Follow-up Technetium-99m Stannous Pyrophosphate
Myocardial Scintigrams after Acute Myocardial Infarction

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SUMMARY Technetium-99m stannous pyrophosphate (99mTc-PYP) myocardial scintigrams were obtained in 68 patients during acute myocardial infarction (AMI) and at follow-up 15.9 ± 8.8 weeks later. All patients with AMI had a positive scintigram (2+ or greater); only one of 46 control patients (2%) had a positive (2+) scintigram. At follow-up scintigraphy 6 to 37 weeks following AMI, 57% of patients had a persistently positive scintigram even though recurrent AMI was suspected in only one of these patients. Patients with persistently positive scintigrams tended to have more severe disease as evidenced by compensated congestive heart failure (41%), persistent angina (77%), and ECG evidence of ventricular dyssnergy (51%). We conclude that 1) in patients with prior AMI, a 2+ abnormality on 99mTc-PYP scintigrams may not represent new AMI; 2) a persistently positive 99mTc-PYP scintigram may have prognostic implications since it occurs predominantly in patients with severe symptomatic coronary disease.

THE USEFULNESS OF MYOCARDIAL IMAGING by various radionuclides in the diagnosis of acute myocardial infarction (AMI) in man has been demonstrated.1-9 It has been suggested that “hot spot” imaging agents such as technetium-99m stannous pyrophosphate (99mTc-PYP) may be helpful in separating acute from remote myocardial infarction.9,10 This hypothesis is based on observations of myocardial scintigrams in patients and animals studied during the first two weeks following AMI.5,4,11,12

Recently, however, several groups have reported positive 99mTc-PYP scintigrams in patients with left ventricular aneurysms or segmental dysfunction who did not have evidence of recent myocardial infarction, thus challenging the concept that 99mTc-PYP scintigrams can always discriminate between chronic and acutely infarcted myocardium.13-15 To further investigate this question, the present study was undertaken to assess the value and limitations of

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greater than 1 mm above the baseline defined by the T-P segment in at least two leads was defined as probably representing left ventricular dyssynergy.

Myocardial imaging using $^{99m}$Tc-PYP was performed in all 68 patients $3.0 \pm 1.1$ days after the onset of the AMI. Nineteen of the 68 patients (28%) had a second scintigram $12.6 \pm 2.8$ days after their acute infarction prior to their discharge from the hospital. None of these 19 patients had any clinical evidence of extension of their infarction prior to their discharge scintigram. However, it is possible that silent extension of myocardial infarction may have occurred in some of these patients prior to their discharge scintigram.15

All 68 patients had a follow-up myocardial scintigram on an ambulatory basis $15.9 \pm 8.8$ weeks (range 6–37 weeks) after their myocardial infarction. During the interval between acute infarction and the follow-up myocardial scintigram, no patient had any symptoms suggesting recurrent myocardial infarction or unstable angina pectoris.

Myocardial imaging was performed in the anterior, 45° left anterior oblique, and left lateral positions two hours after the intravenous injection of $20 \text{ mCi of }^{99m}$Tc-PYP. The radiopharmaceutical was prepared from a Squibb Pyrophosphate Kit and a Squibb Mo-Tc Generator. Chromatography was performed prior to each injection. The preparation was developed with 85% Methanol on Whatman #1 paper to detect free technetium and with saline on silica gel impregnated glass fiber sheet to separate reduced forms of technetium. In all studies, the free technetium was less than 1%, and the reduced hydrolyzed technetium was less than 5%. These methods of chromatography were chosen to document the labeling efficiency and chemical purity of the radiopharmaceutical.

Myocardial scintigrams were recorded using a Searle Pho/Gamma HP scintillation camera with a Divcon collimator in the converging mode. Each view contained 500,000 counts which were obtained over 100–200 seconds with a 20% window and the photo peak centered on 140 keV.

Myocardial scintigrams were classified according to the distribution and intensity of radioactivity in the area of the left ventricle. Regional uptake was considered when activity could be accurately localized to an anatomical wall of the left ventricle (anterior, inferior, lateral, etc.). Diffuse uptake was assigned when the anatomical location was indeterminant.

The intensity of activity was graded from 0 to 3+. Zero activity indicated no activity in the area of the left ventricle. An intensity of 1+ was assigned for activity less than that of the ribs, 2+ for activity equal to or greater than rib activity, and 3+ for activity equal to or greater than sternal activity (fig. 1). A scintigram with 2+ or greater activity in at least two views was considered positive.

For comparing the follow-up scintigrams with the initial scintigram, a scoring system was used. Follow-up scintigrams were interpreted as being improved if there was a decrease in the intensity of the activity or if there was a change in the distribution pattern from a regional pattern to a diffuse pattern; the follow-up scintigram was also interpreted as improved if the area of activity was diminished. Follow-up scintigrams were interpreted as unchanged if there was no change in the intensity, distribution, or area of activity. Follow-up scintigrams were interpreted as being worse if there was an increase in intensity of the activity or if there was a new regional distribution pattern. In addition, a negative scintigram prior to discharge but positive at follow-up was interpreted as being worse.

The scintigrams were interpreted by two independent observers who had no knowledge of the patients' status or previous history. If there was any disagreement in the interpretation, the scintigram was assigned the lower score. There was complete agreement between the two independent observers in 90% of the myocardial scintigrams interpreted.

In addition to a follow-up myocardial scintigram, all 68 patients had a follow-up clinical evaluation by a cardiologist unaware of the results of the myocardial scintigrams, blood drawn for serum CPK, SGOT, LDH, and HBD analysis, and a 12-lead electrocardiogram. Each patient was assigned a clinical classification according to the New York Heart Association classification.15

Finally, to assess the sensitivity and specificity of $^{99m}$Tc-PYP myocardial imaging, 46 consecutive patients without a history of heart disease and no evidence of infarction by electrocardiography also had a myocardial scintigram following diagnostic bone scanning. These patients included 43 men.
and three women, mean age 55.6 years (range 37–85 years). Myocardial imaging in the control patients was performed in the same manner as for the patients with myocardial infarction. The preparations of $^{99m}$Tc-PYP given to the control patients were from the same lots as those given to the patients with myocardial infarction.

The data are presented as the mean ±1 standard deviation. Student’s t-test and the chi square were utilized to test for significant differences.

Results

Myocardial Scintigraphy during AMI (table 1)

All patients with AMI had a positive $^{99m}$Tc-PYP scintigram during the first week following their infarction. Patients with transmural infarctions tended to have scintigraphic abnormalities which were 3+ in intensity and the distribution pattern was regional, whereas patients with subendocardial infarctions tended to have scintigraphic abnormalities which were 2+ in intensity with a diffuse pattern of distribution. These observations are similar to what other investigators have reported.8,9

Myocardial Scintigraphy in Control Patients (table 1)

Only one of the 46 control patients (2%) had a positive $^{99m}$Tc-PYP scintigram. However, 30% of the control patients had a 1+ diffuse $^{99m}$Tc-PYP abnormality. Thus, in this study a scintigraphic abnormality with 1+ intensity and a diffuse pattern of distribution occurred frequently in patients without AMI.

Myocardial Scintigraphy 2–3 Weeks after AMI (table 2)

Of the 19 patients who had repeat scintigrams 2–3 weeks following AMI, 58% had persistent scintigraphic abnormalities. The scintigraphic abnormalities were either improved or unchanged compared to their appearance during the first week following their infarction.

Myocardial Scintigraphy 6–37 Weeks after AMI (tables 2 and 3)

More than half (57%) of the 68 patients with positive scintigrams and AMI had persistently positive scintigrams 6–37 weeks after AMI (table 2, fig. 2). In comparing the scintigraphic abnormalities obtained during AMI with those at late follow-up, it is notable that in 90% of cases, the scintigraphic abnormalities were either improved or negative (table 2).

Table 3 shows the distribution and intensity of activity in the myocardial scintigrams obtained 6 to 37 weeks after AMI. Positive follow-up scintigrams differed from acute infarction scintigrams in intensity and distribution of activity. Positive follow-up scintigrams were usually 2+ in intensity and had a diffuse distribution pattern. Three of 39 positive scintigrams (8%) at follow-up (table 3) had 3+ activity compared to 40 of 68 patients (59%) during acute infarction (table 1) ($P < 0.001$). Twenty-six of 39 positive scintigrams (67%) at follow-up had a diffuse distribution pattern compared to 16 of 68 scintigrams (24%) during acute myocardial infarction ($P < 0.001$).

In three of the patients with persistently positive scintigraphic abnormalities, the follow-up scintigrams showed greater abnormalities than those seen during AMI. One patient had a strongly positive scintigram during AMI which became negative at discharge. At follow-up six weeks later he had a positive scintigram with 2+ activity localized in the area of AMI (fig. 3). One patient, who had an acute inferior myocardial infarction, developed localized uptake in the anterior wall at follow-up. In the third patient, the scintigram changed from 2+ diffuse activity to 3+ diffuse activity at follow-up. The patient who developed a new area of uptake had elevated enzymes suggestive of recurrent myocardial infarction at the time of the repeat scintigram. The other two patients had normal enzyme studies at the time of follow-up scintigraphy, and none of the three patients had electrocardiographic or clinical evidence of recurrent infarction. Nonetheless, it is possible that the three patients whose scintigrams became more abnormal at follow-up did have

Table 2. Characteristics of $^{99m}$Tc-PYP Scintigrams Obtained Early and Late Following Acute Myocardial Infarction

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Scintigraphic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Early follow-up</td>
<td></td>
</tr>
<tr>
<td>(2–3 weeks post AMI)</td>
<td>19</td>
</tr>
<tr>
<td>Late follow-up</td>
<td></td>
</tr>
<tr>
<td>(6–37 weeks post AMI)</td>
<td>68</td>
</tr>
</tbody>
</table>

In the early follow-up group, six of the persistently positive scintigrams changed from 3+ to 2+ and five changed from a regional to a diffuse pattern. Ten of the 11 scans that were positive at 2 to 3 weeks were also positive at 6 to 37 weeks. One of the eight scans that were negative at 2 to 3 weeks was positive at 6 to 37 weeks.
recurrent AMI which was clinically silent. None of the other patients with persistently positive scintigraphic abnormalities which had either improved or remained unchanged had electrocardiographic, enzymatic, or clinical evidence of recurrent AMI.

Although only 19 of 68 patients (28%) had discharge scintigrams, the results of these early follow-up scintigrams correlated very well with the late follow-up scintigrams obtained in these patients (table 2).

Table 4 shows the clinical status of the patients at follow-up and their follow-up myocardial scintigram. A positive follow-up scintigram was not significantly correlated with the time of follow-up scintigram, transmural versus subendocardial infarction, first versus multiple infarctions, and the location of the infarction, whether anterior or inferior.

The patients with persistently positive scintigraphic abnormalities tended to have more severe disease as evidenced by the persistence of angina (77%), the presence of compensated congestive heart failure (41%), and electrocardiographic evidence of left ventricular dyssnergy (51%) (table 4). Three of three patients with 3+ activity on their follow-up scintigram had ST-segment elevation on their follow-up electrocardiograms.

There was no tendency for the percentage of persistently positive scintigrams to decrease as the interval between AMI and late scintigraphy increased (table 4). Thus, it is possible that if scintigrams following AMI were obtained later, they would also be positive.

**Discussion**

Although recent studies have elucidated the dynamics of Tc-PYP myocardial imaging in the AMI setting, long-term follow-up studies are lacking. In man, detection of myocardial damage can be demonstrated by Tc-PYP 12 hours after the onset of symptoms of AMI. In both man and animals, Tc-PYP scintigrams become increasingly more positive 48–72 hours after the onset of infarction. In the absence of reinfarction or extension of injury, there is a gradual decrease of the extent of radioactivity in the infarction zone six days after the acute infarction.

Willerson and associates performed serial scintigraphy in 34 patients with AMI. Twenty patients (59%) had an improved or negative scintigram at a mean follow-up period of 370 ± 173 hours, and 13 (38%) had no change in their scin-
The top panel shows 3+ regional activity localized to the anterior wall during acute myocardial infarction (positive scintigram). The middle panel indicates zero activity 14 days after infarction (negative scintigram prior to discharge). The lower panel shows 2+ regional activity localized to the anterior wall eight weeks after infarction (worse follow-up scintigram). The patient also has increased costochondral junction activity in two ribs.

Figure 3. The top panel shows 3+ regional activity localized to the anterior wall during acute myocardial infarction (positive scintigram). The middle panel indicates zero activity 14 days after infarction (negative scintigram prior to discharge). The lower panel shows 2+ regional activity localized to the anterior wall eight weeks after infarction (worse follow-up scintigram). The patient also has increased costochondral junction activity in two ribs.

Our study showed that 39 of 68 patients (57%) who had positive myocardial scintigrams during AMI continued to have a positive scintigram at a follow-up period of 6 to 37 weeks. However, 32 of these 39 patients (82%) had an improved scintigram. In these 32 patients, the image pattern was generally characterized by 2+ diffuse activity. These data demonstrate that unless a $^{99m}$Tc-PYP scintigram in a patient with prior myocardial infarction shows a 3+ abnormality, it may not represent AMI. In addition, the diagnosis of new myocardial infarction in patients with persistently positive scintigrams will have to depend on involvement of a new area and/or an increase in activity following some original diminution.

The data from our control patients obtained with quality control of preparation of the radiopharmaceutical and careful control of the imaging technique indicate that 1+ activity on myocardial scintigraphy is nonspecific and should
not be interpreted as myocardial infarction. These data support data reported by other investigators.25, 26 The cause of the 1+ activity on myocardial scintigraphy may be unsuspected blood pool imaging.25

The mechanism for the persistence of positive scintigrams at follow-up in our patients after acute myocardial infarction is speculative. It is reasonable to suggest that the similar mechanism of localization of 99mTc-PYP by calcium apatite-like crystals, which has been proposed by Bonte, as the mechanism for the positive scintigram during acute myocardial infarction, is operative at a remote time, when the infarction is healed.11 Disordered calcium homeostasis with deposition of intramyocardial calcium complexes has been demonstrated experimentally early in the zone of ischemic injury.25 26 Persistently positive 99mTc-PYP scintigrams following AMI may be due to unresorbed calcium complexes in the infarcted area, dystrophic myocardial calcification in a ventricular aneurysm or the presence of ventricular dyssynergy, or continuing cell death occurring in the margins of a previous myocardial infarction.13, 14

The data from our patients are consistent with the early resorption of calcium complexes in the AMI setting. Sixteen of 19 patients (84%) had an improved or negative scintigram 12.6 ± 2.8 days after their acute infarction. Unresorbed calcium complexes in the infarcted area may be responsible for the persistent scintigraphic abnormalities at late follow-up.

Twenty of our 24 patients (83%) with ST-segment elevation at follow-up had a positive scintigram. The ST-segment elevation in these patients probably represents ventricular dyssynergy but may represent myocardial ischemia.27, 28

Our study also showed that patients who are asymptomatic at follow-up were most likely to have a negative scintigram, whereas patients with class III angina or with compensated congestive heart failure were most likely to have a positive scintigram. Positive scintigrams have been described in patients with unstable angina4, 20 21 and in patients with myocardial infarction.29 Recent pathologic studies indicate that continuing cell death occurring in the margins of a previous myocardial infarction might be a reason for a persistently positive myocardial scintigram.13, 14 Whether the positive scintigrams in our patients with class III angina following their myocardial infarction represent new myocardial necrosis, scar tissue, or chronic ischemia is unclear.

The serial myocardial scintigrams in the patient illustrated in figure 3 may represent acute deposition of intramyocardial calcium complexes during acute myocardial infarction (positive scintigram), early resorption of these complexes (negative scintigram at discharge), and dystrophic calcification of the myocardial infarction or persistent silent myocardial necrosis during the late healing phase (positive follow-up scintigram).

The follow-up scintigrams in our study were performed at a time when the myocardial infarction would have been expected to be healed. The incidence of positive scintigrams six to eight weeks after myocardial infarction was not significantly different from the incidence of positive scintigrams 33 to 37 weeks after infarction (table 4). Since 38 of the 39 patients with persistently positive scintigrams at late follow-up did not have clinical, electrocardiographic, or enzymatic evidence of recurrent myocardial infarction, the persistently positive myocardial scintigrams are not likely due to recurrent infarction.

Our data indicate that patients with class III angina, compensated congestive heart failure, or ST-segment elevation on their 12-lead electrocardiogram are more likely to have a positive follow-up scintigram. These data suggest that follow-up myocardial scintigraphy in patients with myocardial infarction may be of potential prognostic value in determining their clinical course. A larger study is needed to determine whether or not a persistently positive scintigraphic abnormality provides independent prognostic information.

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