Early exercise testing and elective coronary artery bypass surgery after uncomplicated myocardial infarction

Effect on morbidity and mortality

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SUMMARY One hundred and nineteen consecutive patients were studied prospectively after uncomplicated myocardial infarction by maximal exercise electrocardiography at two weeks and coronary angiography at six weeks. At angiography 87 patients had a stenosis $> 70\%$ in one major coronary artery supplying residual viable myocardium outside the infarction zone. In 82 (94%) of these the 12 lead maximal exercise electrocardiogram correctly identified these areas of ischaemic but viable myocardium. Based on ST criteria alone five patients had a false negative exercise electrocardiogram for additional disease. Nevertheless, three developed angina or a significant fall in systolic blood pressure or both at a low workload.

On the basis of the anatomical lesions, symptoms, and the results of the European Coronary Surgery Study Group 55 patients were allocated for surgery. Of these, 54 underwent coronary artery bypass grafting within three months of myocardial infarction. One patient died perioperatively and another died after a reinfarction at four months while awaiting surgery. The remaining 53 were symptom free during a mean follow up period of 37 months. Sixty four patients received medical treatment. At angiography 32, 24, and eight patients had one, two, and three vessel coronary disease respectively. The exercise electrocardiogram correctly predicted the anatomy in 60 (94%), with two false positive and two false negative results for additional disease. The eight patients with three vessel disease treated medically had generalised inoperable disease, and at follow up three had died after a further infarction and five remained symptomatic with full medical treatment. Thus of those designated as at high risk and considered suitable for surgery the 37 month survival was 53 of 54 patients treated surgically.

After uncomplicated myocardial infarction the one year morbidity and mortality may be predicted by early exercise testing.^{1,2} In patients with exercise induced ST segment depression the mean mortality is 19%³ with one study giving a one year mortality of 27% in contrast to only 2% in those with normal exercise electrocardiograms.¹ We have shown previously that early exercise testing is safe and has considerable potential for the early identification of coronary disease additional to that which subtends the infarcted area.⁴

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As the mortality in patients with uncomplicated infarction is related to ST depression³ on exercise and as this ST depression relates to the presence of additional significant coronary disease⁴ the prognosis for these uncomplicated patients is probably dictated by their coronary anatomy. Whereas additional studies have outlined the importance of the degree of left ventricular damage and exercise induced haemodynamic abnormalities we carefully selected a consecutive series of patients with uncomplicated infarcts in whom adverse haemodynamic responses would be unlikely. In this way a more direct comparison may be made with the initial reports on early exercise testing after uncomplicated infarction.^{1,2}

The European coronary artery bypass surgery

study⁵ of angina patients reported increased survival in the surgical group for those with significant three vessel coronary disease. A review of the European study and discussion with its authors showed that 46% of the patients had had a confirmed previous myocardial infarction. Myocardial infarction could not be excluded in a further 30% leading to the possibility of previous infarction in 78% of the medical group and 73% of the surgical group. With the high incidence of previous infarction and the proved surgical benefits in certain anatomical subsets it seems likely that similar anatomical prognostic criteria will apply to the uncomplicated infarct patient. This is supported by the observation that ST segment depression^{1,2} reflecting additional disease⁴ determines one year survival given that the selected group by virtue of being uncomplicated would not be expected to have sustained major left ventricular damage. The absence of haemodynamic abnormalities in the previous reports would support this premise.^{1,2}

There is no doubt that heart failure and ventricular arrhythmias secondary to left ventricular damage are important prognostic predictors, but of perhaps greater concern is the observation that in the absence of these markers those with ST depression on early exercise testing have a reduced life expectancy. Because of the high one year mortality in patients with ST depression on early postinfarct exercise testing we evaluated prospectively the role of coronary artery bypass grafting in this selected uncomplicated group.

Patients and method

STUDY POPULATION

One hundred and nineteen consecutive patients with uncomplicated myocardial infarction were studied prospectively by 12 lead maximal treadmill stress testing and coronary angiography at two and six weeks respectively. All patients entered the study at two weeks after infarction. Table 1 summarises their clinical data. Patients were excluded from the study if any complications had occurred and specifically if they

had unstable angina, heart failure, cardiac arrhythmia, bundle branch block, or valvar heart disease.⁶ No patient was dependent on cardiac drugs, and thus none had taken digoxin or beta blocking agents for at least 48 hours before the stress test. In all patients the diagnosis of myocardial infarction was considered to be confirmed if in addition to symptoms of an acute coronary event the patient had (a) a rise to at least twice the upper limit of normal in serum creatine kinase activity measured daily for the first three days, or (b) electrocardiographic changes consistent with an acute evolving coronary event, or both.⁷

EXERCISE TESTING

All patients underwent 12 lead maximal stress testing two weeks after infarction according to the Bruce protocol. Although the details of the test have been described previously⁴ the description has been amplified to detail the end point and criteria for a positive test. The test was terminated if there was cardiac pain, a fall in systolic blood pressure of 15 mm Hg, ST segment depression of 3 mm, dyspnoea, or exhaustion. Unlike our previous study⁴ a test was considered to be positive when a net horizontal or down sloping depression of the ST segment >1 mm persisted for 80 ms after the QRS complex in a non-infarct area. The ischaemic area criteria used to predict further disease were: (a) in the presence of an anterior infarct additional ischaemic changes in the inferior and lateral leads would suggest right or circumflex coronary artery disease or both respectively; and (b) in the presence of an inferior infarct additional ischaemic changes in the anterior leads would indicate left anterior descending coronary artery disease.

CORONARY ANGIOGRAPHY

Within four weeks of the exercise test each patient underwent selective coronary angiography and left ventriculography. There were no complications. The anatomy was reported without knowledge of the results of the exercise test. Significant coronary artery disease was defined as a luminal narrowing >70% in

Table 1 Patients' characteristics

	Surgical group (n=55)	Medical group (n=64)	p value
Mean (SEM, range) age (yr)	51(1) (34-68)	50(1) (31-65)	NS
Sex (% male)	92.5	95	NS
Location of infarct (No of patients):			
Anterior	15	38	<0.001
Inferior	40	26	<0.001
Mean (SEM) blood pressure on admission (mm Hg):			
Systolic	124(2)	127(3)	NS
Diastolic	79(2)	83(1)	NS
Mean (SEM) heart rate on admission (beats/min)	83(3)	81(2)	NS

any of the three major coronary arteries. The occluded artery to the infarct area was classed as one vessel disease.

CORONARY ARTERY BYPASS SURGERY

Based on the anatomy, symptoms, and the criteria dictating the prognosis in the European Coronary Surgery Study Group, the patients with additional significant coronary artery disease were offered coronary artery bypass surgery. Our criteria for surgery were: (a) significant three vessel coronary artery disease; (b) a strongly positive exercise electrocardiogram in patients with a critical proximal stenosis of the left anterior descending coronary artery constituting a component of either two or three vessel disease; and (c) patients who had angina refractory to optimum medical treatment whose disease was suitable for surgery. All patients were seen regularly during a mean follow up period of 37(0.5) months.

STATISTICAL ANALYSIS

Data are expressed as mean (SEM). Logarithmic analysis was used, and the difference between continuous variables was assessed by the unpaired *t* test.

Results

COMPARISON OF MEDICAL AND SURGICAL TREATMENT GROUPS

The 55 patients managed surgically and the 64 managed medically were remarkably similar with regard to age, sex, and location and extent of infarction (Table 1). As would be expected from our selection criteria, however, the surgical group had significantly more ST segment depression on exercise testing at a significantly reduced exercise time (Table 2). At catheterisation they also had more coronary arteries with >70% stenosis than the medical group (3.2(0.1) *v* 1.6(0.1), *p*<0.001). Patients with inferior infarcts had a significantly greater chance of additional disease than those with anterior infarcts (*p*<0.001).

EXERCISE DATA AND CORONARY ANGIOGRAPHY RESULTS

Sixty six patients had inferior and 53 anterior infarction.³ Based on the ST segment change alone, 84 patients had a positive stress test for additional coronary artery disease in vessels supplying residual viable myocardium remote from the infarct zone. At angiography all but two had additional coronary disease. The two patients with single vessel disease in whom the stress test was positive in the infarct area underwent successful coronary artery dilatation and subsequently remained asymptomatic during the follow up period. In 112 of our 119 patients the exercise electrocardiogram correctly identified the coronary anatomy with a predictive value of 98%.

A positive stress test had a sensitivity of 94%, the specificity of a negative maximal treadmill test soon after infarction was 94%, and the accuracy rate for the whole group was 94%.

Surgical group—Based on our selection criteria for surgery 55 (50 with three vessel and five with two vessel disease) of the 82 patients who had a true positive stress test were allocated to surgery. There was one perioperative death, and one patient died after reinfarction at four months while awaiting surgery. The remaining 53 were symptom free during the follow up period.

Medical group—In 32 patients, angiography showed single vessel disease to the infarct area, and this was correctly predicted by the exercise test in 30 (94%). Twenty four patients had two vessel disease; these patients were allocated to the medical group because of the distal distribution of the coronary lesions and the fact that they did not fulfil our selection criteria for surgery. All were asymptomatic during the follow up period, although 11 patients were receiving anti-anginal agents. Eight patients with positive stress tests had inoperable distal and diffuse three vessel coronary disease, and they were offered intensive medical

Table 2 Exercise testing and coronary angiography data. Values are mean (SEM) unless stated otherwise

	Surgical group (n=55)	Medical group (n=64)	<i>p</i> value
Heart rate (beats/min):			
Resting	83(3)	81(2)	NS
Peak	149.5(2)	152(3)	
Peak systolic blood pressure (mm Hg)	136(4.2)	145(3.3)	NS
Exercise time (min)	5.5(0.3)	7.5(0.28)	<0.001
ST segment change (mm)	2(0.14)	1(0.17)	<0.001
Coronary artery disease*:			
One vessel	0	32	
Two vessel	5	24	<0.001
Three vessel	50	8	

*No of patients with >70% stenosis in any of the three major coronary arteries.

Table 3 Correlation between maximal stress testing and coronary angiography in both groups of patients

Treatment	Location of infarct	Stress test				Coronary artery disease*			
		TP	FP	TN	FN	1	2	3	Total
Medical (n=64)	Anterior (n=38)	15	1	21	1	22	12	4	38
	Inferior (n=26)	15	1	9	1	10	12	4	26
Surgical (n=55)	Anterior (n=15)	15	0	0	0	0	3	12	15
	Inferior (n=40)	37	0	0	3	0	2	38	40
Total		82	2	30	5	32	29	58	119

T, true; F, false; P, positive; N, negative.

*No of vessels with >70% stenosis.

treatment; of these, three subsequently died and five were restricted by angina or dyspnoea despite full medical treatment. Of the 64 patients in the medical group, the exercise test correctly predicted the anatomy in 60. In all 30 patients who had true negative stress tests for additional ischaemia, the exercise test correctly predicted the coronary anatomy (Table 3).

Discussion

By exercising patients at two weeks after an uncomplicated myocardial infarction mortality and morbidity may be accurately predicted.^{1,2} This has particular advantages for physicians who have more ready access to exercise testing facilities than angiography, reducing the need for and the number of unnecessary angiograms. It is important, however, to emphasise the strictly defined group of patients under study and the precise nature of our protocol. In patients whose course after myocardial infarction is uncomplicated then the one year mortality is of the order of 7.5%.³ However if patients are subdivided on the basis of the early postinfarct exercise ST response the figures range from a 3% one year mortality in those with a normal electrocardiogram to 20% in those with ST depression.³ This ST segment derived data have also been shown to reflect underlying coronary disease accurately.⁴ Our predictive value is superior to that of others⁶ because of our stricter protocol. We used 12 lead electrocardiography, and a maximal end point, and in contrast to others excluded cardiac drugs which have an effect on the ST segment.^{6,8} We do not dispute the importance of a reduced left ventricular ejection fraction in determining prognosis, but our study group was specifically designed to exclude patients with major left ventricular impairment and therefore cannot be directly compared with studies with a more diffuse patient population.

Although exercise testing after infarction clearly has considerable potential for the early identification of multivessel coronary disease, clear guidelines for subsequent management do not exist. In view of the

high one year mortality figure of up to 27% for those with positive exercise tests after uncomplicated infarction and an overall mean one year mortality of 20%,^{3,9,10} it is reasonable to assume that a means of identifying and modifying the anatomy may influence survival. On the basis of the proved benefits of surgery in patients with angina and the belief that the disease process is the same we electively referred our postinfarct patients with additional significant coronary artery disease for early surgery (6–12 weeks). Of 54 patients undergoing surgery, one died and 53 remained well at a mean follow up of 37 months (surgical mortality 2%).

As expected the 53 patients considered for surgery had significantly more ST segment depression (2(0.14) v 1(0.17) mm) on exercise testing at a significantly shorter exercise time (5.5(0.3) v 7.5(0.28) minutes) than the medically managed patients, and at angiography they had significantly more coronary arteries with a stenosis >70% than the medical group. Thus maximal stress testing after early infarction can predict the anatomy and has the potential to define an at risk group with an expected mortality of up to 27%. Our overall medical and surgical mortality at 37 months was 4% (five patients), and all deaths occurred in the high risk group—one at operation, one awaiting operation, and three receiving medical treatment because of inoperable lesions. The patient who died after a reinfarction at four months regrettably had his operation delayed by factors outside our control. Eight patients were considered unsuitable for surgery because of advanced disease; three subsequently died and five were symptomatic although stable with full medical treatment. The remaining 56 patients in the medical group were active and symptom free.

Although this was a prospective study we recognise the absence of a randomised control trial and the use of historical controls. Despite our excellent results we believe a large scale randomised trial is scientifically justified, particularly in view of the contrasting observations of the CASS study.¹¹ In favour of a more aggressive surgical approach is the European angina study and our overall mortality of 4% and the strik-

ingly high survival rate in these patients with high risk lesions. An expected one year mortality of 20% in those with ST segment depression on early postinfarct exercise testing has been reduced to 2% in those undergoing coronary bypass surgery. This benefit continued to 37 months after surgery.

We have shown that maximal treadmill stress testing early after uncomplicated myocardial infarction is a safe and effective diagnostic test that helps in the early identification of patients with high risk multivessel coronary artery disease and that early bypass surgery in these patients has a low mortality rate of 2% at 37 months. It is clearly imperative that other workers substantiate our observations in this uncomplicated group of patients. An additional re-evaluation of those whose infarcts are associated with extensive left ventricular damage is needed but study protocols must clearly define the subgroups under evaluation.

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