Detecting asymptomatic coronary artery disease using routine exercise testing and exercise thallium scintigraphy in patients with atherosclerotic vascular disease

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Summary

ECG-monitored exercise testing has been proposed as a relatively inexpensive and effective means of screening for asymptomatic coronary artery disease in patients presenting for peripheral vascular surgery. Despite the fact that exercise thallium scintigraphy is also dependent on the patient's ability to exercise, using this test in conjunction with ECG-monitored exercise testing may enhance sensitivity and specificity of non-invasive evaluation. Thirty-two patients were subjected to ECG-monitored exercise testing, exercise thallium scintigraphy and coronary angiography. The sensitivity of ECG-monitored exercise testing for detecting coronary artery disease was calculated at 81,8% and the specificity at 87,5%, while the figures for exercise thallium scintigraphy were 73,1% and 33,3% respectively. Using these two methods in combination yielded a predictive accuracy of 90,6%. The only advantage of exercise thallium scintigraphy over exercise ECG appears to be in patients in whom the latter test could not be interpreted or was non-diagnostic.

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Pre-operative cardiac evaluation of surgical patients has evolved greatly since a multifactorial risk index was first described by Goldman *et al.*[1] The need to estimate operative risk prospectively is of particular importance in patients undergoing major vascular surgery, where the incidence of associated coronary artery disease (CAD) and related cardiac complications is alarmingly high.[2,3]

While routine pre-operative coronary angiography has been suggested,[4] non-invasive tests, such as exercise stress testing,[5] gated blood pool scanning[6] and dipyridamole-thallium scanning,[7] have been emphasised as the first step in identifying high-risk patients. The ability of patients presenting for vascular surgery to participate in exercise studies is often hampered by severe claudication, ischaemic rest pain, ischaemic ulceration and previous limb amputation. An added problem is that certain drugs, such as digitalis, diuretics and β-blocking agents, may complicate interpretation of the test. Despite the fact that exercise thallium scanning is also dependent on the patient's ability to exercise, the addition of this method of examination to ECG-monitored stress testing may result in a greater sensitivity and specificity being achieved.

A study was undertaken to determine whether the addition of thallium imaging to conventional exercise stress testing holds any benefits in detecting associated asymptomatic but haemodynamically significant CAD in patients admitted to hospital for peripheral vascular surgery.

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Patients and methods

Thirty-two patients admitted to the Department of Surgery, Universitas Hospital, Bloemfontein, with either atherosclerotic disease of the extremities (peripheral vascular disease (PVD)), carotid artery stenosis (CAS) or abdominal aortic aneurysm (AAA) were included in the study. Symptom-limited exercise testing was carried out using the Bruce protocol[8] on a programmed Bürdick T500 treadmill. Patients unable to achieve at least 85% of maximum predicted heart rate (MPHR) and who did not develop angina, ischaemic ST changes, hypotension or complex arrhythmias were subsequently exercised using an adaptable Würburg arm ergometer according to the protocol suggested by Williams *et al.*[9] Continuous 12-lead ECG monitoring was used during the period of exercise, and resting ECGs were recorded in a supine and a standing position before and after completion of exercise. The test was terminated in the event of claudication, dyspnoea, fatigue, angina, ventricular arrhythmias, hypotension or marked ischaemia on ECG. All ECGs were interpreted by a cardiologist familiar with exercise testing but who did not have prior knowledge of the patient's clinical condition. Tests were taken as positive in the presence of horizontal or down-sloping ST-segment depression of 1 mm or more, a fall in systolic blood pressure of $\geqslant$ 10 mmHg and exercise-induced angina or complex ventricular arrhythmias.

Thallium stress imaging was performed with arm ergometry in 12 patients and with treadmill exercise in 20 patients. Approximately 60 seconds before the termination of exercise, 2 - 3 mCi thallium-201 was administered through a peripheral line. Single photon emission computed tomography (SPECT) was then performed within 5 minutes, using a General Electric Starcam 400 ACT gamma camera. Images were photographed in 32 steps over 180° rotation. Redistribution images were photographed approximately 3 hours later. Pre-processing of the data was performed followed by back projection with a ramp filter. Orthogonal reconstructions of the vertical long axis, horizontal long axis and short axis of the heart were obtained. On these three images the anterior, lateral, inferior, septal and apical areas of the heart could be distinguished. The three sets of reconstructions were displayed on the computer screen and the five territories of the heart visually assessed by one or two experienced observers. A territory was classified as positive for CAD when a reduction in radioactivity existed on the stress images. A reversible defect was classified as an area where redistribution of the ^{201}Tl occurred.

Coronary angiography was performed using the transcutaneous femoral Seldinger technique. Obstruction of more than 50% in at least one of the major coronary arteries was considered haemodynamically significant.

The sensitivity, specificity and predictive accuracy of exercise stress testing and exercise thallium scintigraphy were calculated by comparing the results with coronary angiography. Data were then analysed to simulate a stepwise clinical decision-making process. In this algorithm, clinical evaluation and resting ECG (definite angina, previous myocardial infarction or ischaemic changes on the resting ECG) were followed by treadmill stress testing, arm ergometry and, finally, exercise ^{201}Tl scintigraphy. A positive history or resting ECG were not regarded as an end-point for the purpose of the algorithm and all patients were routinely subjected to an exercise test. Exercise tests were considered negative if the patient reached 85% of MPHR and the ECG remained normal.

Results

The age range of the patients included in the study was 36 - 69 years (mean 59 years) and the group consisted of 28 men and 4 women. Four patients presented with CAS, 22 with PVD and 6 with AAA. After evaluating the clinical history and resting ECG, 18 patients (56,3%) had a previous myocardial infarction, angina or ischaemic ECG changes. The predictive accuracy of this evaluation was 68,8%. The results of ^{201}Tl-stress scanning (9 patients with reversible defects, 14 with fixed defects and 9 normal) and ECG are shown in Tables I and II. Two patients showed signs of left bundle branch block on resting ECG and were not included in the ECG part of the study. Fifteen patients had positive treadmill tests and 2 others managed to reach 85% of their MPHR with a normal stress test. Another 4 patients showed signs of myocardial ischaemia during arm ergometry, while 3 arm ergometry tests remained normal in spite of patients reaching 85% of their MPHR (Fig. 1). Fourteen treadmill tests were discontinued prematurely because of claudication (7 patients), fatigue (6) and asthma (1). The final decision-making algorithm had a predictive accuracy of 90,6% (Fig. 2).

TABLE I. SUMMARY OF EXERCISE TESTS PERFORMED

	Tests performed	THR reached	Positive tests	+ test/THR
Treadmill	**23**	**10**	**15**	**17**
Arm ergometry	**13**	**5**	**4**	**7**
Total	**36**	**15**	**19**	**24**

THR = 85% of maximum predicted heart rate reached.

Coronary angiographic findings are shown in Table III. Two of the patients classified as having normal coronary arteries had previous coronary angioplasties after myocardial infarctions and were expected to have corresponding fixed defects on ^{201}Tl-scintigraphy but a normal exercise ECG. Twelve of the 32 patients were referred for CABS before their PVD procedure, while 2 other patients were referred for CABS after PVD surgery.

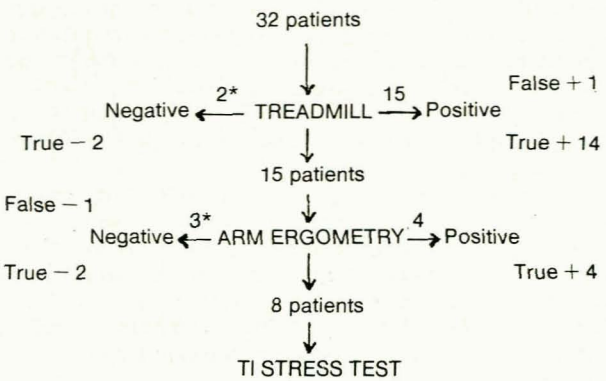
Discussion

CAD commonly accompanies PVD and is the most common cause of early and late postoperative death after major vascular

TABLE II. ACCURACY OF EXERCISE TESTING AND EXERCISE ^{201}Tl SCANNING COMPARED WITH CORONARY ANGIOGRAPHY TO DETECT CAD IN VASCULAR PATIENTS

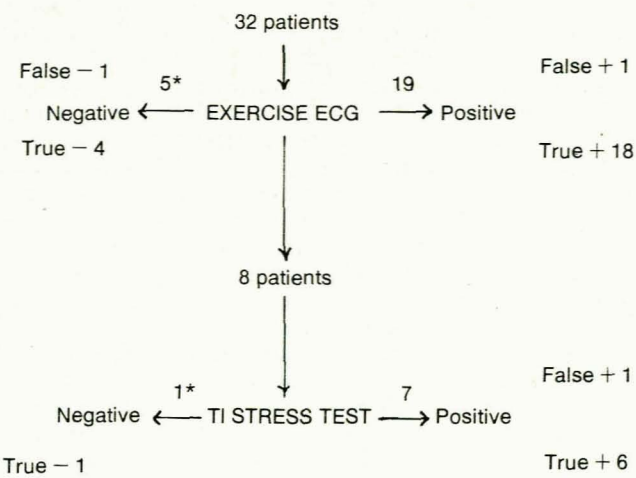
	Exercise ECG		Exercise ^{201}Tl	
	All	THR*	All	THR
Total	**30**	**15**	**32**	**14**
All +	**19**	**11**	**23**	**11**
True +	**18**	**10**	**19**	**8**
False +	**1**	**1**	**4**	**3**
All −	**11**	**5**	**9**	**3**
True −	**7**	**4**	**2**	**1**
False −	**4**	**1**	**7**	**2**
CAD +	**22**	**10**	**26**	**10**
Sensitivity (%)	**81,8**	**100**	**73,1**	**80,0**
Specificity (%)	**87,5**	**80,0**	**33,3**	**25,0**
+ predicted value (%)	**94,7**	**90,9**	**82,6**	**72,7**
− predicted value (%)	**63,6**	**80,0**	**22,2**	**33,3**
Predicted accuracy (%)	**83,3**	**93,3**	**65,6**	**64,3**

*85% of maximum predicted heart rate reached.



*Negative test but 85% of MPHR reached.

Fig. 1. ECG section of non-invasive algorithm.



*Negative test but 85% of MPHR reached.

Fig. 2. Non-invasive algorithm to detect CAD in vascular patients.

TABLE III. CLASSIFICATION OF CORONARY ANGIOGRAPHIC FINDINGS IN RELATION TO SYMPTOMS OF CAD

	No. of patients	Asymptomatic	Accepted for CABS
Three-vessel disease	8	3	6
Two-vessel disease	10	8	6
Single-vessel disease	6	4	2
Normal	8	6	0
Total	32	15*	14

*15/24 patients (62,5%) with significant CAD were asymptomatic.
CABS = coronary artery bypass surgery.

surgery.[2,3] Surgeons and anaesthetists have traditionally relied on the evaluation of risk factors, such as previous history of myocardial infarction, hypertension and angina, in an attempt to predict potential intra- and postoperative myocardial complications. Some objectivity was added to this approach by Cooperman *et al.*,[10] Goldman *et al.*[1] and others,[11] who used multivariate analysis of risk factors to identify patients likely to have peri-operative myocardial complications. The accuracy of clinical history and resting ECGs in predicting the presence of significant CAD in the present study was high (68,8%) when compared with the study by Youngman *et al.*[12] (36%). Different interpretation of resting ECGs may partially account for this.

Angiographic studies have shown that 22 - 30%[4,13] of patients with a negative cardiac history and a normal resting ECG have significant CAD. Accordingly, some centres recommend routine pre-operative coronary angiography,[4,14] followed, when indicated, by CABS or coronary angioplasty. It would, however, be more practical, safer and more cost-effective if an algorithm consisting of non-invasive tests could be used to identify patients with haemodynamically significant CAD who qualify for coronary angiography. Various algorithms have been suggested.[12,15]

ECG-monitored exercise testing has been proposed as a relatively inexpensive, easily applicable means of screening for asymptomatic CAD in patients presenting for major vascular surgery.[5,16] The frequent inability of vascular patients to participate in treadmill exercise has led to the use of arm ergometry as an alternative to or in conjunction with treadmill testing.[5,12] The addition of arm ergometry to a pre-operative algorithm using treadmill testing and exercise radionuclide ventriculography increased the predictive capacity of the algorithm from 64% to 89%.[12] The combination of treadmill stress resting and arm ergometry alone had a predictive accuracy of 74%. Despite the fact that arm ergometry is less sensitive than treadmill exercise in eliciting exercise-induced ischaemic abnormalities (Van der Watt, Nel, Jordaan and Travers — unpublished data), the combination of these two methods had a predictive accuracy of 83,3% and a positive predictive value of 94,7% in the present study.

The advent of more sensitive and specific screening tests for cardiac performance may have reduced the importance of exercise testing in the pre-operative assessment of major vascular surgery patients. Melin *et al.*[17] compared exercise ECG and ^{201}Tl scanning in 130 men and 30 women with no previous myocardial infarction, who were referred for evaluation of chest pain. Although the sensitivity (87% v. 74%) and specificity (89% v. 70%) were higher for ^{201}Tl scanning in the group as a whole, the predictive value for the presence of CAD of a positive ^{201}Tl scan v. a positive exercise ECG in patients with typical angina was not significantly different (99% v. 93%). McCarthy *et al.*[18] studied 128 patients undergoing diagnostic angiography as well as exercise ^{201}Tl scanning for angina. The overall sensitivity of ^{201}Tl scanning was 85% and the specificity 79%, compared with 67% and 91% for exercise ECG. However, the improved sensitivity of ^{201}Tl scanning resulted primarily from inclusion of patients with inadequate ECG stress tests (< 85% of MPHR and without ST changes) and from other ECG stress tests that could not be interpreted (e.g. presence of left bundle branch block or baseline ST-T changes). In those patients who achieved > 85% of their MPHR, there was no difference in sensitivity and specificity between exercise ^{201}Tl scanning and exercise ECG. In patients with non-diagnostic or stress tests that could not be interpreted, ^{201}Tl scanning appeared to offer a similar sensitivity and specificity for the diagnosis of CAD as in those with diagnostically adequate exercise tests. The sensitivity, specificity and predictive accuracy of ECG-monitored exercise testing in the present study were surprisingly high but the same variables for exercise ^{201}Tl scanning were disappointingly low (Table II). Analysing the data in stepwise fashion, however, yielded a predictive accuracy of 90,6% (Fig. 2). Although the sensitivity of ^{201}Tl scanning decreases slightly if 85% of MPHR is not attained, the predictive accuracy of the test is not influenced (Table II).

Using the proposed non-invasive algorithm enabled us to identify 15 patients with asymptomatic but haemodynamically significant CAD. Fourteen patients were subsequently referred for CABS and in 12 cases this was done before the initially planned PVD procedure (Table III). Eleven of the 14 patients referred for CABS were totally asymptomatic, while 6 of the 14 had signs of a previous myocardial infarction or ischaemia on resting ECG.

Conclusions

The very high prevalence of significant but asymptomatic CAD in patients under consideration for peripheral revascularisation (Table III), was one of the most important features of the present study. Bearing in mind the systemic nature of atherosclerosis, the admission to hospital of a patient for vascular surgery offers the ideal opportunity to diagnose associated CAD. The only value of exercise ^{201}Tl scanning appears to be in patients with non-diagnostic stress tests (< 85% of MPHR) and stress tests that cannot be interpreted. The proposed non-invasive algorithm proved to be a very accurate means of selecting patients for pre-operative coronary angiography.

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