Thallium-201 scintigraphy in diagnosis of coronary stenosis¹

Comparison with electrocardiography and coronary arteriography

ROBERT A. CORNE, MERVYN S. GOTSMAN, AVRAHAM WEISS, DEREK ENLANDER, LARRY D. SAMUELS, JEAN A. SALOMON, BERNARD WARSHAW, AND HENRI ATLAN

From the Department of Medicine, Section of Cardiology, University of Manitoba, Canada, and the Departments of Medicine (Cardiology) and Medical Biophysics, Hebrew University of Jerusalem, Israel

SUMMARY The sensitivity of rest and exercise thallium-201 scintigraphy for the detection of significant coronary artery disease and myocardial ischaemia was compared with rest and exercise electrocardiography in 46 patients with chest pain. Of 26 patients with greater than 70 per cent coronary stenosis, 16 had abnormal rest thallium-201 scintigrams and 13 had Q waves. Myocardial perfusion defects in the resting scintigram correlated very well with evidence of previous myocardial infarction (16 of 17 patients, 94%); significant Q waves were present in 13 of these 17 patients (76%).

After exercise, abnormal thallium-201 scintigrams consistent with ischaemia were found in 21 patients (81%). Abnormal exercise electrocardiograms were present in 15 patients (58%). The combination of abnormal exercise thallium-201 scintigrams or exercise electrocardiograms (23/26, 88%) exceeded abnormal exercise electrocardiograms alone (15/26, 58%). The two procedures were thus complementary. Abnormal rest or exercise thallium-201 scintigrams were obtained in 25/26 patients (96%) compared with abnormal rest or exercise electrocardiograms in 21/26 patients (84%). Twenty patients with less than 50 per cent coronary stenosis had normal rest thallium-201 scintigrams and no Q waves. Two had abnormal exercise thallium-201 scintigrams and 7 had abnormal exercise electrocardiograms. Thus, exercise thallium scintigraphy has higher sensitivity than exercise electrocardiography in detecting exercise induced ischaemia and is more specific. Scintigraphy appears to have a higher sensitivity than electrocardiography in detecting coronary artery disease.

While each of the patients with triple vessel coronary disease had positive exercise perfusion scintigrams and positive exercise electrocardiograms, the thallium-201 scintigram was more sensitive than the rest or exercise electrocardiogram in patients with single vessel disease.

The correlation of thallium perfusion defects at rest and/or exercise with angiographically significant coronary stenosis was higher for the left anterior descending and right coronary arteries than for the circumflex coronary artery.

Myocardial perfusion scintigraphy following the intravenous injection of radionuclides at rest and during peak exercise represents a non-invasive method for the diagnosis of haemodynamically significant coronary artery disease (Zaret *et al.*, 1973b).

The major determinant of the myocardial distribution of cationic tracers such as potassium-43 and thallium-201 is blood flow (Prokop *et al.*, 1974; Strauss *et al.*, 1975). Reduced tracer uptake at peak exercise but not at rest indicates transient myocardial ischaemia. Perfusion defects at rest which do not change with exercise are consistent with myocardial infarction, while rest defects associated with an increased perfusion defect with exercise are consistent with both previous infarction and myocardial ischaemia.

¹This work was performed while Dr Corne was a Lady Davis Visiting Professor in Medicine at the Hebrew University of Jerusalem.

Thallium-201 has generally replaced potassium-43 and rubidium-81 because it has an energy spectrum more favourable for imaging with currently available scintillation cameras, and a longer physical half-life (Bradley-Moore *et al.*, 1975). The thallium-201 scan has been reported to be more sensitive than the exercise electrocardiogram in patients with significant coronary artery disease (Bailey *et al.*, 1977; Ritchie *et al.*, 1977a, b; Botvinick *et al.*, 1978). The present study was undertaken (1) to evaluate rest and exercise thallium-201 myocardial perfusion imaging in the detection of significant coronary stenosis determined by coronary arteriography; (2) to compare the sensitivity of thallium-201 myocardial imaging with rest and exercise electrocardiography; and (3) to correlate the thallium-201 scintigram with the number of coronary arteries involved and with the location of significant coronary stenosis.

Subjects and methods

Forty-six patients with known or suspected coronary artery disease were studied. There were 39 men and 7 women, with a mean age of 56 years (range 35 to 74 years). Of the 46 patients, 17 had prior myocardial infarction documented by two or more of the following criteria: (a) typical history; (b) pathological Q waves (duration 0.04 s or greater); (c) characteristic serial enzyme changes (serum creatine kinase and/or aspartate transaminase (SGOT)); (d) asynergy on left ventriculography. All patients had a history of chest pain suggestive of angina pectoris at the time of the study.

MYOCARDIAL PERFUSION IMAGING

Myocardial imaging was performed after exercise and at rest. Before starting the exercise study an indwelling catheter was inserted percutaneously into an antecubital vein. The patient exercised on a treadmill according to the Bruce procedure (Bruce, 1971) until he reached his maximal heart rate or developed chest pain or fatigue. Thallium, 2 mCi, was then injected, and the exercise was continued for an additional 60 seconds. The electrocardiogram was continuously monitored throughout the exercise study and during the imaging procedure which was performed in an adjacent room. Imaging began 10 minutes after injection. Rest myocardial images were obtained in two ways: (1) 29 patients were imaged one week before the exercise imaging procedure. Thallium, 2 mCi, was injected intravenously with the patient erect after fasting for 12 hours in

order to minimise gastric and hepatic activity. Imaging began 10 minutes after injection; (2) 17 patients were re-imaged 4 hours after the exercise study according to the method of Pohost *et al.* (1977). Images were recorded in the anterior and 45 degree left anterior oblique position by rotating the detector with the patient supine, and in the left lateral position with the patient on his left side over the detector. Five hundred thousand counts were recorded in each position. An Elscint Model CE-1 scintillation camera (37 photomultiplier tube, 30 cm crystal diameter) equipped with a high resolution parallel hole collimator was used for all studies. Images were recorded with a 20 per cent window centred on 75 keV. Images were recorded on Polaroid film from the camera console and also digitised on line on magnetic disc as 128 × 128 static byte matrix pictures on a PDP¹ 11/45 computer running the GAMMA 11¹ nuclear medicine software. Polaroid pictures from the analogue data were flood corrected at the camera console during data collection using a built-in camera feature. Flood correction was performed by software on all computer images after data collection.

All studies were interpreted by two observers who had no knowledge of the angiographic or electrocardiographic findings. Five segments of the left ventricle (septal, anterolateral, posterolateral, inferior, and apical) were analysed using both the Polaroid (unprocessed) data and the computer processed data. Polaroid data were interpreted qualitatively according to the following criteria. Resting images were categorised as (a) normal if there was homogeneous tracer distribution of tracer uptake; or (b) abnormal if there was a focal reduction in tracer uptake in regions which normally have homogeneous distribution of radioactivity. The exercise study was considered positive if a new perfusion defect developed or if there was an increase in the rest defect.

The computer-processed images were displayed in 128 × 128 matrix and activity from equal regions of interest determined from the 5 segments of the left ventricle defined above. A significant perfusion defect was considered present at rest when there was a reduction of 20 per cent or greater in counts between one or more of the anatomical segments of the left ventricle (Strauss and Pitt, 1977). The exercise image was considered positive for ischaemia if a new perfusion defect as defined above appeared after exercise or if there was an increase in a defect also observed in the scintigrams obtained at rest.

¹Digital Equipment Corporation.

EXERCISE ELECTROCARDIOGRAPHY

Exercise electrocardiography was performed twice in each patient, initially during the clinical evaluation and again for exercise imaging. Standard graded treadmill exercise using the Bruce procedure (Bruce, 1971) was performed until the patient attained his maximal heart rate or developed angina pectoris or severe fatigue. The Frank lead system (Frank, 1956) and praecordial leads V4-6 were employed for monitoring before, during, and for 10 minutes after exercise. The treadmill exercise electrocardiogram was interpreted as positive if 1 mm or greater horizontal or downsloping ST segment depression of duration 0.08 s or more appeared during or immediately after exercise.

CORONARY ARTERIOGRAPHY

Coronary arteriography was performed using the Judkins technique in multiple projections on 35 mm film with a 4½ inch mode General Electric image intensifier. Coronary arteriograms were evaluated by an independent observer unaware of the myocardial perfusion image results. The percentage luminal narrowing of each angiographic lesion was measured and the location noted. Stenosis of greater than 70 per cent of one or more of three major coronary arteries was considered haemodynamically significant. Left ventriculography was performed in the right anterior oblique projection in all patients. Results were analysed statistically using the binomial test (Siegel, 1956).

Results

The results of the clinical data, resting and exercise electrocardiograms, thallium-201 myocardial perfusion scintigrams at rest and exercise, coronary arteriography, and left ventriculography are summarised in Table 1 for the patients with 70 per cent or greater coronary stenosis.

MYOCARDIAL PERFUSION SCAN

INTERPRETATION

There was complete interobserver agreement in 38 of the 46 cases (84%) using the Polaroid images. Consensus was achieved in the remaining 8 cases using the computer processed data. In 3 of the 38 cases the Polaroid data were considered normal at rest by both observers, while a clinically confirmed defect was shown using the computer processed data.

ANGIOGRAPHY

Twenty-six of the patients had greater than 70 per cent stenosis of at least 1 of the 3 major coronary arteries. Six had single vessel disease, 11 had two

Fig. 1 Normal thallium-201 myocardial perfusion scintigram at rest (upper panels) and exercise (lower panels) in a patient with normal coronary arteries on selective coronary arteriography. ANT, anterior view; LAO, left anterior oblique view; LL, left lateral view.

vessel disease, and 9 patients had triple vessel disease. The remaining 20 patients had either normal coronary arteriograms or less than 50 per cent stenosis of a major coronary artery. No patient had lesions between 50 and 70 per cent stenosis

Fig. 2 A patient with myocardial ischaemia and 95 per cent stenosis of the left anterior descending coronary artery. The thallium-201 scintigram is normal at rest (upper panels). After exercise there is a perfusion defect involving the apex and lower portion of the septum (lower panels).

Fig. 3 Thallium-201 myocardial perfusion scintigram in a patient with 100 per cent obstruction of the left anterior descending and right coronary arteries. There are focal defects involving the septum, apex and inferior walls of the left ventricle at rest (upper panels) which are unchanged after exercise (lower panels), consistent with myocardial infarction without ischaemia.

Fig. 4 A patient with triple vessel coronary disease and a previous myocardial infarction. On the rest injected thallium scintigram (upper panel), there is decreased tracer concentration in the interior wall seen best in the LAO view. With injection at peak exercise (lower panel) the inferior defect becomes more obvious and there is decreased perfusion of the apex (ANT view), septum, and posterolateral walls (LAO view), consistent with myocardial infarction and ischaemia.

Fig. 5 Thallium-201 myocardial perfusion scintigram 10 minutes after exercise (upper panel) and 4 hours later (lower panel). The decreased tracer concentration 10 minutes after exercise is not present 4 hours later, indicative of myocardial ischaemia. Coronary arteriography revealed 90 per cent obstruction of the left anterior descending coronary artery.

without at least 1 major coronary artery narrowed more than 70 per cent.

PATTERNS OF THALLIUM-201 SCINTIGRAMS

Rest and exercise thallium-201 scintigrams in each patient were compared and classified as follows: (1) normal rest and normal exercise (Fig. 1); (2) normal rest and abnormal exercise, indicative of myocardial ischaemia (Fig. 2); (3) abnormal rest with no change on exercise, consistent with myocardial infarction without ischaemia (Fig. 3); (4) abnormal rest and abnormal exercise, consistent with myocardial infarction and ischaemia (Fig. 4). Scintigrams obtained 4 hours after exercise were similar to those obtained at a separate rest study 1 week before exercise. Exercise induced perfusion defects were not present in the scintigram 4 hours later in patients with myocardial ischaemia without infarction (Fig. 5).

ELECTROCARDIOGRAPHY AND PERFUSION SCINTIGRAPHY

The results of the rest and exercise electrocardiograms and the rest and exercise thallium-201 scintigrams are shown in Tables 1 and 2.

Resting thallium defects were present in 16 patients (62%) with significant coronary artery stenosis, while pathological Q waves were recorded

Table 1 Data in patients with coronary stenosis

Case no.	Age	Sex	Clinical		ECG		²⁰¹ Tl		Coronary angio % stenosis			LV angio wall motion
			MI	Angina (NYHA class)	Q	ETT	R	E	LAD	Cx	RCA	
1	44	M	+	III	I	-	I	I	-	50	100	+2I
2	54	M	-	III	-	+	-	S, PL	90	70	60	0
3	60	M	+	II	-	+	I	I, S, PL	70	100	100	0
4	44	M	+	III	I, AS	+	I, S	I, S, PL	100	100	80	+1Ap
5	60	M	+	III	-	+	I, S	-	100	-	100	0
6	63	M	+	III	I	+	I, PL	I, PL, S	80	95	80	+1I
7	48	M	-	III	-	-	-	S	100	40	-	0
8	55	M	+	II	AS	-	S, I	-	100	80	50	+2Ap
9	56	M	+	III	A, L	-	S, PL	-	100	60	40	+3Ap
10	60	M	-	III	-	-	-	I, S, PL	95	60	-	0
11	61	M	+	IV	I	-	I	I, S	100	95	100	+2I
12	63	F	+	IV	I	+	I	I, S, PL	100	90	90	0
13	72	M	+	II	AS	+	-	I, S, PL	100	90	100	0
14	60	M	-	II	-	+	-	I, S, PL	95	95	70	0
15	67	M	+	III	AS	-	S	S, I, PL	100	100	-	+1A
16	55	M	-	III	-	+	-	S, I	100	40	60	0
17	74	M	+	III	I	+	I	I, S	90	-	100	+2I
18	60	F	-	III	-	+	-	-	90	-	80	0
19	53	M	+	III	I, AS	+	I, S	I, S, Ap	90	100	80	+2Ap
20	69	M	+	IV	AS	+	S	S, PL, I	100	70	60	0
21	49	M	+	III	-	+	S	S, I	100	90	30	0
22	52	M	-	II	-	-	-	I, PL	100	100	90	0
23	58	M	+	II	S	-	S	S, I	100	-	90	+2Ap
24	65	M	+	III	-	+	I, PL	-	50	100	100	+1I
25	57	M	-	III	-	-	-	S	90	-	-	0
26	63	F	-	II	-	-	-	S, I	95	-	80	0

Abbreviations: MI = myocardial infarction; NYHA = New York Heart Association Functional classification; ECG = electrocardiogram; Q = Q wave ≥ 0.04 s; ETT, exercise tolerance test; ²⁰¹Tl, thallium myocardial perfusion scintigram; R, rest; E, exercise; LAD, left anterior descending coronary artery; Cx, circumflex coronary artery; RCA, right coronary artery; wall motion: o, normal; +1, hypokinesis; +2, akinesis; +3, dyskinesis; A, anterior; AS, antero-septal; I, inferior; S, septum; L, lateral; PL, posterolateral; Ap, apex; +, present or abnormal -, absent or negative.

in 13 patients (50%). Myocardial perfusion defects in the resting scintigram correlated very well with evidence of previous myocardial infarction (16 of 17 patients, 94%); significant Q waves were present in 13 of these 17 patients (76%). Of the 17 patients with documented past evidence of infarction but without significant Q waves in current electro-

cardiograms, 3 had localised perfusion defects at rest. Of the 16 patients with rest thallium-201 defects, 11 had asynergy whereas of the 13 patients with Q waves, 10 had asynergy.

The proportion of patients with a positive exercise thallium-201 scintigram (21 of 26 patients, 81%) was greater than the proportion with a positive

Table 2 Results of electrocardiogram and thallium-201 myocardial imaging interpretation in 26 patients with > 70 per cent coronary stenosis

	No.	Per cent
<i>Rest</i>		
Q > 0.04 second	13	50
Scintigram abnormal	16	62
Q > 0.04 second/abnormal scintigram	17	65
<i>Exercise</i>		
Exercise ECG abnormal	15	58*†
Scintigram abnormal	21	81*
Exercise ECG abnormal/scintigram abnormal	23	88†
<i>Combined</i>		
Q > 0.04 second or exercise electrocardiogram abnormal	21	81
Rest or exercise scintigram abnormal	25	96

* P < 0.05 abnormal scintigram compared with abnormal exercise electrocardiogram.

† P < 0.01 abnormal exercise electrocardiogram/abnormal scintigram compared with abnormal exercise electrocardiogram.

Table 3 Sensitivity and specificity of thallium exercise scintigraphy and exercise electrocardiography

	Coronary arteriography	
	Coronary stenosis	
	Significant stenosis (> 70%)	No significant stenosis (< 50%)
<i>Exercise scintigram</i>		
Abnormal	21	2
Normal	5	18
Total	26	20
Sensitivity 81%* Specificity 90%†		
<i>Exercise electrocardiogram</i>		
Abnormal	15	7
Normal	11	13
Total	26	20
Sensitivity 58%* Specificity 65%†		

* P < 0.05—sensitivity exercise scintigram compared with exercise electrocardiography.

† P < 0.05—specificity exercise scintigram compared with exercise electrocardiography.

Table 4 Results of electrocardiogram and thallium-201 imaging related to number of coronary vessels with > 70 per cent stenosis

Coronary vessels involved	No.	Abnormal electrocardiogram			Abnormal thallium-201 scintigram		
		Q	Exercise ECG	Q wave or exercise ECG	Rest	Exercise	Rest or exercise
1	6	2	1	3	2	4	6
2	11	6	6	9	8	8	10
3	9	5	8	9	6	9	9

Abbreviations: Q, Q wave 0.04 s or longer; ECG, electrocardiogram.

exercise electrocardiogram (15 of 26 patients, 58%, $P < 0.05$). The sensitivity for the detection of ischaemia was increased when the results of the two procedures at exercise were combined (23 of 26 patients, 88%), being significantly greater than with the exercise electrocardiogram alone ($P < 0.01$).

Of the 26 patients with coronary stenosis greater than 70 per cent, significant Q waves at rest and/or a positive exercise electrocardiogram were present in 21 (81%). Abnormal rest and/or exercise thallium-201 perfusion defects were present in 25 of the 26 patients (96%). The results were unchanged when coronary stenosis greater than 50 per cent was classed as significant.

Each of the 20 patients with normal coronary arteriograms had normal thallium-201 myocardial perfusion scintigrams at rest. Two of the 20 patients with normal rest scintigrams developed perfusion defects on exercise associated with chest pain and positive exercise electrocardiograms. Five additional patients with normal rest and exercise thallium-201 scintigrams had positive exercise electrocardiograms. No patient had significant Q waves. The specificity and sensitivity of exercise thallium scintigrams and exercise electrocardiograms are shown in Table 3.

The sensitivity of thallium-201 myocardial

perfusion scintigraphy and electrocardiography related to the number of coronary arteries with greater than 70 per cent stenosis is shown in Table 4. While each of the patients with triple vessel disease had positive exercise perfusion scintigrams and positive exercise electrocardiograms, the thallium-201 (rest or exercise) scintigram was more sensitive than the rest or exercise electrocardiogram in patients with single vessel disease (6 of 6 patients vs. 3 of 6 patients). There was a progressive increase in both positive exercise scintigrams and exercise electrocardiograms with the number of coronary arteries involved.

The correlation of perfusion defects on the rest or exercise thallium-201 study with the anatomical location of coronary artery stenosis greater than 70 per cent is presented in Table 5. Anterior, apical, or septal perfusion defects were present in 22 of the 24 patients with left anterior descending disease, inferior defects in 15 of the 16 patients with right coronary disease, and posterolateral defects in 11 of the 15 patients with circumflex disease. The correlation is similar when coronary stenosis greater than 50 per cent is considered significant.

Discussion

DETERMINANTS OF THALLIUM MYOCARDIAL DISTRIBUTION

The initial distribution of thallium-201 in the myocardium is dependent on both coronary blood flow and cellular extraction (Strauss *et al.*, 1975; Strauss and Pitt, 1977). Strauss *et al.* (1975) compared the regional myocardial distribution of thallium-201 with that of radioactive microspheres under conditions of normal flow, and partial and complete coronary occlusion; the data indicate that the major determinant of thallium-201 distribution is blood flow. The results of studies of extraction efficiency under various experimental conditions are conflicting (Costin and Zaret, 1976; Weich *et al.*, 1977). Image defects in the rest thallium-201

Table 5 Correlation of thallium-201 scintigraphy and arteriography

Coronary artery % Stenosis	No. of cases	Abnormal thallium-201
LAD		
≥ 50%	25	22
≥ 70%	24	22
Cx		
≥ 50%	18	13
≥ 70%	15	11
RCA		
≥ 50%	20	18
≥ 70%	16	15

LAD, left anterior descending coronary artery; Cx, circumflex coronary artery; RCA, right coronary artery; abnormal thallium-201, abnormal rest or exercise thallium perfusion scintigrams.

scintigram generally represent myocardial infarction (Hamilton *et al.*, 1977). In the resting non-ischaemic state, viable myocardial regions supplied by stenotic coronary arteries are usually adequately perfused in either an anterograde or retrograde fashion. Resting coronary blood flow and regional distribution were both normal in animals, despite coronary stenosis of 85 per cent in diameter (Gould *et al.*, 1974). However, the ability to increase coronary flow in response to stress became progressively abnormal with coronary stenosis exceeding 45 per cent. In the present study, normal thallium-201 rest images were found in patients with 90 to 95 per cent coronary stenosis, unless prior infarction had occurred. Under stress, myocardial segments supplied by coronary arteries with 50 per cent or greater luminal narrowing became transiently ischaemic resulting in a perfusion defect that correlated well with the specific coronary artery which was stenosed.

SENSITIVITY AND SPECIFICITY OF PERFUSION SCINTIGRAPHY AND ELECTROCARDIOGRAPHY
Significant coronary artery stenosis may result in myocardial infarction, in myocardial ischaemia, or it may be silent. Therefore, the demonstration of infarction and/or ischaemia is considered evidence of significant coronary stenosis. Both abnormal Q waves in the resting electrocardiogram and exercise induced ST segment depression lack specificity and sensitivity (Horan *et al.*, 1971; Borer *et al.*, 1975; Fortuin and Weiss, 1977). The results of the present study show that the sensitivity of exercise induced scintigraphic abnormalities (81%) is higher than ST segment depression (58%) on the exercise electrocardiogram ($P < 0.05$), confirming recent studies evaluating these procedures in patients with myocardial ischaemia (Bailey *et al.*, 1977; Ritchie *et al.*, 1977a, b; Botvinick *et al.*, 1978). Combined exercise thallium-201 scintigraphic and electrocardiographic evaluation was more sensitive than the exercise electrocardiogram alone ($P < 0.01$). Therefore the two procedures are complementary. Rest and exercise thallium-201 scintigraphy seem more sensitive in the detection of haemodynamically significant coronary artery disease than rest and exercise electrocardiography but because of the small number of patients studied this was not statistically significant ($0.01 > P > 0.05$). The specificity of thallium-201 exercise scintigraphy in this study was 90 per cent while the specificity of exercise electrocardiography was 65 per cent ($P < 0.05$). These results, similar to those of Ritchie *et al.* (1977a) and Botvinick *et al.* (1978), were obtained from a selected population; more experience is necessary before the specificity of thallium scintigraphy is definitely established.

FALSE NEGATIVE EXERCISE THALLIUM SCINTIGRAMS

Five patients with significant coronary stenosis exercised to the development of angina pectoris had false negative exercise thallium-201 scintigrams. Four had an old extensive myocardial infarction documented by Q waves 0.04 s or greater and an abnormal rest thallium-201 image. The absence of an increase in the rest image defect with exercise may be the result of the infarct concealing an adjacent region of exercise-induced ischaemia. The exercise electrocardiogram was negative in 3 of these 4 patients. While previous studies have suggested that in patients with severe triple vessel disease, global ischaemia may be produced by exercise and a focal perfusion defect may not appear (Pitt and Strauss, 1976), it is noteworthy that each of our patients with angiographically significant triple vessel disease had positive exercise thallium-201 scintigrams. Two of the 5 patients with false negative exercise scintigrams had single vessel disease and 3 had double vessel disease. It is important to remember that the coronary arteriogram reflects an anatomical state, whereas the myocardial perfusion scan reflects the functional regional status of myocardial perfusion. A direct relation between the two techniques does not always exist. Furthermore, the appearance of chest pain during exercise in the absence of ST segment depression and/or a myocardial perfusion defect does not indicate that the patients were in fact ischaemic and, therefore, that the above tests were true false negatives.

SCINTIGRAPHY AND CORONARY ARTERIOGRAPHY

The correlation of thallium perfusion defects at rest and/or exercise with angiographically significant coronary stenosis was higher for the left anterior descending and right coronary arteries than for the circumflex coronary artery. These results are similar to those reported by McLaughlin *et al.* (1977) though the correlation in the present study was slightly higher for circumflex artery disease.

ADVANTAGES OF 4-HOUR POST-EXERCISE STUDY

Our results with patients imaged 10 minutes after exercise and 4 hours later agree with those of Pohost *et al.* (1977) and Blood *et al.* (1977). Exercise induced perfusion defects were not apparent after 4 hours in patients with coronary stenosis without infarction. The images obtained 4 hours after exercise were similar to rest images obtained 1 week before the exercise study. This confirms that 2 separate studies 1 week apart are not necessary. In addition to the information being available the same day, the

exercise and 4-hour post-exercise study technique requires only 1 dose of thallium-201 and, therefore, is less expensive and provides less radiation exposure.

CLINICAL IMPLICATIONS

Myocardial perfusion scintigraphy with thallium-201 is a safe, non-invasive diagnostic technique. The images are of good quality, and can be obtained with a conventional gamma scintillation camera. Thallium-201 scintigraphy represents an objective screening test for identifying significant coronary artery disease in patients with an atypical clinical history and a negative exercise electrocardiogram, and for confirming suspected myocardial infarction. This technique is helpful in assessing the presence or absence of coronary disease in asymptomatic patients with a positive exercise electrocardiogram (Zaret *et al.*, 1973a; Caralis *et al.*, 1977), and for evaluating the results of aortocoronary bypass surgery (Greenberg *et al.*, 1977; Kostuk *et al.*, 1977; Narahara *et al.*, 1977; Ormand *et al.*, 1977; Sbarbaro *et al.*, 1977; Wainwright *et al.*, 1977; Corne *et al.*, 1979), pharmacological interventions (Salel *et al.*, 1974), and modifications of risk factors for coronary artery disease. More experience with this technique is necessary before the specificity is established. We have found that the quantitative computer method employed in this study was of value in those cases of interobserver disagreement using non-processed analogue images and also increased the sensitivity in the interpretation of rest scintigrams. It is anticipated that when comparative studies of medical and surgical treatment are evaluated a more accurate estimate of regional myocardial perfusion will be available than with visual analysis of analogue images.

The authors thank Rafael Vaknine, PhD, for the statistical analysis.

References

- Bailey, I. K., Griffith, L. S. C., Rouleau, J., Strauss, H. W., and Pitt, B. (1977). Thallium 201 myocardial perfusion imaging at rest and during exercise. Comparative sensitivity to electrocardiography in coronary artery disease. *Circulation*, **55**, 79-87.
- Blood, D. K., McCarthy, D. M., Sciacca, R. R., and Cannon, P. J. (1977). Comparison of thallium-201 myocardial scans at rest with scans four hours after exercise (abstract). *Circulation*, **55** and **56**, Suppl. 111, 229.
- Borer, J. S., Brensike, F. J., Redwood, D. R., Itscoitz, S. B., Passamani, E. R., Stone, N. J., Richardson, J. M., Levy, R. I., and Epstein, S. E. (1975). Limitations of the electrocardiographic response to exercise in predicting coronary artery disease. *New England Journal of Medicine*, **293**, 367-371.
- Botvinick, E. H., Taradash, M. R., Shames, D. M., and Parmley, W. W. (1978). Thallium-201 myocardial perfusion scintigraphy for the clinical clarification of normal, abnormal, and equivocal electrocardiographic stress tests. *American Journal of Cardiology*, **41**, 43-51.
- Bradley-Moore, P. R., Lebowitz, E., Green, M. W., Atkins, H. L., and Ansari, A. N. (1975). Thallium-201 for medical use. II. Biologic behaviour. *Journal of Nuclear Medicine*, **16**, 156-160.
- Bruce, R. A. (1971). Exercise testing of patients with coronary heart disease. Principles and normal standards for evaluation. *Annals of Clinical Research*, **3**, 323-332.
- Caralis, D. G., Kennedy, H. L., Bailey, I. K., and Pitt, B. (1977). Thallium-201 myocardial perfusion scanning in the evaluation of asymptomatic patients with ischemic ST segment depression (abstract). *American Journal of Cardiology*, **39**, 320.
- Corne, R. A., Gotsman, M., Weiss, A., Baron, J., Salomon, J., and Atlan, H. (1979). Radionuclide assessment pre- and post-coronary bypass surgery: results of thallium-201 myocardial perfusion scintigraphy and radionuclide angiography compared with coronary arteriography and left ventricular angiography. *Annals of the Royal College of Physicians and Surgeons of Canada*. In press.
- Costin, J. C., and Zaret, B. J. (1976). Effect of propranolol and digitalis upon radioactive thallium and potassium uptake in myocardial and skeletal muscle (abstract). *Journal of Nuclear Medicine*, **17**, 535.
- Frank, E. (1956). An accurate clinically practical system for spatial vectorcardiography. *Circulation*, **13**, 737-749.
- Fortuin, N. J., and Weiss, J. L. (1977). Exercise stress testing. *Circulation*, **56**, 699-712.
- Gould, K. L., Lipscomb, K., and Hamilton, G. W. (1974). Physiological basis for assessing critical coronary stenosis. *American Journal of Cardiology*, **33**, 87-94.
- Greenberg, B., Hart, R., Werner, J., Brundage, B., Botvinick, E., Chatterjee, K., and Parmley, W. (1977). Thallium-201 stress imaging in the follow up evaluation of coronary bypass patients (abstract). *Circulation*, **55** and **56**, Suppl. 111, 230.
- Hamilton, G. W., Trobaugh, G. B., Ritchie, J. L., Williams, D. L., Weaver, W. D., and Gould, K. L. (1977). Myocardial imaging with intravenously injected thallium-201 in patients with suspected coronary artery disease. *American Journal of Cardiology*, **39**, 347-354.
- Horan, L. G., Flowers, N. C., and Johnson, J. C. (1971). Significance of the diagnostic Q wave of myocardial infarction. *Circulation*, **43**, 428-436.
- Kostuk, W. J., Deatrich, D., and Chamberlain, M. J. (1977). Non-invasive follow up of aortocoronary bypass surgery (abstract). *Circulation*, **55** and **56**, Suppl. III, 188.
- McLaughlin, P. R., Martin, R. P., Doherty, P., Daspit, S., Goris, M., Haskell, W., Lewis, S., Kriss, J. P., and Harrison, D. C. (1977). Reproducibility of thallium-201 myocardial imaging. *Circulation*, **55**, 497-503.
- Narahara, K., Ritchie, J. L., Williams, D., and Hamilton, G. (1977). Pre- and post-operative thallium-201 myocardial imaging: non-invasive assessment of graft patency and regional myocardial perfusion (abstract). *Circulation*, **55** and **56**, Suppl. III, 231.
- Ormand, J., Platt, M., Mills, L., Shapiro, W., Pugh, B., Bloomqvist, C. G., Parkey, R. W., and Willerson, J. T. (1977). Thallium-201 scintigraphy and exercise testing in evaluating patients prior to and after coronary bypass surgery (abstract). *Circulation*, **55** and **56**, Suppl. III, 131.
- Pitt, B., and Strauss, H. W. (1976). Myocardial imaging in the non-invasive evaluation of patients with suspected ischemic heart disease. *American Journal of Cardiology*, **37**, 797-806.
- Pohost, I. J., Zir, L. M., Moore, R. H., McKussick, K. A., Guiney, T. E., and Bellar, G. A. (1977). Differentiation of

- transiently ischemic from infarcted myocardium by serial imaging after a single dose of thallium-201. *Circulation*, **55**, 293-302.
- Prokop, E. H., Strauss, H. W., Shaw, J., Pitt, B., and Wagner, H. N., jun (1974). Comparison of regional myocardial perfusion determined by ionic potassium-43 to that determined by microspheres. *Circulation*, **50**, 978-984.
- Ritchie, J. L., Trobaugh, G. B., Hamilton, G. W., Gould, K. L., Narahara, K. A., Murray, J. A., and Williams, D. L. (1977a). Myocardial imaging with thallium-201 at rest and during exercise. Comparison with coronary arteriography and resting and stress electrocardiography. *Circulation*, **56**, 66-71.
- Ritchie, J. L., Zaret, B., Strauss, W., Pitt, B., Berman, D., Schelbert, H., Ashburn, W., Berger, H., and Hamilton, G. (1977b). Myocardial imaging with thallium-201 at rest and exercise. A multicentre study (abstract). *Circulation*, **55** and **56**, Suppl. III, 230.
- Salel, A. F., Berman, D. S., DeNardo, G. L., and Mason, D. T. (1974). Clinical effects of tolamolol on myocardial ischemia assessed by rest and exercise rubidium-81 imaging. In *Proceedings of Symposium on Tolamolol (Royal College of Physicians)*, London, pp. 79-85. Excerpta Medica, Amsterdam.
- Sbarbaro, J. A., Karunaratne, H., Cantez, S., Harper, P., and Resnekov, L. (1977). TI-201 imaging in the assessment of coronary artery bypass graft patency (abstract). *Circulation*, **55** and **56**, Suppl. III, 231.
- Siegel, S. (1956). *Nonparametric Statistics for the Behavioral Sciences*, McGraw-Hill, London.
- Strauss, H. W., Harrison, K., Langan, J. K., Lebowitz, E., and Pitt, B. (1975). Thallium-201 for myocardial imaging: relation of thallium-201 to regional myocardial perfusion. *Circulation*, **51**, 641-645.
- Strauss, H. W., and Pitt, B. (1977). Thallium-201 as a myocardial imaging agent. *Seminars in Nuclear Medicine*, **7**, 49-58.
- Wainwright, R. J., Maisey, M. N., and Sowton, E. (1977). Quantitative thallium scintigraphy in the assessment and follow up of coronary artery bypass grafts (abstract). *Journal of Nuclear Medicine*, **18**, 594.
- Weich, H. F., Strauss, H. W., and Pitt, B. (1977). The extraction of thallium-201 by the myocardium. *Circulation*, **56**, 188-191.
- Zaret, B. L., Stenson, R. E., Martin, N. D., Strauss, H. W., Wells, H. P., jun, McGowan, R. L., and Flamm, M. D., jun (1973a). Potassium 43 myocardial perfusion scanning for the non-invasive evaluation of patients with false positive exercise tests. *Circulation*, **48**, 1234-1241.
- Zaret, B. L., Strauss, H. W., Martin, N. D., Wells, H. P., jun, and Flamm, M. D., jun (1973b). Non-invasive regional myocardial perfusion with radioactive potassium: study of patients at rest, exercise and during angina pectoris. *New England Journal of Medicine*, **288**, 809-812.

Requests for reprints to Dr Robert A. Corne, Section of Cardiology, Health Sciences Centre, 700 William Avenue, Winnipeg, Manitoba, Canada, R3E0Z3.