Fortnightly Review

Management of patients after their first myocardial infarction

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In the past 20 years there has been a steady improvement in the short term prognosis of patients with myocardial infarction,¹ following the introduction of β blockers, thrombolysis, and aspirin. Patients treated with thrombolytic drugs have a lower overall mortality after myocardial infarction but remain at risk of non-fatal reinfarction or death, and in one study almost half of all survivors of acute myocardial infarction died or suffered a further ischaemic event within three years.² It is therefore important to have a strategy to identify patients at high risk, to reduce the subsequent development of cardiac failure and mortality, and to have effective measures for secondary prevention to reduce the incidence of reinfarction as well as to promote rehabilitation.

Risk stratification

The amount of myocardial damage and the degree of left ventricular dysfunction, which may be limited by the presence of a patent infarct related artery, together with the extent of underlying coronary disease, influence prognosis after myocardial infarction.^{3,4} In the 1960s Killip and Kimball showed that the presence and increasing severity of cardiac failure predicted a poor outcome and that hospital mortality was more than 80% if cardiogenic shock developed.⁵ A decade later Norris developed an index including the patient's

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BMJ 1994;309:1129-34

Investigations available for stratification of risk after acute myocardial infarction

Left ventricular dysfunction

Non-invasive investigations:

Clinical features, 12 lead electrocardiography, chest x ray examination, measurement of cardiac enzymes, echocardiography, exercise testing, radionuclide ejection fraction

Invasive investigations:

Left ventricular angiography

Residual ischaemia

Non-invasive investigations:

Clinical features, 12 lead electrocardiography, ambulatory electrocardiography, exercise testing, radionuclide studies

Invasive investigations:

Coronary arteriography

Tendency to arrhythmias

Non-invasive investigations:

Clinical features, 12 lead electrocardiography, ambulatory electrocardiography, exercise testing, signal averaged electrocardiography,* estimation of heart rate variability*

Invasive investigations:

Baroreceptor sensitivity,* electrophysiological study†

*Not yet established in routine clinical practice.

†Not widely available, requires referral to specialist centre.

Summary points

A poor prognosis after myocardial infarction is suggested by:

- Increasing age
- Cardiac failure
- Low ejection fraction
- Positive result on exercise testing
- Frequent ventricular extrasystoles (more than 10 an hour)
- Ventricular tachycardia

A good prognosis is suggested by:

- Young age
- Good residual left ventricular function
- Negative result on exercise testing

age, history of previous infarction, systolic blood pressure on admission, site of infarction, and radiographic evidence of cardiac enlargement or pulmonary congestion.⁶ Increasing age, a history of previous infarction, and radiographic evidence of cardiac failure and cardiomegaly were shown to be associated with a worse prognosis.

The extent of myocardial damage can now be estimated from straightforward, non-invasive investigations that can quantify the degree of ventricular dysfunction. Residual myocardial ischaemia and a tendency to ventricular arrhythmias also influence prognosis after infarction, and the investigation and assessment of all three are discussed below.

EXTENT OF VENTRICULAR DYSFUNCTION

The degree of ventricular dysfunction can be assessed clinically by the presence or absence of a tachycardia, a third heart sound, and signs of cardiac failure. The extent of infarction can be crudely assessed from an electrocardiogram—by the presence, site, and number of Q waves—and from the degree of elevation of cardiac enzymes. In patients given thrombolytic drugs, creatine phosphokinase concentrations may rapidly reach a high peak, which rapidly falls after reperfusion as it is washed out, and so peak creatine phosphokinase concentrations may overestimate size of infarct. Cardiac size can be measured from a chest x ray, and the lung fields may show pulmonary congestion or oedema. Radionuclide ventriculography can reliably measure ejection fraction. Mortality in the first year after infarction increases with falling ejection fraction (fig 1).⁷ Echocardiography can also be used to assess left ventricular function and the site and size of infarction.

FIG 1—Association between mortality in first year after myocardial infarction and ejection fraction. Modified from the Multicenter Postinfarction Research Group.⁷

The challenge to doctors is to identify patients without clinical evidence of cardiac failure but with important left ventricular impairment. Radionuclide ventriculography is not available in all hospitals, and while echocardiography can identify large infarcts, overall left ventricular function is not easily measured. An intriguing possibility currently being investigated is that concentrations of brain natriuretic peptides mirror the degree of left ventricular dysfunction; if so, it might be possible to use a blood test to identify patients who should have formal assessment of left ventricular function.⁸ Clinical criteria and these simple measures of left ventricular function at rest can be used to identify patients with substantial ventricular impairment whose prognosis may be improved by the prescription of angiotensin converting enzyme inhibitors, as shown by the results of the acute infarction ramipril efficacy study and the survival and ventricular enlargement study.^{9,10}

RESIDUAL ISCHAEMIA

Routine early elective coronary arteriography (with a view to coronary angioplasty or bypass grafting of a stenosed artery related to the infarct) after thrombolysis for acute myocardial infarction has not been shown to be beneficial.¹¹ Patients experiencing angina at rest or on mild exertion despite optimal medical treatment are likely to have important residual ischaemia, often in the territory supplied by the infarct related artery (especially in patients treated with thrombolytic drugs). Such patients should be referred for urgent coronary arteriography because their symptoms may be due to a critical lesion suitable for treatment by coronary angioplasty or bypass grafting.

Treadmill exercise test

In patients making a good recovery residual ischaemia may be provoked by a treadmill exercise test. It is widely available and provides information on the presence and degree of residual ischaemia, ventricular dysfunction, and the tendency to arrhythmias.¹²

Features of positive result on exercise testing after acute myocardial infarction associated with poor prognosis

- ST segment depression (at least 0.1 mV, measured 80 ms after the J point)
- Development of angina at low workload
- Failure of systolic blood pressure to rise, or a fall by more than 10 mm Hg, on exercise
- Ventricular extrasystoles or ventricular arrhythmia during exercise or recovery
- ST segment elevation (ischaemia or left ventricular dysfunction)
- Supraventricular arrhythmias

It may also be an important step in rehabilitation. Patients with a negative result have a good prognosis, with an annual mortality of 0.5-4%, and can be reassured, while those with a positive result have an overall annual mortality of about 15-25%. A poorer than average prognosis is suggested by an exercise test that is associated with depression of the ST segment in an electrocardiogram of 2 mm or more, angina at a low workload, limited exercise tolerance (adjusted for age and sex), failure of the systolic blood pressure to rise, and ventricular extrasystoles or arrhythmias (see box).¹³ These findings alone or in combination suggest extensive coronary disease or impaired left ventricular function, or both. All patients who might reasonably be considered for coronary revascularisation by coronary artery bypass surgery or angioplasty should, if possible, have an exercise test. The test may be performed before discharge by means of a submaximal protocol¹⁴ or at four to six weeks after discharge with a maximal stress protocol. The early test may be used in uncomplicated cases to identify patients suitable for early discharge from hospital.¹⁵

β Blockers may interfere with the interpretation of the exercise test by blunting the response of the heart rate to exercise and so altering its prognostic value. However, because of concern about the withdrawal of β blockers from patients with known ischaemic heart disease, there is considerable variation in whether β blockers are stopped before the exercise test is performed.¹⁶ Much of the original data about exercise testing and prognosis after infarction were collected in patients taking β blockers. A positive result on exercise testing for a patient taking β blockers suggests important ischaemia despite treatment, and if this occurs at a low workload it warrants referral for coronary arteriography. A negative result suggests that β blockers are effective in controlling exercise induced ischaemia and may therefore be as effective as angioplasty or coronary artery surgery.¹⁷

Myocardial uptake of thallium radionuclide during exercise is a more sensitive test for myocardial ischaemia than routine exercise testing,¹⁸ but it is expensive, requires additional expertise for interpretation, and in practice provides little extra information when assessing patients after infarction.

Thrombolysis and aspirin—Most of the data relating to exercise testing after myocardial infarction were collected before the widespread use of thrombolysis and aspirin. Patients treated with thrombolytic drugs have a lower mortality, reflecting a reduction in the amount of myocardial damage. The ability of the exercise test to identify patients at risk of reinfarction or death after thrombolysis has been questioned. Recent studies of exercise testing in patients given thrombolytic drugs for acute infarction showed that a negative result carries an excellent prognosis.¹⁹⁻²² Although most patients who had further ischaemic events had had an abnormal exercise test, the predictive accuracy of a positive result was low: a large proportion of patients with a positive result remained free of further events. Clearly patients with a positive result and limiting angina should be referred for coronary arteriography with a view to revascularisation to improve their symptoms and possibly their prognosis. Patients with no or minimal angina and a positive result on exercise testing may be at risk of further infarction or death, but many are not and it is difficult to recommend a logical strategy for such patients. One approach would be to follow them up and refer them for coronary arteriography if symptoms develop.²³

Ambulatory monitoring of ST segment after acute myocardial infarction is easily performed and can be done early after the acute event and in patients who cannot be easily exercised. Substantial evidence exists that transient ischaemia provides prognostic

information in these patients, but how this relates to future ischaemic events is unclear, and the precise role of monitoring ambulatory ST segment in clinical practice is yet to be established.²⁴

Arteriography—It could be argued that all patients should have left ventricular cineangiography and coronary arteriography, and then all other tests become unnecessary: only arteriography can define the number, site, and severity of coronary stenoses. The exercise test, however, gives an indication of the functional effect of underlying coronary artery stenoses, and this will allow many patients who are at low risk and clinically stable to avoid coronary arteriography (performed mainly at larger centres, many of which have long waiting lists). Results from the second thrombolysis in myocardial infarction trial support this view: there was no difference between the invasive treatment group (immediate (2 hours) and delayed (18–48 hours) coronary arteriography with coronary angioplasty or bypass surgery) and the conservative treatment group in the incidence of death and non-fatal reinfarction after one year.²⁵ Coronary artery bypass surgery may be recommended to patients found to have disease of the left main coronary artery or severe disease of all three coronary arteries and impaired left ventricular function. Angioplasty has not yet been shown to improve prognosis in patients who are stable after myocardial infarction, but it may be offered as an alternative to surgery for patients with limiting angina.

TENDENCY TO ARRHYTHMIAS

During the convalescent phase of myocardial infarction, ventricular extrasystoles and supraventricular and ventricular arrhythmias recorded during ambulatory electrocardiography or provoked during exercise testing are associated with a poor prognosis.^{7,26} An count of 10 or more ventricular extrasystoles an hour is associated with a mortality in the first year of at least 15%.⁴ It may be present in up to 20% of patients treated by thrombolysis and is an independent risk factor for all deaths and sudden death after acute myocardial infarction.^{26,27} These observations led to the hypothesis that antiarrhythmic drugs would reduce the incidence of sudden death after myocardial infarction. The cardiac arrhythmia suppression trial compared flecainide, encainide, moracizine, and placebo in patients with asymptomatic ventricular extrasystoles after infarction but was terminated prematurely because of an excess of deaths in the groups receiving flecainide or encainide.²⁸ A trial of mexiletine also failed to show any benefit despite successful suppression of ventricular extrasystoles and arrhythmias confirmed by 24 hour ambulatory electrocardiography.²⁹

Many antiarrhythmic drugs have considerable negative inotropic properties, but amiodarone is the least negatively inotropic of these. A recent randomised double blind study compared the effects of one year of treatment with amiodarone or placebo on mortality, ventricular arrhythmias, and clinical complications in high risk postinfarction patients who could not tolerate β blockers and who did not show obvious ventricular arrhythmias. In this relatively small trial (305 patients took amiodarone, 308 took placebo) amiodarone significantly reduced cardiac mortality and ventricular arrhythmias; there were 21 deaths in the amiodarone group and 33 in the placebo group.³⁰ In contrast to β blockers, amiodarone did not appear to reduce the rate of reinfarction. Larger studies are required before the use of amiodarone, which is associated with a high rate of serious side effects, becomes widespread.

Patients who get ventricular tachycardia after their infarct because of exercise induced ischaemia should have coronary arteriography with a view to revascularisation. Patients in whom ventricular tachycardia occurs spontaneously should be considered for specific

antiarrhythmic treatment guided by ambulatory electrocardiography, exercise testing, or programmed ventricular stimulation.

Newer non-invasive methods for determining potential ventricular arrhythmias include the detection of late potentials by signal averaged electrocardiography,³¹ measurement of decreased variability in heart rate by 24 hour ambulatory electrocardiography,³² and estimation of baroreceptor sensitivity.³³ These have not yet become established in routine clinical practice, but they may become useful in selecting patients for further investigation of an arrhythmogenic substrate.³⁴

Secondary prevention

SMOKING AND LIFESTYLE

Patients who have just suffered a myocardial infarction are receptive to suggestions about changes in diet and lifestyle, many of which can be emphasised during rehabilitation. The benefits gained from modification of stress and a type A personality are modest compared with those gained from stopping smoking.³⁵ Stopping smoking is the most effective contribution a patient can make towards reducing risk. Mortality in patients who stop smoking after a myocardial infarction is 50% lower at five years than in patients who continue to smoke.³⁶ Stopping smoking also delays the start of angina after myocardial infarction.³⁷ Losing weight and taking regular sensible exercise lead to a feeling of wellbeing and allow patients to feel that they are contributing to their own recovery.

DIET AND LIPIDS

It seems sensible to recommend a reduction in the intake of saturated fat and an increase in the amount of fruit and vegetables. Obese patients should be encouraged to lose weight. Adding two portions a week of oily fish (salmon, trout, mackerel, herring, sardines) to the diet has been associated with a reduction in deaths from ischaemic heart disease and total mortality, but the rate of non-fatal reinfarction was not reduced.³⁸

Alcohol—There is strong evidence that a high intake of alcohol is an important preventable cause of death and is associated with increased blood pressure.³⁹ In contrast, a modest intake of alcohol (less than two drinks a day) might be beneficial. Alcohol increases the concentration of high density lipoprotein, and moderate alcohol consumption has been associated with a lower total mortality than abstinence and heavy consumption.⁴⁰ Alcohol consumption should not be recommended as a specific measure for secondary prevention.

Hypercholesterolaemia—While the debate about primary prevention and screening of populations continues, the evidence for secondary prevention in patients with myocardial infarction is less controversial. The greatest benefit in treating hyperlipidaemia appears to be in those most at risk, and survivors of myocardial infarction represent a high risk group.⁴¹ In all patients with myocardial infarction aged under 65 (the benefits of treating elderly patients have yet to be established) plasma lipids should be measured within 24 hours of the infarction as there is often a fall in plasma cholesterol concentrations over the next three months. Substantially elevated plasma cholesterol concentrations in patients aged under 50 suggests familial hypercholesterolaemia, particularly in association with signs such as tendon xanthomata, and first degree relatives should be screened. Recently, the British Cardiac Society, European Atherosclerosis Society, and British Hyperlipidaemia Association have issued guidelines on the management of hyperlipidaemia.⁴² Patients should first be given dietary advice to reduce their intake of saturated fats. After three to six months of successful dietary intervention a

full fasting lipid profile—including total cholesterol, high density lipoprotein and low density lipoprotein cholesterol, and triglycerides—should be performed. Ideally, total cholesterol should be lowered to less than 5.2 mmol/l and low density lipoprotein cholesterol to less than 3.4 mmol/l; the second target value is important as many patients, especially postmenopausal women, have a high total cholesterol concentration due partly to a high concentration of high density lipoprotein cholesterol.

Hypertriglyceridaemia—The role of triglycerides remains unclear. Hypertriglyceridaemia is often associated with obesity, sedentary lifestyle, hypertension, high alcohol intake, and diabetes mellitus. These should all be controlled before treating hypertriglyceridaemia, but if the triglyceride concentration remains above 2.3 mmol/l despite such measures then drug treatment should be considered, especially if this occurs in association with hypercholesterolaemia.

Drug treatment should be conventional, with bile acid sequestering drugs being used for hypercholesterolaemia the fibrates for mixed hyperlipidaemia. Inhibitors of hydroxymethyl glutaryl coenzyme A reductase are potent, well tolerated, and preferred by many patients to cholestyramine, but the results of long term trials with these drugs are not yet available.

ASPIRIN

Aspirin is established as a simple, safe, and effective immediate treatment for myocardial infarction and for secondary prevention. Treatment should begin as soon as possible after the start of symptoms and should be continued indefinitely. Pooled data show that the rates of non-fatal myocardial infarction and non-fatal stroke are reduced by about a third, and all vascular events by about a quarter.⁴³ It is effective in doses of 75–325 mg, lower doses being associated with fewer side effects.

β BLOCKERS

Three large randomised double blind studies of oral β blockers (timolol,⁴⁴ metoprolol,⁴⁵ and propranolol⁴⁶) have shown a clear benefit in the secondary prevention of death in patients after myocardial infarction. Patients with bradycardia, heart block, hypotension, pronounced cardiac failure, asthma, chronic airways disease, and important peripheral vascular disease may not tolerate β blockers. Indeed, in most trials of β blockers over half of the eligible patients were excluded. In the absence of side effects treatment should be continued indefinitely since stopping β blockers may be associated with sudden worsening of angina and in some cases myocardial infarction.⁴⁷

Patients with mild cardiac failure have a high risk of sudden death, and in the β blocker heart attack trial those patients with cardiac failure who could tolerate treatment appeared to derive most benefit.⁴⁸ It is important to control hypertension in survivors of acute myocardial infarction, and β blockers are a good choice because of their cardioprotective properties.

ANGIOTENSIN CONVERTING ENZYME INHIBITORS

In animal and human studies angiotensin converting enzyme inhibitors were found to reduce ventricular remodelling and enlargement after myocardial infarction. The potential for these drugs to benefit patients with myocardial infarction has been assessed in four large trials (see table), and it can be seen that the trials that included patients with the highest risk showed the greatest benefit. The implication from these trials is that patients with a large infarct complicated by clinical evidence of cardiac failure, or with an ejection fraction of less than 40% determined by radionuclide ventriculography, are likely to receive considerable benefit from angiotensin converting enzyme inhibitors. Once started, treatment should be continued indefinitely.

CALCIUM ANTAGONISTS

Trials of calcium antagonists have not shown benefit to patients after infarction and may be harmful in patients with impaired left ventricular function.⁵⁰ In the Danish verapamil in myocardial infarction trial, analysis of subsets showed that verapamil decreased mortality and major events after acute myocardial infarction in patients without cardiac failure.⁵¹ Verapamil therefore may be an alternative to β blockers in patients with contraindications to β blockers (for example, asthma). Otherwise calcium antagonists should only be used if there is a specific indication, such as angina or hypertension not responsive to β blockers (see fig 2 for summary of drug treatments).

ANTICOAGULANTS

In trials comparing oral anticoagulants with placebo reinfarction, cerebrovascular events, and total mortality were reduced in patients with myocardial infarction. The increased risk of intracerebral haemorrhage was outweighed by a reduction in ischaemic stroke. The risk of major extracranial haemorrhage also increased.^{52–53} In trials comparing oral anticoagulation with aspirin no significant differences in total mortality were found, but patients treated with aspirin had a lower coronary mortality.^{54–55}

In uncomplicated cases of myocardial infarction the increased risk of major extracranial haemorrhage and the greater cost and complexity of treatment with anticoagulants clearly favour the use of aspirin. Anticoagulants should be considered for patients with high risk of systemic embolisation because of atrial fibrillation, severe cardiac failure, or mobile mural thrombus. Aspirin can be started when the risk of systemic embolisation has resolved and treatment with anticoagulants is stopped.⁵⁶

Rehabilitation

Rehabilitation should begin at the start of the illness. Communication with patients and their families should be frequent and in plain language. A positive attitude

Summary of results of trials of angiotensin converting enzyme inhibitors in patients after myocardial infarction

Study	Drug used	Entry criteria	Time treatment started	Length of follow up	No (%) of patients who died		P value of difference
					Placebo	Treatment	
Acute infarction ramipiril efficacy study ^a	Ramipiril	Clinical cardiac failure	Within 3–10 days of myocardial infarction	Average 15 months	222/992 (22)	170/1014 (17)	0.002
Survival and ventricular enlargement study ^a	Captopril	Ejection fraction < 40% but no evidence of cardiac failure	Within 3–16 days of myocardial infarction	Average 42 months	275/1116 (25)	228/1115 (20)	0.019
International study of infarct Survival IV ^a	Captopril	All patients with acute myocardial infarction excluding those with hypotension	Within 24 hours of myocardial infarction	6 months	2008/27 382 (7.3)	1886/27 442 (6.9)	0.03
Cooperative new Scandinavian Enalapril Survival Study II ^a	Enalapril	All patients with acute myocardial infarction excluding those with hypotension	On admission with myocardial infarction	41–180 days	286/3046 (9.4)	312/3044 (10.2)	0.26

^aPersonal communication.

hospital based rehabilitation programme.⁵⁷ Booklets may be obtained from the British Heart Foundation, but in our coronary care unit we use a "heart manual," which is a complete package that includes relaxation techniques, education, and exercise training.⁵⁷

DISCHARGE FROM HOSPITAL

After discharge it is natural for patients to have further anxieties, but early contact with their general practitioner will allay much of this anxiety. Patients should be warned to expect some feelings of tiredness, malaise, aches, and pains and instructed about the use of glyceryl trinitrate and its side effects. Physical activity should be encouraged, with emphasis that care should be taken to gently increase activities for the first four to six weeks. Thereafter, patients' progress should be reviewed, with exercise testing carried out as appropriate. If the result of an exercise test is satisfactory then further increases in physical activity should be encouraged: recent reports of controlled studies suggest that physical activity and cardiac rehabilitation programmes based on exercise are of great value in reducing long term mortality and increasing a general sense of wellbeing.⁵⁸

Sexual intercourse should be avoided initially, but patients and spouses can be reassured that cardiovascular demands during intercourse are normally less than those during the exercise test.⁵⁹ Libido may be affected by drugs and may not return for some time after the infarct.

At about four weeks after infarction most patients may resume driving after informing their insurance companies—although drivers of heavy goods vehicles and public service vehicles will require special assessment. Air travel is usually safe after six weeks, and up to 90% of patients return to their previous occupations after two to three months.

Conclusions

Figure 3 summarises the investigations and treatment for patients after myocardial infarction. Patients

FIG 2—Summary of drug treatment for secondary prevention after myocardial infarction

about expected recovery from early in hospital, with stress laid on the active role that the family and patient can have, may be all that is required. Common emotional problems such as denial, anxiety, and depression should be recognised and dealt with. Patients should be able to discuss their illness and problems with the hospital team and should be made to realise that it is largely through their own efforts that they will recover; this helps patients' motivation to comply with any changes required for secondary prevention.

While many hospitals run organised postinfarction rehabilitation programmes, many others do not. Booklets for patients and families can complement explanations by medical and nursing staff since some patients find medical staff intimidating. Together with a self help programme, they may be as beneficial as a

FIG 3—Protocol for investigation and treatment after acute myocardial infarction

should undergo exercise testing whenever possible; it identifies most patients after their first infarction who are at low risk of reinfarction with an excellent prognosis and require no further investigation. It also identifies patients who may be at increased risk of further ischaemic events and who require more careful observation and investigation.

An optimistic approach that stresses the actions that patients may take themselves makes recovery from a myocardial infarction and return to normal activity more likely. Aspirin should be prescribed for all patients except those with absolute contraindications, and β blockers for those who can tolerate them. Patients with persistent angina should be referred for coronary arteriography as they may benefit from revascularisation. Angiotensin converting enzyme inhibitors should be prescribed for patients with large infarcts and cardiac failure or those who are shown on non-invasive investigation to have important left ventricular impairment.

- De Vreede JJM, Gorgels AP, Verstraaten GMP, Vermeer F, Dassen WRM, Wellens HJJ. Did prognosis after acute myocardial infarction change during the past 30 years? *J Am Coll Cardiol* 1991;18:698-706.
- Stevenson R, Ranjadayan K, Wilkinson P, Roberts R, Timmis AD. Short and long term prognosis of acute myocardial infarction since introduction of thrombolysis. *BMJ* 1993;307:349-53.
- Morgan CD, Roberts RS, Haq A, Baigrie RS, Daly PA, Gent M, *et al* for the TPAT Study Group. Coronary patency, infarct size and left ventricular function after thrombolytic therapy for acute myocardial infarction: results from the tissue plasminogen activator Toronto placebo controlled trial. *J Am Coll Cardiol* 1991;17:1451-7.
- Roubin GS, Harris PJ, Bernstein L, Kelly DT. Coronary anatomy and prognosis after myocardial infarction in patients 60 years of age and younger. *Circulation* 1983;67:743-9.
- Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol* 1967;20:457-64.
- Norris RM, Caughey DE, Deeming LW, Mercer CJ, Scott PJ. Coronary prognostic index for predicting survival after recovery from acute myocardial infarction. *Lancet* 1970;ii:485-7.
- The Multicenter Postinfarction Research Group. Risk stratification and survival after myocardial infarction. *N Engl J Med* 1983;309:331-6.
- Struthers AD. Plasma concentrations of brain natriuretic peptide: will this new test reduce the need for cardiac investigations? *Br Heart J* 1993;70:397-8.
- The Acute Infarction Ramipril Efficacy Study Investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. *Lancet* 1993;342:821-8.
- Results of the survival and ventricular enlargement trial. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1992;327:669-77.
- SWIFT Trial Study Group. SWIFT trial of delayed intervention elective intervention versus conservative treatment after thrombolysis with anistreplase in acute myocardial infarction. *BMJ* 1991;302:555-60.
- Theroux P, Waters DD, Halphen C, Debaisieux JC, Mizgala F. Prognostic value of exercise testing soon after myocardial infarction. *N Engl J Med* 1979;301:341-5.
- Jennings K, Reid DS, Hawkins T, Julian DG. Role of exercise testing early after myocardial infarction in identifying candidates for coronary surgery. *BMJ* 1984;288:185-7.
- Weld FM, Chu KL, Bigger JT Jr, Rolnitzky LM. Risk stratification with low level exercise testing 2 weeks after acute myocardial infarction. *Circulation* 1981;64:306-14.
- Moss AJ, Benhorin J. Prognosis and management after a first myocardial infarction. *N Engl J Med* 1990;322:743-53.
- Muir KW, Rodger JC, DeBono JS, McDonald H, Irving JB. Drugs and the exercise test. *BMJ* 1992;305:808-9.
- Lim R, Dymond DS. Should antianginal drugs be stopped for exercise testing. *Lancet* 1992;340:161-2.
- Moss AJ, Goldstein RE, Hall WJ, Bigger JT, Fleiss JL, Greenberg H, *et al* and the Multicenter Myocardial Ischaemia Research Group. Detection and significance of myocardial ischaemia in stable patients after recovery from an acute coronary event. *JAMA* 1993;269:2379-85.
- Stevenson R, Umachandran V, Ranjadayan K, Wilkinson P, Marchant B, Timmis AD. Reassessment of treadmill stress testing for risk stratification in patients with acute myocardial infarction treated by thrombolysis. *Br Heart J* 1993;70:415-20.
- Cross SJ, Shiang Lee H, Kenmure A, Walton S, Jennings K. First myocardial infarction in patients under 60 years old: the role of exercise tests and symptoms in deciding whom to catheterise. *Br Heart J* 1993;70:428-32.
- Arnold AER, Simoons ML, Detry JMR, von Essen R, Van de Werf F, Deckers JW, *et al* for the European Cooperative Study Group. Prediction of mortality following hospital discharge after thrombolysis for acute myocardial infarction: is there a need for coronary arteriography? *Eur Heart J* 1993;14:306-15.
- Piccalo G, Pirrelli S, Massa D, Cipriani M, Sarullo FM, De Vita C. Value of negative predischarge exercise testing in identifying patients at low risk after acute myocardial infarction treated by systemic thrombolysis. *Am J Cardiol* 1992;70:31-3.
- Murray RG. Which patients should have exercise testing following myocardial infarction treated by thrombolysis. *Br Heart J* 1993;70:399.
- Mickley H. Ambulatory ST segment monitoring after myocardial infarction. *Br Heart J* 1994;71:113-4.
- Williams DO, Braunwald E, Knatterud G, Babb J, Bresnahan J, Greenberg MA, *et al* and the TIMI II investigators. One year results of the thrombolysis in myocardial infarction investigation (TIMI) phase II trial. *Circulation* 1992;85:533-42.
- Bigger JT, Fleiss JL, Kleiger R, Miller JP, Rolnitzky LM and the Multicenter Postinfarction Research Group. The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. *Circulation* 1984;64:250-8.
- Maggioli AP, Zuanetti G, Franzosi MG, Rovelli F, Santoro E, Staszewsky L, *et al* on behalf of the GISSI-2 investigators. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. *Circulation* 1993;87:312-22.
- The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: the effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989;321:406-12.
- The IMPACT (international mexiletine and placebo antiarrhythmic coronary trial) research group. International mexiletine and placebo antiarrhythmic coronary trial.I: Report on arrhythmia and other findings. *J Am Coll Cardiol* 1984;4:1148-63.
- Ceremuzynski L, Kleczar E, Krzeminska-Pakula M, Kuch J, Nartowicz E, Smielak-Korombel J, *et al*. Effect of amiodarone on mortality after myocardial infarction. *J Am Coll Cardiol* 1992;20:1056-62.
- Simson MB. The use of signals in the terminal QRS complex to identify patients with ventricular tachycardia after myocardial infarction. *Circulation* 1981;64:235-42.
- Kleiger RE, Miller JF, Bigger JT Jr, Moss AJ and the Multicenter Postinfarction Research Group. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. *Am J Cardiol* 1987;59:256-62.
- La Rovere MT, Specchia G, Mortara A, Schwartz PJ. Baroreflex sensitivity, clinical correlates and cardiovascular mortality among patients with a first myocardial infarction. A prospective study. *Circulation* 1988;78:816-24.
- Farrell TG, Bashir Y, Cripps T, Malik M, Poloniecki J, Bennett D, *et al*. Risk stratification for arrhythmic events in postinfarction patients based on heart rate variability, ambulatory electrocardiographic variables and the signal-averaged electrocardiogram. *J Am Coll Cardiol* 1991;18:687-97.
- Friedman M, Thoresen CE, Gill JJ, Ulmer D, Powell LH, Price VA, *et al*. Alteration of type A behaviour and its effect on cardiac recurrences in post myocardial infarction patients: summary results of the recurrent coronary prevention project. *Am Heart J* 1986;112:653-65.
- Wilhelmsson C, Vedin A, Elmfeldt D, Tibbin G, Wilhelmsen L. Smoking and myocardial infarction. *Lancet* 1975;ii:415-20.
- Daly LE, Graham IM, Hickey M, Mulcahy R. Does stopping smoking delay onset of angina after infarction? *BMJ* 1985;291:935-7.
- Burr ML, Fehily AM, Gilbert JF, Rogers S, Holliday RM, Sweetnam PM, *et al*. Effects of changes in fat, fish, and fibre intakes on death and reinfarction. Diet and reinfarction trial. *Lancet* 1989;ii:757-61.
- Kannel WB, Sorlie P. Hypertension in Framingham. In: Paul O, ed. *Epidemiology and control of hypertension*. New York: Stratton, 1975:553-92.
- Marmot MG, Rose G, Shipley MJ. Alcohol and mortality: a U shaped curve. *Lancet* 1981;i:580-3.
- Davey Smith G, Song F, Sheldon TA. Cholesterol lowering and mortality: the importance of considering initial level of risk. *BMJ* 1993;306:1367-73.
- Betteridge DJ, Dodson PM, Durrington PN, Hughes EA, Laher MF, Nicholls DP, *et al*. Management of hyperlipidaemia: guidelines of the British Hyperlipidaemia Association. *Postgrad Med J* 1993;69:359-69.
- Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy. I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. *BMJ* 1994;308:81-106.
- Pedersen TR and the Norwegian Multicenter Study Group. Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. *N Engl J Med* 1981;304:801-7.
- Herlitz J, Elmfeldt D, Holmberg S, Malek I, Nyberg G, Pennert K, *et al*. The Göteborg metoprolol trial: Mortality and causes of death. *Am J Cardiol* 1984;53:9D.
- Beta-blocker Heart Attack Study Group. A randomized trial of propranolol in patients with acute myocardial infarction. *JAMA* 1981;246:2073-4.
- Olsson G, Oden A, Johansson L, Sjogren A, Rehnqvist N. Prognosis after withdrawal of chronic postinfarction metoprolol treatment: a 2 to 7 year follow up. *Eur Heart J* 1988;9:365-72.
- Chadda K, Goldstein S, Byington R, Curb JD. Effect of propranolol after acute myocardial infarction in patients with congestive heart failure. *Circulation* 1986;73:503-10.
- Swedberg K on behalf of the CONSENSUS II Study Group. Effects of the early administration of enalapril on mortality in patients with acute myocardial infarction. *N Engl J Med* 1992;327:678-84.
- Held PH, Yusuf S, Furberg CD. Calcium channel blockers in acute myocardial infarction and unstable angina: an overview. *BMJ* 1989;299:1187-92.
- The Danish Study Group On Verapamil in Myocardial Infarction. Effect of verapamil on mortality and major events after acute myocardial infarction (the Danish verapamil infarction trial II—DAVIT II). *Am J Cardiol* 1990;66:779-85.
- Smith P, Arnesen H, Holme I. The effect of warfarin on mortality and reinfarction after myocardial infarction. *N Engl J Med* 1990;323:147-52.
- Anticoagulants in the Secondary Prevention of Events in Coronary Thrombosis Research Group (ASPECT). Effect of long term oral anticoagulant treatment on mortality and cardiovascular morbidity after myocardial infarction. *Lancet* 1994;343:499-503.
- Breiddin K, Loew D, Lechner K, Urbela K, Walter E. The German-Austrian aspirin trial: a comparison of acetylsalicylic acid, placebo and phenprocoumon in secondary prevention of myocardial infarction. *Circulation* 1980;62(suppl V):V63-72.
- The EPSIM Research Group. A controlled comparison of aspirin and oral anticoagulants in prevention of death after myocardial infarction. *N Engl J Med* 1982;307:701-8.
- Cairns JA. Oral anticoagulants or aspirin after myocardial infarction? *Lancet* 1994;343:497-8.
- Lewin B, Robertson IH, Cay EL, Irving JB, Campbell M. Effects of self-help post-myocardial infarction rehabilitation on psychological adjustment and use of health services. *Lancet* 1992;339:1036-40.
- Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. *JAMA* 1988;260:945-50.
- Cooper AJ. Myocardial infarction and advice on sexual activity. *Practitioner* 1985;229:575-9.

(Accepted 19 April 1994)