Improved detection of myocardial infarction by emission computed tomography with thallium-201

Relation to infarct size

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SUMMARY Emission computed tomography with thallium-201 was compared with planar imaging in its ability to detect myocardial infarctions of various sizes four weeks after the onset. Tomography was performed after planar imaging at rest in 160 patients with a first myocardial infarction, in whom infarct size was prospectively estimated by the peak value of creatine kinase activity at the time of the acute episode and in 39 patients without infarction. The planar images and the transaxial, short axial, and long axial tomograms were interpreted qualitatively. Tomography was significantly more sensitive than planar imaging in detecting anterior (87% *v* 96%), inferior (73% *v* 97%), and non-transmural (47% *v* 87%) infarcts. The increased sensitivity was confined to detecting small infarcts as assessed by the peak creatine kinase value (44% *v* 89% when peak creatine kinase activity was ≤ 1000 IU/l). The overall sensitivity was 96% for tomography and 78% for planar imaging. The specificity was similar (92%) with the two techniques.

Thus emission computed tomography can improve the detection rate of small infarcts that cannot be identified on planar images, by showing the three dimensional distribution of thallium-201, and increases the diagnostic value of thallium-201 scintigraphy.

Thallium-201 myocardial scintigraphy has been extensively used in the detection of myocardial infarction¹⁻³ as well as of coronary artery stenosis.⁴⁻⁶ Although more sensitive and specific than electrocardiography, the sensitivity of planar imaging for detecting infarction is still not 100%,^{3,7,8} possibly because of the difficulty in detecting small infarcts owing to the geometric constraints of a two dimensional display.^{9,10} Emission computed tomography with a rotating gammacamera provides tomographic sections with little of the interplanar propagation^{11,12} seen in pinhole tomography.^{13,14} Although several preliminary studies have suggested that emission tomography is superior to planar imaging in assessing myocardial infarction with thallium-201,¹⁵⁻¹⁷ the

advantage of this technique in detecting myocardial infarction has not been adequately studied in a large series of patients. Moreover, it is still not clear how the detection of small infarcts can be improved by tomography. Accordingly, we undertook this prospective study in patients with myocardial infarction in whom infarct size was estimated by enzymatic analysis during the acute episode. We assessed the ability of both planar imaging and emission computed tomography with thallium-201 to detect myocardial infarction four weeks after its onset with particular reference to the infarct size.

Patients and methods

We studied 160 patients (133 men and 27 women, mean age 58 (range 31-78) years) after their first myocardial infarction documented by a history of typical chest pain lasting one hour or more, the presence of a characteristic pattern of increase in the serum

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creatinine kinase activity above normal values, and the appearance of Q waves or the evolution of ST-T changes characteristic of infarction on the electrocardiogram. These patients were selected from consecutive patients admitted to our coronary care unit with acute myocardial infarction between September 1981 and December 1983 on the basis of the following criteria: (a) a first acute myocardial infarct with neither clinical nor electrocardiographic evidence of a previous infarction; (b) no recurrence of myocardial infarction after the completion of the enzyme assay until the time of the scintigraphic study; and (c) a peak creatine kinase value measured from serial serum determinations.

To evaluate the problem of false positive test results, we studied 39 additional patients without myocardial infarction (29 men and 10 women, mean age 53 (range 42–64) years). These patients were selected on the basis of normal left ventricular function and regional wall motion at cardiac catheterisation. Twenty of these patients had completely normal coronary arteries. The remaining 19 patients had <75% narrowing of at least one coronary artery.

Serum creatine kinase activities were determined at four hourly intervals for 48 hours from the time of admission and every 12 hours for the following 48 hours. The peak value in the serum creatine kinase curve was used as a biochemical estimate for the extent of the acute myocardial necrosis.^{18,19} The upper limits of normal for creatine kinase in our laboratory is 80 IU/l for men and 70 IU/l for women.

ELECTROCARDIOGRAPHY

Standard 12 lead electrocardiograms were recorded at the time of admission and at least once daily for the following seven days. Transmural infarction was defined as the development of new pathological (0.04 s) Q waves and non-transmural infarction as transient ST-T changes without the subsequent development of Q waves. The electrocardiographic localisation of the transmural infarction was determined according to the criteria of the American Heart Association.²⁰ For analysis, antero-septal and anterolateral transmural infarcts were grouped as anterior, whereas inferior and inferoposterior transmural infarcts were grouped as inferior infarctions.

MYOCARDIAL SCINTIGRAPHY

Thallium-201 myocardial scintigraphy was performed four weeks after the onset of infarction in all patients with infarction and 1–7 days before or after cardiac catheterisation in the control patients. Images were obtained approximately 10 minutes after an intravenous injection of 71.3 MBq (2 mCi) of thallium-201 at rest using a large field of view gammacamera (Hitachi: Gamma View) equipped with a low energy high resolution parallel hole collimator. Planar views included the anterior, 30°, 45°, and 60° left anterior oblique, and left lateral projections, and 300 000 counts were collected for each image.

COMPUTED TOMOGRAPHY

After planar imaging, tomography was performed

Fig. 1 Normal emission computed tomograms with thallium-201: (a) transaxial images (viewed from below with anterior surface up) from the cranial (left) to the caudal region (right); (b) short axis images (viewed from the apex) from the apex (left) to the base (right); (c) long axis images (viewed from the right anterior oblique projection) from the septal (left) to the lateral region (right).

Thallium-201 emission tomography in myocardial infarction

using a rotating gammacamera with a high resolution parallel hole collimator supported by a gantry (General Electric: Maxi-400 T) interfaced to a digital computer (DEC: PDP 11/60). The camera rotated from a 45° left posterior oblique to a 45° right anterior oblique position of the patient so that data from only the anterior half of the heart were collected. A total of 32 discrete view images (one image every 5.8°) were acquired over 180°. Each image was acquired for 30 s for a total acquisition time of 16 minutes. Contiguous transaxial tomograms were reconstructed into 12 mm thick multiple sections by a filtered back projection method using a convolution algorithm^{17,21} without attenuation correction. Thereafter, the tomographic images along the short and long axes of the heart were reorganised from the set of transaxial tomograms according to the method described by Borrello *et al.*²² Each reconstructed section contained 150 000 to 200 000 counts. The reconstructed images were displayed in a 64×64 matrix (Fig. 1).

All planar and tomographic images were interpreted qualitatively and independently by two experienced observers unaware of the clinical findings. A perfusion defect was defined as a discrete region of absent or decreased thallium-201 activity, present in at least two views of the planar images and at least two sections of the tomographic images. In eight cases in the planar study and in four in the tomographic study there was observer disagreement and a consensus was reached.

Sensitivity was calculated as the number of true positives divided by the number of true positives plus false negatives multiplied by 100(%). Specificity was calculated as the number of true negatives divided by the number of false positives plus true negatives multiplied by 100(%). The sensitivity and specificity of the two techniques was compared using McNemar's test. χ^2 analysis was used to determine the significance of differences between the groups. A *p* value of <0.05 was considered to be significant.

Results

SITE AND EXTENT OF INFARCTION

Of the 160 patients with infarction, the electrocardiographic site of transmural infarction was anterior in 85 and inferior in 60. Fifteen patients had non-transmural infarction. The extent of the myocardial necrosis estimated by the peak creatine kinase value ranged from 175 to 6469 IU/l (Fig. 2). These values ranged from 180 to 6469 IU/l among the 85 patients with anterior myocardial infarction, from 175 to 3706 IU/l among the 60 with inferior infarction, and from 178 to 1180 IU/l among the 15 with non-transmural infarction. Overall, the peak creatine kinase value was ≤ 1000 IU/l in 63 patients (27 with anterior, 24 with

Fig. 2 Distribution of infarctions according to size (peak creatine kinase value) and location among 160 patients with myocardial infarction: (a) anterior, (b) inferior, and (c) non-transmural infarctions, and (d) all patients.

inferior, and 12 with non-transmural infarction) and >1000 IU/l in the remaining 97 patients (58 with anterior, 36 with inferior, and three with non-transmural infarction).

THALLIUM-201 MYOCARDIAL SCINTIGRAPHY

The results of both planar imaging and tomography are given in Tables 1 and 2. In 125 of 160 (78%)

Table 1 Results of planar imaging and tomography with thallium-201 in 160 patients with and 39 patients without myocardial infarction. Figures are numbers (%) of patients

	Planar imaging	Tomography	Significance
Sensitivity:			
Anterior	74/85 (87)	82/85 (96)	<i>p</i> <0.02
Inferior	44/60 (73)	58/60 (97)	<i>p</i> <0.001
Non-transmural	7/15 (47)	13/15 (87)	<i>p</i> <0.05
Overall	125/160 (78)	153/160 (96)	<i>p</i> <0.001
Specificity	36/39 (92)	36/39 (92)	NS

Table 2 Detection of myocardial infarction with respect to the location, type, and size of infarction. Figures are numbers (%) of patients

Location and peak CK value (IU/l)	Planar imaging	Tomography	Significance
Anterior			
≤1000	16/27 (59)	24/27 (89)	p<0.02
≥1001	58/58 (100)	58/58 (100)	NS
Inferior			
≤1000	8/24 (33)	22/24 (92)	p<0.001
≥1001	36/36 (100)	36/36 (100)	NS
Non-transmural			
≤1000	4/12 (33)	10/12 (83)	p<0.05
≥1001	3/3 (100)	3/3 (100)	NS
Overall			
≤1000	28/63 (44)	56/63 (89)	p<0.001
≥1001	97/97 (100)	97/97 (100)	NS

CK, creatine kinase.

patients with myocardial infarction, perfusion defects were detected by both planar imaging and tomography. In 28 of 160 (18%) patients perfusion defects were identified only by tomography. In seven patients, both planar imaging and tomography were normal. In no patient were defects detected by planar imaging and not by tomography. Overall sensitivity in detecting myocardial infarction was 125 of 160 (78%) by planar imaging and 153 of 160 (96%) by tomography ($p<0.001$). In the 39 patients without myocardial infarction, all but three patients were correctly identified as normal by each technique. These three patients had an apical defect on both planar and tomographic images. Specificity was thus 92% for both planar imaging and tomography.

Table 1 also shows the sensitivities of scintigraphy with respect to the electrocardiographic location and type of infarction. Planar imaging less commonly detected inferior or non-transmural infarcts than anterior infarcts ($p<0.05$), whereas tomography significantly improved the detection of infarcts independent of the location and type of infarction. The increased sensitivity of tomography was, however, confined to the detection of small infarcts as assessed by the peak creatine kinase value (Table 2). In 97 patients with a peak creatine kinase value >1000 IU/l, sensitivity was 100% for both techniques. In 63 patients with a peak creatine kinase of ≤ 1000 IU/l, by contrast, sensitivity was only 44% for planar imaging and 89% for tomography ($p<0.001$) (Table 3).

In all cases, the sites of perfusion defects were concordant when present in both planar and tomographic studies and corresponded closely with the electrocardiographic location.

Fig. 3 illustrates the case of a patient with inferior myocardial infarction in whom the planar images were normal. The tomographic study, however, showed a definite inferior perfusion defect, seen best on the short axial and long axial images.

Discussion

With planar imaging, numerous studies have reported the ability of thallium-201 myocardial scintigraphy to evaluate patients with myocardial infarction.^{3,7,10} Good qualitative relations have been found between the location of thallium-201 perfusion defects and evidence of myocardial infarction by electrocardiography,³ ventriculography,²⁸ coronary angiography,^{4,6} cardiac enzymes,²³ and postmortem studies.²⁴ Sensitivity in acute myocardial infarction has been reported by Wackers *et al* to be 100% within the first six hours, 76% within 24 hours, and 73% after 48 hours.⁷ Ritchie *et al* found sensitivities of 85% within the first seven days and of 70% after that period.³ This reduction in the sensitivity with increasing time from the onset of myocardial infarction may be related to a decrease in defect size due to the resolution of ischaemia around a small area of infarction.^{3,7}

Because in this study we aimed to detect residual myocardial scarring rather than ischaemia, these studies were performed at rest in stable patients four weeks after the onset of infarction, when ischaemia would not play a large role. The overall sensitivity and specificity of planar imaging were 78% and 92% respectively (Table 1). These results are in good agreement with the findings of other workers.^{3,6,7} We

Table 3 Results of planar imaging and tomography with thallium-201 in 63 patients with a peak creatine kinase value of ≤ 1000 IU/l. Figures are numbers (%) of patients

Peak CK value (IU/l)	Planar imaging	Tomography
≤200	0/6 (0)	3/6 (50)
201-400	1/10 (10)	7/10 (70)
401-600	7/16 (44)	15/16 (94)
601-800	8/15 (53)	15/15 (100)
801-1000	12/16 (75)	16/16 (100)
Total	28/63 (44)	56/63 (89)

CK, creatine kinase.

Fig. 3 (a) Planar images and (b) tomograms in a patient with inferior myocardial infarction. No apparent perfusion defects were identified on the planar images. The tomograms showed a definite inferior defect (arrows), seen best on the short axis and long axis images. LAO, left anterior oblique.

also found that a significant incidence of false negative results in patients with a small infarct accounted for the unsatisfactory sensitivity of planar imaging (Tables 2 and 3).

In planar imaging, background or non-myocardial activity overlaps myocardium, and some normal myocardium from an adjacent or opposing myocardial wall is partly superimposed on a given regional defect.

These may mask the presence of perfusion defects. Experimental studies by Mueller *et al* showed that a minimum of 5 g of myocardium must be affected in an abnormal thallium-201 uptake for a defect to be visualised on a planar image.⁹ Clinically, Niess *et al* showed that generally 6% or more of the left ventricle must be damaged to be detected on a planar image at rest.¹⁰ When all these findings, including those of the

present study, are taken together thallium-201 planar imaging appears to be of limited value as a diagnostic tool in patients with myocardial infarction if the studies are not performed soon after infarction.

Tomographic imaging, although offering no intrinsic improvement of spatial resolution by itself, can help to detect small areas of ischaemia by avoiding the effects of activity from surrounding structures and by increasing contrast between normal and infarcted myocardium.^{25 26} Indeed, tomography showed a significant improvement in detecting small infarcts as assessed by the serum enzyme values independent of the location and type of infarction (Tables 2 and 3). Our equipment can reorganise not only transaxial tomograms but also short axial and long axial tomograms, which greatly helped the accurate assessment of radionuclide distribution (Fig. 3). As a result, tomography yielded a higher overall sensitivity than planar imaging in the detection of infarction without significant loss of specificity (Table 1). This improvement is of clinical importance because the diagnosis or exclusion of myocardial infarction is a common and sometimes difficult problem in clinical practice.

In addition to its diagnostic value, thallium-201 scintigraphy provides prognostic information.^{27 28} Moreover, this technique has been recently used for assessing the effect of intracoronary thrombolysis on myocardial salvage.^{29 30} Another advantage of tomography is in improving the quantification of the extent of perfusion abnormalities as reported previously.¹⁷ Although cardiac motion and attenuation corrections are still problems that prevent accurate quantification, tomography can provide more detailed information of the changes in myocardial perfusion resulting from therapeutic interventions.

The relatively short data collection time allows this tomographic approach to be applied to transient perfusion abnormalities induced by exercise. Tomography might be expected to increase the accuracy of thallium-201 imaging to detect individual coronary artery involvement and even less pronounced coronary artery disease. But this subject requires further study.

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