior oblique projections 45 minutes to one hour after the intravenous injection of 15 mCi of $^{99m}$Tc tagged to 5 mg of stannous pyrophosphate (PYP)* with continuous ECG monitoring. Informed consent was obtained from each patient. Neither arrhythmia nor obvious side effects were observed from either the injection of the radionuclide or from the imaging process itself. The imaging time for 3-5 views was approximately 15 minutes.

The initial myocardial images were obtained 1-3 days after the onset of chest pain suggesting possible myocardial infarction. The scintigrams were graded from zero to 4+ depending on the activity over the myocardium by one of the authors (R.P.) without prior knowledge of the clinical condition of the patient. Zero represented no activity and a negative myocardial scintigram; 1+ was considered to be questionable activity; 2+ represented definite but faint activity and a positive myocardial scintigram; 3+ and 4+ represented definite and increased activity within the myocardial scintigram. In this study as well as in previous ones, we have regarded 2-4+ myocardial scintigraphic uptake as representing a positive myocardial scintigram. In those scintigrams that were positive, the area of increased uptake was also described as being anterior, inferior, lateral, or true posterior.*

Results

Seventeen patients with electrocardiograms suggestive of subendocardial ischemia or infarction had $^{99m}$Tc-PYP myocardial scintigrams obtained (table 1). The mean age of these patients was 64.3 ± 3.26 (SE) years; nine were males and the remainder females. The initial scintigrams were obtained 64 ± 4.34 hours after the onset of chest pain suggesting the possibility of myocardial infarction. Each of these patients had prominent ST depression and or prominent T wave inversion electrocardiographically consistent with subendocardial ischemia or infarction (fig. 1). The only ECG evolution in these 17 patients was a return to baseline of the deep ST depression over a period of several days. Cardiac enzymes were elevated in all of these patients (either serum glutamic oxaloacetic transaminase or creatine phosphokinase or both) and subsequently evolved in the expected manner for acute myocardial infarction. In these patients there was not another obvious reason for the enzyme elevation other than myocardial infarction. The myocardial scintigrams were positive in each of these 17 patients with subendocardial infarction (figs. 2, 3, and 4) (table 1). The patterns of radionuclide activity varied from a faintly but diffusely positive uptake in 11 patients (figs. 2 and 3) to prominent and apparently more localized uptake in six patients (fig. 4). In the six patients with subendocardial infarction with well localized $^{99m}$Tc-PYP myocardial uptake the correlation between ECG and scintigraphic localization is shown in table 2. Serial follow-up myocardial scintigrams demonstrated a decrease in the myocardial uptake of $^{99m}$Tc-PYP in six patients (second scintigram obtained 369 ± 173.1 hours after initial one) and unchanged uptake in four (second scintigram obtained 203 ± 45.5 hours after initial one). The remaining seven patients did not have repeat myocardial scintigrams obtained. None of these patients died so that histological data are not available.

The remaining 71 patients did not subsequently evolve electrocardiographic or enzymatic evidence of myocardial infarction. Their mean age was 54.6 ± 1.89 years; 44 were males and the remainder females. The mean time of myocardial imaging in these patients was 75.4 ± 4.09 hours after the onset of chest pain resulting in their hospital admission. The discharge diagnoses in these patients were angina pectoris 54 patients; pericarditis, four patients; primary myocardial disease, one patient; cardiac arrest of unknown etiology, two patients; aortic stenosis, one; mitral regurgitation, one; hypertension, two patients; congestive heart failure, one patient; cerebrovascular accident, one patient; polyarteritis nodosa, one

*MP4018 (stannous pyrophosphate), Mallinckrodt Chemical Works, St. Louis, Mo.
Table 1

Patients with Acute Subendocardial Myocardial Infarction

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>ECG localization of infarction</th>
<th>Time myocardial scintigram performed after infarction (hr)</th>
<th>Myocardial scintigram</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.D.</td>
<td>60/M</td>
<td>Subendocardial</td>
<td>48</td>
<td>3+ high lateral</td>
</tr>
<tr>
<td>E.S.</td>
<td>63/F</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>K.L.</td>
<td>44/M</td>
<td>Subendocardial</td>
<td>96</td>
<td>3+ posterior</td>
</tr>
<tr>
<td>A.D.</td>
<td>63/M</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>W.W.</td>
<td>80/M</td>
<td>Subendocardial</td>
<td>72</td>
<td>4+ inferolateral</td>
</tr>
<tr>
<td>H.M.</td>
<td>60/M</td>
<td>Subendocardial</td>
<td>72</td>
<td>2+ anterior diffuse</td>
</tr>
<tr>
<td>L.J.</td>
<td>52/M</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>R.M.</td>
<td>63/M</td>
<td>Subendocardial</td>
<td>48</td>
<td>3+ posterior</td>
</tr>
<tr>
<td>L.C.</td>
<td>52/F</td>
<td>Subendocardial</td>
<td>72</td>
<td>2+ inferolateral, diffuse</td>
</tr>
<tr>
<td>C.M.</td>
<td>44/F</td>
<td>Subendocardial</td>
<td>96</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>C.R.</td>
<td>82/F</td>
<td>Subendocardial</td>
<td>48</td>
<td>3+ anterior</td>
</tr>
<tr>
<td>E.W.</td>
<td>80/M</td>
<td>Subendocardial</td>
<td>72</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>J.N.</td>
<td>91/F</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>M.E.</td>
<td>66/F</td>
<td>Subendocardial</td>
<td>72</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>C.G.</td>
<td>76/F</td>
<td>Subendocardial</td>
<td>72</td>
<td>3+ posterior</td>
</tr>
<tr>
<td>L.V.D.</td>
<td>58/M</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
<tr>
<td>D.D.</td>
<td>50/F</td>
<td>Subendocardial</td>
<td>48</td>
<td>2+ diffuse</td>
</tr>
</tbody>
</table>

Figure 2

The top panel demonstrates a myocardial scintgram obtained in an anteroposterior projection (ANT) from a patient with a subendocardial infarction. Note the diffuse and relatively faint uptake of 99mTc-PYP in the scintgram. The bottom panel demonstrates a negative myocardial scintgram obtained from a patient without myocardial infarction for comparison.
patient; Parkinson’s disease, one patient; syncope etiology unknown, one patient; and chest wall trauma, one patient. In each of these patients the myocardial scintigram was negative.

Discussion

The data obtained in these patients demonstrate that acute subendocardial infarction can be recognized in at least some patients utilizing 99mTc-PYP myocardial scintigrams. In the patients in this study that had ECGs suggestive of subendocardial myocardial infarction and subsequent evolution of at least one of the cardiac enzymes, the myocardial scintigrams were positive. The pattern of uptake of 99mTc-PYP in the heart varied from being diffusely and faintly positive to being well localized and strongly positive. Just as is the case for 99mTc-PYP myocardial scintigrams in patients with acute transmural myocardial infarction, there is a tendency for the scintigram to become less positive or negative seven or more days after infarction. It has not been possible to accurately localize the area of myocardial damage in most patients with subendocardial infarction from the positive myocardial scintigram; this is in contrast to the ability to localize fairly precisely the area of damage in transmural myocardial infarctions.

The reason for positive myocardial scintigrams in patients with acute subendocardial infarctions as well as in those with acute transmural myocardial infarctions is presumably due to the incorporation of the pyrophosphate into hydroxyapatite which is itself deposited near the region of mitochondria in irreversibly damaged cells after myocardial injury.

However this hypothesis remains to be proven and more importantly we are not yet certain that some ischemic but not necessarily irreversibly damaged cells do not label with 99mTc-PYP. 99mTc-PYP and other phosphates have been used as bone-scanning agents for several years. Earlier investigations conducted in our laboratory demonstrated that 99mTc-PYP myocardial scintigrams are positive in dogs with experimental myocardial infarction; in experimental animals the myocardial scintigrams become positive approximately 12–14 hours after infarction and become less positive or negative 7–14 days later. Earlier studies have also suggested that the 99mTc-PYP myocardial scintigram may be negative in patients with acute transmural myocardial infarction if one waits more than six days after infarction to perform the test. False positive scintigrams might occur in breast tumors, healing rib fractures, and or possibly in some patients with myocardial necrosis not based on coronary artery disease, but the frequency with which any of these are mistaken for myocardial infarction is presently uncertain.

Other agents have been used in the past for myocardial imaging and at least one, technetium-99m
tetracycline, has been utilized to perform myocardial scintigrams in a few patients with nontransmural myocardial infarction. The $^{99m}$Tc-PYP appears to have certain advantages over other imaging agents that have been studied; however, it becomes positive relatively early after infarction, is inexpensive, safe, does not label the liver (making identification of diaphragmatic or inferior myocardial infarctions relatively easy), and it is given intravenously. Technetium-$^{99m}$ tetracycline has the advantage that it may also be given intravenously but the disadvantage of not becoming positive until 24 hours after infarction and an additional 24 hours after the injection of $^{99m}$Tc tetracycline is necessary for optimal imaging concentration in the infarct.

In summary, the data obtained in this study suggest that $^{99m}$Tc-PYP myocardial scintigrams identify the presence of acute subendocardial myocardial infarction in patients. Thus this myocardial imaging procedure should be of diagnostic help in identifying whether ST-segment depression on the ECG implies subendocardial infarction in patients admitted to the hospital with chest pain of varying etiology. However, the exact frequency with which $^{99m}$Tc-PYP myocardial scintigrams are positive in patients with subendocardial infarction and how often the scintigrams are positive in patients with histological evidence of subendocardial infarction but equivocal cardiac enzyme changes and electrocardiograms will have to be determined in a larger number of patients in the future.

Acknowledgments

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References


6. **Shen AC, Jennings RB**: Kinetics of calcium accumulation in acute myocardial ischemic injury. Am J Pathol 67: 441, 1972

7. **Subramanian G, McAfee JC, Bell EG, Blaha RJ, O’Mara RE, Ralston PH**: 99mTc-labeled polyphosphate as a skeletal imaging agent. Radiology 102: 701, 1972


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