Exercise testing soon after myocardial infarction: its relation to course and outcome at one year in patients aged less than 55 years

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SUMMARY A consecutive series of 184 patients aged < 55 years who had an acute myocardial infarction were enrolled in a study to examine outcome at one year. One hundred of these patients underwent a maximal exercise test six weeks after infarction to evaluate its ability to predict cardiac events. The in-hospital mortality for the series was 7.6% (14 deaths) and the one year mortality for the 170 survivors was 3.8% (seven deaths). During the exercise test 31 patients had angina and 21 had ST depression. During the one year follow up period 39 of 100 patients had angina on exertion, 15 patients underwent coronary artery surgery, three patients had a reinfarction, and one patient died. Angina during the exercise test but not ST segment depression during the exercise test predicted angina on exertion and the need for coronary artery surgery. In the year of follow up angina occurred during everyday exertion in 25 (81%) (95% confidence interval 62 to 92%) of the 31 patients who developed angina during the exercise test and in only 14 (20%) (95% confidence interval 12 to 32%) of 69 patients who did not, and coronary artery surgery was performed in 11 (35%) (95% confidence interval 19 to 54%) of the 31 patients with angina during the exercise test and only four (6%) (95% confidence interval 2 to 15%) of 69 patients without angina.

The outcome after myocardial infarction in patients aged < 55 years was good and the occurrence of angina, but not ST segment depression, during a maximal exercise test six weeks after infarction was an indication for further investigation.

The aims of management in younger survivors of acute myocardial infarction include full rehabilitation of the patients so that they can return to normal lives and, if possible, a reduction in subsequent morbidity and mortality. To achieve this those patients who are at increased risk of death, reinfarction, and other cardiac events must be identified. This requires a reliable and preferably non-invasive method of predicting important cardiac events and of selecting patients who may benefit from further investigation. There have been several studies to assess the value of exercise testing soon after infarction. Unfortunately most included substantial numbers of elderly patients (over 60 years and even up to 79 years) and presented no information specific to younger patients, despite strong evidence of the independent effect of age on outcome in survivors of acute myocardial infarction. This study was therefore designed to determine the outcome and value of a symptom limited exercise test six weeks after infarction in predicting cardiac events during the first year after infarction in a consecutive group of patients aged < 55.

Patients and methods

STUDY POPULATION
The study population was drawn from 184 consecutive patients under the age of 55 years admitted to our coronary care unit between October 1981 and February 1984 with confirmed acute myocardial infarction. The diagnosis of acute myocardial infarction was based on the presence of the following: (a) a history of typical chest pain lasting at least 30 minutes and (b) a rise in the activity of cardiac enzymes (creatine kinase, lactic dehydrogenase, or...
artery stenosis was defined as at least twice the upper limit of normal or (c) characteristic electrocardiographic changes—that is a sequential rise of ST segment, inversion of T waves, and appearance of new Q waves.

Fourteen (7.6%) patients died in hospital. Seventy patients were excluded from the study for various reasons. Three could not be exercised because of left ventricular failure and nine because of limiting neurological or orthopaedic disease. Thirteen patients were excluded because of severe non-cardiac disease and 22 patients refused to take part in the study. Six patients lived too far away for adequate follow up, and 17 patients were excluded for various administrative reasons.

So we studied 100 survivors of an acute myocardial infarction under the age of 55 years (10 women and 90 men; mean age 46-6 years (range 32-54)). Five patients had a history of previous myocardial infarction and four were taking β blockers at entry into the study.

EXERCISE TESTING
All patients had a symptom limited treadmill exercise test during a modified Bruce protocol (table) six weeks after infarction (range 35–50 days, mean 42.7 days). Exercise was stopped if: (a) the patient developed limiting symptoms of chest pain, dyspnoea, or fatigue; (b) there was a sustained fall in systolic blood pressure of ≥ 20 mm Hg from values attained earlier during exercise; (c) ventricular extrasystoles occurred in runs of three or more; or (d) there was ST segment depression of ≥ 4 mm.

Throughout the exercise test leads II, V2, and V5 were monitored continuously. Blood pressure and standard 12 lead electrocardiograms were recorded every three minutes during exercise and at 1, 3, and 5 minutes after exercise or until the electrocardiogram was normal and the patient was comfortable, whichever was longer. We analysed the following exercise test variables: (a) the development of angina, (b) significant ST depression defined as at least 1 mm horizontal or downsloping ST segment depression measured 0-08 s from the J point of the QRS complex, and (c) the duration of exercise.

CORONARY ARTERIOGRAPHY
All patients had a coronary arteriogram and left ventricular angiogram at a mean of three months after infarction. The left ventricular angiograms were recorded in both the 30° right anterior oblique and either 60° left anterior oblique or lateral projections. At least two orthogonal views of each coronary artery were obtained. Clinically significant coronary artery stenosis was defined as at least a 70% reduction in intraluminal diameter. Each angiogram was reported independently by two observers and differences of opinion were settled by consensus. Left ventricular ejection fractions were calculated from the 30° right anterior oblique angiogram by the area-length method for single plane angiograms. There were no complications associated with angiography or exercise testing.

FOLLOW UP
All patients, including those excluded from exercise testing, were followed up as outpatients. The frequency of review depended on their progress and severity of symptoms. A full, formal clinical assessment of all patients was undertaken at one year. The events of interest were death, reinfarction defined by the same criteria for infarction as for entry into the study, coronary artery surgery, and the development of stable or unstable angina pectoris. Coronary artery surgery was recommended for two patients with severe left main stem lesions but was only advised because of symptoms in the other patients.

STATISTICAL ANALYSIS
Exercise test variables were examined in relation to the selected end points. The χ² test with Yates’ correction for small numbers and Fisher’s exact test were applied as appropriate. Values of p < 0.05 were considered to be significant. Proportions are presented with their 95% confidence intervals (CI). The mortality rates in the exercised patients and in those excluded from exercise testing were compared by calculating a standardised mortality ratio for the two groups. This relates the mortality rate within each of the groups to the expected mortality rate of an age and sex matched group of the general population and is expressed as a percentage ± standard error.

Results

EXERCISE TEST END POINTS
The exercise test was terminated because of angina in 31 patients, exhaustion in 67 patients, and a fall in systolic blood pressure in two patients. Neither the extent of ST segment depression nor the occurrence of ventricular arrhythmias was an end point to any of the exercise tests.

CORONARY ANATOMY
Twelve patients had three vessel disease, 36 had two vessel disease, and 47 single vessel disease. Five patients had no significant coronary artery disease.

During follow up exertional angina occurred in 39 patients: five (42%) of the 12 patients with three vessel disease, 19 (53%) of the 36 patients with two vessel disease, and 13 (28%) of the 47 patients with single vessel disease. Two (40%) of the five patients
Exercise testing soon after myocardial infarction

without significant coronary artery disease had mild exertional angina at the one year follow up examination. Angina was therefore significantly more common in patients with multivessel (two or three vessel) disease, 24 (50%) (95% CI 35 to 65%) of 48 patients, than in patients with single vessel disease, 13 (28%) (95% CI 16 to 43%) of 47 patients (p < 0.05).

EJECTION FRACTION
At the time of cardiac catheterisation, the ejection fraction was > 50% in 55 patients, 40–49% in 23 patients, 30–39% in 11 patients, and < 30% in 10 patients. The quality of the left ventricular angiogram was not good enough for analysis in one patient.

ANGINA
Angina occurred in 31 patients during their six week exercise test (fig 1a). Of these, 25 (81%) (95% CI 62–92%) continued to experience angina during everyday life in the first year after infarction; but only 14 (20%) (95% CI 12 to 32%) of the 69 patients who had no angina on exercise testing (p < 0.001) did so. Of the 39 patients who experienced exertional angina during everyday life in the one year follow up period 36 (92%) had developed their first symptoms by the time they presented for their six week exercise test. Only 25 (69%) (95% CI 51 to 83%) of these 36 patients experienced angina during the exercise test, while two (5%) had significant ST segment depression alone and nine (25%) had a negative exercise test.

ST DEPRESSION
Significant ST depression occurred in 21 patients during their six week exercise test (fig 1b). Of these, five (24%) (95% CI 9–48%) experienced angina on exertion during follow up compared with 34 (43%) (95% CI 32–55%) of the 79 patients who did not have ST depression on exercise testing. This difference is not significant.

Only nine patients had ST depression of > 2 mm and of these, four (44%) (95% CI 15 to 77%) had a clinical history of angina during follow up compared with 35 (38%) (95% CI 28 to 49%) of the 91 patients with less or no ST depression. This difference is not significant.

DEATH
During the one year follow up period there was only one death in the study cohort (standardised mortality ratio 222 ± 220%). Death was sudden and occurred 11 months after infarction. Necropsy did not show recent infarction, and death was assumed to be caused by an arrhythmia. This patient had single vessel right coronary artery disease and an ejection fraction of 36%; and six weeks after infarction he exercised for 18 minutes with a normal haemodynamic response, without angina, and with 1 mm ST segment depression in lead aVL only. There were six further deaths in the group of patients excluded from the study cohort and these are discussed below.

REINFARCTION
Reinfarction occurred in only three patients: one with single vessel circumflex disease and two with two vessel (left anterior descending and circumflex) disease. Of these three patients only one had angina during his exercise test and none had ST depression. The ejection fraction was 27% in one patient and > 55% in the other two.

CORONARY ARTERY SURGERY (fig 2)
Coronary artery surgery was performed on 15 patients during the one year follow up period with no operative mortality. Apart from two patients with significant narrowing of the left main stem, coronary artery surgery was performed only for limiting angina. Of these 15 patients, five had single vessel, seven had two vessel, and three had three vessel coronary artery disease. One of the patients with left main stem disease is included in the group with two vessel disease and the other in the group with three

![Fig 1](http://heart.bmj.com/)

**Fig 1** (a) Relation of occurrence of angina during follow up to angina on exercise testing and (b) to ST depression on exercise testing.
vessel disease (there was additional significant right coronary artery disease).

Angina during the six week exercise test was an indicator of the later need for coronary artery surgery (fig 2a). Eleven (35%) (95% CI 19 to 54%) of the 31 patients with angina as the end point for their six week exercise test needed an operation and only four (6%) (CI 2 to 15%) of the 69 patients who did not develop angina (p < 0.001) later needed an operation.

Neither the presence of nor the degree of ST depression on exercise was a useful predictor of the need for subsequent coronary artery surgery (fig 2b). Four (19%) (95% CI 6 to 43%) of the 21 patients with ST depression and 11 (14%) (95% CI 8 to 24%) of the 79 patients without ST depression underwent coronary artery surgery during the first year of follow up (p = NS). Only one (11%) of the nine patients with ST depression of > 2 mm had coronary artery surgery.

Coronary artery surgery was needed in significantly more patients with impaired left ventricular function: eight (38%) (95% CI 19 to 61%) of the 21 patients with an ejection fraction < 40% but only seven (9%) (95% CI 4 to 18%) of the 78 patients with an ejection fraction > 40% (p < 0.01).

**UNSTABLE ANGINA**
There were no cases of unstable angina.

**EXCLUDED PATIENTS**
Six of the 70 patients who were not included in the study cohort died of cardiac causes in the first year of follow up (standardised mortality ratio 1980 ± 6530%). All deaths occurred suddenly at home in the first two months after discharge from hospital. Three died in the first three weeks—before the exercise test. Only one of these patients was excluded on medical grounds (because of severe systemic lupus erythematosus). The overall mortality for the 184 consecutive patients is, therefore, 3.8% (7/184).

Eight (11%) of these 70 patients had coronary artery surgery in the first year of follow up for limiting symptoms.

Three patients were lost to follow up.

**Discussion**

Prognostic information in subgroups of survivors of acute myocardial infarction can be applied to the management of these patients since those who have a good outlook can be reassured and those at increased risk of death and reinfarction can be investigated and managed appropriately. In recent years exercise testing soon after infarction has been suggested as one means of obtaining such information. The increased workload on departments performing non-invasive tests is considerable when all patients are investigated. It is, therefore, important to identify patients in whom such an approach provides little additional information on which to base long term management. Most of the previous studies of exercise testing after myocardial infarction have included older patients, and their conclusions may not be valid when applied to the management of younger patients in whom the outcome was better. Differences in study design, exercise test protocol and timing, and population selection make comparison between studies difficult. However, many workers have recommended an exercise test soon after infarction as a means of predicting significant cardiac events such as death and reinfarction, having shown that several variables identified during the exercise test correlate with a worse prognosis. Starling et al studied patients up to 79 years of age and found...
that a combination of angina, inadequate blood pressure response, and ST segment depression identified those patients with the highest mortality. However, 24% of their patients had a history of previous myocardial infarction. In a similar study of patients up to 70 years of age, DeBusk et al found that exercise induced ST depression of at least 2 mm at a heart rate of <135 beats per minute predicted increased morbidity and mortality. The results of these and similar studies have been applied to the management of younger patients in whom the clinical course after infarction may be very different.

Studies of the course of disease in younger patients after infarction suggest that the outlook in patients under 60 years is very good. Roubin et al for instance, found a one year mortality of 3.6% in their study of 229 patients followed over a mean period of 34 months. No previous studies have reported on the correlation between exercise test data and prognosis in a young group of patients. Our study has therefore examined the outcome and the role of exercise testing six weeks after infarction in predicting important cardiac events in a consecutive series of patients under 55 years.

The study confirms that the prognosis in young survivors of myocardial infarction is very good. The inpatient mortality of 7.6% was similar to that reported by Norris et al in their study of 325 patients under 60 years of age. The overall mortality in the present series was only 3.8%; there was one death in those who underwent exercise testing and six among those who were excluded. The reasons for the increased mortality in those patients excluded from the study cohort is unclear. However, the calculated standardised mortality ratios of 222 ± 220% for the exercised patients and 1980 ± 6530% for the excluded patients show that the suggestion of a higher mortality rate amongst the “excluded” group is not an artefact of the age and sex distributions of the two populations. We confirmed that angina during the exercise test frequently predicted exertional angina during follow up. Interestingly, 92% of our patients with a history of exertional angina at one year follow up had experienced their first symptoms within six weeks of their acute infarction, although not all actually experienced it during the exercise test. As might be expected, the need for coronary artery surgery because of symptoms was significantly more common in patients with angina during the exercise test, a finding similar to that of Davidson and DeBusk. Neither ST segment depression nor an abnormal haemodynamic response to exercise was a useful predictor of subsequent cardiac events.

Naturally, our results must be examined against factors that might influence mortality, such as left ventricular function, coronary artery disease, coronary artery surgery, and treatment with β blockers.

Taylor et al found that an ejection fraction of <40% and a history of previous myocardial infarction (probably operating through a reduced ejection fraction) were the best predictors of subsequent mortality over a 30 month follow up period. Norris et al also suggested that mortality was primarily related to left ventricular dysfunction, with exercise test variables and coronary artery disease playing a secondary role. Other evidence in favour of left ventricular dysfunction as a major prognostic factor has been provided by Sanz et al and De Feyter et al. An abnormal haemodynamic response to exercise (shown to relate to impaired left ventricular function) has been shown to correlate with outcome. In one study patients with an inadequate blood pressure response to exercise early after infarction had a mortality that was five times as high as that in patients in whom blood pressure rose by at least 30 mm Hg. In that study 300 patients underwent exercise testing on a bicycle ergometer and the mortality rate in the 212 patients in whom the blood pressure increased by ≥30 mm Hg was 3% compared with 16% among the 88 patients in whom the blood pressure increased <30 mm Hg. An exercise induced reduction of >5% in left ventricular ejection fraction also identified patients at high risk of cardiac death and other cardiac events. Conversely, a good haemodynamic response to exercise was used as a pointer to low risk patients. Seventy eight of our patients had ejection fractions >40% and 21 had ejection fractions <40%, figures that resemble those in other studies. In the present study, however, there was no correlation between exercise test variables such as short exercise time or an abnormal blood pressure response to exercise and either left ventricular function or subsequent prognosis.

The severity of coronary artery disease in our series is similar to that in previous studies. Twelve (12%) of our patients had three vessel disease compared with 7% and 9% respectively in the studies by De Feyter et al and Roubin et al in which the mortality rates in the first year of follow up were also low—between 3% and 4%.

Fifteen (15%) of our patients had coronary artery surgery during the year of follow up. This compares with 10–13.4% in the studies by Roubin et al, Krone et al, and De Feyter et al. Seventy seven (24%) of the 325 patients in the Norris study had coronary artery surgery in the first three months after infarction. In that study, however, the indications for operation were different from those used in this study. Some of their patients were operated on for limiting angina, others because of heart failure, and, in some, as part of a randomised study. In the present study, patients were only operated on for limiting
symptoms (with the exception of the two patients with stenoses of the left main stem) and, although our patients with low ejection fractions were more likely to have operation, in all cases they also had limiting angina. Most (70%) of our patients with low ejection fractions have not had an operation and only one of them has died.

β Blockers have been shown to produce a small but definite reduction in mortality after infarction but the rationale and cost benefit ratio of treating all patients after infarct need closer study. It was not our practice routinely to treat our patients with β blockers; we reserved them for specific indications such as angina or hypertension. The choice of antianginal preparation was left to the individual doctor, but at one year 22 patients were taking β blockers and less than half of them had been taking them for more than six months. Because mortality is worse in the first six months after myocardial infarction it is unlikely that β blockers had any significant effect on overall survival in this study.

The unique feature of our study population is their age. Davis et al. in their study of 940 survivors of myocardial infarction under 66 years old, found that significantly more patients died in the 61–65 year age group than in the younger age groups. Two further studies showed that apart from complex ventricular arrhythmias, age was the most important prognostic variable. The present study is thus further evidence that age is an important prognostic factor in survivors of myocardial infarction. Most of the patients with poor left ventricular function had angina and most of these could in turn be identified by a clinical history of angina as early as six weeks after infarction. Our findings suggest that routine angiography in all young patients after infarction is unnecessary although in the past, mainly for emotional reasons, this is the very patient group in which coronary arteriography has been used routinely. The exercise test six weeks after infarction provides little additional prognostic information for the first year follow up. It is chiefly performed to reassure both patient and clinician. Symptom free patients do not seem to need long term follow up but more prolonged study of the patients in this study may qualify this impression.

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