Acute Myocardial Infarction Imaged with ^{99m}Tc-Stannous Pyrophosphate and ^{201}Tl: A Clinical Evaluation

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Twenty-six patients suspected of having acute myocardial infarction (AMI) underwent myocardial scintigraphy sequentially with ^{201}Tl and ^{99m}Tc-stannous pyrophosphate (^{99m}Tc-PP$_i$). Of the 26 patients, 24 had AMI documented by enzyme and electrocardiographic changes. Nineteen had transmural and five had subendocardial myocardial infarctions. The remaining two patients had "unstable angina pectoris." The mean time from onset to imaging was 4 days. Of the 24 patients with AMI, 22 had positive ^{99m}Tc-PP$_i$ scintigrams. In 20 the area of acute myocardial damage appeared to be the same by ^{99m}Tc-PP$_i$ scintigram as by ECG; in two, the location could not be precisely determined. The two patients with negative ^{99m}Tc-PP$_i$ scintigrams at the time of combined myocardial imaging had had positive ^{99m}Tc-PP$_i$ images previously. In all 24 patients, the ^{201}Tl images were abnormal in at least the location suggested by the electrocardiogram. In seven patients, the area of decreased ^{201}Tl activity was grossly equal to the positive area on the ^{99m}Tc-PP$_i$ images; in 15, the ^{201}Tl defect was definitely larger; and in two, the ^{201}Tl defect appeared slightly smaller. Although the ^{99m}Tc-PP$_i$ and ^{201}Tl myocardial images provide different information, both are valuable in determining the overall integrity of the myocardium in patients with ischemic heart disease.

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We have previously described the ability of ^{99m}Tc-stannous pyrophosphate* (^{99m}Tc-PP$_i$) to identify directly the presence and location of acute myocardial infarction in dogs (*1–3*) and patients (*4–6*). These findings have been confirmed by several investigators in both animals and patients (*7–11*). Strauss et al. (*12*) and Jambroes et al. (*13*) have shown ^{201}Tl to be an excellent agent for imaging the normal myocardium and for detecting areas of decreased regional perfusion. Wackers et al. (*14*) found that ^{201}Tl can show areas of acute myocardial infarction. The present study was designed to determine whether additional information could be obtained by sequential imaging with both ^{201}Tl and ^{99m}Tc-PP$_i$ in patients with acute myocardial infarction.

MATERIALS AND METHODS

Twenty-six patients suspected of having acute myocardial infarction were imaged with both ^{201}Tl and ^{99m}Tc-PP$_i$. Their mean age was 51 years; 15 were men. The mean time since onset was 4.2 days (range 3–10 days). Informed consent was obtained from each patient. The myocardial images were obtained using a Searle Radiographics Pho/Gamma HP scintillation camera with a 16,000-hole high-resolu-

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* TechneScan PYP™ (Mallinckrodt, St. Louis, Mo.).

tion collimator. The camera was interfaced to a PDP-8/I computer and images were placed on nine-track magnetic tape for later retrieval. The images were simultaneously recorded on an Ohio-Nuclear Series 150 data system.

Each patient was injected intravenously with 2 mCi of ^{201}Tl-chloride supplied as a sterile nonpyrogenic isotonic solution (New England Nuclear Corp., North Billerica, Mass.). The tracer was carrier free and contained less than 0.2% ^{203}Pb and less than 1.5% ^{202}Tl. Thallium-201 has biologic properties similar to those of potassium. It decays by electron capture with a half-life of 74 hr with gamma emissions at 135 and 160 keV (12%) and an x-ray at 81 keV (95%). In this study, the x-ray was used with a 10% window for myocardial imaging. Imaging was begun within 10 min after injection, and a minimum of three views (anterior, left anterior oblique, and left lateral) were obtained. Additional left and right anterior oblique views were also obtained on some patients. The imaging time for 3–5 views was approximately 30 min.

When the ^{201}Tl images were completed, the patient was injected intravenously with 15 mCi of ^{99m}Tc tagged to 5 mg of stannous pyrophosphate. Images were obtained 1 hr later in the anterior, left lateral, and one or more left anterior oblique projections. Imaging time for 3–5 views was approximately 15 min. During imaging the patients had continuous ECG monitoring. Neither arrhythmia nor obvious side effects were observed either from the injection of the radiopharmaceuticals or from the imaging process itself.

The clinical diagnosis of acute myocardial infarction was made on the basis of a typical history of prolonged chest pain and classical ECG and serum enzyme evolution for infarction (*4–6*). The ECG recognition of acute transmural infarction depended on identifying acute ST-segment elevation and T-wave inversion, followed by the development of significant Q waves. The ECG recognition of subendocardial infarction depended on the presence of deep ST depression and T-wave inversion, subsequently returning to normal over a period of several days.

The ^{99m}Tc-PP_i images were graded from 0 to 4+ depending on the activity over the myocardium (*4–6*): 0 represented no activity and a negative myocardial scintigram; 1+ was considered to be questionable activity but a negative scintigram; 2+ represented definite but faint activity and a positive myocardial scintigram; and 3+ and 4+ represented definite marked activity within the myocardium. This grading scheme is based on visibility and not on the size of the lesion. Sizing of the ^{99m}Tc-PP_i scintigrams was done in a crude quantitative manner by comparing the area of ^{99m}Tc-PP_i uptake to the gross area of the left ventricle as seen in one projection on the ^{201}Tl scintigrams. An area of ^{99m}Tc-PP_i uptake less than ¼ of this area was considered small; one between ¼ and ½ was considered moderate; and one greater than ½ was considered large. This scheme seemed to work on all infarctions except inferior ones, where the damaged area could not be imaged perpendicularly.

The ^{201}Tl images were compared with images previously obtained in six patients with no evidence of old or acute myocardial infarction. These normal images were similar to the normal images taken with ^{129}Cs published by Romhilt et al. (*14*). The normal

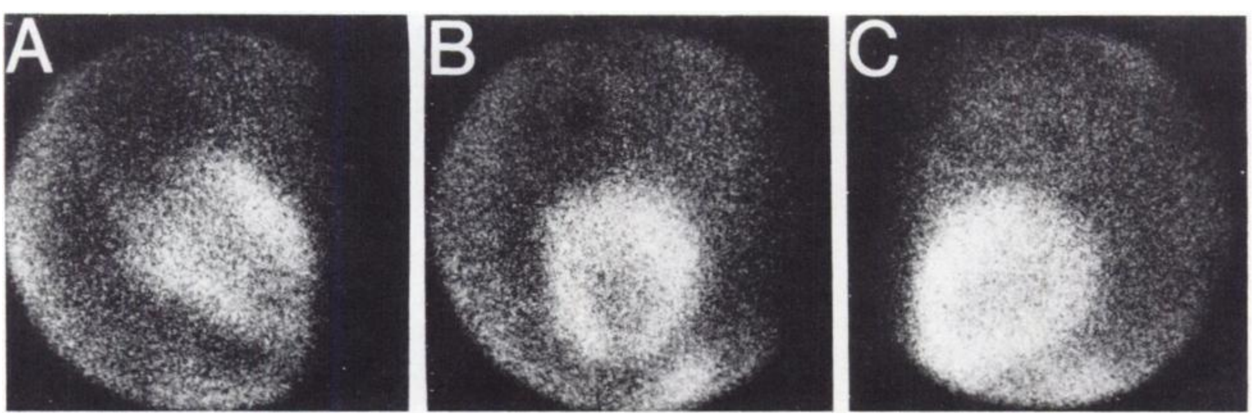

FIG. 1. Normal ^{201}Tl images in anterior (A), 45° left anterior oblique (B), and left lateral (C) views of patient with no known myocardial disease. Activity is seen in muscle volume representing left ventricle. Decreased activity at center is due to relatively decreased activity in blood pool of left ventricle. Decreased activity at base is due to origins of great vessels, and decreased activity at apex is variable finding probably representing muscle thinning at apex. The images usually appear circular in 45° LAO and left lateral projections. Images were obtained 5–15 min after intravenous injection of 2 mCi of ^{201}Tl.

images showed a doughnut or horseshoe appearance with the myocardium of the left ventricle surrounding the intraventricular cavity (Fig. 1). The right ventricle was not consistently visualized but, when seen, it appeared as a thin curvilinear structure extending from the interventricular septum.

The gross size of the abnormal areas on the ^{99m}Tc-PP_i and ^{201}Tl scintigrams were compared by considering areas involved on the three views (Fig. 2). Small, moderate, and large areas were considered on each view, along with the number of anatomic locations. The gross anatomic location of ^{201}Tl defects is mapped in Fig. 3. This method lacks the quantitative accuracy of direct measurements but seems to have clinical value. A quantitative measurement by the computer of the area of abnormality is currently being performed as a part of another study, but this approach involves such problems as registration and the difficulty of measuring what is not seen on the ^{201}Tl images.

RESULTS

Twenty-four of the 26 patients had acute myocardial infarctions documented by enzyme and electrocardiographic changes. Five of the 24 were subendocardial and 19 were transmural: 14 anterior, anterolateral, or lateral; 5 inferior, inferoposterior, or posterolateral (Table 1). One of the two remaining patients had Prinzmetal's angina, with no enzyme or ECG changes and normal ^{99m}Tc-PP_i and ^{201}Tl scintigrams. The other patient had the clinical syndrome of unstable angina pectoris with no enzyme or ECG changes, a normal ^{201}Tl scintigram, but a 2+ positive ^{99m}Tc-PP_i scintigram.

Twenty-two of the 24 patients with acute infarc-

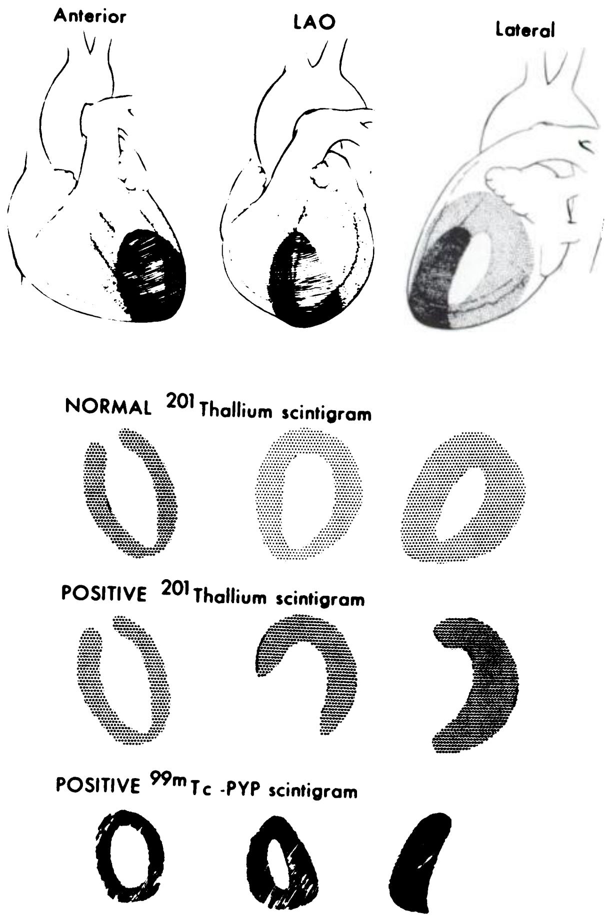

FIG. 2. Line drawings showing change in configuration of ^{201}Tl and ^{99m}Tc-PP_i scintigrams with rotation of heart. Top row of figures shows location of left ventricular myocardium (dotted area) in anterior, LAO, and left lateral views. Linear shading denotes area of anterior wall infarction. Second row represents normal ^{201}Tl images, while third row shows anterior wall defect in ^{201}Tl images caused by anterior myocardial infarction. Fourth row represents ^{99m}Tc-PP_i images of anterior myocardial infarction in anterior, LAO, and left lateral views.

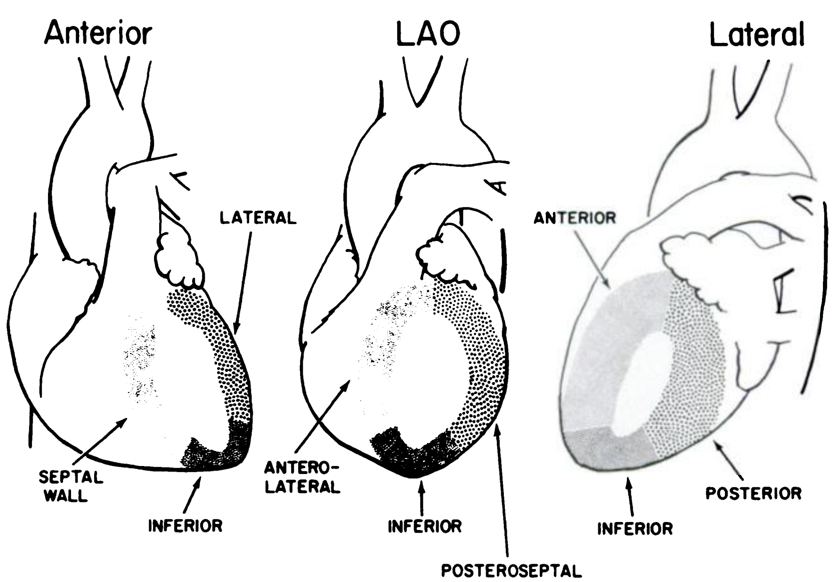

FIG. 3. Anterior, LAO, and left lateral views showing portion of left ventricular myocardium seen in each position with ^{201}Tl. Myocardium perpendicular to scintillation camera face is seen best because of "end on" effect with increased depth of radioactivity.

TABLE 1. PATIENT DATA

Patient	Age/Sex	Previous history of myocardial infarction	ECG diagnoses	^{99m}Tc-PP$_i$ images	^{201}Tl images	Complications of present infarctions
1	50 F	Previous anterior subendocardial myocardial infarction (MI)	Acute anterolateral MI	3+ positive small apical	Small apical defect $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None
2	50 F	No, but did have saphenous view bypass to RCA & LAD 4 yr previously	Acute anteroseptal & apical MI	4+ postive large anterior-apical	Markedly decreased activity anterior, apical $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None
3	55 F	None	Acute anterolateral MI	4+ positive large anterior, lateral, possible septal	Markedly decreased activity septal, anterior, lateral, posterior, and inferior $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	Congestive heart failure
4	56 M	None	Acute anterolateral MI	2–3+ positive small apical	Decreased activity apical and inferior with ? decrease in septum $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	None
5	68 M	Old inferior MI	Acute anterior MI	2+ positive small anterior apical	Markedly decreased activity anterior, apical, and some decrease inferiorly $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	None
6	36 F	None	Acute inferior MI	4+ positive small inferior	Markedly decreased activity inferior $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None
7	51 F	None	Unstable angina pectoris	Negative	Normal $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None
8	51 M	None	Acute anterolateral MI	4+ positive large anterior lateral	Large markedly decreased activity anterior lateral $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None
9	49 F	Old anterior MI	Acute subendocardial MI	3+ positive small apical-inferior	Small moderately decreased activity apical & inferior $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	Congestive heart failure
10	54 M	None	Acute anterior MI	4+ positive large anterior lateral	Large markedly decreased activity, anterior & lateral $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	None
11	84 F	None	Acute anterior apical MI	3+ positive small apical	Slightly decreased activity apical $^{201}Tl < {}^{99m}Tc\text{-}PP_i$	None
12	72 F	None	Acute subendocardial MI	Negative, but was 2+ positive 6 days earlier on admission	Decreased activity septum and posterior $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	Congestive heart failure
13	60 M	None	Acute inferoposterior MI	3+ positive small inferior	Markedly decreased activity, anterior, septal, and inferior $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	None
14	49 M	None	Acute anterolateral MI	4+ positive large anterolateral	Markedly decreased activity anterior, & high septal $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	Congestive heart failure
15	47 M	Old inferior MI	Acute anterolateral MI	3+ positive moderate anteroapical	Moderately decreased activity anterior, apical, inferior, high posterior $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	None
16	34 M	Old anterior MI	Acute inferolateral MI	3+ positive large lateral apical	Markedly decreased activity anterior, inferior, and lateral $^{201}Tl > {}^{99m}Tc\text{-}PP_i$	Congestive heart failure
17	63 F	None	Acute anterior MI	Negative	Normal $^{201}Tl \simeq {}^{99m}Tc\text{-}PP_i$	None

TABLE 1. (*Continued*)

Patient	Age/Sex	Previous history of myocardial infarction	ECG diagnoses	$^{99m}Tc-PP_i$ images	^{201}Tl images	Complications of present infarctions
18	50 F	None	Acute lateral subendocardial MI	3+ positive small anterior apical	Moderately decreased activity anterior, apical $^{201}Tl > ^{99m}Tc-PP_i$	None
19	55 M	None	Acute anterior MI	3+ positive small anterior	Moderately decreased activity anterior, high posterior $^{201}Tl > ^{99m}Tc-PP_i$	Congestive heart failure
20	59 M	None	Acute inferior MI	2+ positive small inferior	Markedly decreased activity, inferior & septal $^{201}Tl > ^{99m}Tc-PP_i$	Congestive heart failure
21	49 M	None	Acute posterolateral MI	4+ positive small apical posterior	Markedly decreased activity apical, inferior, & posterior $^{201}Tl > ^{99m}Tc-PP_i$	None
22	37 M	None	Acute anterior MI	4+ positive moderate anterior	Markedly decreased activity anterior, lateral, & inferior $^{201}Tl > ^{99m}Tc-PP_i$	Congestive heart failure
23	52 M	None	Unstable angina pectoris	2+ positive small anterior view only	Questionably decreased activity anterior wall $^{201}Tl \simeq ^{99m}Tc-PP_i$	None
24	35 F	Old anteroseptal MI	Acute subendocardial MI	3+ positive small apical	Generalized markedly decreased activity $^{201}Tl > ^{99m}Tc-PP_i$	None
25	59 M	Old inferior MI	Acute anterolateral subendocardial MI	3+ positive small lateral	Markedly decreased activity lateral & posterior wall $^{201}Tl > ^{99m}Tc-PP_i$	None
26	30 M	Old inferior MI	Acute lateral MI	3+ positive large lateral posterior	Moderately decreased activity apical, inferior $^{201}Tl < ^{99m}Tc-PP_i$	Congestive heart failure

tion had positive $^{99m}Tc-PP_i$ scintigrams at the time of sequential imaging (Figs. 4A–4C), and the location of the increased $^{99m}Tc-PP_i$ uptake correlated with the ECG location. Both patients with negative $^{99m}Tc-PP_i$ scintigrams at the time of dual myocardial imaging had acute subendocardial infarctions, and their $^{99m}Tc-PP_i$ images had been positive 4 and 7 days earlier.

In all 24 patients with acute myocardial infarction, the ^{201}Tl scintigrams were abnormal (Figs. 4, 6, and 8), showing defects in the ventricular ring. Abnormal areas were seen best when viewed edge on. Thus, defects in the lateral wall appeared best in the anterior view, and those in the anterior wall were viewed best in the lateral projection (Fig. 3). Determination of gross area of increased activity required at least three views so that each wall (septal, lateral, anterior, posterior, and inferior) could be evaluated. Comparisons between $^{99m}Tc-PP_i$ and ^{201}Tl regarding the areas of abnormality (small, moderate, or large and the number of anatomic locations) was done on a crude quantitative basis by two of the authors (RWP and SEL). All seven of the patients with previous transmural myocardial infarction had abnormal ECGs indicating the area of old injury, while six of the seven had ^{201}Tl images abnormal in this area.

In seven patients, the area of decreased ^{201}Tl activity was approximately equal to the area of increased $^{99m}Tc-PP_i$ activity (Fig. 4). The defects in the ^{201}Tl images fit the positive $^{99m}Tc-PP_i$ images in the same view as if the two were parts of a puzzle. Two of these seven patients had histories of previous myocardial infarction. Both of these patients' previous infarcts were in an area adjacent to the newly infarcted myocardium and were not seen as two separate areas. Fifteen patients had ^{201}Tl defects definitely larger than the areas of $^{99m}Tc-PP_i$ uptake (Figs. 5–8), and the defects usually included areas other than those suspected of being acutely infarcted. Five of these 15 patients had a history of previous myocardial infarction; four of these five had ^{201}Tl defects in the region of the old infarction separate from the new area. The fifth (patient No. 25) had

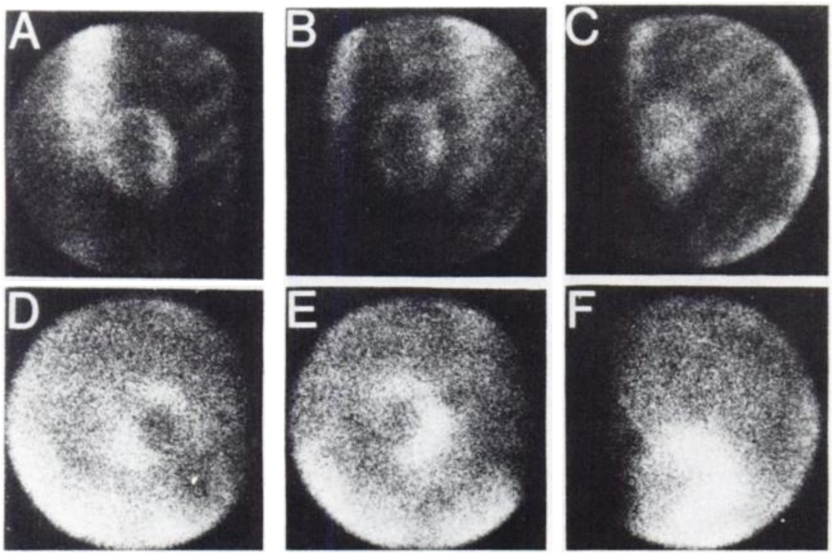

FIG. 4. Scans of 54-year-old man (Patient No. 10) with large acute anterolateral myocardial infarction show area of abnormality to be approximately equal on ^{99m}Tc-PP$_i$ and ^{201}Tl images. Parts A, B, and C represent anterior, 45° LAO, and left lateral scintigrams done 1 hr after injection of 15 mCi of ^{99m}Tc-PP$_i$. Note doughnut pattern due to variability of blood flow in acutely infarcted tissue. Parts D, E, and F represent anterior, 45° LAO, and left lateral scintigrams done approximately 1 hr before ^{99m}Tc-PP$_i$ scintigrams with injection of 2 mCi of ^{201}Tl. Note decreased activity in anterior and lateral myocardium.

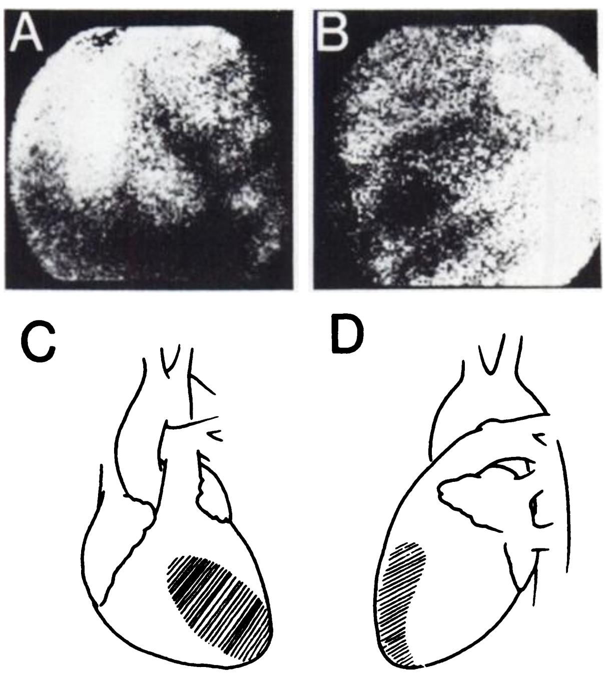

FIG. 5. Scans of 47-year-old man (Patient No. 15) with acute anterolateral and old inferior myocardial infarction on ECG. Parts A and B are anterior and left lateral scintigrams done 1 hr after injection of 15 mCi of ^{99m}Tc-PP$_i$. 3+ positive anteroapical infarction is best seen on anterior view with activity on lateral view poorly seen on far left side of image. C and D are line drawings showing myocardial location.

an acute anterolateral subendocardial infarction with a previous inferior transmural infarction. The ^{201}Tl scintigrams showed markedly decreased activity including the lateral and posterior wall. Two patients had ^{201}Tl defects somewhat smaller than the area of ^{99m}Tc-PP$_i$ uptake. One of these patients had a history of a previous inferior myocardial infarction and the ^{201}Tl images showed some decreased activity inferiorly, but the new infarction (apical–lateral) was much smaller on the ^{201}Tl image than the large lateral area of increased ^{99m}Tc-PP$_i$ activity.

Congestive heart failure was present in nine patients; seven of these were in the group whose ^{201}Tl defects were larger than the ^{99m}Tc-PP$_i$ defects. There was one patient in each of the other two groups.

DISCUSSION

Imaging of the myocardium in patients with acute myocardial infarction has been performed both with radiopharmaceuticals that visualize the normal myocardium (^{42}K, ^{43}K, ^{81}Rb, ^{84}Rb, ^{86}Rb, ^{129}Cs, ^{131}Cs, ^{134m}Cs, ^{201}Tl) and with those that visualize the abnormal myocardium (^{99m}Tc-tetracycline, ^{67}Ga, ^{99m}Tc-glucoheptonate, ^{99m}Tc-phosphates) (*15*). Each class of radiopharmaceuticals has advantages and disadvantages.

The most widely used radionuclides that concentrate in the normal myocardium are potassium and its analogs. Of these agents, ^{43}K, ^{129}Cs, and ^{201}Tl have shown clinical usefulness. Romhilt et al. (*16*) showed ^{129}Cs to be a good imaging agent (half-life 33 hr, emissions at 372 and 412 keV), but ^{201}Tl, with its 74-hr half-life and 81-keV x-ray, appears to be the current agent of choice. The disadvantages of ^{201}Tl are its cost and its restricted availability. Furthermore, abnormal scintigrams obtained with ^{201}Tl and related agents cannot be considered specific for acute myocardial infarction. Lack of activity in the myocardium after injection of a potassium analog can be due not only to an acute myocardial infarction, but also to old infarction or ischemia. Strauss et al. (*17*) and Zaret et al. (*18*) previously used these agents to show areas of transient myocardial ischemia. Because of this nonspecificity, coupled

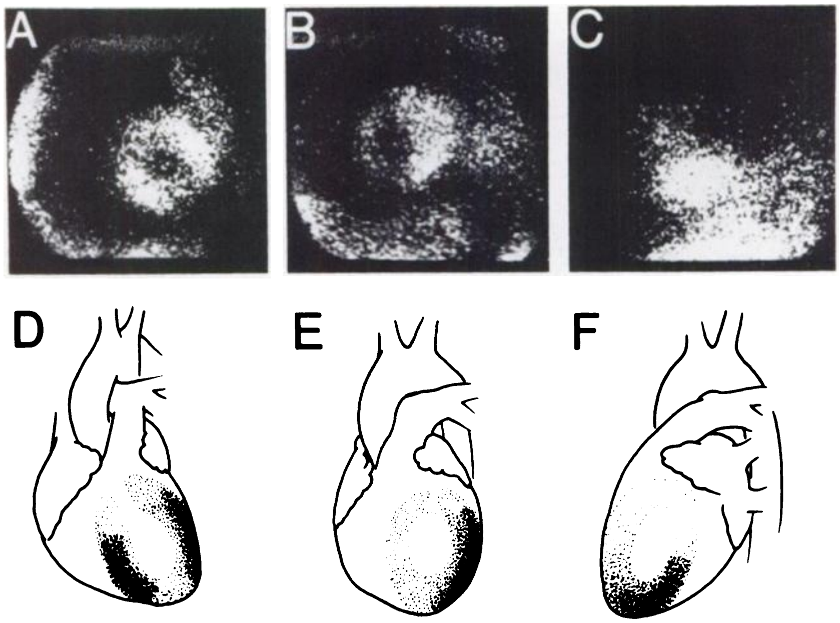

FIG. 6. Thallium-201 scintigrams done on Patient No. 15 1 hr before scintigrams in Fig. 5. Images were obtained 5–30 min after intravenous injection of 2 mCi of ^{201}Tl. Parts A, B, and C represent anterior, 45° LAO, and left lateral views, while D, E, and F are line drawings showing myocardial location. Note decreased activity apically (anterior view), anterior and inferior (LAO view), and anterior and high posterior (left lateral view). Abnormal myocardium detected on ^{201}Tl images is more extensive than that seen on ^{99m}Tc-PP$_i$ because ^{201}Tl identifies myocardium that is ischemic or fibrotic as well as acutely infarcted.

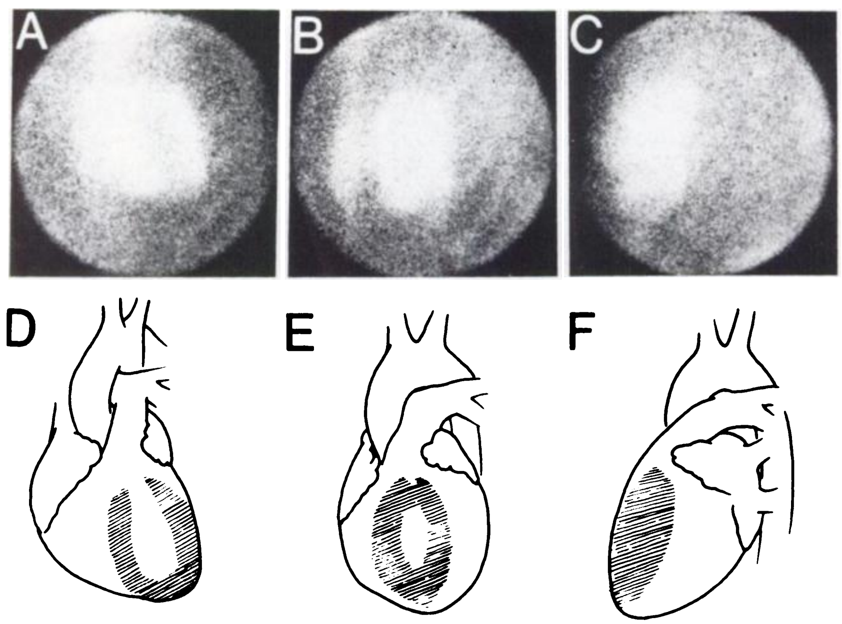

FIG. 7. Scans of 55-year-old woman (Patient No. 3) with acute anteroseptal myocardial infarction by ECG. Parts A, B, and C are anterior, 45° LAO, and left lateral scintigrams done 1 hr after injection of 15 mg of ^{99m}Tc-PP$_i$. Scintigrams show 4+ positive large acute myocardial infarction involving septal, anterior, and lateral myocardium. As in Fig. 2, note doughnut pattern of ^{99m}Tc-PP$_i$ uptake due to variability of blood flow in acutely infarcted tissue. Parts D, E, and F are line drawings showing myocardial location.

with the fact that potassium-analog scintigrams show abnormalities as negative defects, sizing of acute myocardial infarcts with these agents may prove difficult.

At present, ^{99m}Tc-phosphates are the most widely used radiopharmaceuticals for imaging acutely infarcted tissue. Animal studies have indicated that only irreversibly damaged tissue concentrates ^{99m}Tc-PP$_i$ (*3*), although occasional uptake by severely ischemic but still viable myocardium has not been excluded. Acutely infarcted myocardium appears as a "positive" image without interference from the normal myocardium. Activity in the bony structures is present, but this disadvantage is minimized if imaging is performed 1 hr after the intravenous injection of the ^{99m}Tc-PP$_i$.

Imaging with ^{99m}Tc-PP$_i$ has been shown to identify accurately the presence and location of acute myocardial infarction in patients (*4–6,9–11*). Sizing of acute anterior myocardial infarcts in dogs with ^{99m}Tc-PP$_i$ correlates well with histologic sizing (*8,19–21*).

If ^{99m}Tc-PP$_i$ can identify and size acute anterior or lateral myocardial infarction as suggested, why is there any advantage in dual imaging with a potassium analog such as ^{201}Tl? The answer may be found in the 15 patients in whom the ^{201}Tl images showed defects that were definitely larger than the areas of

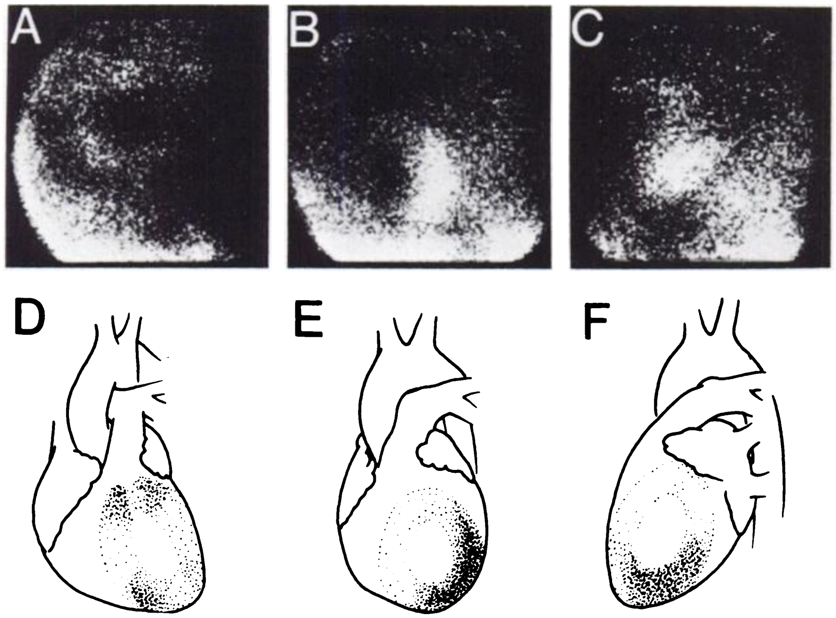

FIG. 8. Thallium-201 scintigrams done on Patient No. 3 1 hr before scintigrams in Fig. 7. Images were obtained 5–30 min after intravenous injection of 2 mCi of ^{201}Tl. Parts A, B, and C represent anterior, 45° LAO, and left lateral views, while D, E, and F are line drawings showing myocardial location. Note markedly decreased activity involving septal, inferior, and lateral myocardium (anterior view), and anterior and high posterior myocardium (LAO and left lateral views). Thallium-201 shows additional areas of abnormality because it also identifies areas of ischemia and fibrosis.

^{99m}Tc-PP$_i$ uptake and usually included areas other than those suspected of being acutely infarcted. While ^{201}Tl images may add little new information in patients with only normal and acutely infarcted myocardium, they provide additional valuable information as to the integrity of the total myocardium in the patients with superimposed chronic infarction or ischemia.

Two patients in whom the ^{201}Tl defects were smaller than the areas of ^{99m}Tc-PP$_i$ uptake raise questions as to the mechanism of ^{201}Tl uptake. It has generally been thought that ^{201}Tl would not be found in areas of acute myocardial infarction because its sequestration requires not only blood flow, but also active cellular transport mechanisms. Buja et al. (*22*) showed that ^{201}Tl was present in the outer margins of 24-hr-old acute myocardial infarcts in animals. There was a relationship between the amount of ^{201}Tl present and blood flow as measured by radioactive microspheres. It was not clear if the ^{201}Tl was in irreversibly damaged tissue or in foci of viable tissue scattered through the irreversibly injured tissue. Another cause for overlapping of the ^{201}Tl and ^{99m}Tc-PP$_i$ on scintigrams could be subendocardial extension of the infarction at the margins between viable and nonviable tissue. In this case the ^{99m}Tc-PP$_i$ could sequester in the subendocardial tissue while the ^{201}Tl could be present in the overlapping epicardial tissue. Further studies are needed to understand this phenomenon better.

Although congestive heart failure was seen in all three groups, its incidence was highest in the patients in whom the ^{201}Tl-designated areas were larger than those shown by ^{99m}Tc-PP$_i$. This group of patients may have had significant areas of fibrosis or ischemia as well as acute myocardial infarcts. Using ^{99m}Tc-PP$_i$ images to locate acutely infarcted myocardium and ^{201}Tl images to show additional abnormal areas should offer the clinician a clearer picture of the overall extent of myocardial damage and, possibly, prognosis. In addition, combined myocardial imaging with ^{99m}Tc-PP$_i$ and ^{201}Tl may make sizing inferior and subendocardial infarcts possible in patients; with ^{99m}Tc-PP$_i$ alone this is currently difficult and perhaps impossible (*20*).

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