Positive myocardial scintigraphy at the bedside – evaluation using a portable gamma camera

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Summary

A study was undertaken to evaluate the role of positive infarct scintigraphy in the diagnosis of acute myocardial infarction (AMI), using Technetium^{99m} stannous pyrophosphate (Tc-PYP) and a portable gamma camera. Sixty-one patients admitted to the Coronary Care Unit (CCU) with a presumptive diagnosis of AMI or ischaemic cardiac pain were studied. Positive scans were present in 24/25 (96%) patients with AMI and new Q waves, and in 10/12 (83%) patients with AMI and no Q waves. Nine of eleven (82%) patients with chest pain and no infarction had negative scans. Of thirteen patients with unstable angina, ten (77%) had positive scans. A further eight patients undergoing coronary artery bypass surgery for angina pectoris were studied pre- and post-operatively. Two patients had strongly positive postoperative scans. The Tc-PYP scan is valuable in the detection of peri-operative infarction following coronary artery surgery, and in patients with unstable angina the technique may detect small amounts of myocardial necrosis undetectable by more conventional means. When the diagnosis of infarction is obvious from the ECG, enzymes, or a combination of the two, the Tc-PYP scan provides no extra information helpful in patient management.

Introduction

The radiopharmaceutical Technetium^{99m} stannous pyrophosphate (Tc-PYP) is known to accumulate in acutely infarcted myocardium (Bonte *et al.*, 1974) and positive infarct imaging has been widely applied in the assessment of patients with chest pain (Parkey *et al.*, 1974; Willerson *et al.*, 1975a). The development of the mobile gamma camera means that myocardial imaging may be carried out at the

bedside of acutely ill patients, such as those on a coronary care unit (CCU), or recovering from open-heart surgery. A study was therefore designed to assess the value of such positive infarct scintigraphy in patients on a CCU and in the detection of peri-operative infarction following coronary artery vein grafting.

Patients and methods

Sixty-one patients were admitted to the CCU with a presumptive diagnosis of acute myocardial infarction (AMI), or ischaemic cardiac pain. There were forty-eight men and thirteen women, aged between 28 and 73 years, with a mean of 56 years. All patients had twelve lead ECGs performed on admission, and daily for 3 days. Estimations of serum glutamic-oxaloacetic-transaminase (SGOT) and hydroxybutyric dehydrogenase (HBD) were performed daily for 3 days. An SGOT level of below 40 i.u./l and HBD of less than 140 i.u./l were considered normal, levels of 40–50 i.u./l and 140–150 i.u./l of SGOT and HBD respectively were considered equivocally raised and levels above 50 and 150 i.u./l respectively were deemed definitely abnormal. AMI was diagnosed by the conventional electrocardiographic and enzymatic criteria, and patients with AMI were classified into two groups according to whether the acute episode caused new Q waves to appear on the ECG or not. The terms 'transmural' and 'subendocardial' infarctions for these patients have been avoided, as the presence of Q waves is not necessarily synonymous with transmural infarction (Helfant, 1976) and infarctions without Q waves may not be truly subendocardial. Myocardial scans were performed at the bedside, 2.0–2.5 hr after the intravenous injection of 15

FIG. 1. Representative examples of the five grades of scan from 0 to 4. Grade 0=no myocardial uptake, Grade 1=questionable uptake, Grade 2, definite myocardial uptake, Grades 3 and 4 increasing density of Tc-PYP uptake.

mCi of Tc-PYP, using a mobile Portacamera (General Electric) with a standard medium-energy parallel-hole collimator and nineteen photomultiplier tubes. The average time between the onset of symptoms and the scan was 48 hr, with a range of 4 hr to 8 days. Scans were performed in the anteroposterior (AP), left anterior oblique (LAO), and left lateral (LL) projections. One million counts per view were collected, taking between 4 and 6 min. The data were recorded on 4-inch square Dupont X-ray plates. Each scan was independently assessed by five observers, unaware of the clinical diagnosis, on the basis of all three projections and assigned a grade of 0-4, following a documented scoring scheme (Parkey *et al.*, 1974). Examples of the five grades of scan are shown in Fig. 1. Grades 0 and 1 were considered negative and grades 2-4 positive. Scans were labelled negative unless a majority of 4 to 1 observers deemed them positive but inter-observer variation was on average less than one grade. Computer processing of the data was not considered necessary to decide if a particular scan was positive or negative.

A further eight patients undergoing coronary artery bypass surgery for angina pectoris had scans performed 24 hr pre-operatively and between 48 and 96 hr postoperatively, following the protocol above. In addition to conventional enzyme testing, the patients had estimates of total creatine kinase (CK) and of the cardiospecific MB-CK, determination of the isoenzyme being carried out using the Merck diagnostic method based on the use of an inhibiting antibody to the CK-M subunit (Neumeier *et al.*, 1976). Levels of MB-CK between 4 and 50 i.u./l

were considered mildly elevated, and levels over 50 i.u./l grossly elevated (Coleman *et al.*, 1976).

Results

Coronary care unit

Patients with acute myocardial infarction. Twenty-five patients had typical electrocardiographic criteria for infarction with Q wave evolution, there being seventeen anterior and eight inferior infarctions. All twenty-five had unequivocally raised enzymes, and twenty-four (96%) had positive scans. The one patient in this group with a negative scan was studied only 4 hr after the onset of symptoms and was not re-studied at the optimal imaging time of 24-72 hr. Since early detection of infarction appears to be related to blood flow to the infarcted area (Bruno *et al.*, 1976) re-perfusion of the infarcted area in this patient may not yet have been established.

In twenty of the twenty-five patients, the uptake of Tc-PYP was localized and the site of uptake correlated with the electrocardiographic site of infarction. This was so, even for small infarctions.

TABLE 1. Correlation between the presence of a positive scan and the presence of infarction in the group of forty-eight patients

	Scan +	Scan -	Total
Clinically positive	34	3	37
Clinically negative	2	9	11
Total	36	12	48

χ^2 analysis - $P < 0.001$.

TABLE 2. Data on the patients undergoing coronary vein graft surgery

Patient	Pre-op scan	Post-op scan	Post-op ECG	Peak total CK i.u./l	Peak MB-CK i.u./l
J.G.	+	—	ST changes	570	9
B.G.	—	—	ST changes	192	0
R.C.	—	+	Lateral Q waves	1425	190
G.R.	—	—	No change	214	23
R.R.	—	—	No change	229	0
K.B.	—	—	ST changes	185	7
J.A.	—	+	ST changes	783	43
E.W.	+	—	ST changes	748	23

Three patients had diffuse Tc-PYP uptake, and localization to one part of the ventricle was not possible. The remaining patient with a large antero-lateral infarction electrocardiographically showed a typical 'doughnut' pattern (Buja *et al.*, 1975) of uptake (Fig. 2). There was no correlation between the peak serum enzymes and the grade of intensity of Tc-PYP uptake.

It is evident from these results that from the purely diagnostic point of view, the Tc-PYP scan is not superior to either the electrocardiogram or the serum enzymes in this group of patients. If imaging is not performed too early in the evolution of the infarct (i.e. within the first 24 hr) then the scan is probably no worse than conventional tests.

FIG. 2. Typical 'doughnut' scan, with increased Tc-PYP uptake in a horseshoe distribution around the periphery.

Twelve patients had infarction without Q waves, diagnosed from a combination of electrocardiographic and enzyme changes. Eleven patients showed definite ST segment and T wave abnormalities of varying severity and eight (67%) had unequivocally raised cardiac enzymes. The diagnosis was made in all cases from electrocardiographic and enzymatic

FIG. 3. (a) Twelve lead electrocardiogram showing minor inferior changes only. (b) A-P scan showing definite 'hot spot' inferiorly.

data combined, as the ECG changes alone are not diagnostic of infarction, unlike the situation when Q waves are present. Ten patients in this group (83%) had positive scans. In only four was it possible to localize the Tc-PYP uptake, and the remaining six showed diffuse uptake. Although others have labelled such infarcts as subendocardial (Willerson *et al.*, 1975b), this term has been avoided for the reasons outlined above. One patient in this group had only minor ECG changes, and cardiac enzymes in the equivocal range. The Tc-PYP scan showed a definite area of increased uptake inferiorly (Fig. 3).

Although the scan alone appears superior to the enzymes alone in detecting infarction without Q waves (83% versus 67%), in everyday clinical practice the combination of electrocardiography and serum enzyme estimation is more often than not perfectly adequate to diagnose infarction in this syndrome. This is true even though the ECG changes

are non-specific and may not on their own be able to discriminate between acute ischaemia and infarction.

Patients without acute infarction. Eleven patients had chest pain without infarction. In this group (four with pericarditis, four with stable angina pectoris, and three with non-cardiac pain) nine had negative scans. The two positive scans were both found in cases of pericarditis, possibly indicating associated myocarditis, and it is of note that none of the four patients with stable angina had Tc-PYP uptake.

Statistical analysis of the data from these forty-eight patients shows a highly significant correlation between the presence of infarction and the presence of a positive scan ($P < 0.001$, Table 1).

No valid statistical comparison between the abilities of the electrocardiograms, serum enzymes, and Tc-PYP scans to detect infarction can be made, either in those with Q waves, or those without. This is because this study has relied upon the electrocardiogram and the enzymes for the basic diagnosis of infarction, with which to compare the Tc-PYP scan.

Only if there were another, foolproof technique for diagnosing infarction in any particular patient would it be possible to make such statistical comparisons.

Unstable angina. Of thirteen patients with unstable angina, as defined by the criteria laid down by the ongoing Myocardial Infarction Research Unit (MIRU) study (Mundth *et al.*, 1975), ten had positive scans (77%). All ten with positive scans were grade 2, and the pattern of uptake was diffuse and not localizable to any one ventricular region. This change is similar to the usual pattern seen in infarctions without Q waves. A typical example is the grade 2 scan in Fig. 1. Thus, in terms of the Tc-PYP scan, there appears to be a similarity between unstable angina and infarction without Q waves, and it must be stressed that none of the patients with unstable angina had raised cardiac enzymes.

Patients undergoing coronary artery surgery. The results of pre- and postoperative scans, the postoperative ECG, peak total CK and peak MB-CK postoperatively in eight patients are summarized in Table 2. Two patients had grade 2 diffusely positive scans pre-operatively which were negative post-operatively, despite a high total CK and mild to moderately elevated MB-CK. One of these (E.W.) had had unstable angina, with no ECG changes or enzyme rises, and had not responded to conventional medical therapy; coronary arteriography had shown three-vessel coronary disease, and he was revascularized during the same admission. The reason for the positive pre-operative scan in the other patient is unclear. The remaining six patients all had negative pre-operative scans and, of these, two

FIG. 4. (a) pre-operative, and (b) postoperative electrocardiograms from a patient undergoing coronary artery vein grafting.

had strongly positive postoperative scans. One of these (R.C.) had grossly elevated MB-CK and new Q waves appearing on the ECG; the other (J.A.) had moderate MB-CK elevation and ST segment changes only (Fig. 4). The postoperative scan of this latter patient is the grade 3 scan in Fig. 1. Of the remaining four patients with negative pre- and postoperative scintigrams, two had no MB-CK detectable in the blood and two had mild to moderate elevations. Thus there is a tendency for MB-CK levels to be raised postoperatively and mild to moderate elevations (4 to 50 i.u./l) may occur in the absence of definitive ECG or scintigraphic changes. No patient with negative postoperative scans had new Q waves on the postoperative ECG.

Discussion

Many earlier techniques for infarct imaging have relied upon failure of damaged myocardium to take up potassium analogues, producing an image

defect or 'cold spot' (Romhilt *et al.*, 1973; Martin *et al.*, 1974), but it is impossible to differentiate old from acute infarction using these techniques. Since Tc-PYP is only taken up by acute infarcts, this 'hot spot' imaging is advantageous in the diagnosis of acute myocardial infarction. The authors have utilized Tc-PYP with a portable gamma camera to obviate the necessity for moving ill patients away from the intensive care environment by taking imaging to the bedside. This CCU study indicates the high detection rate (96%) in patients with AMI and new Q waves, in agreement with other workers (Berman *et al.*, 1975; Lessem *et al.*, 1977). One patient with Q waves had a positive scan as late as 8 days after symptoms but, in general, scans tend to become negative at about 7 days after infarction (Parkey *et al.*, 1974; Willerson *et al.*, 1975a). The only patient with Q waves and a negative scan was imaged very soon (4 hr) after symptoms. As current evidence indicates that the delivery of Tc-PYP to the infarct is flow dependent (Bruno *et al.*, 1976; Marcus *et al.*, 1976), early detection of acute infarction, i.e. before 6 hr after symptoms, may be unsatisfactory. Uptake of Tc-PYP may depend on the length of duration of ischaemia and the rapidity with which flow is re-established (Bruno *et al.*, 1976). The authors, in common with other groups, have found a good correlation (20/24) between the site of ECG Q waves and the site of Tc-PYP uptake (Lessem *et al.*, 1977). The 'doughnut' appearance seen in Fig. 2 has been previously described as being due to accumulation of radioactivity at the infarct periphery, around a central zone of relatively decreased activity (Buja *et al.*, 1975). The same study demonstrated calcification in the infarct periphery leading to preferential deposition of Tc-PYP in these areas, the uptake of the agent mediated by incorporation into calcium salts in the mitochondria of irreversibly damaged cells (D'Agostino and Chiga, 1970). It is possible that residual perfusion of the peripheral zones of the infarct via a coronary collateral circulation offers the most likely explanation.

The possibility of obtaining negative scans early in the evolution of the infarct, and scans which only visualize peripheral infarct zones, imposes serious limitations on the ability of the Tc-PYP scan (a) to act as an accurate screening test for admission to a CCU, and (b) to provide data on the size of an infarct. Experimental work has shown a correlation between image infarct activity, and infarct weight (Botnick *et al.*, 1975), but attempts to apply sizing techniques *in vivo* have been disappointing. Thus, although detection of infarcts with Q waves is reliable, the scan offers little in terms of patient management when the diagnosis is obvious electrocardiographically.

Twelve patients had infarction without Q waves, diagnosed from electrocardiographic and enzyme changes. That such a diagnosis is not easily made from the ECG alone is evident when one considers the non-specific nature of ST segment and T wave changes, and the difficulty in differentiating between acute ischaemia and infarction without Q waves electrocardiographically. Enzymes are relied upon to substantiate the diagnosis but the levels may be equivocal. Hence, when comparing the reliability of various techniques in making the diagnosis, one has to compare the ability of the scan with that of the ECG and enzymes combined, as in clinical practice both these tests are used, and in clinical practice, as with infarctions with Q waves, conventional ECG and enzyme testing is more often than not perfectly adequate to make the diagnosis. However, not only do the present data indicate that the Tc-PYP scan can identify over 80% of infarcts without Q waves, but that it can also locate the infarct in approximately 25%. In certain circumstances, therefore, such as when conduction defects make ECG interpretation difficult, or when serum enzymes are equivocal, the scan may provide confirmatory or refutatory evidence as to the presence of infarction.

The detection rate in this study is similar to that of Willerson *et al.* (1975b) but some have reported disappointing results in this syndrome (Walsh *et al.*, 1976). The diffuse pattern of uptake generally found in these patients (grade 2 – Fig. 1) has been suggested by some as specific for this type of infarction (Poliner *et al.*, 1976), although this is not the experience of the present nor of other workers.

Of particular interest was the finding of positive scans in ten of thirteen patients (77%) with unstable angina, and with a similar pattern of uptake to those with infarcts without Q waves. This phenomenon has been noted previously with an incidence varying from 35 to 100% (Donsky *et al.*, 1976; Walsh *et al.*, 1976; Lessem *et al.*, 1977). The question is raised as to whether these patients have sustained small amounts of myocardial necrosis undetectable by other means, or whether Tc-PYP is taken up by severely ischaemic but non-necrotic cells. Experimental work in animals suggests that Tc-PYP uptake is confined to necrotic cells (Buja *et al.*, 1975; Marcus *et al.*, 1976; Coleman *et al.*, 1977) and post-mortem data in humans have supported this (Holman, Ehrie and Lesch, 1976). No Tc-PYP uptake has occurred in patients with coronary artery disease and exercise-induced ischaemia (Klein *et al.*, 1977) and, although a recent report has asserted that patients with stable angina pectoris may have a higher scintigraphic score at rest than normals (Mason *et al.*, 1977), the scans were still in the negative range by most criteria. None of the authors' four patients with stable angina pectoris

had positive scans, although no statistical comment may be made from this small group. No other patient group without frank infarction has been shown to have such a consistently high rate of positive scans as this group with unstable angina, even though many with stable angina have been studied (Donsky *et al.*, 1976).

This evidence, plus the well recognized fact that at post-mortem many patients with coronary artery disease have been found to have small areas of infarction without any evidence of such during life (Allison *et al.*, 1963), would suggest that Tc-PYP scans are in fact detecting small areas of necrosis hitherto undetectable by conventional methods, and that in terms of the Tc-PYP scan, unstable angina and myocardial infarction appear to be different clinical manifestations of the same pathological process of necrosis, and may warrant the same management.

It is unclear why positive scans occurred in two patients with pericarditis. Although false positives do occur, the scans may in these two patients reflect a concomitant myocarditis, with small areas of necrosis occurring in this condition leading to Tc-PYP uptake. The scans were diffusely positive, further refuting the claim of specificity of the diffuse pattern for infarction without Q waves. Diffusely positive scans have been reported in such conditions as left ventricular aneurysms and cardiomyopathies (Ahmad *et al.*, 1976; Chacko *et al.*, 1977) but it is very important to delay imaging long enough after the Tc-PYP administration to allow activity to clear from the blood pool (Klein *et al.*, 1977); imaging at only 1 hr after injection may be including a blood pool image (Klein *et al.*, 1977), producing a diffusely but inappropriately positive scan.

Peri-operative patients

The incidence of peri-operative AMI following coronary artery surgery has been reported as varying from 7 to 40% (Alderman *et al.*, 1973a; Brewer, Bilbro and Bartel, 1973; Espinoza *et al.*, 1974) but variation in statistics is largely due to the difficulty in making the diagnosis, and most data have been gleaned from inspection of postoperative electrocardiograms. Only the appearance of new Q waves is of value in the postoperative ECG, and even the specificity of these for AMI has been questioned (Bassan *et al.*, 1974). Conventional serum enzymes are often non-specifically increased after open heart surgery (Alderman *et al.*, 1973b), and although the isoenzyme MB-CK has been reported as reflecting only myocardial damage following bypass surgery (Dixon *et al.*, 1973), other reports contradict this belief (Coleman *et al.*, 1976; Righetti *et al.*, 1977), and the present data as summarized in Table 2, show that MB-CK elevations generally occur in patients after coronary artery surgery.

No patient, however, had a severely raised MB-CK without any other evidence of infarction, and further work is necessary to determine a true 'upper normal' MB-CK after open-heart surgery that does not indicate AMI, but may be due to surgical trauma, myocardial hypothermia, or intra-operative defibrillation. It appears that Tc-PYP uptake is a more specific marker of peri-operative infarction in patients undergoing coronary artery bypass grafting, although the small number studied to date preclude statistical analysis. Some workers (Platt *et al.*, 1976) however, have found the scan significantly more sensitive than the ECG or enzymes in this context, and others find the scan a highly valuable adjunct to the ECG (Klausner *et al.*, 1977).

Conclusion

In conclusion, therefore, the Tc-PYP scan performed at the bedside is a quick, reliable and non-invasive method for detecting acute infarction. As far as patient management is concerned, the scan offers little extra when the diagnosis is evident from the electrocardiographic appearance of Q waves, but in those cases where a clinical history is unobtainable, Q waves are not present, or when enzymes are equivocal, a positive scan confirms that such patients should be managed as having suffered acute infarctions. A negative scan early after symptoms is not enough evidence that infarction has not occurred, however, and the Tc-PYP scan cannot therefore serve as a screening technique for admission to a CCU.

In the syndrome of unstable angina, it appears that scintigraphic detection of necrosis is an expression of the high sensitivity of this method, but further studies, including improved cardiac isoenzyme techniques are required before the exact sensitivity of the scan in this context is realized.

In the peri-operative environment, the Tc-PYP scan is of major value in detecting acute infarction given the limitations of conventional investigations in this setting; but the positive scans should be interpreted, as in all patients, in the light of the entire clinical picture.

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