Sequential Myocardial Scintigraphy with Technetium-99m Stannous Pyrophosphate Following Myocardial Infarction

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Studies have shown that technetium-99m stannous pyrophosphate (Tc-PPi) is effective for the detection and imaging of acute myocardial infarction. Positive Tc-PPi myocardial scintigrams, however, have been reported in patients with other forms of heart disease and no evidence of recent myocardial infarction. To help define the usefulness of this test, we undertook a prospective study to ascertain when Tc-PPi myocardial scintigrams return to normal after myocardial infarction. Twenty patients with acute myocardial infarction were followed with Tc-PPi scintigrams at 1 and 2 wk, and 1, 2, 3, 6, and 9 mo after infarction. The serial scintigrams revealed that a) 15 of 18 scintigrams were positive within the first week after infarction, b) the number of markedly positive scintigrams decreased promptly after the first week, and c) some scintigrams (11 of 18 at 1 mo, and 3 of 18 at 9 mo) remained positive throughout the study. The possible explanations for persistently positive scintigrams are discussed. Persistently positive scintigrams may hinder the usefulness of Tc-PPi myocardial scintigraphy for the diagnosis of acute myocardial infarction in patients who have had a myocardial infarction within the previous 9 mo.

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Recent studies have shown that technetium-99m stannous pyrophosphate (Tc-PPi) is effective for the detection and imaging of acute myocardial infarction in experimental animals and humans (*1,2*). Experimentally infarcted myocardium has been shown to accumulate radioactivity within 12–16 hr after infarction, to reach peak activity 2–6 days after infarction, and have little or no ability to accumulate tracer by 15 days (*1,2*). This technique has proven simple and safe, and has been rapidly applied as a clinical test (*3*). As more clinical data have accumulated, however, some investigators have questioned whether positive Tc-PPi myocardial scintigrams are specific for acute myocardial infarction. Positive Tc-PPi myocardial scintigrams have now been reported in patients with no evidence of recent myocardial infarction but with left-ventricular aneurysm (*4*), unstable ischemic heart disease (*5*), myocardiopathy (*5*), and stable ischemic heart disease (*6,7*).

During the early use of Tc-PPi at this center, positive myocardial scintigrams were also noted in patients with no evidence of recent myocardial infarction, although most did have definite evidence of cardiac disease (*7,8*). To help define the usefulness of this test in the documentation of acute myocardial infarction, we undertook a prospective study to find out when Tc-PPi myocardial scintigrams return to normal after myocardial infarction.

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METHODS

Twenty patients who suffered an acute myocardial infarction between August 1975 and March 1976 were studied. All were males. The age range was 31–85 yr, with a mean of 61. The diagnosis of myocardial infarction was based on clinical history, physical examination, ECG, and serum enzymes, including myocardial-specific fraction of CPK (CPK-MB). The study protocol consisted of Tc-PPi myocardial scintigraphy at the following intervals after myocardial infarction: within 1 wk, 2 wk, 1 mo, 2 mo, 3 mo, 6 mo, and 9 mo.

The myocardial scintigrams were performed 2 hr after the i.v. injection of 15 mCi Tc-99m bound to 20 mg of stannous pyrophosphate*. The binding of the Tc-99m-pyrophosphate complex was confirmed with paper chromatography, and 95% binding was the lower limit accepted before the material was used. The images were recorded by a scintillation camera with high-resolution collimator. Images were recorded in the anterior, left anterior oblique, and left lateral projections.

The scintigrams were graded on a 0–4+ scale after the method of Parkey et al. (*2*). Zero represents no activity; 1+ questionable activity; 2+ definite activity; and 3+ and 4+ increasing degrees of activity, with 2+, 3+ and 4+ considered positive scintigrams. The scintigrams were graded independently and blindly by two observers, and if there was disagreement, the lower grade was used. The scintigrams were graded in a random fashion, but no control scintigrams (patients without myocardial infarction) were included.

Each patient was seen by one of us (F.M.) at the time of each scintigram. If there was any historical suggestion of a recent increase in cardiac ischemia, the study was postponed. Each patient had a routine ECG at the 6- or 9-mo interval to check for "silent" myocardial infarction in the interim.

This study was approved by the Human Experimentation Committees and participants gave informed consent.

RESULTS

Clinical data. Relevant clinical information and serial scintigram scores for each patient are presented in Table 1. Because of the relatively small number of subjects and the lack of precision inherent in such a scintigram-scoring system, it is difficult to draw conclusions regarding clinical parameters and scintigram results. We felt that cases 2, 4, 6, and 17

TABLE 1. CLINICAL DATA AND INDIVIDUAL SCINTIGRAM SCORES

Case No.	Age & sex	Location of infarction	Peak CPK*	Clinical course	Scintigram scores 1 wk	2 wk	1 mo	2 mo	3 mo	6 mo	9 mo
1	64 M	Inferior	748+†	Asymptomatic	–	0	0	–	0	1	0
2	52 M	Anterior	694+	CHF‡ and angina	3	1	2	2	2	2	2
3	65 M	Inferior	120+	Angina—CABG‖ at 2 mo	–	0	3	3	2	0	1
4	55 M	Inferior	805+	Angina	–	1	0	2	2	2	2
5	67 M	Inferior	382+	Asymptomatic	3	0	2	2	1	1	0
6	84 M	Subendocardial	190+	CHF	3	3	2	3	1	2	2
7	59 M	Subendocardial	335+	Asymptomatic	0	2	2	1	1	0	0
8	58 M	Subendocardial	375+	Asymptomatic—sudden death at 4 mo	1	2	2	1	0	deceased	
9	85 M	Inferior	305+	Asymptomatic	2	–	1	0	1	1	0
10	52 M	Subendocardial	247+	Repeat MI at 1 mo—CABG at 2 mo	4/2§	0/2	0	0	–	0	0
11	69 M	Inferior	463+	Asymptomatic	3	1	2	1	1	1	0
12	55 M	Inferior	211+	CHF	2	2	–	0	0	1	1
13	52 M	Anterior	650+	Angina	4	0	0	1	1	1	0
14	69 M	Inferior	493+	Asymptomatic	4	1	2	2	1	0	1
15	58 M	Anterior	233+	Repeat MI at 1 month—CHF	1/4	–/3	–	1	–	2	0
16	52 M	Anterior	415+	Angina, CHF, CABG at 3 mo	3	4	2	0	2	1	0
17	61 M	Inferior	282+	CHF	4	2	2	3	3	3	1
18	31 M	Anterior	806+	Asymptomatic—sudden death at 3 mo	3	1	0	0	deceased		
19	69 M	Anterior	444+	Angina	4	1	1	0	0	0	0
20	60 M	Inferior	299+	Asymptomatic	–	2	3	2	2	1	0

* CPK normals 0–100 U.
† + = positive CPK-MB fraction.
‡ CHF = congestive heart failure.
‖ CABG = coronary-artery bypass graft.
§ Denominator is scan after repeat infarction.

TABLE 2. SERIAL CUMULATIVE SCINTIGRAM SCORES

	1 wk	2 wk	1 mo	2 mo	3 mo	6 mo	9 mo
Total scans obtained	18	20	18	19	17	18	18
Scans graded 3+-4+	12	3	2	3	1	1	0
Scans graded 2+	3	6	9	5	5	4	3
Scans graded 1+	2	6	2	5	7	8	4
Scans graded 0	1	5	5	6	4	5	11

represented the best examples of persistently positive scans, and it is noteworthy that all of these patients were symptomatic and three of the four had congestive heart failure suggesting extensive myocardial disease. Two patients experienced repeat myocardial infarction between 2 and 4 wk and were reentered into the study, making a total of 22 potential scintigrams at 1 and 2 wk. Also, one patient died suddenly after 2 mo, and another died suddenly after 3 mo, making a total of 18 potential scintigrams after 3 mo. The results of the routine ECG taken at 6 or 9 mo on all patients showed no evidence of "silent" myocardial infarction during the study.

Serial scintigrams. The results of the serial scintigrams are listed in Table 2. The scores presented here are the results of independent interpretation by two observers. There was interobserver disagreement on approximately one third of the scintigram scores in which case the lower score was always used. From Table 2 several conclusions can be reached. First, most patients (15/18) had positive scintigrams within the first week after infarction. Second, the number of markedly positive scintigrams (3+ and 4+) decreased promptly after the first week. Third, a number of scintigrams with moderate uptake (2+) persisted throughout the study. Finally, the majority of scintigrams returned to normal (0–1+) during the study. Representative scintigrams from two patients are seen in Figs. 1 and 2.

DISCUSSION

The skeletal imaging agent Tc-99m stannous pyrophosphate (Tc-PPi) has recently been used to detect acute myocardial infarction. The original reports of Bonte, Parkey, and associates demonstrated Tc-PPi uptake in acute experimental canine myocardial infarction (*1*) and in humans with acute myocardial infarction (*2*). They extended their observations and defined scintigraphic patterns of localized uptake in acute transmural infarction and diffuse uptake in acute subendocardial infarction (*9,10*). Other groups confirmed these observations (*11*) and the Tc-PPi myocardial scintigram was then recommended for general use as a clinical test for acute myocardial infarction (*3*).

As further experience with Tc-PPi accumulated, it became clear that a positive Tc-PPi myocardial scintigram was not always associated with acute myocardial infarction. Willerson and associates (*9*), in their original clinical application of the technique, noted that some patients (9 of 101) with positive scintigrams had no other laboratory confirmation of acute myocardial infarction. They were uncertain whether these were false-positive scintigrams or whether the scintigrams were more sensitive in identifying myocardial damage than ECG or serum enzymes.

Other groups have reported positive scintigrams in situations clearly not explained by acute myocardial necrosis. Ahmad and associates (*4*) reported positive scintigrams in patients with prior myocardial infarction and left-ventricular wall-motion abnormalities. Similar findings have been noted at our own institution (*7*) and by others (*12*). Patients with stable arteriosclerotic heart disease (*6*) and cardiomyopathy (*5*) have frequently been shown to have positive scintigrams, and routine skeletal imaging has shown tracer accumulation in the heart region in from 11–32% of cases (*8,13,14*).

The findings of this study corroborate the foregoing observations. Most of our patients had intense, localized scintigraphic images within the first week after myocardial infarction; the intensity of the scintigraphic images faded rapidly after the first week, and at the close of the study the majority of scans were normal and none was markedly positive. A small number of scintigrams (3 of 19 at 2 mo), however, remained markedly positive (3+-4+) longer than expected, and a number of scintigrams (5 of 18 at 6 mo) remained moderately positive (2+) for an extended period.

The explanation for persistently positive scintigrams remains speculative. In considering the technical aspects of the procedure, the major concern is whether some of the positive scintigrams are related to the imaging of blood-pool radioactivity (*13–15*). Procedural controls to prevent blood-pool imaging include imaging 2 hr after injection of the radionuclide, when blood background should be low due to rapid skeletal uptake and renal excretion, and ensur-

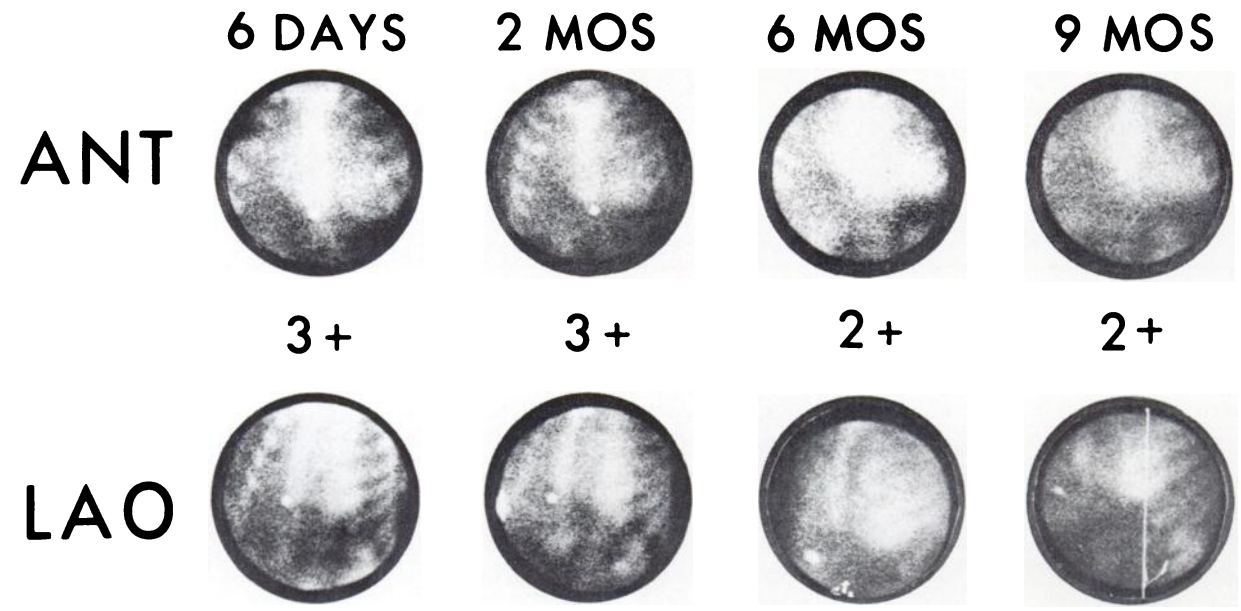

FIG. 1. Representative sequential scintigrams in Case 6. Scintigram at 6 days shows diffuse 3+ activity, which some authors have equated with acute subendocardial infarction. Scintigrams remain diffusely positive.

ing by paper chromatography that the technetium-99m is at least 95% bound to the stannous pyrophosphate. In spite of these precautions, studies of Berman et al. (*16,17*) suggest that blood-pool labeling could explain the "2+ diffuse pattern."

There is a tenable pathologic explanation for the persistently positive myocardial scintigrams after myocardial infarction. It has been shown that intramitochondrial calcium phosphate crystals are formed in acutely infarcted myocardium (*18,19*). Buja and coworkers established a temporal and topographic association between calcium accumulation in acute myocardial infarcts and Tc-PPi uptake (*20*), and concluded that complexes of calcium phosphate with Tc-99m form in acute myocardial infarcts and are responsible for the scintigraphic images. In patients with positive scintigrams remote from myocardial infarction, radiographic evidence of aneurysmal cal-

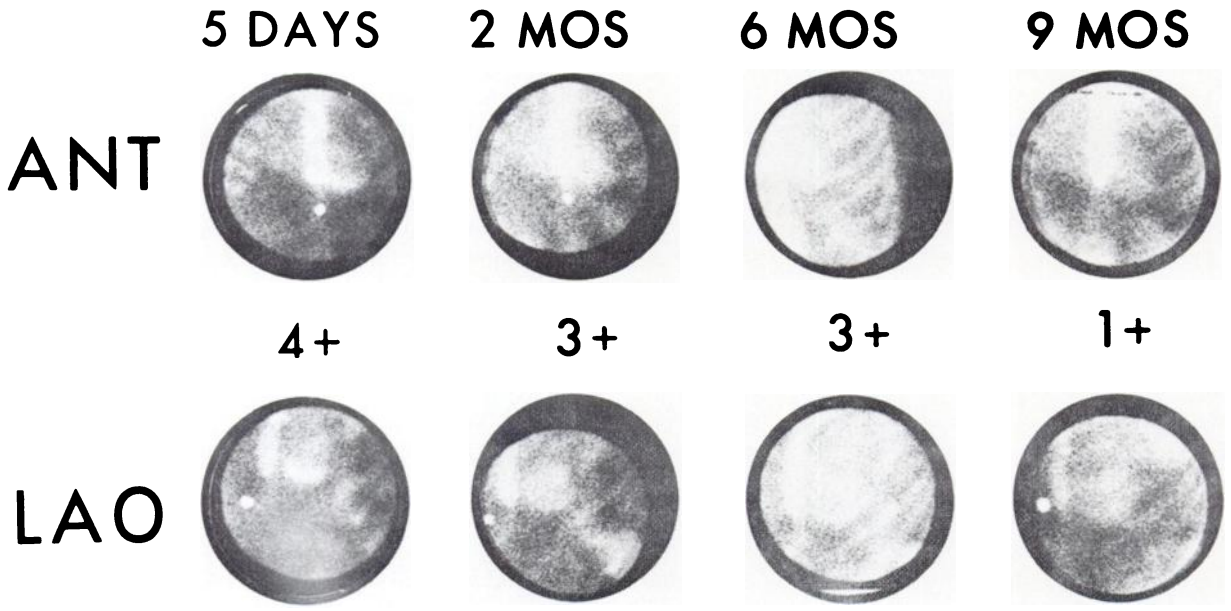

FIG. 2. Representative sequential scintigrams in Case 17. Scintigram at 5 days shows 4+ inferior-wall activity. Scintigrams at 2 and 6 mo show diffuse 3+ activity. Scintigram at 9 mo shows 1+ activity.

cification (*4*) and microscopic evidence of myocardial calcification (*12*) have been documented. Persistent myocardial dystrophic calcification is a possible mechanism for persistent myocardial scintigrams following myocardial infarction.

We feel that these persistently positive scintigrams hinder the usefulness of Tc-PPi for the diagnosis of acute myocardial infarction in patients who have had a previous myocardial infarction. In this series, five of 18 patients still had positive scintigrams 6 mo after infarction. We urge caution in the scintigraphic diagnosis of acute infarction in such a situation. Special caution should be exercised in interpreting diffuse moderately positive (2+) scintigrams as diagnostic of subendocardial infarction. In the scintigraphic diagnosis of recurrent myocardial infarction, the comparison of intensity and distribution of scintigraphic images, the use of routine Tc-PPi scintigrams at some point after infarction, and the addition of myocardial perfusion imaging may prove helpful but await clinical application.

FOOTNOTE

* Phosphotec, Squibb, Princeton, N.J.

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