# THALLIUM-201 MYOCARDIAL STRESS IMAGING: A STUDY OF ITS VALUE IN THE DIAGNOSIS OF CORONARY ARTERY DISEASE AND THE LOCATION OF DISEASED VESSEL

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## SYNOPSIS

**Nuclear cardiology techniques have a definitive role in detection and evaluation of coronary artery disease. In particular myocardial imaging with injection of Thallium-201 at peak exercise, has been found useful in future decisions regarding coronary angiography and surgery. 61 patients had thallium myocardial stress imaging (TSMI) in SGH over a period of one year. Of these 34 had coronary arteriography as well. The thallium study was used to predict coronary vessel disease and compared with results of angiography. TSMI gave a sensitivity of 91.3% and specificity of 88.9% which is similar to results obtained in other centres for planar thallium-201 imaging.**

## INTRODUCTION

Thallium myocardial stress imaging (TSM) is now widely accepted as a useful method for the evaluation of suspected or known coronary artery disease (1-3). Its high sensitivity and specificity (4) for coronary artery disease and its non-invasive nature have made it valuable for the evaluation of atypical chest pain and when the ECG stress test is equivocal or difficult to interpret. It is also useful for the evaluation of patients with known coronary artery disease, after coronary artery bypass surgery and, in special circumstances, to determine the viability of myocardium distal to an anatomical lesion delineated by coronary angiography.

The successful application of TSMI, however, requires meticulous attention to scanning technique and each laboratory must continually review its results especially in relationship to coronary ateriography.

In this study, we retrospectively examined the results of TSMI performed in the Department of Nuclear Medicine, Singapore General Hospital, between July 1983 and September 1984 and compare them with the results of coronary arteriography.

## METHODS

### Patient selection

A total of sixty-one patients underwent TSMI during the stated period. Thirty-four (or 56%) of these patients had coronary arteriography and left ventricular angiogram performed within six months of TSMI as part of their diagnostic evaluation. There were thirty-one males and three females with a mean age of 46.5 years (range 31 to 65 years). Two patients were excluded from the study because they were inadequately stressed — one a 55 year old male who developed exercise induced bronchospasm and the other a 60 year old female with osteoarthritis of both knees. The 32 patients with adequate stress had a mean age of 45.9 years (range 31 — 65 years) and 15 (46%) of them had a history of previous myocardial infarction.

### Exercise Thallium-201 Imaging Protocol

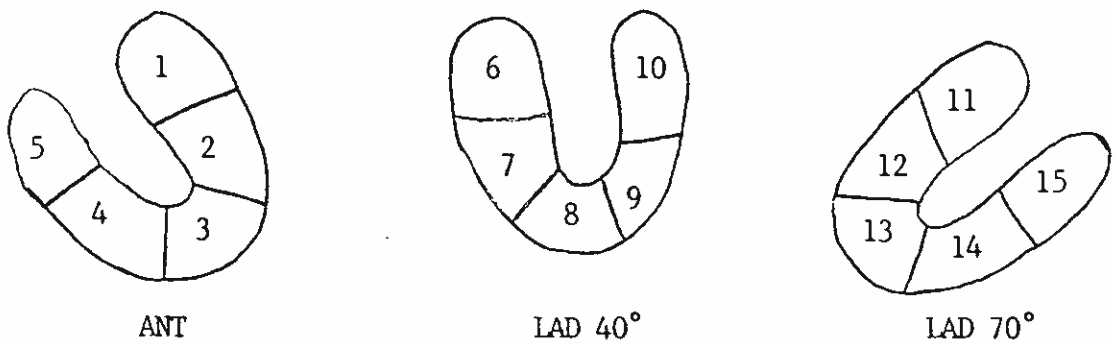
Patients were exercised either on a bicycle ergometer or a treadmill with no attempt to alter drug therapy prior to exercise. Each patient was exercised to achieve a heart rate equal to or better than 85% of his or her predicted maximum or until the onset of limiting symptoms (chest pain, severe breathlessness or fatigue) or signs (ST segment depression — 3mm or a drop in systolic blood pressure of 10 mmHg below the previous blood pressure recording).

1.5 to 2.0 mCi (55 to 74 MBq) of thallium-201 was then injected intravenously through an indwelling cannula in the forearm and flushed with saline. Exercise was continued for another 30—60 seconds as long as symptoms and signs did not deteriorate.

Thallium imaging was then performed immediately and again 3—4 hours later. On each occasion images were obtained in the anterior, left anterior oblique 45 (LAO 45) and left anterior oblique 70 (LAO 70) projections with the patient supine. The gamma camera used was either an Ohio Nuclear Series 100 gamma camera (with a single 20% window centred on the 80 keV X-ray peak) or a General Electric 400A LFOV gamma camera (with two windows centred on the 80 keV X-ray and the 167 keV gamma ray peaks respectively). All early images contained 300,000 counts per view while the delayed images were taken over period of time equal to that required for the corresponding early view of 300,000 counts. The analog images were recorded on film as well as stored in digital form on a General Electric Star computer.

### Interpretation of thallium images

The analog images were reviewed by two nuclear medicine physicians independently without knowledge of the clinical history of the result of other investigations. Each image was divided into 5 equal segments for a total of 15 segments according to the method of Rigo et al (see figure 1). Segments 1, 2, 6, 7, 11




LAD: 1, 2, 6, 7, 11, 12
RCA: 4, 5, 14, 15
LCx: 9, 10
Indeterminate: 3, 8, 13 (usually assigned to anterior circulation [LAD])

Fig 1: Diagram showing the division of the three thallium planar images into 15 segments for identification of the major vascular territories.

and 12 are considered the vascular territory of the left anterior descending artery (and the diagonals), segments 4, 5, 14 and 15 for the right coronary artery and segments 9 and 10 for the left circumflex coronary artery (and the marginals). Segments 3, 8 and 13 are non-specific segments and are described separately unless they extend in continuity into one of the specific segments in a typical pattern.

An abnormal segment is described as MI (myocardial infarction) if the perfusion defect seen in the early stress images persist without change in the delayed images. It is described as Is (Ischaemic) if reperfusion is demonstrated in the delayed images.

## CORONARY ARTERIOGRAPHY

All 31 patients had selective coronary arteriography and left ventricular angiography by the percutaneous femoral technique by the cardiologists and the results were reviewed by one experienced angiographer without knowledge of the clinical history. Each patient was considered to have three major coronary arteries: left anterior descending (LAD), left circumfled (LCx) and right coronary artery (RCA). Coronary artery stenosis of $>50\%$ of the lumen was considered haemodynamically significant. Significant lesions in large diagonal or marginal branches are considered lesions of the left anterior descending or circumflex respectively. Left main disease was not encountered in the study.

## CLINICAL HISTORY

A special attempt was made to identify patients with a past history of myocardial infarction. The presence of Q waves and a definite clinical episode accepted by a cardiologist as a transmural myocardial infarct must be documented. The patient is then considered to have a transmural myocardial infarction (MI) in the area delineated electrocardiographically by the Q waves.

## RESULTS

Nine of our thirty-two patients (9/32 or 28%) did not have significant coronary artery disease. Eight of them had normal coronary arteries on arteriography while the remaining one had only minor irregularities of the left anterior descending artery (patient 27).

Twenty-three (23/32 or 72%) had one or more coronary arteries with 50% narrowing of the lumen. Sixteen of them (16/32 or 70%) had single vessel disease [13 with left anterior descending disease, 2 with circumflex and one right coronary artery], three had two vessel disease and four had three vessel disease (examples of normal and abnormal scans are shown in figures 2—3.

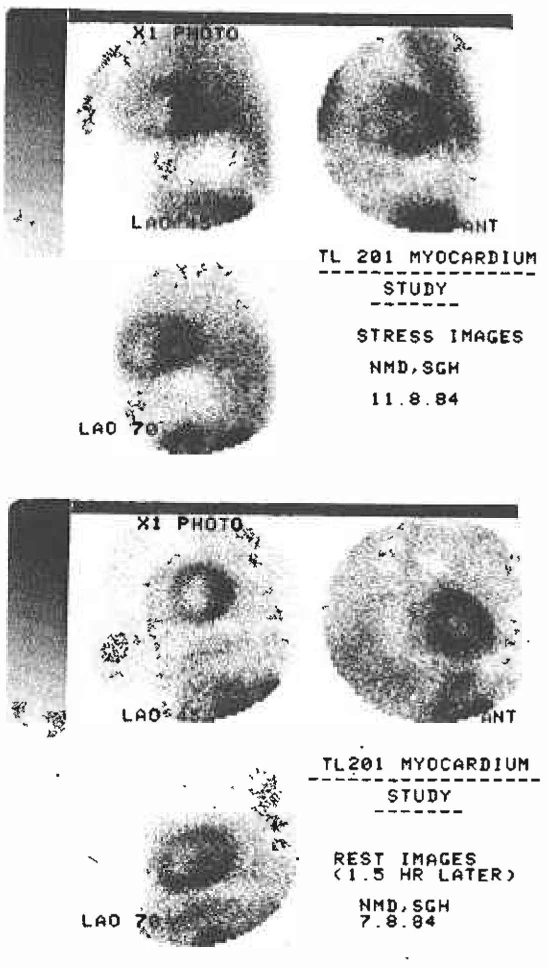



Fig. 2: TMSI; stress and delayed images showing septal ischemia (LAD disease), and lung uptake of Tl-201.

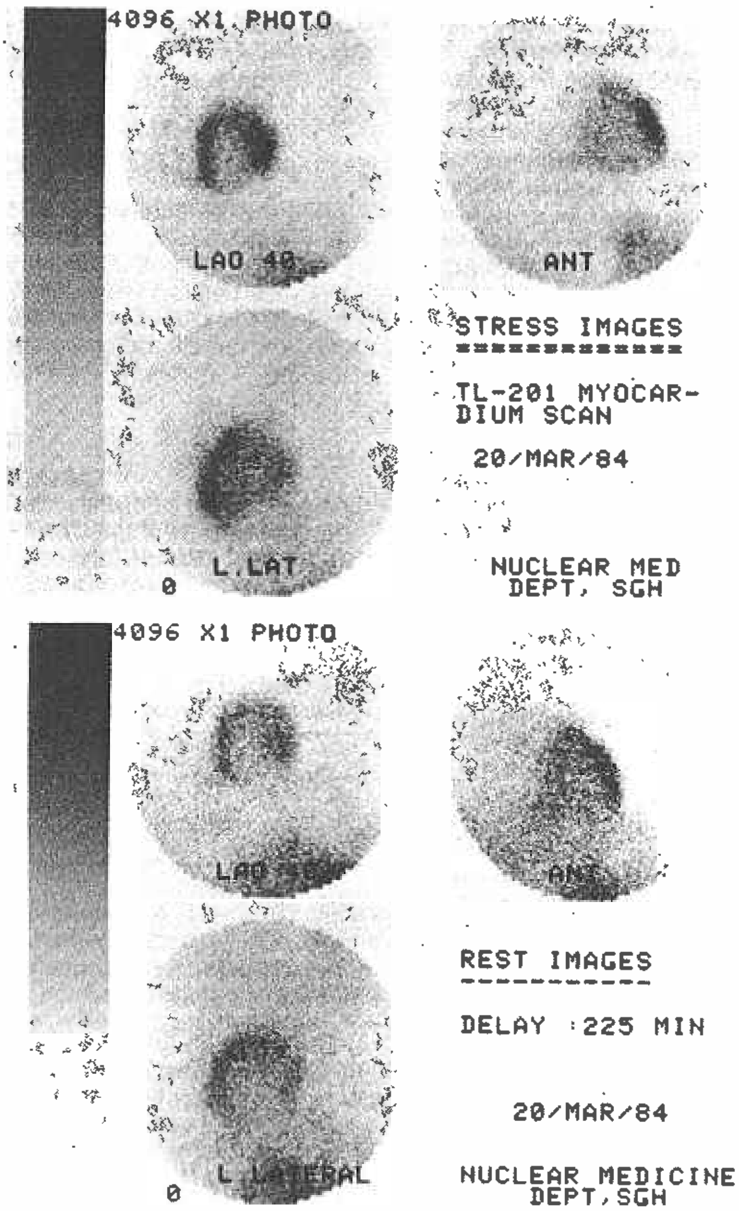



Fig. 3A

Fig. 3A: TMSI; stress and delayed images showing inferior wall defect with no reperfusion.

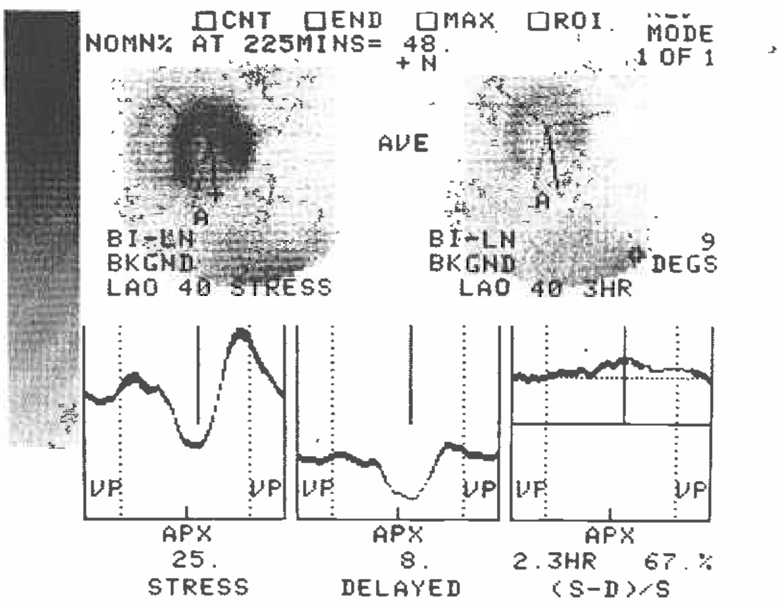



Fig. 3B: Quantitative analysis confirms poor T1-201 uptake in inferoapical region with no reperfusion.

No significant coronary artery disease

Eight of the nine patients without significant coronary artery disease had normal thallium scan while one (patient case no. 30) had an ischaemic defect in the LAD territory. This last patient was admitted two weeks prior to coronary arteriography, with a history of chest pain. His ECG was suggestive of an acute non-transmural anteroseptal myocardial infarction although the cardiac enzymes were only minimally raised.

Significant coronary artery disease

Twenty-one of the twenty-three patients with significant coronary artery disease (21/23 or 91%) had positive thallium scans. Fourteen of the sixteen patients with single vessel disease had positive scans while all the patients with two and three-vessel disease had positive thallium scans. The two patients with false negative thallium scans were cases no 31 and 32. The former had 90% obstruction of the obtuse marginal which supplies a large segment of the anterolateral wall of the left ventricle, while the latter had 80% obstruction of the LAD.

Overall Sensitivity and Specificity for detection of coronary artery disease

The sensitivity and specificity of thallium scan for the detection of coronary artery disease in this study are:-

$$\text{Sensitivity} = \frac{\text{Number of true positives}}{\text{Number of true positives} + \text{Number of false negatives}} \times 100$$

$$= \frac{21}{21 + 2} \times 100 = 91.3\%$$

$$\text{Specificity} = \frac{\text{Number of true negatives}}{\text{Number of true negatives} + \text{Number of false negatives}} \times 100$$

$$= \frac{8}{8 + 1} \times 100 = 88.9\%$$

Prediction of no of vessels involved with TSMI

Table 1 is a comparison of the results of TSMI when compared with coronary arteriography. Fourteen of sixteen patients with single vessel disease were found to have a single area of reduced perfusion on TSMI (14/16 or 87.5%). Although there were two false negatives, no patient was diagnosed to have two vessel disease. All three patients with two-vessel disease had only one perfusion defect on TSMI. Three of the four patients with three-vessel disease had perfusion defects in the territories of two arteries while the remaining patient had a perfusion defect in only one vascular territory.

**TABLE 1**
**COMPARISON OF TSMI PREDICTION OF NO OF VESSELS INVOLVED WITH RESULTS OF CORONARY ARTERIOGRAPHY**

| Coronary Arteriography | | TSMI | | |
|---|---|---|---|---|
| | Nos | OVD | 1VD | 2VD |
| 0 VD* | 9 | 8 | 1 | 0 |
| 1 VD | 16 | 2 | 14 | 0 |
| 2 VS | 3 | 0 | 3 | 0 |
| 3 VD | 4 | 0 | 1 | 3 |

*VD = vessel disease

Identification of diseased vessel with TSMI

Table II is an analysis of all the true positive TSMI scans with respect to the vessel(s) identified as significantly obstructed. TSMI was highly accurate in identifying the individual diseased vessel. Fourteen out of fifteen diseased vessels (14/15 or 93%) in the patients with single vessel disease were correctly identified.

**TABLE II**
**COMPARISON OF IDENTITY OF DISEASED VESSEL DIAGNOSED BY TSMI IN PATIENTS WITH SINGLE VESSEL DISEASE WHEN COMPARED WITH CORONARY ARTERIOGRAPHY (TRUE POSITIVE SCANS ONLY)**

| Coronary arteriography | TSMI | | |
|---|---|---|---|
| | LAD | Cx | RCA |
| LAD | 12 | 1 | — |
| Cx | — | 1 | — |
| RCA | — | — | 1 |

Effect of location of disease and previous history of myocardial infarction on sensitivity of TSMI

TSMI was able to detect twenty-three out of 32 of the diseased vessels (23/323 or 72%); of the twenty LAD arteries with significant obstruction, sixteen (16/20 or 80%) were detected while three of six (3/6 or 50%) affected LCx arteries and four of seven (4/7 or 57%) affected RCA were detected (see table III).

**TABLE III**
**COMPARISON OF TSMI DIAGNOSIS OF DISEASED VESSEL WITH RESULTS OF ARTERIOGRAPHY**

| | Proportion of diseased vessels with corresponding scintigraphic defects | | | |
|---|---|---|---|---|
| | LAD | Cx | RCA | All Vessels |
| All patients with CAD | 16/20 (80%) | 3/6 (50%) | 4/7 (57%) | 23/32 (72%) |
| No history of MI in that vascular territory | 6/9 (67%) | 2/5 (40%) | 3/6 (50%) | 11/20 (55%) |
| History of MI in that vascular territory | 10/11 (91%) | 1/1 (100%) | 1/1 (100%) | 12/13 (92%) |
| 1 VD | 12/13 (92%) | 1/1 (100%) | 1/1 (100%) | |
| 2 VD | 1/3 (33%) | 1/1 (100%) | 3/4 (75%) | |
| 3 VD | 3/4 (75%) | 1/4 (25%) | 0/2 (0%) | |

The sensitivity of TSMI was higher in the presence of a histoy of myocardial infarction. When there was a history of previous myocardial infarction, twelve of the thirteen diseased vessels (12/13 or 92%) were detected. When such a history was absent, only 11 of 20 diseased vessels were detected (11/20 or 55%).

The sensitivity for the detection of any diseased vessel was also higher for 1 vessel in comparison with 2-vessel and 3-vessel disease. In those patients with 1-vessel disease, 93% (or 14/15) of all diseased vessels were detected, and 91% (or 12/13) of LAD disease were detected while both the patients with diseased LCx and RCA were also correctly diagnosed. The sensitivity with two and three-vessel disease was lower.

**TABLE IV**
**RELATIIONSHIP OF NON-REPERFUSION (MI) AND REPERFUSION (Is) DEFECTS ON TSMI TO A PREVIOUS HISTORY OF MYOCARDIAL INFARCTION**

| P/H MI | TSMI | |
|---|---|---|
| | MI | Is |
| MI (12) | 10 | 2 |
| Nil (11) | 3 | 8 |

## DISCUSSION

The value and limitations of stress thallium myocardial imaging in identifying disease in individual coronary arteries have been described (Lenaers et al 1979 (3), Rigo et al 1980 (2, 5, 6). Thallium-201 (T1-201) myocardial perfusion scintigraphy is an important non-invasive method to evaluate the presence and extent of coronary artery disease. Injection of T1-201 at peak exercise followed by imaging at 5 mins and at 3 hours, can differentiate areas of reversible perfusion, representing myocardial scarring (Pohost, 1977 (7). Myocardial distribution of thallium activity during exercise is linearly related to the region myocardial blood flow, (Nielsen 1980 [8]) and the thallium myocardial stress image is an indication of physiologic coronary blood supply to the myocardium.

The sensitivity and specificity of T1-201 imaging obtained in this study are in agreement with those obtained elsewhere. (T1-201 sensitivity 82% for detection of CAD specificity 91% (Okada 1980 [4] and Massie et al 1979 [5]). In the single patient whose coronary arteriogram was normal but TSMI showed LAD disease, it is possible that borderline visual luminal narrowing may be associated with markedly reduced maximal hyperemic response (White, 1984 [9]. The number of patients studied with two and three vessel disease is small, but inaccuracies may be greater due to the arbitrary manner in which myocardial segments are assigned to vascular territories (Reisman et al 1985 [10]). It also appears that with the presence of a prèvious history of MI, the accuracy of TSMI is higher (91%), than in patients without any history (80%) [2]. In patients without previous infarction a negative scan can be useful to defer coronary angiography in patients with mild atypical symptoms (Rigo et al 1981 [11]). In patients with previous infarction the thallium scan can be used to identify individual coronary artery narrowings and estimate extent of disease in a given patient, and help assess necessity for coronary arteriography.

Previous studies, (Lenares 1979 [3], Massie 1979 [5] have shown low sensitivity for circumflex disease, and disease of the left circumflex coronary artery and corresponding posterior wall abnormalities are less frequently recognised. There is a tendency for stress thallium scintigraphy to underestimate the extent of coronary artery disease (Rigo 1980 [2]) and this could be due to inadequate exercise or because only the most ischaemic area appears abnormal, whereas other areas may also have insufficient flow. Significant right or left circumflex disease is more likely to be missed than left anterior descending disease. Also collateral vessels to the right, and left circumflex arterial bed may be more important functionally than those to the left anterior descending arterial bed, and may therefore mask a significant coronary arterial lesion (Eng et al 1979 [12]).

In summary, thallium-201 myocardial stress imaging has high specificity for coronary artery disease. Segmental analysis of the stress thallium scintigrams reveals information about the regions at highest risk of ischemia, though all the vessels with significant stenoses may not be identified. Abnormal studies are uncommon in patients without significant narrowings, while regional abnormalities are rare except in the distribution of the stenosed vessels. In patients with previous infarction the sensitivity of TSMI is increased, while in patients without previous infarction, normal TSMI makes LAD, or triple vessel disease unlikely. In many patients however, some regions of myocardium at risk will not be detected, particularly that supplied by left circumflex, and less severe lesions may also be missed. Tomographic approaches to TSMI have improved the diagnostic accuracy of this test (Nohara et al 1984 [13]) and, in this Department, all thallium-201 stress studies have been tomographic since the end 1984, the results of which have been reported elsewhere (Sundram et al 1986 [14]).

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