

Guidelines

Acute myocardial infarction: pre-hospital and in-hospital management

The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology

Introduction

The management of acute myocardial infarction has undergone major changes in recent years. Good practice can now be based on sound evidence derived from well-conducted clinical trials. Because of this, the European Society of Cardiology decided that it was opportune to provide guidelines and appointed a Task Force to formulate these. It must be recognised, however, that many aspects of treatment, such as the management of cardiac arrest and shock, depend upon experience rather than upon randomized controlled experiments. Furthermore, even when excellent clinical trials have been undertaken, their results are open to interpretation. Finally, treatment options may be limited by resources; cost-effectiveness is an important issue when deciding upon therapeutic strategies.

In setting out these guidelines, the Task Force has attempted to define which treatment strategies are based on unequivocal evidence and which are open to genuine differences of opinion. As always with guidelines, they are not prescriptive. Patients vary so much from one another that individual care is paramount and there is still an important place for clinical judgment, experience and common sense.

The natural history of acute myocardial infarction

The true natural history of myocardial infarction is hard to establish for a number of reasons: the common occurrence of silent infarction, the frequency of acute coronary death outside hospital and the varying methods used in the diagnosis of the condition. Community studies^{1,2} have consistently shown that the overall fatality of acute heart attacks in the first month is about

50%, and of these deaths about one-half occur within the first 2 h. This high mortality seems to have altered little over the last 30 years. By contrast with community mortality, there has been a profound fall in the fatality of those treated in hospital. Prior to the introduction of coronary care units in the 1960s, the in-hospital mortality seems to have averaged some 25–30%³. A systematic review of mortality studies in the pre-thrombolytic era of the mid-1980s showed an average fatality of 18%⁴. The overall one-month mortality has since been reduced, but remains high in spite of the widespread use of thrombolytic drugs and aspirin. Thus, in the recent MONICA (monitoring trends and determinants in cardiovascular disease) review of five cities, the 28 day mortality was 13–27%⁵. Other studies have reported one month mortality figures of 10–20%^{6–10}.

It was found many years ago that certain factors were predictive of death in patients admitted to hospital with myocardial infarction³. Chief among these were age, previous medical history (diabetes, previous infarction) indicators of large infarct size, including site of infarction (anterior vs inferior), low initial blood pressure, the presence of pulmonary congestion and the extent of ischaemia as expressed by ST elevation and/or depression on the electrocardiogram. These factors remain operative today.

Aims of management

While the primary concern of physicians is to prevent death, those caring for victims of myocardial infarction aim to minimize the patient's discomfort and distress and to limit the extent of myocardial damage. The care can be divided conveniently into three phases:

- (1) Emergency care when the main considerations are to relieve pain and to prevent or treat cardiac arrest.
- (2) Early care in which the chief considerations are to initiate reperfusion therapy to limit infarct size and to prevent infarct extension and expansion and to treat immediate complications such as pump failure, shock and life-threatening arrhythmias.
- (3) Subsequent care in which the complications that usually ensue later are addressed, and consideration is given to preventing further infarction and death.

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These phases may correspond to pre-hospital care, the coronary care unit (CCU), and the post CCU ward, but there is much overlap and any categorization of this kind is artificial.

Emergency care

Initial diagnosis

A working diagnosis of myocardial infarction must first be made. This is usually based on the history of severe chest pain lasting for 15 min or more, not responding to nitroglycerine. But the pain may not be severe and, in the elderly particularly, other presentations such as dyspnoea, faintness or syncope are common. Important clues are a previous history of coronary disease, and radiation of the pain to the neck, lower jaw, or left arm. There are no individual physical signs diagnostic of myocardial infarction, but most patients have evidence of autonomic nervous system activation (pallor, sweating) and either hypotension or a narrow pulse pressure. Features may also include irregularities of the pulse, bradycardia or tachycardia, a third heart sound and basal rales. An electrocardiogram should be obtained as soon as possible. Even at an early stage, the ECG is seldom normal^[11,12]. However, the ECG is often equivocal in the early hours and even in proven infarction it may never show the classical features of ST elevation and new Q waves. Repeated ECG recordings should be obtained and, when possible, the current ECG should be compared with previous records. ECG monitoring should be initiated as soon as possible in all patients to detect life-threatening arrhythmias. When the diagnosis is in doubt, rapid testing of serum markers is valuable. In difficult cases, echocardiography and coronary angiography may be helpful.

Relief of pain, breathlessness and anxiety

Relief of pain is of paramount importance, not only for humane reasons but because the pain is associated with sympathetic activation which causes vasoconstriction and increases the work of the heart. Intravenous opioids — morphine or, where available, diamorphine — are the analgesics most commonly used in this context; intramuscular injections should be avoided. Repeated doses may be necessary. Side-effects include nausea and vomiting, hypotension with bradycardia, and respiratory depression. Antiemetics may be administered concurrently with opioids. The hypotension and bradycardia will usually respond to atropine, and respiratory depression to naloxone, which should always be available. If opioids fail to relieve the pain after repeated administration, intravenous beta-blockers or nitrates are often effective. Paramedics have a limited choice of non-addictive opioids that they may use, the availability of which varies from country to country. Oxygen should

be administered especially to those who are breathless or who have any features of heart failure or shock.

Anxiety is a natural response to the pain and to the circumstances surrounding a heart attack. Reassurance of patients and those closely associated with them is of great importance. If the patient becomes excessively disturbed, it may be appropriate to administer a tranquilliser, but opioids are frequently all that is required.

Cardiac arrest

BASIC LIFE SUPPORT

Those not trained or equipped to undertake advanced life support should start basic life support as recommended by The European Resuscitation Council^[13].

ADVANCED LIFE SUPPORT

Trained paramedics and other health professionals should undertake advanced life support, as described in the guidelines of the European Resuscitation Council^[14].

Early care

Restoring and maintaining patency of the infarct related artery

For patients with the clinical presentation of myocardial infarction and with ST elevation or bundle branch block, early reperfusion should be attempted.

THROMBOLYTIC TREATMENT

THE EVIDENCE FOR BENEFIT. More than 100 000 patients have been randomized in trials of thrombolysis vs control, or one thrombolytic strategy compared with another^[15-20]. For patients within 12 h of the onset of symptoms of infarction, the overall evidence for the benefit of treatment with thrombolysis is overwhelming.

For those presenting within 6 h of symptom onset, and ST elevation or bundle branch block, approximately 30 deaths are prevented per 1000 patients treated, with 20 deaths prevented per 1000 patients treated for those between 7 and 12 h. Beyond 12 h there is no convincing evidence of benefit for the group as a whole.

The ISIS-2^[16] study demonstrated the important additional benefit of aspirin so that there was a combined reduction of approximately 50 lives per 1000 patients treated. There is consistency of benefit across pre-stratified subgroups and across the range of data derived subgroup analyses. Overall, the largest *absolute* benefit is seen among patients with the highest risk, even though the proportional benefit may be similar. Thus, more lives are saved per 1000 higher risk patients treated; for example, among those over 65 years of age, those with presenting systolic pressure <100 mmHg, or those with anterior infarction or more extensive evidence of ischaemia.

Time to treatment. Most benefit is seen in those treated soonest after the onset of symptoms. An analysis of studies in which patients were randomized to pre-hospital or in-hospital thrombolysis suggests that saving an hour reduces mortality significantly^[21], but the relatively small size of these studies precludes precise quantification of the benefit. The fibrinolytic overview^[15] reported a progressive decrease of about 1.6 deaths per hour of delay per 1000 patients treated. This calculation, based on studies in which the time to treatment was not randomized, must be interpreted with caution because the time to presentation is not random.

Hazards of thrombolysis. Thrombolytic therapy is associated with a small but significant excess of approximately 3.9 extra strokes per 1000 patients treated^[15] with all of the excess hazard appearing on the first day after treatment. The early strokes are largely attributable to cerebral haemorrhage; later strokes are more frequently thrombotic or embolic. There is a non-significant trend for fewer thrombo-embolic strokes in the later period in those treated with thrombolysis. Part of the overall excess of stroke is among patients who subsequently die and is accounted for in the overall mortality reduction (1.9 excess per 1000). Thus, there is an excess of approximately two non-fatal strokes per 1000 patients treated. Of these, half are moderately or severely disabling. The risk of stroke varies with age. There is a substantially increased risk for those above 75 years of age and also for those with systolic hypertension. Other major non-cerebral bleeds, requiring blood transfusion or that are life-threatening, occur in about 7 per 1000 patients treated. No specific subgroup is associated with an excess of bleeds, but smaller studies have demonstrated a clear association between arterial and venous punctures and the development of major haematomas. The risks are increased if arterial punctures are performed in the presence of a thrombolytic agent.

Administration of streptokinase and anistreplase may be associated with hypotension, but severe allergic reactions are rare. Routine administration of hydrocortisone is not indicated. Where hypotension occurs, it should be managed by temporarily halting the infusion, lying the patient flat or elevating the feet. Occasionally atropine or intravascular volume expansion may be required.

Comparison of thrombolytic agents. Neither the International Trial^[19] nor the Third International Study of Infarct Survival (ISIS 3)^[17] found a difference in mortality between the use of streptokinase and tissue plasminogen activator or anistreplase. Furthermore, the addition of subcutaneous heparin did not reduce mortality compared with the use of no heparin. However, the GUSTO Trial (Global Utilisation of Streptokinase and Tissue Plasminogen Activator for occluded coronary arteries)^[20] employed an accelerated t-PA (tissue type plasminogen activator) regimen given over 90 min rather than the previously conventional period of 3 h. Accelerated t-PA with concomitant aPTT (activated partial thromboplastin time) adjusted intravenous heparin was

reported to result in 10 fewer deaths per 1000 patients treated. The risk of stroke is higher with t-PA or anistreplase than with streptokinase^[16,20]. In the GUSTO trial, there were three per 1000 additional strokes with accelerated t-PA and heparin in comparison with streptokinase and subcutaneous heparin^[20], but only one of these survived with a residual deficit. In assessing the net clinical benefit, this must be taken into account with the reduced death rate in the t-PA group. The choice of reperfusion strategy will depend on an individual assessment of risk, and also on factors such as availability and cost benefit^[22].

Clinical implications. Based upon the substantial evidence now accumulated, there is unequivocal benefit, in terms of morbidity and mortality for prompt treatment of acute myocardial infarction with thrombolysis and aspirin, the two agents being additive in their effect. Where appropriate facilities exist, with trained medical or paramedical staff, pre-hospital thrombolysis may be instituted provided that the patient exhibits the clinical features of myocardial infarction and the ECG shows ST elevation or bundle branch block.

Unless clearly contraindicated, patients with infarction, as diagnosed by clinical symptoms and ST segment elevation or bundle branch block, should receive aspirin and thrombolytic therapy with the minimum of delay. If the first ECG does not show diagnostic changes, frequent or continuous ECG recordings should be obtained. Rapid enzyme analysis, echocardiography and, occasionally, coronary angiography may be helpful. A realistic aim is to initiate thrombolysis within 90 min of the patient calling for medical treatment ('call to needle' time). In patients with slowly evolving, or stuttering myocardial infarction, a series of ECGs and clinical assessments should be performed to detect evolving infarction (with rapid cardiac enzyme analysis, if available).

Thrombolytic therapy should not be given to patients in whom:

The potential for benefit is low, e.g. if the ECG remains normal, or demonstrates only T wave changes as these patients are at low risk but experience all of the hazards of therapy. Trials have not demonstrated benefit in those with ST depression, even though the risk in these patients is relatively high; they have not, however, excluded the possibility of some benefit;

infarction has been established for more than 12 h, unless there is evidence of ongoing ischaemia, with the ECG criteria for thrombolysis.

Contra-indications to thrombolytic therapy

Stroke

Recent major trauma/surgery/head injury (within preceding 3 weeks)

Gastro-intestinal bleeding within the last month

Known bleeding disorder

Dissecting aneurysm

Methods of administration

Table 1 Thrombolytic regimens for acute myocardial infarction

| | Initial treatment | Heparin therapy | Specific contra-indications |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|----------------------------------------------------------------------------|
| Streptokinase (SK) | 1.5 million units 100 ml of 5% dextrose or 0.9% saline over 30–60 min | None or subcutaneous 12 500u b.d. | Prior (>5 days) SK/anistreplase |
| Anistreplase | 30 units in 3–5 min i.v. | | Prior SK or anistreplase >5 days Known allergy to SK/anistreplase |
| Alteplase (t PA) | 15 mg i.v. bolus 0.75 mg . kg ⁻¹ over 30 min then 0.5 mg . kg ⁻¹ over 60 min i.v. Total dosage not to exceed 100 mg. | i.v. for 48 h* | |
| Urokinase** | 2 million units as an i.v. bolus or 1.5 million units bolus + 1.5 million units over 1 h | i.v. for 48 h* | |

This table describes frequently used thrombolytic regimens. Alternative strategies and newer agents may confer advantages over these regimens but the potential advantages have not been validated in large scale studies.

*Dosage determined by aPTT.

**Not licensed in some countries for use in myocardial infarction.

N.B. Aspirin should be given to all patients without contraindications.

Relative contra-indications

- Transient ischaemic attack in preceding 6 months
- Coumadin/warfarin therapy
- Pregnancy
- Non-compressible punctures
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mmHg)
- Recent retinal laser treatment

Re-administration of thrombolytic agent. If there is evidence of re-occlusion or reinfarction with recurrence of ST elevation or bundle branch block, further thrombolytic therapy should be given, or angioplasty considered. Streptokinase and anistreplase should not be re-administered in the period between 5 days and a minimum of 2 years following initial treatment with either of these drugs. Antibodies to streptokinase persist for at least 2 years, at levels which can impair its activity. Alteplase (t-PA) and urokinase do not result in antibody formation.

Adjunctive antithrombotic and antiplatelet therapy. The independent and additive benefits of aspirin have been described above. It is not clear whether aspirin works by enhancing thrombolysis, preventing reocclusion or by limiting the microvascular effects of platelet activation. In studies on late reocclusion, aspirin was more effective in preventing recurrent clinical events than in maintaining patency^[23]. The first dose of 150–160 mg should

be chewed, and the same dosage given orally daily thereafter.

Heparin has been extensively tested after thrombolysis, especially with tissue plasminogen activator. Heparin does not improve immediate clot lysis^[24] but coronary patency evaluated in the hours or days following thrombolytic therapy with tissue plasminogen activator appears to be better with intravenous heparin^[25,26]. No difference in patency was apparent in patients treated with either subcutaneous or intravenous heparin and streptokinase^[27]. Prolonged intravenous heparin administration has not been shown to prevent reocclusion after angiographically proven successful coronary thrombolysis, nor has intravenous heparin followed by coumadin^[28]. Heparin infusion after tissue plasminogen activator therapy may be discontinued after 24–48 h^[29]. Close monitoring of heparin therapy is mandatory; aPTT values over 90 s are correlated with an unacceptable risk of cerebral bleeding. In the ISIS-3 trial^[17], subcutaneous heparin (12 500 b.d.) did not affect mortality when combined with aspirin and streptokinase, alteplase, or anistreplase.

PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA)

The role of coronary angioplasty (PTCA) during the early hours of myocardial infarction can be divided into primary angioplasty, angioplasty combined with thrombolytic therapy, and 'rescue angioplasty' after failed thrombolysis.

Table 2 Spectrum of haemodynamic states in myocardial infarction

| | |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Normal | Normal blood pressure, heart and respiration rates, good peripheral circulation |
| Hyperdynamic state | Tachycardia, loud heart sounds, good peripheral circulation. ?beta-blocker therapy |
| Bradycardia-hypotension | 'Warm hypotension', bradycardia, venodilatation, normal jugular venous pressure, decreased tissue perfusion. Usually in inferior infarction, but may be provoked by opiates. Responds to atropine or pacing |
| Hypovolaemia | Venoconstriction, low jugular venous pressure, poor tissue perfusion. Responds to fluid infusion |
| Right ventricular infarction | High jugular venous pressure, poor tissue perfusion or shock, bradycardia, hypotension. See text. |
| Pump failure | Tachycardia, tachypnoea, small pulse pressure, poor tissue perfusion, hypoxaemia, pulmonary oedema. See text. |
| Cardiogenic shock | Very poor tissue perfusion, oliguria, severe hypotension, small pulse pressure, tachycardia, pulmonary oedema. See text. |

Primary angioplasty. This is defined as PTCA without prior or concomitant thrombolytic therapy, and is a therapeutic option only when rapid access (<1 h) to a catheterization laboratory is possible. It requires an experienced team, which includes not only interventional cardiologists, but also skilled supporting staff. This means that only hospitals with an established interventional cardiology programme can use PTCA as a routine treatment option for patients presenting with the symptoms and signs of acute myocardial infarction. For patients admitted to a hospital without these facilities on site, a careful individual assessment should be made of the potential benefits of PTCA in relation to the risks and treatment delay of transportation to the nearest interventional catheterization laboratory. It should be reserved for those in whom the benefits of reperfusion would be great but the risks of thrombolytic therapy high.

Primary PTCA is effective in securing and maintaining coronary patency and avoids some of the bleeding risks of thrombolysis. Randomized clinical trials comparing primary PTCA with thrombolytic therapy have shown more effective restoration of patency, better ventricular function and a trend towards better clinical outcome^[30-32]. PTCA may have a special role in the treatment of shock.

Patients with contra-indications to thrombolytic therapy have a higher morbidity and mortality than those eligible for this therapy^[33]. Primary PTCA can be performed with success in a large majority of these patients^[34], but experience is still limited and effectiveness and safety outside major centres may be less good than they have been in trials. Large multicentre randomized trials are needed.

Angioplasty combined with thrombolysis. PTCA performed as a matter of policy immediately after thrombolytic therapy, in order to enhance reperfusion or reduce the risk of reocclusion, has proved disappointing in a number of trials^[35-37], which have shown a tendency to an increased risk of complications and death. Routine PTCA after thrombolysis cannot, therefore, be recommended.

'Rescue' angioplasty. Currently the only exception to this general rule is 'rescue PTCA' which is defined as PTCA performed on a coronary artery which remains occluded

despite thrombolytic therapy. Limited experience from two randomized trials^[38,39] suggests a trend towards clinical benefit if the infarct-related vessel can be re-canalized at angioplasty. Although angioplasty success rates are high, an unsolved problem is the unreliability of non-invasive methods in assessing patency.

CORONARY ARTERY BYPASS SURGERY (CABG)

Coronary artery bypass surgery has a very limited place in the management of the acute phase of myocardial infarction. It may, however, be indicated when PTCA has failed, when there has been a sudden occlusion of a coronary artery during catheterization, if PTCA is not feasible, or in association with surgery for a ventricular septal defect or mitral regurgitation due to papillary muscle dysfunction and rupture.

Pump failure and shock

The various haemodynamic states that can arise in myocardial infarction are tabulated in Table 2.

HEART FAILURE

Left ventricular failure during the acute phase of myocardial infarction is associated with a poor short and long-term prognosis^[40]. The clinical features are those of breathlessness, a third heart sound and pulmonary rales which are at first basal but may extend throughout both lung fields. However, pronounced pulmonary congestion can be present without auscultatory signs. Repeated auscultation of the heart and lung fields should be practised in all patients during the early period of myocardial infarction, together with the observation of other vital signs.

General measures include monitoring for arrhythmias, checking for electrolyte abnormalities, and for the diagnosis of concomitant conditions such as valvular dysfunction or pulmonary disease. Pulmonary congestion can be assessed by portable chest X-rays. Echocardiography is valuable in assessing ventricular function, and determining the mechanisms, such as mitral regurgitation and ventricular septal defect, which may be responsible for poor cardiac performance. In a few cases, coronary angiography may provide additional information of therapeutic value.

The degree of failure may be categorized according to the Killip classification^[41]: class 1: no rales or third heart sound; class 2: rales over less than 50% of the lung fields or third heart sound; class 3: rales over 50% of the lung fields; class 4: shock.

MILD AND MODERATELY SEVERE HEART FAILURE

Oxygen should be administered early by mask or intranasally, but caution is necessary in the presence of chronic pulmonary disease.

Minor degrees of failure often respond quickly to diuretics, such as frusemide 10–40 mg given slowly intravenously, repeated at 1–4 hourly intervals, if necessary. If there is no satisfactory response, intravenous nitroglycerine or oral nitrates are indicated. The dose should be titrated while monitoring blood pressure to avoid hypotension. The initiation of ACE therapy should be considered within the next 24–48 h in the absence of hypotension or renal failure.

SEVERE HEART FAILURE

Oxygen should be administered and a loop diuretic given as above. Unless the patient is hypotensive, intravenous nitroglycerine should be given, starting with 0.25 $\mu\text{g} \cdot \text{kg}^{-1}$ per minute, and increasing every 5 min until a fall in blood pressure by 15 mmHg is observed or the systolic blood pressure falls to 90 mmHg. Consideration should be given to measuring the pulmonary artery and wedge pressures, and the cardiac output with a balloon flotation catheter with a view to obtaining a wedge pressure of less than 20 mmHg and a cardiac index in excess of 2 $\text{l} \cdot \text{min}^{-1}$.

Inotropic agents may be of value if there is hypotension. If signs of renal hypoperfusion are present, dopamine is recommended intravenously in a dosage of 2.5–5.0 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. If pulmonary congestion is dominant, dobutamine is preferred with an initial dosage of 2.5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. This may be increased gradually at 5–10 min intervals up to 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ or until haemodynamic improvement is achieved. ACE therapy and phosphodiesterase inhibitors may also be considered.

The blood gases should be checked. Continuous positive pressure airways pressure may be indicated if an oxygen tension of more than 60 mmHg cannot be maintained in spite of 100% oxygen delivered at 8–10 $\text{l} \cdot \text{min}^{-1}$ by mask and the adequate use of bronchodilators.

Cardiogenic shock. Cardiogenic shock is defined as a systolic blood pressure <90 mmHg in association with signs of circulatory deterioration expressed as peripheral vasoconstriction, low urinary output (<20 $\text{ml} \cdot \text{h}^{-1}$), and mental confusion and dulling.

The diagnosis of cardiogenic shock should be made when other possibilities for hypotension have been excluded such as hypovolaemia, vasovagal reactions, electrolyte disturbance, pharmacological side-effects, or arrhythmias. It is usually associated with extensive left ventricular damage, but may occur in right ventricular

infarction (vide infra). Ventricular function should be evaluated by echocardiography, and haemodynamics measured with a balloon flotation catheter. A filling pressure (pulmonary wedge) of at least 15 mmHg should be aimed for with a cardiac index of >2 $\text{l} \cdot \text{min}^{-1}$. Low dose dopamine 2.5–5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ may be given to improve renal function and the additional administration of dobutamine 5–10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ should be considered.

Patients in cardiogenic shock can be assumed to be acidotic. Correction of acidosis is important as catecholamines have little effect in an acid medium.

Emergency PTCA or surgery may be life-saving and should be considered at an early stage. Supportive treatment with a balloon pump is a valuable bridge to such intervention.

Cardiac rupture and mitral regurgitation

FREE WALL RUPTURE

This clinical entity is encountered in 1%–3% of all hospitalized patients with acute myocardial infarction^[42]. In 30% to 50% of the cases it occurs in the first 24 h and in 80% and 90% in the first 2 weeks.

Acute free wall rupture. This is characterized by cardiovascular collapse with electromechanical dissociation i.e. continuing electrical activity with a loss of cardiac output and pulse. It is usually fatal within a few minutes, and does not respond to standard cardiopulmonary resuscitation measures. Only very rarely is there time to bring the patient to surgery.

Subacute free wall rupture. In about 25% of cases, small quantities of blood reach the pericardial cavity and produce a progressive haemodynamic burden^[43,44]. The clinical picture may simulate reinfarction because of the recurrence of pain and re-elevation of ST segments, but more frequently there is sudden haemodynamic deterioration with transient or sustained hypotension. The classical signs of cardiac tamponade occur and can be confirmed by echocardiography. Immediate surgery should be considered irrespective of the clinical status of the patient, as an acute episode follows in most cases. Surgical repair is performed by the sutureless technique described by Padro *et al.*^[45], which does not require cardiopulmonary bypass.

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect (VSD) appears early after myocardial infarction, with an incidence of about 1–2% of all infarctions^[42]. Without surgery, the mortality is 54% within the first week, and 92% within the first year^[46]. The diagnosis, first suspected because of the occurrence of a loud systolic murmur accompanied by severe clinical deterioration, is best confirmed by echocardiography and/or by detecting an oxygen step-up in the right ventricle. The murmur may, however, be soft or absent. Pharmacological treatment with vasodilators, such as

intravenous nitroglycerine, may produce some improvement if there is no cardiogenic shock, but intra-aortic balloon counterpulsation is the most effective method of providing circulatory support while preparing for surgery. Operation offers the only chance of survival in large post-infarction VSDs with cardiogenic shock^[47,48]. The primary goal of early surgery is the reliable closure of the defect using the technique of patch augmentation^[49]. Pre-operative coronary angiography should be performed provided it does not compromise the haemodynamic status or cause undue delay to surgery. Bypass grafts are inserted as necessary. Predictors of poor postoperative outcome are cardiogenic shock, posterior location, right ventricular dysfunction, age, and long delay between septal rupture and surgery^[47,48]. Hospital mortality after surgery is estimated to be between 25 and 60%^[50,51], and 95% of survivors are NYHA I or II^[50].

MITRAL REGURGITATION

Most cases of mitral regurgitation after myocardial infarction are mild and the reflux is transitory. In a minority of patients, however, major acute regurgitation is a catastrophic complication that is amendable to aggressive therapy if promptly diagnosed and treated surgically. The incidence of moderately severe or severe mitral regurgitation is about 4% and the mortality without surgery high at about 24%^[52]. It is usually associated with significant narrowing of both the right and left circumflex coronary arteries with posteromedial papillary muscle involvement.

Cardiogenic shock and pulmonary oedema with severe mitral regurgitation require emergency surgery. Intra-aortic balloon pump placement may be helpful during preparation^[50]. Coronary angiography is performed if the patient's condition permits. In congestive heart failure, primary catheterization and reperfusion of the infarct-related artery by thrombolysis or PTCA can be attempted.

Valve replacement is the procedure of choice in papillary muscle dysfunction and rupture, although repair can be attempted in selected cases^[53]. Revascularization is indicated for major vessel obstruction.

Arrhythmias and conduction disturbances

Arrhythmias and conduction disturbances are extremely common during the early hours after myocardial infarction. In some cases, such as ventricular tachycardia and ventricular fibrillation, they are life threatening and require immediate correction. Often, however, arrhythmias are not in themselves hazardous, but are a manifestation of a serious underlying disorder, such as continuing ischaemia, vagal overactivity, or electrolyte disturbance, that requires attention. The necessity for treatment and its urgency depend mainly upon the haemodynamic consequences of the rhythm disorder.

VENTRICULAR ARRHYTHMIAS

Ventricular ectopic rhythms. Ventricular ectopic beats are almost universal on the first day, and complex

arrhythmias (multiform complexes, short runs, or the R-on-T phenomenon) are common. Their value as predictors of ventricular fibrillation is questionable; either ventricular fibrillation follows so quickly that no prophylactic measures can be taken or no serious arrhythmia ensues.

Ventricular tachycardia. Short runs of ventricular tachycardia may be well tolerated and not require treatment, but more prolonged episodes may cause hypotension and heart failure. Lignocaine is the drug of first choice, but several other agents are also effective. An initial loading dosage of 1 mg . kg⁻¹ of intravenous lignocaine is usually given, with half this dose being repeated every 8–10 min to a maximum of 4 mg . kg⁻¹. This may be followed by an intravenous infusion to prevent recurrences. Countershock is indicated if haemodynamically significant ventricular tachycardia persists.

It is important to differentiate true ventricular tachycardia from accelerated idioventricular rhythm, usually a harmless consequence of reperfusion, in which the ventricular rate is less than 120 beats . min⁻¹.

Ventricular fibrillation. When a defibrillator is available, immediate defibrillation should be performed. If it is not, a precordial thump is worth trying. The recommendations of the European Resuscitation Council should be followed (Fig. 1)^[14].

SUPRAVENTRICULAR ARRHYTHMIAS

Atrial fibrillation complicates some 15–20% of myocardial infarctions, and is frequently associated with severe left ventricular damage and heart failure. It is usually self-limited. Episodes may last from minutes to hours, and are often repetitive. In many cases, the ventricular rate is not fast, the arrhythmia is well tolerated, and no treatment is required. In other instances, the fast rate contributes to heart failure and prompt treatment is needed. Digoxin is effective in slowing the rate in many cases, but amiodarone may be more efficacious in terminating the arrhythmia^[54]. Countershock may also be used, but should only be employed if mandatory as recurrences are so common.

Other supraventricular tachycardias are rare, but usually self-limited. They may respond to carotid sinus pressure. Beta-blockers may be effective, if not contraindicated, but verapamil is not recommended. Countershock should be employed if the arrhythmia is poorly tolerated.

SINUS BRADYCARDIA AND HEART BLOCK

Sinus bradycardia is common in the first hour, especially in inferior infarction. In some cases, opioids are responsible. It may be accompanied by quite severe hypotension, in which case it should be treated by intravenous atropine, starting with a dosage of 0.3–0.5 mg, repeated up to a total of 1.5–2.0 mg. Later in the course of myocardial infarction, it is usually a favourable sign and requires no treatment. Occasionally it may, however, be associated with hypotension. If it then fails to respond to atropine, temporary pacing may be advisable.

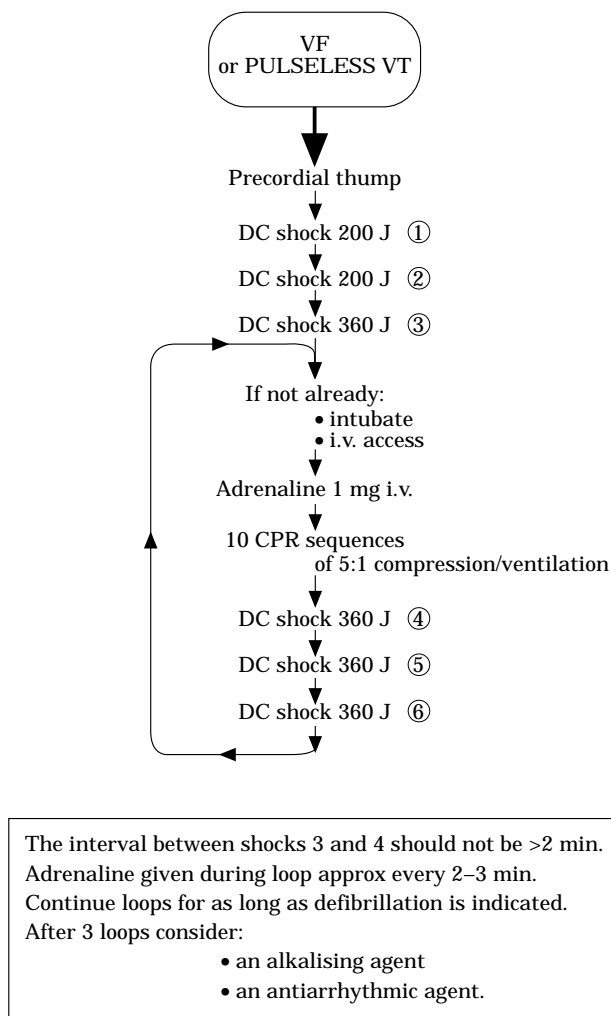


Figure 1 European Resuscitation Council guidelines on the treatment of ventricular fibrillation

First degree heart block needs no treatment.

Type I second degree (Wenckebach) AV (atrio-ventricular) block is usually associated with inferior infarction and seldom causes adverse haemodynamic effects. Should it do so, however, atropine should be given first; if this fails, pacing should be instituted.

Type II second degree (Mobitz) and complete AV block are indications for the insertion of a pacing electrode. Pacing should be undertaken if a slow heart rate appears to be a cause of hypotension or heart failure. If the haemodynamic disturbance is severe, consideration should be given to AV sequential pacing.

Asystole may follow AV block, bi- or trifascicular block, or electrical countershock. If a pacing electrode is in place, pacing should be attempted. Otherwise, chest compression and ventilation should be initiated, and external pacing started.

A transvenous pacing electrode should be inserted, as discussed above, in the presence of advanced atrio-ventricular block, and considered if bifascicular or trifascicular block develop. Many cardiologists prefer

the subclavian route but this should be avoided in the presence of thrombolysis or anticoagulation. Alternative sites should be chosen in this situation.

Prophylactic therapies in the acute phase

Aspirin. Convincing evidence of the effectiveness of aspirin was demonstrated by the ISIS-2 trial^[16], in which it was shown that the benefits of aspirin and streptokinase were additive. In this trial of more than 17 000 patients, the first 160 mg tablet of aspirin was chewed; subsequently one 160 mg tablet was swallowed daily. The mortality in those receiving aspirin in ISIS-2 was 9.4% compared with that of 11.8% in those receiving placebo. It was effective both in those who did and those who did not receive thrombolysis. In an overview of all the aspirin trials^[55], a 29% odds reduction in death was observed, with a vascular mortality of 11.7% in the control population and 9.3% in those receiving aspirin—representing 24 lives saved per 1000 patients treated. There were also fewer non-fatal strokes and non-fatal myocardial reinfarctions in the treated group.

There are few contra-indications to the use of aspirin, but it should not be given to those with a known hypersensitivity, bleeding peptic ulcer, blood dyscrasia, or severe hepatic disease. Aspirin may occasionally trigger bronchospasm in asthmatics. Unlike the situation with thrombolysis, there is no clear evidence of a relationship between effectiveness and the time from the onset of symptoms. Nonetheless, aspirin should be given to all patients with an acute coronary syndrome as soon as possible after the diagnosis is deemed probable. This represents about 85–95% of those sustaining a myocardial infarction.

Anti-arrhythmic drugs. Although it has been demonstrated that lignocaine can reduce the incidence of ventricular fibrillation in the acute phase of myocardial infarction^[56,57], this drug significantly increases the risk of asystole^[57]. A meta-analysis of 14 trials showed a non-significantly higher mortality in lignocaine treated patients than in controls^[58]. The prophylactic use of this drug does not appear justified.

Beta-blockers. Many trials of intravenous beta-blockade have been undertaken in the acute phase of myocardial infarction, because of their potential to limit infarct size, reduce the incidence of fatal arrhythmias, and to relieve pain. The 16 000 patient ISIS-1^[59] study of intravenous atenolol revealed a significant ($2P < 0.05$) 15% reduction in mortality at 7 days. The 7 day mortality of only 4.6% in the placebo arm indicates that only a low risk group were recruited. Pooling of 28 trials^[60] of intravenous beta-blockade reveals an absolute reduction of mortality at 7 days from 4.3% to 3.7% or six lives saved per 1000 treated in this low risk group. It is unknown whether these benefits can be extended to those at higher risk.

These studies were conducted prior to the thrombolytic era. The only large trial of intravenous

Table 3 Dosages in ACE inhibitor trials

| | Initial dosage | Target dosage |
|-------------------------------------------|------------------------------------------------------------------------------------------|--------------------|
| CONSENSUS II ^[68] enalapril | 1 mg i.v. enalaprilat over 2 h followed by 2.5 mg b.d. increasing to 20 mg, if tolerated | up to 20 mg daily |
| GISSI-3 ^[63] lisinopril | 5 mg initially | up to 10 mg daily |
| ISIS-4 ^[64] captopril | 6.25 mg initially, 12.5 mg in 2 h, 25 mg at 10–12 h | up to 50 mg b.d. |
| CHINESE ^[67] captopril | 6.25 mg initially, 12.5 mg 2 h later if tolerated | up to 12.5 mg t.d. |
| SMILE ^[117] zofenopril | 7.5 mg initially, repeated after 12 h and repeatedly doubled if tolerated | up to 30 mg b.d. |
| AIRE ^[116] ramipril | 2.5 mg b.d. increased to 5 mg b.d. if tolerated | up to 5 mg b.d. |
| SAVE ^[115] captopril | test of 6.25 mg, increased if tolerated to 25 mg t.d. | up to 50 mg t.d. |
| TRACE ^[118] trandolapril | test of 0.5 mg | up to 4 mg daily |

beta-blockade undertaken since the widespread use of thrombolysis was a substudy of the TIMI-IIB^[61] but the number of events was too small to allow conclusions to be drawn. As discussed below, the use of beta-blockade in the acute phase of infarction in many countries is extremely low. There is a good case for the greater use of an intravenous beta-blocker when there is tachycardia (in the absence of heart failure), relative hypertension, or pain unresponsive to opioids. It may be prudent to test the patient's response to this form of therapy by first using a short-acting preparation.

Nitrates. A meta-analysis of 10 trials of early intravenous nitrate therapy conducted in 2041 patients showed a mortality reduction of about one-third^[62]. Each of the trials was small and with only 329 deaths in all, the results although highly significant had wide confidence limits. The GISSI-3^[63] trial also tested intravenous nitrate therapy (followed by transdermal nitrate) in 19 394 patients; no significant reduction in mortality was observed, but this finding must be viewed with caution as 44% of the patients assigned to the control group received intravenous nitrate. The ISIS-4 trial^[64], in which oral mononitrate was administered acutely and continued for one month, also failed to show a benefit. Furthermore, a benefit was not seen in the ESPRIM trial of molsidomine^[65], a nitric oxide donor. Again, however, both in ISIS-4 and ESPRIM, the frequent early use of intravenous nitrates in the control group makes deductions difficult. The routine use of nitrates in the initial phase of myocardial infarction has, therefore, not convincingly been shown to be of value.

Calcium antagonists. A meta-analysis of trials involving calcium antagonists early in the course of acute myocar-

dial infarction showed a non-significant adverse trend^[66]. There is no case for using calcium antagonists for prophylactic purposes in the acute phase of myocardial infarction.

Angiotensin converting enzyme (ACE) inhibitors. It is now well established that ACE inhibitors should be started in the later hospital period in patients who have an impaired ejection fraction or who have experienced heart failure in the early phase (see later). Recently, the GISSI-3^[63], ISIS-4^[64] and Chinese Study^[67] have shown that ACE inhibitors started on the first day reduce mortality in the succeeding 4–6 weeks by a small but significant amount. The CONSENSUS II trial^[68], however, failed to show a benefit. This may have been due to the play of chance, or the fact that treatment was initiated with an intravenous formulation. A systematic overview of trials of ACE inhibitions early in acute myocardial infarction indicated that this therapy would result in 4.6 fewer deaths per 1000 patients treated^[64]. Although it is recognised that subgroup analysis is hazardous, it would seem probable that this therapy was especially valuable in certain high risk groups, such as those presenting with heart failure or with previous infarction. The benefits of ACE inhibition in myocardial infarction patients appear to be a class effect. The regimens used in the trials of ACE inhibitors are shown in Table 3.

As discussed later, opinions differ as to whether to administer ACE inhibitor therapy to all patients (for whom it is not contraindicated) on the first day or start it in a more selected group of patients shortly thereafter^[69,70,71]. In the view of the Task Force, there are valid arguments on both sides. Certainly, there should be a low threshold for using these agents early if features

of heart failure do not respond quickly to conventional measures.

Magnesium. A meta-analysis of trials of magnesium therapy in acute myocardial infarction suggested a significant benefit^[72,73], but the later large ISIS-4 trial^[64] did not support this. Although it has been argued that the magnesium regimen in ISIS-4 was not optimal^[74], there does not at present seem enough evidence to recommend its routine use.

Management of specific types of infarction

SUSPECTED MYOCARDIAL INFARCTION WITHOUT ST ELEVATION OR BUNDLE BRANCH BLOCK

Many patients present with symptoms suggestive of recent myocardial infarction, but without the ECG features of ST elevation or bundle branch block which would qualify them for thrombolytic therapy. Some will progress to Q wave infarction, and others to non-Q wave infarction; many will eventually be classified as unstable angina. A sizeable proportion will be regarded as having stable angina and yet others will have a non-cardiac diagnosis. The management will depend on the degree of suspicion of infarction. Thus, if there has been a previous infarction, or there are definite ST and T wave changes short of ST elevation or new Q waves, or if the symptoms or physical signs suggest that this is an acute coronary syndrome, the patient should be closely observed with repeated ECG recordings and enzyme tests. In the absence of contra-indications, all such patients should be given aspirin and considered for heparin therapy and beta-blockade. Continuing chest pain should be treated with nitrates and, if severe, opioids. If pain persists or recurs in spite of this treatment, coronary angiography should be considered with a view to early intervention by angioplasty or surgery.

NON-Q WAVE MYOCARDIAL INFARCTION

A 'non-Q wave' myocardial infarction is one with the characteristic clinical features and enzyme abnormalities, but without new Q waves in the ECG. The incidence is reported as being from 20 to 40% of all infarctions but may be increasing in relation to Q wave infarction^[75]. This variability could be related to the use of reperfusion therapy and/or more sensitive techniques for enzyme detection^[75,76].

Hospital mortality is significantly less than in Q wave infarction. Conversely in the long term, higher mortality and event rates are reported in non-Q infarcts after hospital discharge, so that the mortality is similar at 3–5 years^[75,76]. A higher incidence of residual ischaemia is a constant finding (50%–90% more than in Q wave infarction)^[76,77].

Risk markers. Initial and persistent ST depression, complications present in the acute phase, post-infarction angina with ECG changes, early reinfarction, and the inability to perform a stress test, are all associated with

a higher mortality^[78,79]. A symptom-limited exercise stress test should be performed as in Q wave infarction, but thallium scintigraphy and stress echocardiography may be more sensitive and specific in detecting, quantifying, and localizing ischaemic myocardium in asymptomatic non-Q wave postinfarction patients^[75].

Management. Whether evolving infarction results in Q waves or ends as a non-Q wave infarction is established only after a few days follow-up. Thus, at the time of admission to CCU no distinction can be made between these two groups of patients. Thrombolytic therapy is particularly indicated in patients with ST segment elevation due to extensive ischaemia resulting from occlusion of a coronary artery^[16]. The ISIS-2^[16] and GISSI^[18] trials demonstrated no decrease in mortality with thrombolysis in patients with myocardial infarction and ST depression on admission; these patients have probably not had a complete coronary occlusion. Recent data from TIMI IIIB, confirmed no significant benefit in mortality, or reinfarction rate with t-PA in non-Q wave infarction^[80].

Antithrombotic therapy with oral aspirin and intravenous heparin reduces the incidence of subsequent reinfarction or death^[81,82]. Thrombolysis may prevent the development of Q waves in those who present with ST elevation.

Two small trials have suggested that diltiazem reduces early but not the total incidence of reinfarction;^[83,84] further evidence is needed before this agent can be recommended for this purpose. There are no specific studies designed to demonstrate the effect of betablockers in non-Q AMI. Retrospective analysis of the non-Q subgroup in general trials has been inconclusive^[85].

An early invasive strategy — systematic coronary angiography and revascularization <48 h — was explored in TIMI IIIB^[80]. No difference in death, reinfarction or positive exercise test at 6 weeks was found comparing this with an early conservative strategy.

Revascularization should be considered if spontaneous or readily provoked ischaemia can be detected, provided the coronary anatomy is appropriate for this. At present, there are no data from controlled clinical trials that compare the long-term effects of medical treatment, PTCA or surgery in patients with non-Q wave infarction and residual ischaemia. PTCA of the culprit lesion is safe and effective for relieving angina and recurrent ischaemia^[86] but many patients after non-Q wave infarction are found to have multiple or severe stenoses for which surgical treatment is more suitable^[87].

RIGHT VENTRICULAR INFARCTION

The recognition of right ventricular infarction is important because it may manifest itself as cardiogenic shock, but the appropriate treatment strategy is quite different from that for shock due to severe left ventricular dysfunction.

Right ventricular infarction may be suspected by the specific, but insensitive, clinical triad of hypotension,

clear lung fields, and raised jugular venous pressure in a patient with inferior myocardial infarction^[88]. ST elevation in V_4R is very suggestive of the diagnosis^[89]; this lead should certainly be recorded in all cases of shock, if not done as a routine. Q waves and ST elevation in V_{1-3} also suggest the diagnosis.

When right ventricular infarction can be implicated in hypotension or shock, it is important to maintain right ventricular preload. It is desirable to avoid (if possible) vasodilator drugs such as the opioids, nitrates, diuretics and ACE inhibitors. Intravenous loading is effective in many cases; initially, it should be administered rapidly, for example at a rate of 200 ml in 10 min. It may require 1–2 l normal saline in the first few hours, and 200 ml \cdot h⁻¹ thereafter. Careful haemodynamic monitoring should be instituted during intravenous fluid loading. If cardiac output does not improve on this regimen, dobutamine should be given.

Right ventricular infarction is often complicated by atrial fibrillation. This should be corrected promptly as the atrial contribution to right ventricular filling is important in this context. Likewise, if heart block develops, dual chamber pacing should be undertaken. There has been some question of the effectiveness of thrombolytic therapy in right ventricular infarction, but it certainly seems appropriate in the hypotensive patient. Alternatively, direct angioplasty may result in rapid haemodynamic improvement^[90].

MYOCARDIAL INFARCTION IN DIABETIC PATIENTS

Diabetic patients who sustain a myocardial infarction have a high mortality. Strict attention to the control of hyperglycaemia with insulin has been claimed to reduce long-term mortality^[91]. Diabetes is not a contraindication to thrombolysis, even in the presence of retinopathy.

Management of the later in-hospital course

GENERAL MANAGEMENT

Most patients should rest in bed for the first 12–24 h, by which time it will be apparent whether the infarction is going to be complicated. In uncomplicated cases, the patient can sit out of bed late on the first day, be allowed to use a commode and undertake self-care and self-feeding. Ambulation can start the next day and such patients can be walking up to 200 m on the flat, and walking up stairs within a few days. Those who have experienced heart failure, shock or serious arrhythmias should be kept in bed longer, and their physical activity increased slowly, dependent upon their symptoms and the extent of myocardial damage.

DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

These complications are now relatively uncommon after infarction, except in patients kept in bed because of heart failure. In such patients, they can be prevented by

heparin. When they occur they should be treated with heparin, followed by oral anticoagulation for 3–6 months.

INTRAVENTRICULAR THROMBUS AND SYSTEMIC EMBOLI

Echocardiography will reveal intraventricular thrombi in many cases, especially large anterior infarctions. If the thrombi are mobile or protuberant, they should be treated initially with heparin and subsequently with oral anticoagulants for 3–6 months.

PERICARDITIS

Acute pericarditis may complicate myocardial infarction, giving rise to chest pain that may be misinterpreted as recurrent infarction or angina. The pain is, however, distinguished by its sharp nature, and its relationship to posture and respiration. The diagnosis may be confirmed by a pericardial rub. If the pain is troublesome, it may be treated by high dose oral or intravenous aspirin, non-steroidal anti-inflammatory agents, or steroids. A haemorrhagic effusion with tamponade is uncommon and is particularly associated with anticoagulant treatment. It can usually be recognised echocardiographically. Treatment is by pericardiocentesis if haemodynamic embarrassment occurs.

LATE VENTRICULAR ARRHYTHMIAS

Ventricular tachycardia and ventricular fibrillation occurring on the first day carry only a small adverse prognosis, but when these arrhythmias develop later in the course they are liable to recur and are associated with a high risk of death. This is partly due to their usual association with severe myocardial damage; a careful assessment of coronary anatomy and ventricular function should always be undertaken. If it is probable that the arrhythmia is induced by ischaemia, revascularization by angioplasty or surgery should be considered. If this is unlikely, a variety of therapeutic approaches are available which are, as yet, inadequately researched. These include the use of beta-blockers, amiodarone, and electrophysiologically guided anti-arrhythmic therapy. In some cases, an implantable converter defibrillator is indicated.

POST-INFARCTION ANGINA AND ISCHAEMIA

Mild angina occurring in those with a previous history of the condition may respond satisfactorily to the usual medical treatment, but new, especially rest, angina in the early post-infarction phase requires further investigation.

The routine use of elective PTCA following thrombolytic therapy has been compared with a conservative approach in several randomized trials^[92–94]. It can be concluded that routine PTCA in the absence of spontaneous or provokable ischaemia does not improve left ventricular function or survival. In treating angina or recurrent ischaemia, however, whether due to re-occlusion or to a residual stenosis, PTCA has a definite role. It may also be of value in managing arrhythmias associated with persistent ischaemia. Although analyses

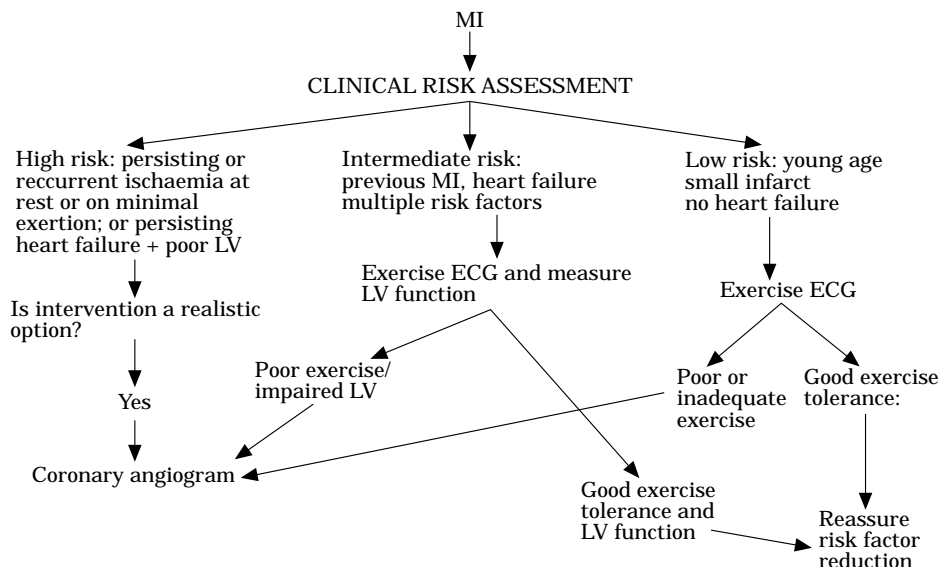


Figure 2 Strategies for assessment of risk.

from several trials have identified a patent infarct-related vessel as a marker for good long-term outcome, it has not been shown that late PTCA with the sole aim of restoring patency influences late events.

Coronary artery bypass surgery may be indicated if symptoms are not controlled by other means or if coronary angiography demonstrates lesions, such as left main stenosis or three vessel disease with poor left ventricular function, for which surgery improves prognosis^[95].

Risk assessment, rehabilitation, and secondary prevention

RISK ASSESSMENT

Risk assessment prior to discharge has the objectives of estimating prognosis, deciding which further investigations are required, and assisting in devising the best individual therapeutic strategy for patients who survive the acute event. This assessment depends partly on clinical data, including age, pre-existing risk factors, previous infarction, diabetes, haemodynamic status and arrhythmias during the acute phase, and partly on functional investigations and imaging.

CLINICAL RISK STRATIFICATION

Clinical risk stratification can be used to divide patients into high, intermediate and low risk categories. This clinical stratification is important because the 'yield' of investigations depends critically on the pre-test probability of a positive result.

Evaluation of high risk cases. Patients at the highest risk are those with persistent heart failure, severely impaired left ventricular function, persistent or early appearance of angina at rest or on minimal exertion, or recurrent

arrhythmias, and those unable to perform a pre-discharge exercise test^[96–99]. Such patients tend to be older, to have multiple risk factors, and to have had previous infarcts. Left ventricular function should be evaluated by echocardiography and/or scintigraphy. Coronary angiography provides independent prognostic information and acts as a guide to further treatment such as revascularization^[100].

Evaluation of medium risk cases. Cases that are clinically at medium risk are likely to be older than 55 years, have had transient heart failure, have had a previous infarction or have risk factors such as hypertension or diabetes. These patients should be assessed for left ventricular dysfunction and for residual ischaemia. The latter may be assessed by exercise electrocardiography, myocardial perfusion scanning or stress echocardiography, depending on local availability. Patients with impaired left ventricular function and/or inducible ischaemia should be considered for angiography. This approach to stratification is shown as a flow chart in Figure 2.

Evaluation of low risk patients. Low risk patients are younger (age <55 years), have had no previous infarcts, and have had an event-free clinical course. Exercise electrocardiography is the most useful first investigation in this group. This may take the form of a submaximal test before discharge or a symptom-limited test on treadmill or cycle ergometer at 3–8 weeks post-infarction, or both. Variables reflecting residual exercise-induced myocardial ischaemia do not seem to be closely related to mortality.

Patients who fail to achieve a satisfactory workload on exercise testing, or who develop angina or electrocardiographic signs of ischaemia, or severe dyspnoea should be considered for further tests. By contrast,

the negative predictive accuracy for patients who can complete stage III of the standard Bruce protocol or its equivalent without chest pain or ischaemic ECG changes is high^[101]. In addition, the effect on patient morale is positive, and the information is helpful in planning rehabilitation. There is no necessity to discontinue medication before exercise testing.

ASSESSMENT FOR ISCHAEMIA

Patients who fail to achieve a satisfactory workload on exercise testing, or who develop angina or electrocardiographic signs of ischaemia at a medium workload should be considered for further evaluation in order to localize the site and quantify the amount of myocardium at risk, as well as the extent of potentially viable myocardium. The choice between stress echocardiography and radioisotope perfusion scanning depends upon the experience of the individual centre and the resources available. In competent hands, both these techniques are more sensitive and specific than exercise electrocardiography.

EVALUATION OF PUMP FUNCTION

Evaluation of cardiac impairment by echocardiography or radionuclide ventriculography is helpful in assessing patients with no evidence of cardiac failure, particularly if performed under conditions of stress, though left ventricular function is likely to be well preserved in low risk cases.

EVALUATION FOR ARRHYTHMIC RISK

Holter monitoring and electrophysiological studies are of value in the assessment of patients considered to be at high risk of arrhythmias. Heart rate variability, QT dispersion, baroreflex sensitivity, and late potentials have all been found to be of prognostic value after myocardial infarction, but further clinical experience is needed to establish whether they add substantially to the more conventional prognostic tests.

EVALUATION OF METABOLIC RISK MARKERS

It is also important to measure metabolic risk markers such as total, LDL and HDL cholesterol, fasting triglyceride and plasma glucose in all patients.

INDICATIONS FOR CORONARY ANGIOGRAPHY

Coronary angiography should be undertaken in the early post-infarction period when there is:

Angina that does not respond to pharmacological therapy

Angina or evidence of myocardial ischaemia at rest
Exercise-induced angina or myocardial ischaemia at a low workload, or on Holter monitoring, when there has been little or no increase in heart rate.

Coronary angiography should be considered when there is:

Angina or objective evidence of provokable myocardial ischaemia (in the absence of the features described above)

Postinfarction angina responding to pharmacological therapy

Severe left ventricular dysfunction

Complex ventricular arrhythmia more than 48 h after the onset.

In selected cases, especially in younger individuals, coronary angiography can be considered for patients with an uncomplicated course to evaluate the success of reperfusion, to identify those with extensive coronary artery disease, and to facilitate early hospital discharge and return to work.

Rehabilitation

Rehabilitation is aimed at restoring the patient to as full a life as possible, and must take into account physical, psychological and socio-economic factors. The process should start as soon as possible after hospital admission, and be continued in the succeeding weeks and months. The details of rehabilitation will not be discussed here, as full consideration of its principles and methods are dealt with in the reports of the Working Group on Rehabilitation of the European Society of Cardiology^[102].

Psychological and socio-economic aspects. Anxiety is almost inevitable, both in patients and their associates, so that reassurance and explanation of the nature of the illness is of great importance and must be handled sensitively. It is also necessary to warn of the frequent occurrence of depression and irritability that more frequently occurs after return home. It must also be recognised that denial is common; while this may have a protective effect in the acute stage, it may make subsequent acceptance of the diagnosis more difficult.

The question of return of work and other activities should be discussed prior to hospital discharge.

Lifestyle advice. The possible causes of coronary disease should be discussed with patients and their partners during hospitalization, and individualized advice on a healthy diet, weight control, smoking and exercise given.

Physical activity. All patients should be given advice with regard to physical activity based upon their recovery from the heart attack, taking into account their age, their preinfarction level of activity, and their physical limitations. Assessment is greatly aided by a pre-discharge exercise test, which not only provides useful clinical information but can be reassuring to the over-anxious patient. A meta-analysis of rehabilitation programmes which included exercise suggested a significant reduction in mortality^[103].

Secondary prevention

Smoking. Although no randomized trials have been undertaken, compelling evidence from observational studies shows that those who stop smoking have a mortality in the succeeding years less than half that of those who continue to do so^[104]. This is, therefore,

potentially the most effective of all secondary prevention measures; much effort should be devoted to this end. Most patients will not have smoked during the acute phase and the convalescent period is ideal for health professionals to help smokers quit the habit. Resumption of smoking is common after return home and continued support and advice is needed during rehabilitation. A randomized study has demonstrated the effectiveness of a nurse-directed programme^[105]: a smoking cessation protocol should be adopted by each hospital.

Diet and dietary supplements. There is little evidence on the effectiveness of dietary treatment of postinfarction patients, but a weight reducing diet should be prescribed for those who are overweight. All patients should be advised to take a diet low in saturated fat and high in fruit and vegetables. One study suggests that taking fatty fish at least twice a week reduces the risk of reinfarction and death^[106]. The role of antioxidants in the prevention of coronary disease has yet to be established.

Antiplatelet and anticoagulant treatment. The Antiplatelet Trialists Collaboration^[55] meta-analysis demonstrated about a 25% reduction in reinfarction and death in post-infarction patients. In the trials analysed, aspirin dosages ranged from 75 to 325 mg daily. There is some evidence that the lower dosages are effective with fewer side-effects.

Clinical trials undertaken before the widespread use of aspirin showed that oral anticoagulants are effective in preventing reinfarction and death in survivors of myocardial infarction^[107,108]. The patients in these trials were randomized at least two weeks after the index infarction. The role of routine early oral anticoagulation following acute myocardial infarction is less clear and has only recently been evaluated after thrombolytic therapy^[29,109]. In such patients there is no clear benefit over antiplatelet therapy. Possibly, subsets of patients, e.g. those with left ventricular aneurysm, atrial fibrillation or echographically proven left ventricular thrombus might benefit from early oral anticoagulation, but large randomized trials in this field are lacking. The ambulant use of subcutaneous heparin may be helpful^[110], but the results should be confirmed in more studies.

Combined anticoagulant and antiplatelet therapy after myocardial infarction is currently being investigated; the first results appear promising^[111].

Beta-blockers. Several trials and meta-analyses have demonstrated that beta-adrenoceptor blocking drugs reduce mortality and reinfarction by 20–25% in those who have recovered from acute myocardial infarction^[60,85]. Positive trials have been conducted with propranolol, metoprolol, timolol and acebutolol, but studies with other beta-blockers, although not significant, are compatible with a comparable effect. About 25% of patients have contra-indications to beta-blockade because of uncontrolled heart failure, respiratory disease or other conditions. Of the remainder, perhaps half can be defined as of low risk^[85,112], in whom

beta-blockade exerts only a marginal benefit, bearing in mind the minor though sometimes troublesome side-effects. Opinion is divided as to whether beta-blockers should be prescribed to all those for whom they are not contra-indicated, or whether they should only be given to those at moderate risk who have the most to gain.

Calcium antagonists. Trials with verapamil^[113] and diltiazem^[114] have suggested that they may prevent reinfarction and death, but caution must be exercised in the presence of impaired ventricular function. They may be appropriate when beta-blockers are contra-indicated (especially in obstructive airways disease).

Trials with dihydropyridines^[66] have failed to show a benefit in terms of improved prognosis after myocardial infarction; they should, therefore, only be prescribed for clear clinical indications, bearing in mind the potentially adverse effects in those with poor left ventricular function.

Nitrates. There is no evidence that oral or transdermal nitrates improve prognosis after myocardial infarction, the ISIS-4^[64] GISSI-3^[63] trials failing to show a benefit at 4–6 weeks after the event. Nitrates, of course, continue to be first line therapy for angina pectoris.

Angiotensin converting enzyme (ACE) inhibitors. Several trials have established that ACE inhibitors reduce mortality after acute myocardial infarction^[115–118]. In the SAVE trial^[115] patients were entered a mean of 11 days after the acute event if they had an ejection fraction less than 40% on nuclear imaging, and if they were free of manifest ischaemia on an exercise test. No mortality benefit was seen in the first year, but there was a 19% reduction in the succeeding 3–5 years of follow-up (from 24.6 to 20.4%). Fewer re-infarctions and less heart failure were, however, seen even within the first year.

In the AIRE trial^[116] patients were randomized to ramipril a mean of 5 days after the onset of a myocardial infarction that was complicated by the clinical or radiological features of heart failure. At an average of 15 months later, the mortality was reduced from 22.6% to 16.9% (a 27% reduction). In the TRACE study^[118], patients were randomized to trandolapril or placebo a median of 4 days after infarction, if they had left ventricular dysfunction as demonstrated by a wall motion index of 1.2 or less. At an average follow-up of 108 weeks, the mortality was 34.7% in the treated group and 42.3% in the placebo group. Taking the three studies together, there is a strong case for administering ACE inhibitors to patients who have experienced heart failure in the acute event, even if no features of this persist, who have an ejection fraction of less than 40%, or a wall motion index of 1.2 or less, provided there are not contra-indications.

As discussed above, there is a case for administering ACE inhibitors to all patients with acute infarction from admission, provided there are no contra-indications. Against such a policy is the increased incidence of hypotension and renal failure in those

receiving ACE inhibitors in the acute stage, and the small benefit in those at relatively low risk, such as patients with small inferior infarctions. With the very early use of ACE inhibitors, consideration should be given to discontinuing these agents at 4–6 weeks if the clinical course has been uncomplicated and the ejection fraction greater than 40%.

Lipid-lowering agents. The Scandinavian Simvastatin Survival Study (4S)^[119] clearly demonstrated the benefits of lipid-lowering in a population of 4444 anginal and/or post-infarction patients with serum cholesterol levels of 5.5–8.0 mmol . l⁻¹ (212–308 mg . dl⁻¹) after dietary measures had been tried. Patients were not entered into the trial until 6 months after an acute infarction, and a relatively low risk group of patients was recruited. Overall mortality at a median of 5.4 years was reduced by 30% (from 12 to 8%). This represented 33 lives saved per 1000 patients treated over this period. There were substantial reductions in coronary mortality, and in the need for coronary bypass surgery. Patients over 60 years of age appeared to benefit as much as younger patients. Women benefited as far as major coronary events were concerned, but a statistically significant reduction in death was not demonstrated; this may have been as a result of the relatively small number of women recruited.

Lipid-lowering agents should, therefore, be prescribed for patients who correspond to those recruited into 4S, but controversy still exists as to how soon treatment should be started after the event, and whether the criteria for treatment should be extended to those with lower lipid levels.

Logistics of care

PRE-HOSPITAL CARE

Patient delay. The most critical time in an acute heart attack is the very early phase, during which the patient is often in severe pain and liable to cardiac arrest. Furthermore, the earlier that some treatments, notably thrombolysis, are administered, the greater the beneficial effect. Yet, it is often an hour or more after the onset before aid is requested. Sometimes this reflects the fact that the symptoms are not severe, or typical, or abrupt in onset, but frequently immediate action is not taken even when they are. It should be a normal part of the care of patients with known ischaemic heart disease to inform them and their partners of the symptoms of a heart attack and how to respond to it. It is less certain what should be the role of education of the general public. Certainly, the public must be aware of how to call the emergency services, but although they have achieved some success, it is questionable whether public education campaigns have had a significant impact on outcome^[120,121].

Public education in cardio-pulmonary resuscitation. The techniques of basic life support should be part of the school curriculum. Those most likely to encounter

cardiac arrest while at work, such as the police and fire service personnel, should be proficient in cardio-pulmonary resuscitation.

The ambulance service. The ambulance service has a critical role in the management of acute myocardial infarction and cardiac arrest. The quality of the care given depends on the training of the staff concerned. At the most simple level, all ambulance personnel should be trained to recognise the symptoms of myocardial infarction, administer oxygen and pain relief, and provide basic life support. All emergency ambulances should be equipped with defibrillators and at least one person on board trained in advanced life support. Doctor-manned ambulances, available in only a few countries, can provide more advanced diagnostic and therapeutic skills, including the authorisation to give opioids and thrombolytic drugs. In some countries, suitably trained nurses undertake these functions.

It is desirable for ambulance staff to record an ECG for diagnostic purposes and either interpret it or transmit it so that it can be reviewed by experienced staff in a coronary care unit or elsewhere. The recording of an ECG prior to admission can greatly accelerate in-hospital management^[122,123].

General practitioners. In some countries, general practitioners play a major role in the early care of myocardial infarction. In these countries, they are often the first to be called by patients. If they can respond quickly and have been suitably trained, they can be very effective, because they may know the individual patient, record and interpret an ECG, be able to administer opioids and thrombolytic drugs, and undertake defibrillation^[123,124]. In most areas, general practitioners are not so trained. In this circumstance, although it is desirable that they attend the patient without delay, they should immediately call for an ambulance.

Admission procedures. The processing of patients once they arrive in hospital must be speedy, particularly with regard to diagnosis and the administration of thrombolysis, if indicated. In some hospitals, direct admission to a coronary care unit may be the best option, but in most, patients are first delivered to an Emergency Department. Delays here can be substantial; it is essential that suitably qualified staff are available to assess and treat patients with suspected myocardial infarction in this environment. Patients with clear-cut features of myocardial infarction, whose ECG demonstrate either ST elevation or left bundle branch block, should enter a 'fast-track' system, in which thrombolysis is instituted in the Emergency Department so that the 'door-to-needle' time is no more than about 20 min. Other cases may require more detailed assessment which may be better undertaken in the coronary care unit.

THE CORONARY (CARDIAC) CARE UNIT (CCU)

All patients with suspected myocardial infarction should initially be assessed and cared for in a designated unit,

where appropriately trained staff are constantly available and where the necessary equipment for monitoring and treatment are immediately at hand. Where the CCU is used, as it usually is, for triage, it is important that satisfactory arrangements exist for the rapid transfer to other wards of those not needing its highly specialised facilities.

Non-invasive monitoring. Electrocardiographic monitoring for arrhythmias should be started immediately in any patient suspected of having sustained an acute myocardial infarction. This should be continued for at least 24 h or until an alternative diagnosis has been made. Further ECG monitoring is dependent upon the perceived risk to the patient and upon the equipment available. When a patient leaves the CCU, monitoring of rhythm may be continued, if necessary, by telemetry. More prolonged monitoring is appropriate for those who have sustained heart failure, shock or serious arrhythmias in the acute phase as the risk of further arrhythmias is high.

Invasive monitoring. All coronary care units should have the skills and equipment to undertake invasive monitoring of the arterial and pulmonary artery pressures. Arterial pressure monitoring should be undertaken in patients with cardiogenic shock. Balloon flotation catheters, such as the Swan-Ganz catheter, are of value for the assessment and care of patients with low cardiac output. They permit measurement of right atrial, pulmonary artery and pulmonary wedge pressures, and cardiac output. Balloon flotation catheters are indicated in the presence of cardiogenic shock, progressive heart failure, and suspected ventricular septal defect or papillary muscle dysfunction.

The current use of therapies tested by clinical trials

The results of clinical trials have often not been implemented in practice and treatments which have been shown to be of little or no value continue to be used widely. It has been difficult to obtain reliable data on the utilization of therapies in myocardial infarction, except from clinical trials, which may not be truly representative of current practice. The European Secondary Prevention Study Group have recently reported^[125,126] on the utilization of drugs in samples of 200–520 representative acute myocardial infarction patients from 11 countries. Thrombolytic therapy was given to an average of 35% of patients (range 13 to 52%). The use of intravenous beta-blockade varied from 0.5–54% (average 13%). Oral beta-blockade at discharge varied from 33–81% (average 52%). These data emphasize the need both for continuing medical education and for ongoing audit to ensure the implementation of therapeutic advances. Centres which participate in multicentre clinical trials are more likely to implement evidence-based changes in clinical practice^[127].

Recommendations

Patients. Patients with a suspected heart attack have a right to expect prompt diagnosis, pain relief, resuscitation and, if indicated, reperfusion treatment.

Patients with suspected or confirmed myocardial infarction should be cared for by staff trained and experienced in modern coronary care. They should have access to advanced methods of diagnosis and treatment either at the initial place of management or following transfer to a specialist unit.

They should have appropriate facilities for post-discharge follow-up, rehabilitation and secondary prevention.

They and their associates should be informed of how to recognise and respond to a further heart attack.

Cardiologists. Cardiologists, in association with emergency care physicians and health authorities, should ensure that an optimal system for the care of heart attack patients is operative in their area. This should include the appropriate training of ambulance personnel and first-line doctors, efficient arrangements for the diagnosis and treatment of suspected myocardial infarctions in the Emergency Department, and protocols for the prompt administration of thrombolytic treatment.

Cardiologists, in association, with anaesthetists and other relevant specialists, should ensure that medical and paramedical hospital staff are competent in resuscitation techniques.

Registers should be kept of the time from the call for care and the administration of thrombolysis ('call-to-needle time') and that from hospital admission to thrombolysis ('door-to-needle time'). The former should be no longer than 90 min and for 'fast track' patients with clear indications for thrombolysis, the 'door-to-needle time' should not exceed 20 min.

Registers should also be kept of the proportion of patients with definite myocardial infarction admitted within 12 h of the onset of symptoms with ST elevation or bundle branch block who receive thrombolysis. This proportion should probably be in excess of 90%.

PTCA may be regarded as a viable and cost-effective alternative to thrombolytic therapy when the appropriate skills and facilities are available. The results of PTCA should be recorded in a national register.

A rehabilitation programme should be made available for all patients, tailored to their individual needs.

There should be a policy for smoking cessation. This must consist of a continuing programme run by health professionals that not only encourages patients to stop, but endeavours to maintain cessation.

Records should be kept of secondary prevention therapy prescribed to survivors of definite myocardial infarction. Suggested minimum target figures at the time of discharge are for aspirin >85%, beta-blockers >35% and ACE inhibitors >20%.

All patients should have their lipids measured, preferably on the day of admission. Those with raised

lipids should first receive dietary advice. Should this fail to reduce raised lipid levels sufficiently, consideration should be given to lipid-lowering drugs, according to the criteria of the Scandinavian Simvastatin Survival Study.

General practitioners. When general practitioners are the first point of contact for cases of suspected myocardial infarction, they must either be able to respond immediately or make provision for the emergency services to do so, or (preferably) both.

If general practitioners can respond quickly and are appropriately trained and equipped, they can provide defibrillation and thrombolysis effectively.

They should be involved in the co-ordinated local programme for the management of cardiac emergencies.

They should see patients as soon as possible after discharge from hospital, ensure that their rehabilitation is properly organised, and oversee the appropriate secondary prevention measures.

Health authorities. Health authorities should encourage the training of the public in basic cardiopulmonary resuscitation techniques and the ambulance personnel in basic and advanced life support.

They should ensure that an optimal system of care is available for patients suspected of sustaining cardiac arrest or myocardial infarction, by co-ordinating the activities of the ambulance service, general practitioners, and the hospital service.

They should ensure that Emergency Departments have appropriate protocols for the prompt management of patients with suspected myocardial infarction, and that there are appropriately trained staff available at all times.

They should provide sufficient beds for the intensive care of patients with myocardial infarction. Physicians with a formal training in cardiology must be available.

They should make provision for the rehabilitation of patients discharged from hospital after myocardial infarction.

They should ensure that facilities are available in their own hospital or district for the advanced investigation and treatment of patients with the complications of myocardial infarction or, if not available locally, arrangements have been made with tertiary centres elsewhere.

Procedure of the Task Force. The Task Force on the Management of Acute Myocardial Infarction was created by the Committee for Scientific and Clinical Initiatives of the European Society of Cardiology in February 1995 and asked to report to the Congress of the Society in August 1995. The members of the Task Force were Prof. D. G. Julian (Chairman) U.K., Prof. J.-P. Boissel (France), Prof. D. P. De Bono (U.K.), Prof. K. A. A. Fox (U.K.), Dr J. Heikkilä (Finland), Dr L. Lopez-Bescos (Spain), Prof. K.-L. Neuhaus (Germany), Prof. R. Schröder (Germany) Prof. P. Sleight (U.K.),

Prof. G. Specchia (Italy), Drs A. Sigurdsson and K. Swedberg (Sweden), Prof. M. Turina, Dr M. Genoni (Switzerland), Prof. F. W. A. Verheugt (The Netherlands), Prof. F. van de Werf (Belgium), Dr F. Zijlstra (The Netherlands).

Individual members were invited to submit draft papers in their area of expertise and these were first discussed at a meeting in London on 15 and 16 May. After several revisions, and consultation with members of the Committee, the members met again on 4 July in Amsterdam. The document was redrafted and widely circulated prior to submission of the final document to the Committee for its approval.

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