

Potential value of thallium-201 scintigraphy as a means of selecting patients for the coronary care unit

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SUMMARY The potential value of thallium-201 scintigraphy as a means of selecting patients for appropriate coronary care unit admission was evaluated. Studies were made prospectively on 203 patients with possible acute myocardial infarction but atypical history and non-diagnostic electrocardiogram at a time when the clinical diagnosis was still in doubt. Under conventional circumstances, this particular group of patients will be admitted to the coronary care unit for observation in order to rule out myocardial infarction by further clinical evaluation. Scintigraphy was performed upon arrival in the coronary care unit and within 10 hours after the last episode of chest pain. Of 203 patients, 49 had positive, 47 had questionable, and 107 had normal thallium-201 scintiscans. Serial serum enzyme determinations and further clinical follow-up disclosed acute myocardial infarction in 34 patients: all had abnormal scans. Of 47 patients subsequently determined to present with unstable angina, 27 had abnormal scans, of whom 7 subsequently developed acute myocardial infarction. Of 24 patients with previous myocardial infarction, 18 patients had abnormal scans. None of either the 25 patients with stable angina or the 73 patients with atypical complaints showed frank perfusion defects, though questionable abnormal scintiscans were obtained in 5 and 12 patients in these groups, respectively.

It is concluded that thallium-201 scintigraphy, when performed within a time interval of 10 hours after the last episode of chest pain, may be of value as a means of selecting those patients requiring further stay in hospital and observation in the coronary care unit.

We have reported previously that thallium-201 scintigraphy is a highly sensitive technique for the detection of acute myocardial infarction, especially during the very early period after the onset of symptoms (Wackers *et al.*, 1975, 1976). In addition, a considerable number of patients with unstable angina will show abnormal thallium-201 scintiscans during the pain free period after an anginal attack (Wackers *et al.*, 1978). The purpose of the present study was to assess the potential of thallium-201 scintigraphy to serve as a more appropriate means of selecting patients for admission to the coronary care unit. In many patients, the diagnosis of acute myocardial infarction is obvious at the time of hospital arrival. However, among the patients referred to the coronary care unit of our hospital, a significant number have complaints which are determined

subsequently not to be caused by acute coronary artery disease. In many of these patients the history and initial electrocardiogram will provide sufficient information to recognise the non-cardiac character of the complaints. Nevertheless, a substantial group of patients still remains in whom initial evaluation provides a questionable history and a non-diagnostic electrocardiogram; in these patients admission and further clinical observation for at least 24 hours seems unavoidable in order to rule out acute myocardial infarction or ischaemia. In order to maximise efficient management and use of the coronary care unit, early and proper characterisation of patients in whom the diagnosis remains in question is essential. The results of the present study indicate that thallium-201 scintigraphy might be of value as a means of selecting those from within the above-mentioned group of patients who, in fact, require coronary care unit admission and further observation.

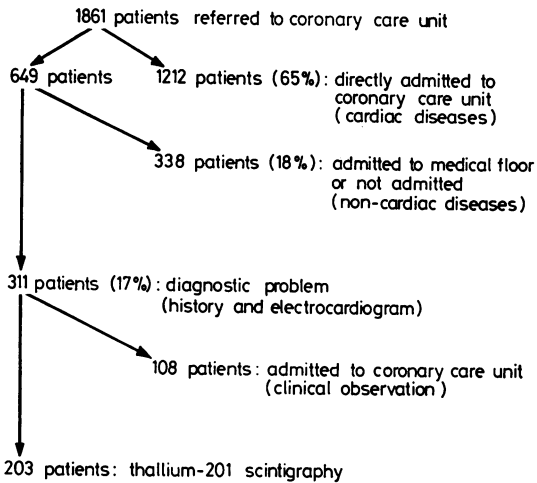


Fig. 1 Admission policy in 1861 patients referred to the coronary care unit. In 203 patients thallium-201 scintigraphy was evaluated as a potential selection method.

Subjects and methods

A prospective study was performed from September 1975 to September 1976. During this period 1861 patients were referred to the coronary care unit because of presumed acute myocardial infarction. The admission policy for these patients is shown in Fig. 1. There were 1212 patients (65%) who were directly admitted because of evident acute cardiac disease from the history and/or electrocardiogram. In 338 patients (18%) cardiac disease could be ruled out by the history, symptoms, physical examination, and electrocardiogram. These patients were either transferred to other departments or they were allowed to return home. A diagnostic problem was posed by 311 (17%) patients because of atypical history and/or non-diagnostic electrocardiogram. Such patients usually are admitted to the coronary care unit for a further evaluation period of at least 24 hours. In 203 of the 311 patients thallium-201 scintigraphy was performed at arrival in the coronary care unit. In these patients the time interval between the last episode of chest pain and scintigraphy did not exceed 10 hours. Entry into the study of these 203 patients in whom the diagnosis initially was unclear was determined only by the availability of the radiopharmaceutical and the gamma camera. The additional 108 diagnostically undefined patients not studied with thallium-201 were admitted for the usual clinical observation period.

SCINTIGRAPHY

All scintigraphic studies were performed with an

Ohio Nuclear ON-100 scintillation camera installed in the coronary care unit. Thallium-201 scintigraphy was performed as soon as possible after arrival of the patients. Using a low energy, high resolution, parallel hole collimator and a 20 per cent energy window set symmetrically over 75 keV, scintiscans were obtained 5 to 10 minutes after intravenous injection of 1.6 to 2.7 mCi thallium-201 chloride. Scintiscans accumulating 300 k counts were obtained in 3 views (anterior 0°, left anterior oblique 45°, and left lateral, the latter with the patient positioned on his right side). The analogue unprocessed images were judged without knowledge of clinical data as positive, questionable, or normal. The judgement concerning diminished or absent regional thallium-201 activity was made qualitatively by comparison of thallium-201 accumulation in different areas of the left ventricular myocardium. The scintiscans read as 'positive' or 'defect', showed a consistent area of definite diminished thallium-201 activity, equal to or less than lung activity, on all three views. 'Questionable' scans represented either a consistent area with diminished activity but slightly higher than background activity on all three views or a defect on only one view. 'Normal' scans showed homogeneous uptake of the radiopharmaceutical in the left ventricle on all three views.

All scintiscans were read by at least two observers. The results in this study represent a consensus of the observers.

ADMISSION POLICY AND FOLLOW-UP

The results of scintigraphy were made available to the attending physician in the coronary care unit and at times affected his final judgment. Of the 203 patients studied, 116 patients were admitted to hospital (63 in the coronary care unit and 53 in the medical floor) and 87 patients were allowed to return home.

All patients admitted to the coronary care unit or medical floor had a similar follow-up for 2 to 3 weeks, while all patients who returned home were seen again after 2 or 3 days, or earlier if either enzyme levels were raised or complaints persisted. In addition, all the latter patients were seen for follow-up after 8 to 12 months (mean 9 months).

ELECTROCARDIOGRAM

Twelve lead electrocardiograms were obtained in all patients at arrival at the coronary care unit, before thallium-201 scintigraphy. The patients who were in hospital had electrocardiograms taken at least twice daily. The patients who returned home all had a follow-up electrocardiogram 2 or 3 days after the scintigraphic study and at the follow-up at 8 to 12 months.

ENZYME DETERMINATIONS

For all patients blood samples were taken approximately at the time of scintigraphy for determination of enzyme levels (SGOT, SGPT, LDH, and CKMB) and subsequently each 6 hours for at least 24 hours in those patients who were in hospital. The patients who returned home all had a second blood sample taken at the second or third day at follow-up.

FINAL DIAGNOSIS

A major objective of this study was to assess the accuracy of thallium-201 scans to detect patients with acute myocardial infarction. Though the remaining patients, without acute infarction, all had an atypical history on admission, further observation allowed separation into several subgroups. The final diagnosis was based upon the results of enzyme level determinations, the development of electrocardiographic changes, and the impression obtained after further clinical evaluation. The following diagnostic criteria were employed.

Acute myocardial infarction

(1) Enzyme levels showing typical rise and fall after admission; (2) electrocardiographic development of diagnostic Q waves (more than 0.03 s in duration), loss of R waves, or T wave inversion.

Unstable angina progressing to acute myocardial infarction

(1) Normal enzyme levels at the time of scintigraphy; (2) the occurrence of a new severe attack of chest pain within 24 hours of admission to hospital, followed by the electrocardiographic development of diagnostic Q waves, loss of R waves, or T wave inversion, and typical rise and fall of enzyme levels.

Unstable angina

(1) Normal enzyme levels during the observation period; (2) upon further questioning, a history suggesting angina pectoris increasing in severity and frequency within a period of approximately 10 days before admission; (3) transient electrocardiographic changes were not required. (*Note:* Since all patients included in this study had an atypical history on admission, the term 'unstable angina' is defined more liberally than usual.)

Previous myocardial infarction

(1) Diagnostic Q waves on the electrocardiogram; (2) normal enzyme levels during the observation period.

Stable angina pectoris

(1) Normal enzyme levels; (2) history of chest

pain occurring on exertion and disappearing at rest, relieved by glyceryl trinitrate.

Atypical complaints

(1) Normal enzyme levels; (2) after further questioning it was felt that the complaints had to be interpreted as atypical and most likely of non-cardiac origin.

SENSIVITY, SPECIFICITY, AND PREDICTIVE ACCURACY

The sensitivity of thallium-201 scintiscans was defined as:

$$\frac{\text{True positives (TP)}}{\text{TP} + \text{false negatives (FN)}} \times 100$$

The specificity was defined as:

$$\frac{\text{True negatives (TN)}}{\text{TN} + \text{false positives (FP)}} \times 100$$

The predictive accuracy of a positive test was defined as:

$$\frac{\text{TP}}{\text{TP} + \text{FP}} \times 100$$

Results

SCINTIGRAPHY

The results of thallium-201 scintigraphy were available within 1½ to 2 hours after arrival of the patients in the coronary care unit. Of the 203 patients, 49 had positive, 47 had questionable, and 107 had normal scans.

ELECTROCARDIOGRAM

Except for one patient who had complete left bundle-branch block, all patients showed normal initial ventricular activation pattern on the electrocardiogram at the time of scintigraphy. The electrocardiogram was normal in 78 patients and showed nonspecific ST segment changes in 125 patients. The relation between the scintigraphic results and the electrocardiographic findings is shown in Table 1.

Table 1 Relation between results of thallium-201 scintigraphy and electrocardiogram in 203 patients

Scintigraphy	Electrocardiogram		Total
	Normal	Nonspecific ST-T segment changes	
Defect	12	37	49
Questionable	17	30	47
Normal	49	58	107

FINAL DIAGNOSIS

On the basis of serum enzyme determinations, 34 patients (17%) had acute myocardial infarction at the time of scintigraphy. Fourteen of these patients evolved electrocardiographic transmural infarctions with peak SGOT rise of more than 4 times upper limit of normal; of these patients 2 had recurrent infarction. Twenty patients had electrocardiographic non-transmural or biochemically small infarctions (SGOT rise less than 4 times upper limit of normal). Forty-seven patients (23%) had 'unstable angina' at the time of thallium-201 scintigraphy; in 7 of these this progressed to acute myocardial infarction within 24 hours after admission, and 4 out of these 7 patients had electrocardiographic transmural infarctions. The remaining 40 patients with 'unstable angina' all had an unremarkable course. Twenty-four patients (12%) had previous myocardial infarction. Twenty-five patients (12%) were considered to have symptoms of stable angina pectoris. In 73 patients (36%) the final impression was of atypical complaints, most likely of non-cardiac origin.

RELATION BETWEEN FINAL DIAGNOSIS AND RESULTS OF THALLIUM-201 SCINTIGRAPHY (FIG. 2)

All patients determined subsequently to have had acute myocardial infarction at the time of scinti-

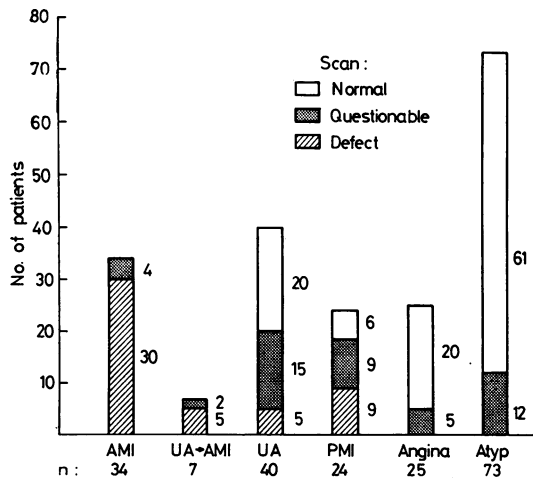


Fig. 2 Final diagnosis and results of scintigraphy in 203 patients referred to the coronary care unit. The final diagnosis is based on the results of enzyme level determinations, the development of electrocardiographic changes, and the re-evaluation of the patient's history. Abbreviations: AMI, acute myocardial infarction; PMI, previous myocardial infarction; UA, unstable angina, UA → AMI, unstable angina progressing to acute myocardial infarction; atyp, atypical complaints.

graphy had abnormal scans: 30 patients showed definite defects on the scintiscans, and in the remaining 4 patients the scintiscans were judged as questionable. The 2 patients with recurrent infarction both had positive scans. Of the 7 patients with 'unstable angina' who developed acute myocardial infarction, 5 patients had positive scans, and 2 had questionable scans. Of the remaining 40 patients with uncomplicated 'unstable angina', 5 had positive scans, 15 had questionable scans, and 20 had normal scans. Of the 24 patients with previous myocardial infarction, 9 showed a defect, 9 had questionable scans, and 6 had normal scans. None of the patients with stable angina pectoris or atypical complaints had a defect on the thallium-201 scans. Five of 25 patients with stable angina had questionable scans, the remaining 20 had normal scans. Of the 73 patients with atypical complaints, 12 patients had questionable scans and 61 patients had normal scans. Thus, positive scans were obtained only in patients with acute or previous myocardial infarction or 'unstable angina'. Questionable scans were obtained in 30 of 105 patients with myocardial infarction or 'unstable angina' compared with 17 of 98 patients with stable angina or atypical complaints. This difference is, however, not significant. Normal scans were obtained in 26 of 105 patients with myocardial infarction or 'unstable angina', compared with 81 of 98 patients with stable angina or atypical complaints ($P < 0.01$).

SENSITIVITY, SPECIFICITY, AND PREDICTIVE ACCURACY OF THALLIUM-201 SCINTISCANS

The sensitivity, specificity, and predictive accuracy of thallium-201 scintiscans to detect patients with acute myocardial infarction, 'unstable angina', and previous myocardial infarction are given in Table 2. Positive thallium-201 scans have an 88 per cent

Table 2 Diagnostic value of thallium-201 scintigraphy for various diagnoses in 203 patients

Scintiscans	Diagnosis	Sensitivity (%)	Specificity (%)	Predictive accuracy (%)
Positive	AMI	88	88	61
	AMI, UA → AMI	85	91	71
	AMI, UA	49	92	81
	AMI, PMI, UA	46	100	100
Positive + Questionable	AMI	100	63	35
	AMI, UA → AMI	100	66	42
	AMI, UA	75	71	63
	AMI, PMI, UA	75	82	82

Abbreviations: AMI, acute myocardial infarction; UA → AMI, unstable angina progressing to AMI; PMI, previous myocardial infarction.

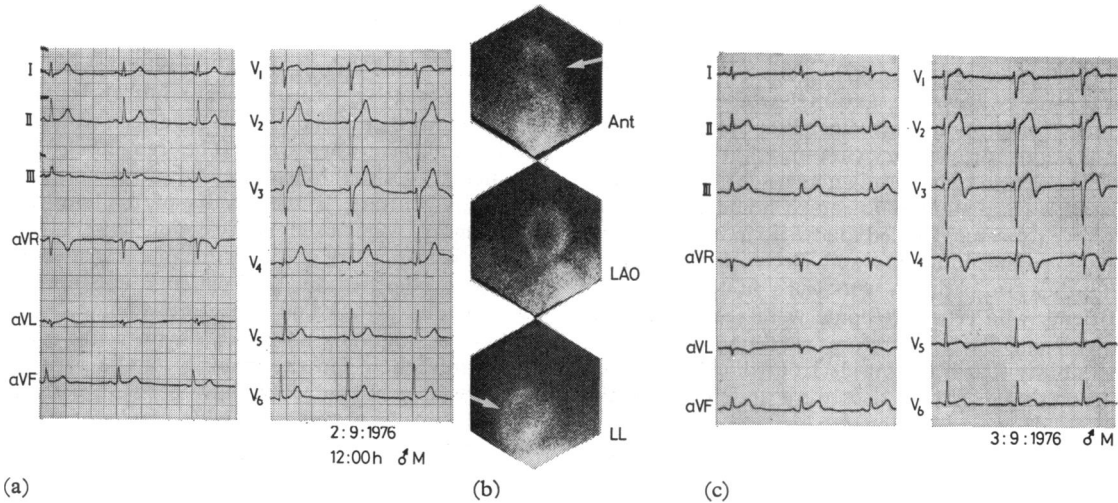


Fig. 3(a) Electrocardiogram on admission of a 37-year-old man. During the night before admission he experienced recurrent attacks of atypical praecordial pain, which had subsided at admission. Though there is loss of R wave in V3, this electrocardiogram is not diagnostic for acute myocardial infarction. (b) Thallium-201 scintiscans at the time of the electrocardiogram in Fig. 3a. An evident area of diminished activity is present at the anterolateral wall (arrows). CKMB level at the same time was raised (10 times the upper limit of normal). Peak SGOT level indicated that the infarction was probably small (2.5 times the upper limit of normal). Abbreviations: Ant, anterior 0° view; LAO, left anterior oblique 45° view; LL, left lateral 90° view. (c) Electrocardiogram of the same patient as in Fig. 3a and 3b 24 hours after admission. Changes compatible with acute anterior wall infarction have developed. These changes occurred 10 hours after admission.

sensitivity, 88 per cent specificity, and 61 per cent predictive accuracy to detect acute myocardial infarction in the particular patient population studied. The sensitivity increases to 100 per cent when questionable scans also are included but then the specificity and predictive accuracy decrease to 63 and 35 per cent, respectively. Positive scans have a specificity of 92 per cent and a predictive accuracy of 81 per cent to detect the group of patients with acute myocardial infarction or 'unstable angina' but the sensitivity is 49 per cent. The sensitivity is 75 per cent in the latter group when questionable scans also are included. The specificity and predictive accuracy to recognise patients in whom perfusion defects may be expected (that is, acute myocardial infarction, 'unstable angina', and previous myocardial infarction) by positive scans are 100 per cent: no false positive scintiscans were obtained. For questionable scans these values were 82 per cent.

Discussion

The present study deals with a common diagnostic dilemma in the coronary care unit or emergency room. Neither the patient's history nor electrocardiogram permitted a definite diagnosis at the time of admission. Yet, 34 patients evolved acute

myocardial infarction, and all these patients had abnormal (positive or questionable) thallium-201 scintiscans on admission. Diagnostic electrocardiographic changes occurred in these patients only hours after admission. Fig. 3 shows an example of such a patient. Behar *et al.* (1977) evaluating the electrocardiogram as a decision making tool in a consecutive series of patients in the emergency room reported that 35 per cent of the patients with acute myocardial infarction showed a normal electrocardiogram at arrival in the emergency room.

In the present study, positive thallium-201 scans also were obtained in 10 patients with 'unstable angina' and in 9 patients with previous myocardial infarction. Of the 10 patients with 'unstable angina' and positive scans, 5 developed acute myocardial infarction after being admitted to hospital; similar progression occurred in 2 of 22 patients with 'unstable angina' and questionable scans. The finding of positive scans in patients with unstable angina is in agreement with our results in a larger series of patients with unstable angina, in which positive scans were obtained in 50 per cent of the patients studied within 6 hours after the last anginal attack (Wackers *et al.*, 1978). This is not surprising since thallium-201 uptake in the myocardium reflects regional myocardial perfusion (Strauss *et al.*, 1975;

DiCola *et al.*, 1977) and the integrity of the Na⁺K⁺-ATPase system (Britten and Blank, 1968; Adolph *et al.*, 1976; Gelbart *et al.*, 1976). This lack of specificity is not necessarily a disadvantage, since both myocardial infarction and unstable angina provide indications for coronary care unit admission.

The design of our study may be criticised since 78 patients were allowed to return home and did not receive the same detailed follow-up in terms of serial enzyme determinations and electrocardiograms as did the 116 patients who were in hospital. The patients who returned home were seen again only after 2 or 3 days. Therefore, we cannot exclude the possibility that transient electrocardiographic changes or slight enzyme rises were undetected in this group. However, in the 116 patients who were in hospital and who were followed up closely, the same excellent agreement existed between final diagnosis and results of thallium-201 scintigraphy as in the patients who returned home. Therefore, it seems unlikely that the results of this study are significantly influenced by this aspect of study design.

The present series of patients represents a highly selected group of patients, in whom neither the electrocardiogram nor the history were diagnostic. Therefore, the value of thallium-201 scintigraphy is maximally challenged. It is in this group of patients that a reliable selection method is needed. A selection procedure for the coronary care unit or emergency room should be able to detect (a) patients with acute myocardial infarction, (b) patients with pre-infarction angina or unstable angina, (c) patients with non-cardiac complaints. The results of this study indicate that thallium-201 scintigraphy might be such a method when positive and questionable scintiscans are considered abnormal. Table 3 illustrates the potential influence of thallium-201 scintigraphy on the admission policy in the coronary care unit. It seems conceivable that in most medical

centres the 203 patients would have been admitted to rule out myocardial infarction. If all patients with acute myocardial infarction and unstable angina are to be admitted to the coronary care unit, then in the present study 81 patients should have been admitted to the intensive care unit. The remaining 122 patients (60%) would have been admitted unnecessarily. In contrast, if the results of thallium-201 scintigraphy were used as selection criteria, 96 patients with positive and questionable scans would have been admitted and 107 patients with normal scans would be allowed to return home. Using thallium scintigraphy all patients with acute myocardial infarction and the majority of the patients with 'unstable angina' would have been correctly in hospital, but 35 patients (18 with previous infarction, 5 with stable angina, and 12 with atypical complaints) would have been in hospital unnecessarily. On the other hand, 20 patients with 'unstable angina' would have been allowed to return home. However, it should be emphasised that 'unstable angina' in the present context represents a liberal use of the terminology. Moreover, all patients with 'unstable angina' and normal scans had an unremarkable and favourable clinical course.

Conclusion

In view of the high cost of the coronary care unit (Peterson, 1976) it could be of value if only those patients with bona fide acute coronary syndromes were admitted. The sensitivity of thallium-201 scintigraphy to detect myocardial perfusion defects indicates that this method might be useful as a selection method for the coronary care unit or emergency room. The standard electrocardiogram may be non-diagnostic during the early hours of an acute infarction in some patients. In addition when abnormal initial ventricular activation pattern is present, such as left bundle-branch block, WPW syndrome, or pacemaker rhythm, the electrocardiographic diagnosis of acute infarction is hampered. Though the use of thallium-201 scintigraphy as a selection method has to be assessed in a prospective controlled study, the following practical guidelines can be given on the basis of the present study: (1) thallium-201 scintigraphy has to be performed within 6 to 10 hours after the last episode of chest pain; (2) in the presence of previous myocardial infarction positive thallium-201 scans have limited value; (3) negative scans within 6 to 10 hours after acute chest pain make acute myocardial infarction unlikely, though acute coronary insufficiency cannot be excluded; (4) positive thallium-201 scans may represent either acute myocardial infarction, previous myocardial infarction, or unstable angina.

Table 3 Evaluation of admission policy in 203 patients: admission based on electrocardiogram and history is compared with that based on thallium-201 scintigraphy and related to final follow-up diagnosis (see text)

	Destination		Incorrect	
	Hospital	Home	Hospital	Home
Electrocardiogram + history	203	—	122 (60%)	—
Thallium-201 scintigraphy	96	107	35 (36%)	20 (18%)
Correct (retrospect)	81 (AMI, UA)	122 (atyp)		

Abbreviations: AMI, acute myocardial infarction; UA, unstable angina; atyp, atypical complaints.

Finally, we should like to emphasize that this study deals with a particular subgroup of patients, in whom the history and electrocardiogram were of little help in the decision making. Thallium-201 scintigraphy has to be considered as an additional diagnostic method, along with history and electrocardiogram, to improve efficient management of the coronary care unit.

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