Acute Coronary Syndrome

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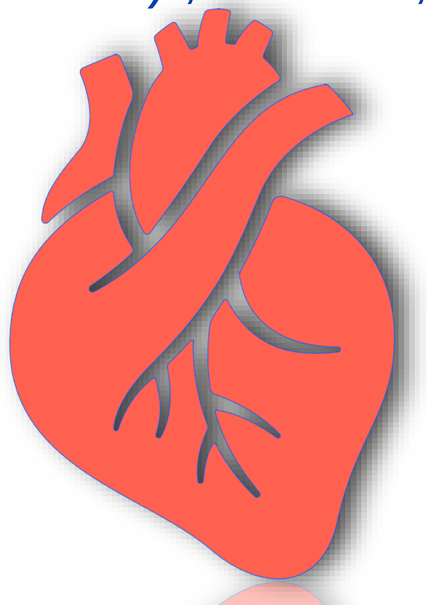


Acute coronary syndrome is a term that encompasses both unstable angina and myocardial infarction. Unstable angina is characterised by new-onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest in the absence of myocardial injury. Myocardial infarction (MI) is distinguished from unstable angina by the occurrence of myocardial necrosis and is diagnosed when myocardial injury occurs in the presence of clinical evidence of acute myocardial ischaemia .

Acute coronary syndrome may present as a new phenomenon in patients with no previous history of heart disease or against a background of chronic stable angina. Approximately 12% of patients with acute coronary syndrome die within 1 month and 20% within 6 months of the index event. The risk markers that are indicative of an adverse prognosis include recurrent ischaemia, extensive ECG changes at rest or during pain, raised plasma troponin I or T concentrations, arrhythmias and haemodynamic complications (hypotension, mitral regurgitation) during episodes of ischaemia. Careful assessment and risk stratification cation are important because these guide the use of more complex pharmacological and interventional treatments which can improve outcome .

Pathogenesis

Acute coronary syndrome almost always occurs in patients who have coronary atherosclerosis. The culprit lesion that precipitates the acute event is usually a complex ulcerated or fissured atheromatous plaque with adherent platelet-rich thrombus and local coronary artery spasm These vascular changes during an acute coronary syndrome are dynamic, such that the degree of obstruction may either increase, leading to complete vessel occlusion, or regress due to the effects of platelet disaggregation and endogenous fibrinolysis.

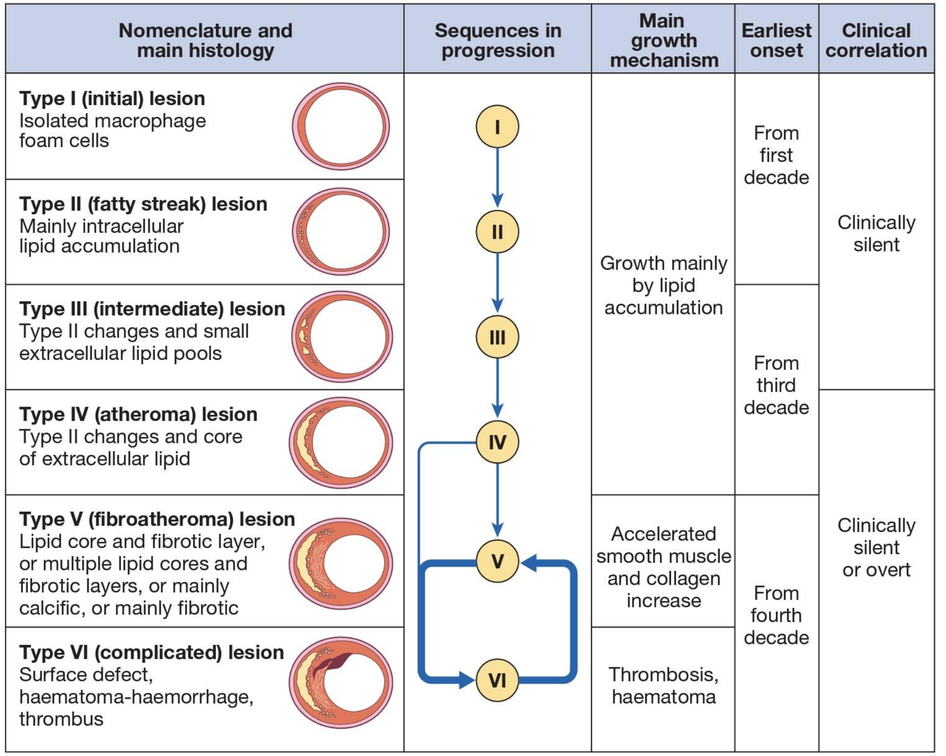


Fig. 16.54 **The six stages of atherosclerosis.** American Heart Association classification. *From Stary HC, Chandler B, Dinsmore RE et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. Circulation 1995; 92:1355–1374. © 1995 American Heart Association.*

Myocardial infarction

In acute type 1 MI, occlusive thrombus is present at the site of rupture or erosion of an atheromatous plaque; so-called atherothrombosis. The thrombus may undergo spontaneous lysis over the course of the next few days, although irreversible myocardial damage will have occurred. Without treatment, the artery responsible for the type 1 MI remains permanently occluded in 20%–30% of patients. Since the process of infarction progresses over several hours , most patients present when it is still possible to salvage myocardium and improve outcome.

Myocardial infarction may also occur as the result of an imbalance between the blood supply and metabolic demands of the heart (type 2 MI). This may occur because of the presence of CAD and major non-cardiac stress, such as sepsis in a patient with three-vessel CAD, or because there is overwhelming demand in the presence of unobstructed coronary arteries, such as an excessively fast heart rate from a primary arrhythmia. For the diagnosis of type 2 MI, there needs to be clinical evidence of ischaemia, such as ECG changes or symptoms of chest pain. This should be distinguished from myocardial injury where there is evidence of elevated cardiac troponin concentration (myocardial necrosis) without evidence of myocardial ischaemia, such as occurs in myocarditis. Myocardial injury can be acute or chronic depending upon its underlying cause. The term type 3 MI is used to describe the situation where there is sudden death presumed to be due to MI. The terms type 4 and type 5 MI are used to describe the situations where MI occurs during or following the conduct of the coronary revascularisation procedures PCI and CABG, respectively. In these situations, clinical evidence of ischaemia is required to distinguish MI from procedure-related myocardial injury.

16.47 Classification and criteria for diagnosis of acute myocardial infarction

Criteria for acute myocardial infarction

The term acute myocardial infarction (MI) should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischaemia and with detection of a rise and/or fall of cardiac troponin values with at least one value above the 99th centile upper reference limit and at least one of the following:

- Symptoms of myocardial ischaemia
- New ischaemic ECG changes
- Development of pathological Q waves
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology
- Identification of a coronary thrombus by angiography or autopsy

Classification of acute myocardial infarction

- **Type 1 MI:** Acute atherothrombosis in the artery supplying the infarcted myocardium
- **Type 2 MI:** An imbalance between myocardial oxygen supply and demand unrelated to acute atherothrombosis
- **Type 3 MI:** Cardiac death in patients with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes before cardiac troponin values become available or abnormal
- **Type 4 MI:** MI caused during percutaneous coronary intervention (PCI; type 4a). Other types include stent thrombosis (type 4b) and restenosis (type 4c) and consistent with type 1 MI
- **Type 5 MI:** MI caused during coronary artery bypass grafting

Coronary procedure-related MI ≤ 48 hours after the index procedure is arbitrarily defined by an elevation of cardiac troponin values > 5× for type 4a MI and > 10× for type 5 MI of the 99th centile upper reference limit in patients with normal baseline values together with at least one of the following:

- New ischaemic ECG changes (this criterion is related to type 4a MI only)
- Development of new pathological Q waves
- Imaging evidence of loss of viable myocardium that is presumed to be new and consistent with an ischaemic aetiology
- Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolisation

Adapted from Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. Eur Heart J 2019; 40: 237–269.

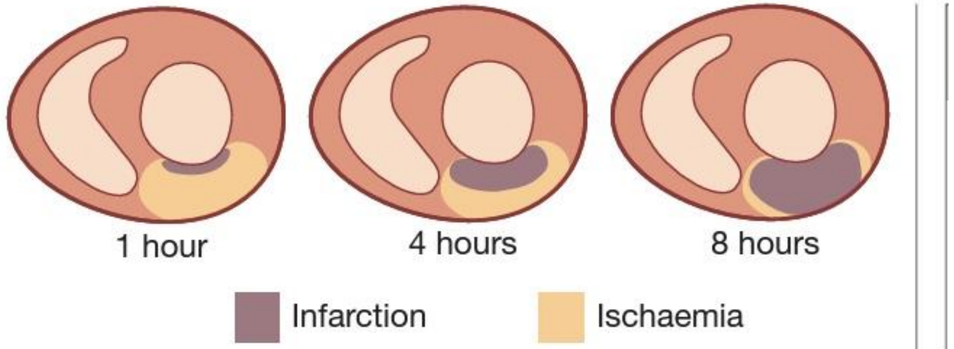


Fig. 16.63 The time course of myocardial infarction. The relative proportion of ischaemic, infarcting and infarcted tissue slowly changes over a period of 12 hours. In the early stages of myocardial infarction, a significant proportion of the myocardium in jeopardy is potentially salvageable.

Clinical features

The differential diagnosis of acute coronary syndrome is wide and includes most causes of **central chest pain or collapse**. **Chest pain at rest** is the cardinal symptom but breathlessness, vomiting and collapse are also common features The pain occurs in the same sites as angina but is usually more severe and lasts longer; it is often described as a tightness, heaviness or constriction in the chest. In acute MI, the pain can be excruciating, and the patient's expression and pallor may vividly convey the seriousness of the situation. Most patients are breathless and, in some, this is the only symptom.

Painless or 'silent' MI may also occur and is particularly common in older patients or those with diabetes mellitus.

If **syncope** occurs, it is usually caused by an arrhythmia or profound hypotension.

Vomiting and sinus bradycardia are often due to vagal stimulation and are particularly common in patients with inferior MI.

Nausea and vomiting may also be caused or aggravated by opiates given for pain relief. Sometimes infarction occurs in the absence of physical signs. Sudden death, from ventricular fibrillation or asystole, may occur immediately and often within the first hour. If the patient survives this most critical stage, the liability to dangerous arrhythmias remains, but diminishes as each hour goes by. It is vital that patients know not to delay calling for help if symptoms occur. Complications may occur in all forms of acute coronary syndrome but have become less frequent in the modern era of immediate or early coronary revascularisation.

16.49 Clinical features of acute coronary syndromes

Symptoms

- Prolonged cardiac pain: chest, throat, arms, epigastrium or back
- Anxiety and fear of impending death
- Nausea and vomiting
- Breathlessness
- Collapse/syncope

Physical signs

Signs of sympathetic activation

- Pallor
- Sweating
- Tachycardia

Signs of vagal activation

- Vomiting
- Bradycardia

Signs of impaired myocardial function

- Hypotension, oliguria, cold peripheries
- Narrow pulse pressure
- Raised jugular venous pressure
- Third heart sound
- Quiet first heart sound
- Diffuse apical impulse
- Lung crepitations

Low-grade fever

Complications

- Mitral regurgitation
- Pericarditis

Complications of ACS

Arrhythmias

Arrhythmias are common in patients with acute coronary syndrome but are often transient and of no haemodynamic or prognostic importance. The risk of arrhythmia can be minimised by adequate pain relief, rest and the correction of hypokalaemia. VF occurs in 5%–10% of patients who reach hospital and is thought to be the major cause of death in those who die before receiving medical attention. Prompt defibrillation restores sinus rhythm and is life-saving. The prognosis of patients with early VF (within the first 48 hours) who are successfully and promptly resuscitated is identical to that of patients who do not suffer VF. The presence of ventricular arrhythmias during the convalescent phase of acute coronary syndrome may be a marker of poor ventricular function and may herald sudden death. Selected patients may benefit from electrophysiological testing and specific anti-arrhythmic therapy, including ICDs, as discussed in the previous section on cardiac arrhythmias. AF is a common but frequently transient arrhythmia, and usually does not require emergency treatment. However, if it causes a rapid ventricular rate with hypotension or circulatory collapse, prompt cardioversion is essential. In other situations, digoxin or a β-blocker is usually the treatment of choice. AF may be a feature of impending or overt left ventricular failure, and therapy may be ineffective if heart failure is not recognised and treated appropriately. Anticoagulation is required if AF persists. Bradycardia may occur but does not require treatment unless there is hypotension or haemodynamic deterioration, in which case atropine (0.6–1.2 mg IV) may be given. Inferior MI may be complicated by AV block, which is usually temporary and often resolves following reperfusion therapy. If there is clinical deterioration due to second-degree or complete AV block, a temporary pacemaker should be considered. AV block complicating anterior infarction is more serious because asystole may suddenly supervene. A prophylactic temporary pacemaker should be inserted in these patients.

16.50 Common arrhythmias in acute coronary syndrome

- Ventricular fibrillation
- Ventricular tachycardia
- Accelerated idioventricular rhythm
- Ventricular ectopics
- Atrial fibrillation
- Atrial tachycardia
- Sinus bradycardia (particularly after inferior myocardial infarction)
- Atrioventricular block

Recurrent angina

Patients who develop recurrent angina at rest or on minimal exertion following an acute coronary syndrome are at high risk and should be considered for prompt coronary angiography with a view to revascularisation. Patients with dynamic ECG changes and ongoing pain should be treated with intravenous glycoprotein IIb/IIIa receptor antagonists (tirofiban 400 ng/kg/min for 30 min, then 100 ng/kg/min for 48 hrs, or abciximab, initially 180 μg/kg, then 2 μg/kg/min for up to 72 hrs). Patients with resistant pain or marked haemodynamic changes should be considered for intra-aortic balloon counterpulsation and emergency coronary revascularisation. Post-infarct angina occurs in up to 50% of patients treated with thrombolysis. Most patients have a residual stenosis in the infarct-related vessel, despite successful thrombolysis, and this may cause angina if there is still viable myocardium downstream. For this reason, all patients who have received successful thrombolysis should be considered for early (within the first 24 hours) coronary angiography with a view to coronary revascularisation.

Acute heart failure

Acute heart failure usually reflects extensive myocardial damage and is associated with a poor prognosis. All the other complications of MI are more likely to occur when acute heart failure is present.

Pericarditis

This only occurs following infarction and is particularly common on the second and third days. The patient may recognise that a different pain has developed, even though it is at the same site, and that it is positional and tends to be worse or sometimes present only on inspiration. A pericardial rub may be audible. Opiate-based analgesia should be used. Non-steroidal (NSAIDs) and steroidal anti-inflammatory drugs may increase the risk of aneurysm formation and myocardial rupture in the early recovery period, and should be avoided.

Dressler syndrome

This syndrome is characterised by persistent fever, pericarditis and pleurisy, and is probably due to autoimmunity. The symptoms tend to occur a few weeks or even months after MI and often subside after a few days. If the symptoms are prolonged or severe, treatment with high-dose aspirin, NSAIDs or even glucocorticoid steroids may be required.

Papillary muscle rupture

This typically presents with acute pulmonary oedema and shock due to the sudden onset of severe mitral regurgitation. Examination usually reveals a pansystolic murmur and third heart sound but the murmur may be quiet or absent in patients with severe regurgitation. The diagnosis is confirmed by echocardiography, and emergency valve replacement may be necessary. Lesser degrees of mitral regurgitation due to papillary muscle dysfunction are common and may be transient

Ventricular septal rupture

This usually presents with sudden haemodynamic deterioration accompanied by a new loud pansystolic murmur radiating to the right sternal border, which may be difficult cult to distinguish from acute mitral regurgitation. Rupture of the intraventricular septum causes leftto-right shunting through a ventricular septal defect, which tends to cause acute right heart failure rather than pulmonary oedema. Doppler echocardiography and right heart catheterisation will confirm the diagnosis. Treatment is by emergency surgical repair; without this, the condition is usually fatal.

Ventricular rupture

Rupture of the ventricle may lead to cardiac tamponade and is usually fatal, although it is occasionally possible to support a patient with an incomplete rupture until emergency surgery can be performed.

Embolism

Thrombus often forms on the endocardial surface of freshly infarcted myocardium. This can lead to systemic embolism and occasionally causes a stroke or ischaemic limb. Venous thrombosis and pulmonary embolism may occur but have become less common with the use of prophylactic anticoagulants and early mobilisation.

Ventricular remodelling

This is a potential complication of an acute transmural MI due to thinning and stretching of the infarcted segment. This leads to an increase in wall stress with progressive dilatation and hypertrophy of the remaining ventricle . As the ventricle dilates, it becomes less efficient and heart failure may supervene. Infarct expansion occurs over a few days and weeks but ventricular remodelling can take years. Beta-blocker, ACE inhibitor and mineralocorticoid receptor antagonist therapies can reduce late ventricular remodelling and prevent the onset of heart failure.

Ventricular aneurysm

Ventricular aneurysm develops in approximately 10% of patients with MI and is particularly common when there is persistent occlusion of the infarct-related vessel. Heart failure, ventricular arrhythmias, mural thrombus and systemic embolism are all recognised complications of aneurysm formation. Other features include a paradoxical impulse on the chest wall, persistent ST elevation on the ECG, and sometimes an unusual bulge from the cardiac silhouette on the chest X-ray. Echocardiography is diagnostic. Surgical removal of a left ventricular aneurysm carries a high morbidity and mortality but is sometimes necessary.

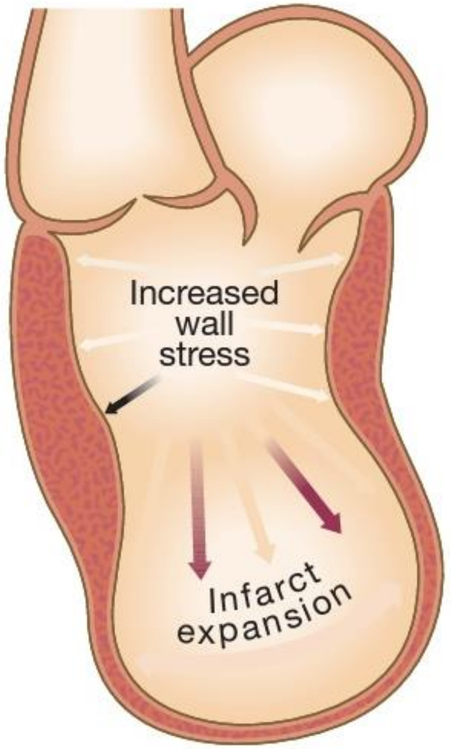


Fig. 16.64 Infarct expansion and ventricular remodelling. Full-thickness myocardial infarction causes thinning and stretching of the infarcted segment (infarct expansion), which leads to increased wall stress with progressive dilatation and hypertrophy of the remaining ventricle (ventricular remodelling).

Investigation

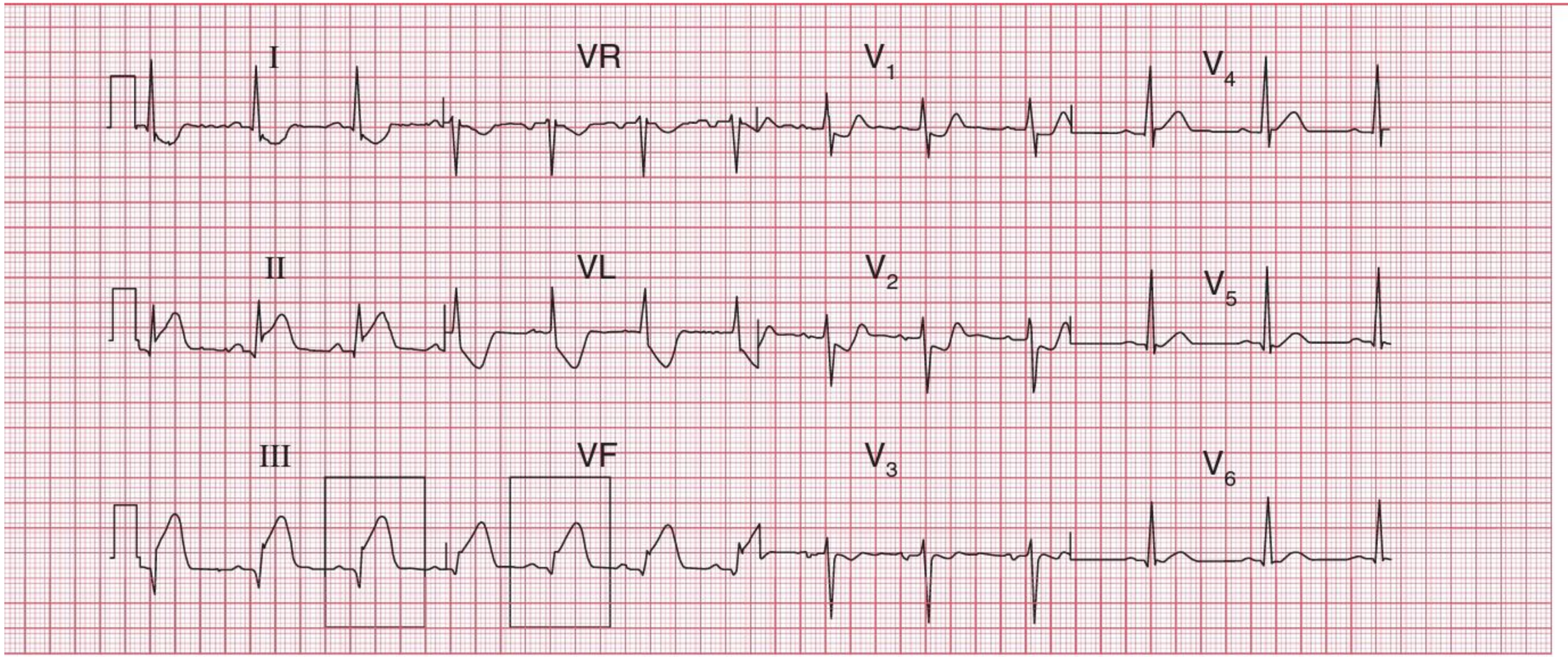
Electrocardiogram

The standard 12-lead ECG is central to confirming the diagnosis and deciding immediate management but may be difficult to interpret if there is bundle branch block or previous MI. The initial ECG may be normal or non-diagnostic in one-third of cases. Repeated ECGs are important, especially where the diagnosis is uncertain or the patient has recurrent or persistent symptoms. The earliest ECG change is usually ST-segment deviation. With proximal occlusion of a major coronary artery, **ST-segment elevation (or new bundle branch block)** is seen initially, with later diminution in the size of the R wave and, in transmural (full-thickness) infarction, development of a Q wave. Subsequently, **the T wave becomes inverted because of a change in ventricular repolarisation; this change persists after the ST segment has returned to normal.** These sequential features are sufficiently reliable for the approximate age of the infarct to be deduced.

In non-ST segment elevation acute coronary syndrome, there is **partial occlusion of a major vessel or complete occlusion of a minor vessel, causing unstable angina or partial-thickness (subendocardial) MI.** This is usually associated with ST-segment depression and T-wave changes. In the presence of infarction, this may be accompanied by some loss of R waves in the absence of Q waves .

The ECG changes are best seen in the leads that ‘face’ the ischaemic or infarcted area. When there has been anteroseptal infarction, abnormalities are found in one or more leads from V1 to V4 , while anterolateral infarction produces changes from V4 to V6 , in aVL and in lead I. Inferior infarction is best shown in leads II, III and aVF, while, at the same time, leads I, aVL and the anterior chest leads may show ‘reciprocal’ changes of ST depression .

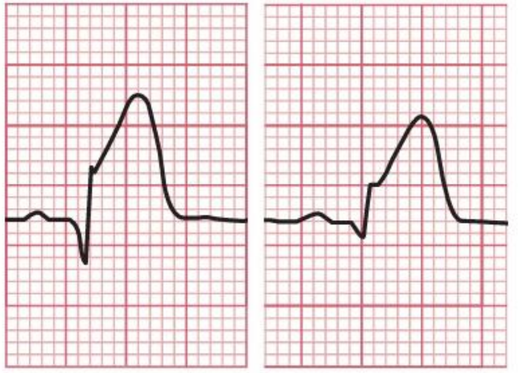
Infarction of the posterior wall of the LV does not cause ST elevation or Q waves in the standard leads, but can be diagnosed by the presence of reciprocal changes (ST depression and a tall R wave in leads V1–V4). Some infarctions (especially inferior) also involve the RV. This may be identified by recording from additional leads placed over the right precordium.



Acute inferior infarction

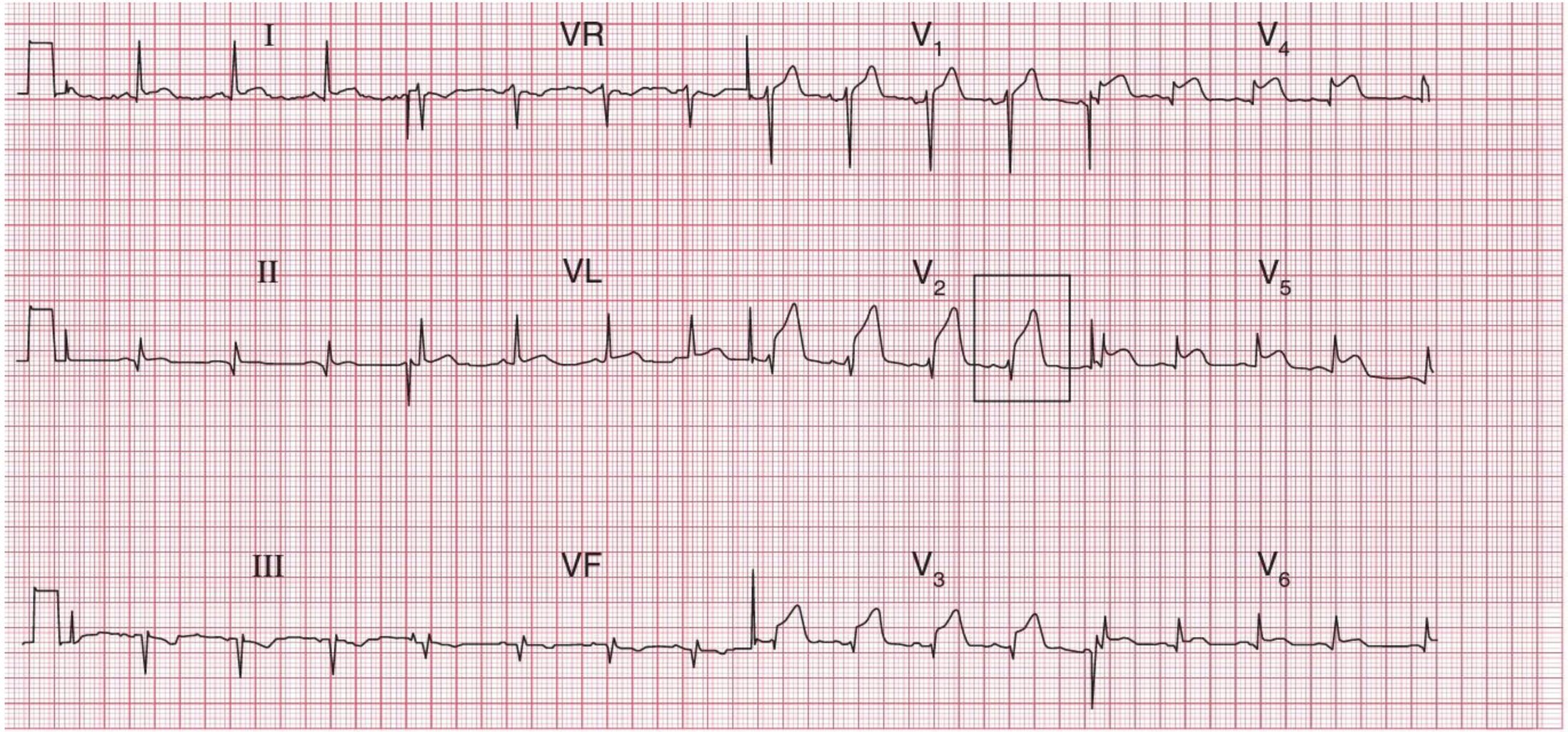
NOTE

- Sinus rhythm
- Normal axis
- Small Q waves in leads II–III, VF
- Raised ST segments in leads II–III, VF
- Depressed ST segments in leads I, VL, V_2–V_3
- Inverted T waves in leads I, VL, V_3

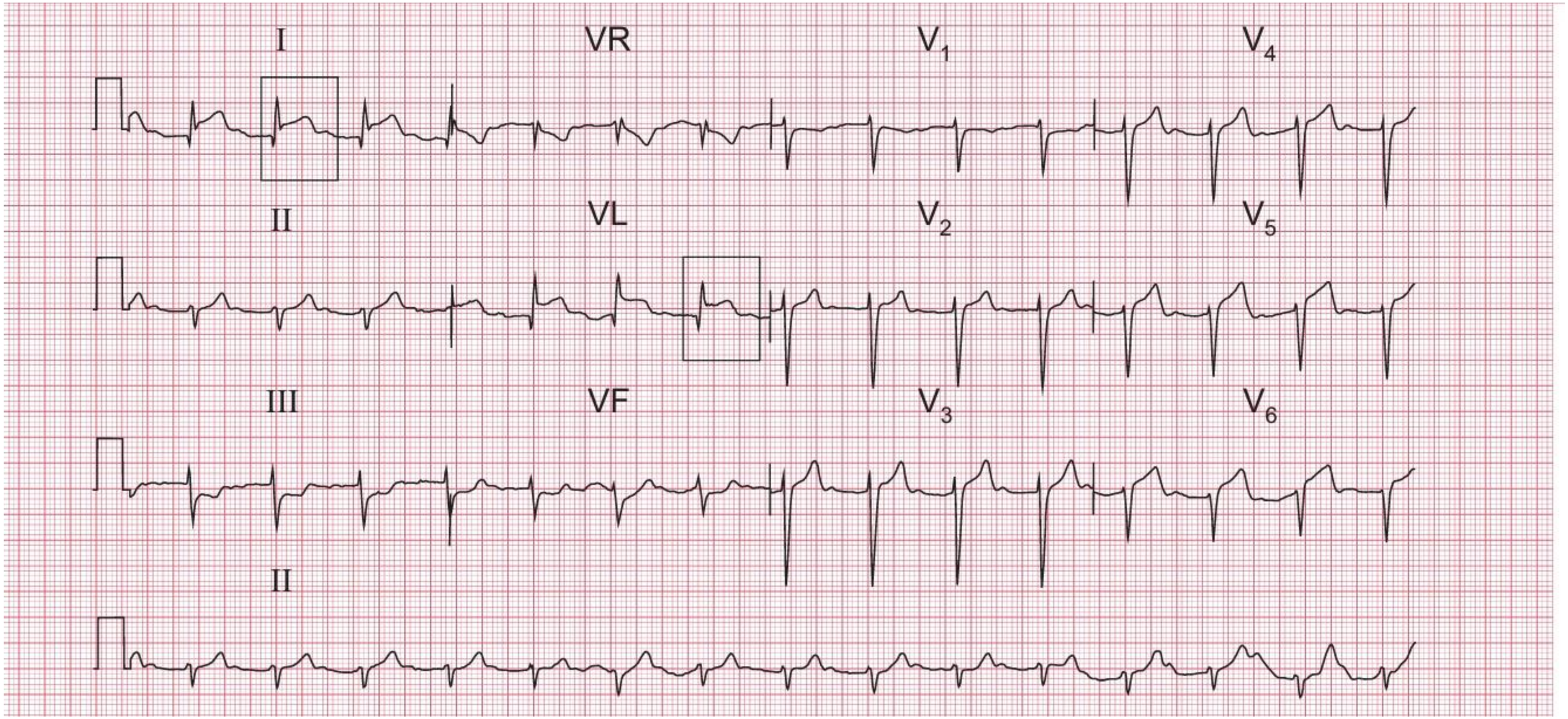


Raised ST segments in leads III and VF

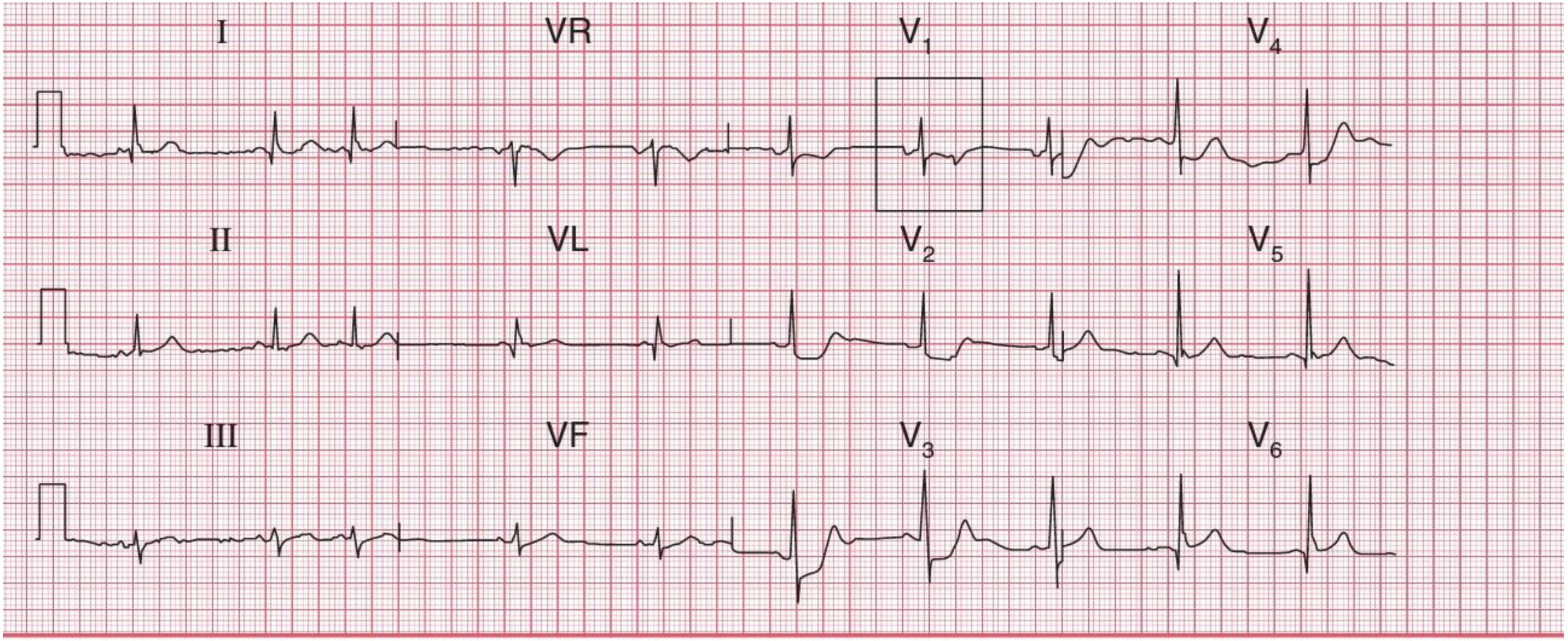
Anterior STEMI



Lateral STEMI



Posterior STEMI



Cardiac biomarkers

Serial measurements of cardiac troponin concentration should be taken. In unstable angina, there is no detectable rise in troponin and the diagnosis is made on the basis of the clinical features and investigations such as ECG or coronary angiography. In contrast, MI causes a rise in plasma concentrations of troponin T and I and other cardiac muscle enzymes . Levels of troponins T and I increase within 3–6 hours, peak at about 36 hours and remain elevated for up to 2 weeks. A full blood count may reveal the presence of a leucocytosis, which reaches a peak on the first day. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are also elevated. Lipids should be measured within 24 hours of presentation because there is often a transient fall in cholesterol in the 3 months following infarction.

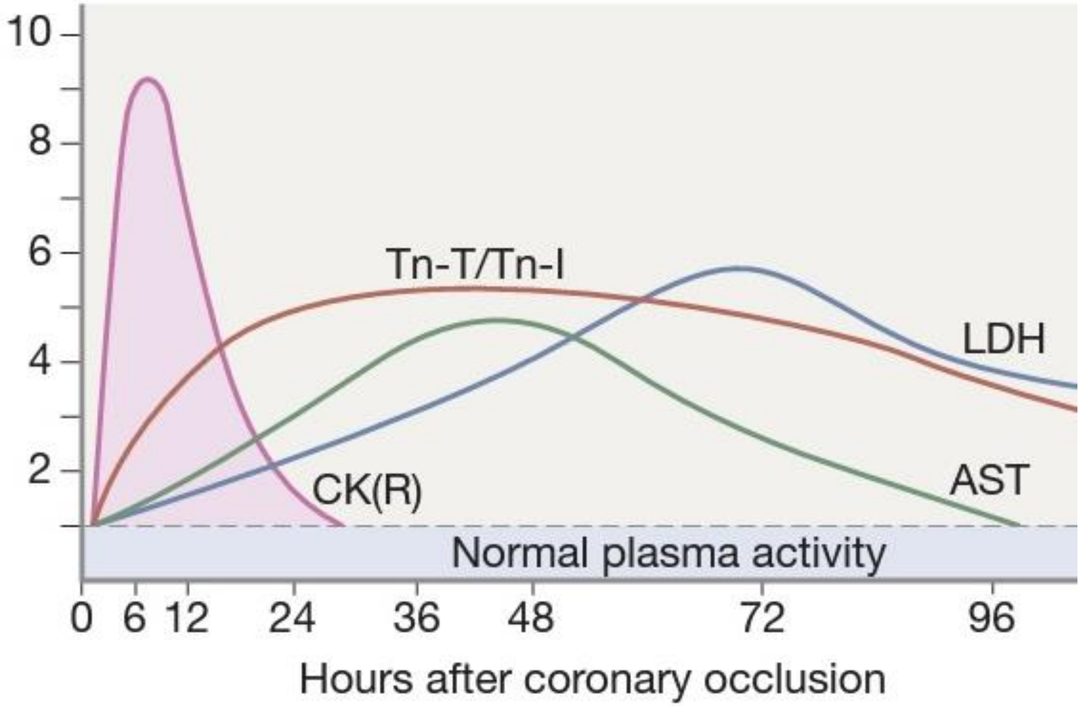


Fig. 16.69 Changes in plasma cardiac biomarker concentrations after myocardial infarction. Creatine kinase (CK) and troponins T (Tn-T) and I (Tn-I) are the first to rise, followed by aspartate aminotransferase (AST) and then lactate (hydroxybutyrate) dehydrogenase (LDH). In patient treated with reperfusion therapy, a rapid rise in plasma creatine kinase (curve CK(R)) occurs, due to a washout effect.

Radiography

A chest X-ray should be performed since this may demonstrate pulmonary oedema that is not evident on clinical examination . The heart size is often normal but there may be cardiomegaly due to pre-existing myocardial damage.

Echocardiography

Echocardiography is normally performed before discharge from hospital and is useful for assessing ventricular function and for detecting important complications, such as mural thrombus, cardiac rupture, ventricular septal defect, mitral regurgitation and pericardial effusion.

Coronary angiography

Coronary arteriography should be considered with a view to revascularisation in all patients at moderate or high risk of a further event, including those who fail to settle on medical therapy, those with extensive ECG changes, those with an elevated cardiac troponin and those with severe pre-existing stable angina . This often reveals disease that is amenable to PCI or urgent CABG

Management

All patients with suspected acute coronary syndrome should be admitted urgently to hospital because there is a risk of death or recurrent myocardial ischaemia during the early unstable phase. Appropriate medical therapy can reduce the incidence of these complications by at least 60%. Patients should ideally be managed in a dedicated cardiac unit, where the necessary expertise, monitoring and resuscitation facilities are available. Clinical risk factor analysis using tools such as the GRACE score should be performed to identify patients that should be selected for intensive therapy, and specifically early inpatient coronary angiography (thresholds vary, but a score of 140 points or more supports early intervention). If there are no complications and risk factor analysis shows that angiography is not required, the patient can be mobilised from the second day and discharged after 2–3 days. Low-risk patients without spontaneous angina may be considered for an exercise tolerance test 4-6 weeks after the acute coronary syndrome. This will help to identify those individuals who may require further investigation, and may help to boost the confidence of the remainder.

Analgesia

Adequate analgesia is essential, not only to relieve distress but also to lower adrenergic drive and thereby reduce vascular resistance, BP, infarct size and susceptibility to ventricular arrhythmias. Intravenous opiates (initially, morphine sulphate 5–10 mg or diamorphine 2.5–5 mg) and antiemetics (initially, metoclopramide 10 mg) should be administered, and titrated until the patient is comfortable. Intramuscular injections should be avoided because the clinical effect may be delayed by poor skeletal muscle perfusion, and a painful haematoma may form following thrombolytic or antithrombotic therapy.

Reperfusion therapy

Immediate reperfusion therapy with PCI is indicated when the ECG shows new bundle branch block or characteristic ST-segment elevation in two contiguous leads of 1 mm or more in the limb leads or 2 mm or more in the chest leads. This is the treatment of choice for those presenting within 12 hours of symptom onset . If PCI cannot be performed within 120 minutes for any reason, and thrombolysis is contraindicated, the procedure should be performed as soon as practically possible. Patients should be considered for PCI within the first 24 hours, even if they have reperfused spontaneously or with thrombolytic therapy. Coronary artery patency is restored in over 95% of patients undergoing PCI. The procedure preserves left ventricular function with a marked reduction in the progression to heart failure, more than halves rates of recurrent MI and dramatically improves mortality with more than 95% 1-year survival rates in clinical trials. Successful therapy is also associated with rapid pain relief, resolution of acute ST elevation and occasional transient arrhythmias. Reperfusion therapy with PCI confers no immediate mortality benefit in patients with non-ST segment elevation acute coronary syndrome. Selected medium- to high-risk patients do benefit from in-hospital coronary angiography and coronary revascularisation but this does not need to take place in the first 12 hours unless there are high-risk features, such as ongoing chest pain or ECG changes.

Thrombolytic therapy

If primary PCI cannot be achieved in a timely manner in patients with ST-segment elevation MI , thrombolytic therapy should be administered. Although the survival advantage is not as good as primary PCI, mortality is reduced and this is maintained for at least 10 years. The benefit of thrombolytic therapy is greatest in those patients who receive treatment within the first 12 hours and especially the first 2 hours. Modern thrombolytic agents, such as tenecteplase (TNK) and reteplase (rPA), are analogues of human tissue plasminogen activator and can be given as an intravenous bolus, allowing prompt treatment to be given in the emergency department or in the pre-hospital setting. The major hazard of thrombolytic therapy is bleeding. Cerebral haemorrhage causes 4 extra strokes per 1000 patients treated, and the incidence of other major bleeds is between 0.5% and 1%. Accordingly, the treatment should be withheld if there is a significant risk of serious bleeding . For some patients, thrombolytic therapy is contraindicated or fails to achieve coronary arterial reperfusion . Emergency PCI may then be considered, particularly where there is evidence of cardiogenic shock. Even where thrombolysis successfully achieves reperfusion, PCI should be considered within 24 hours to prevent recurrent infarction and improve outcome.

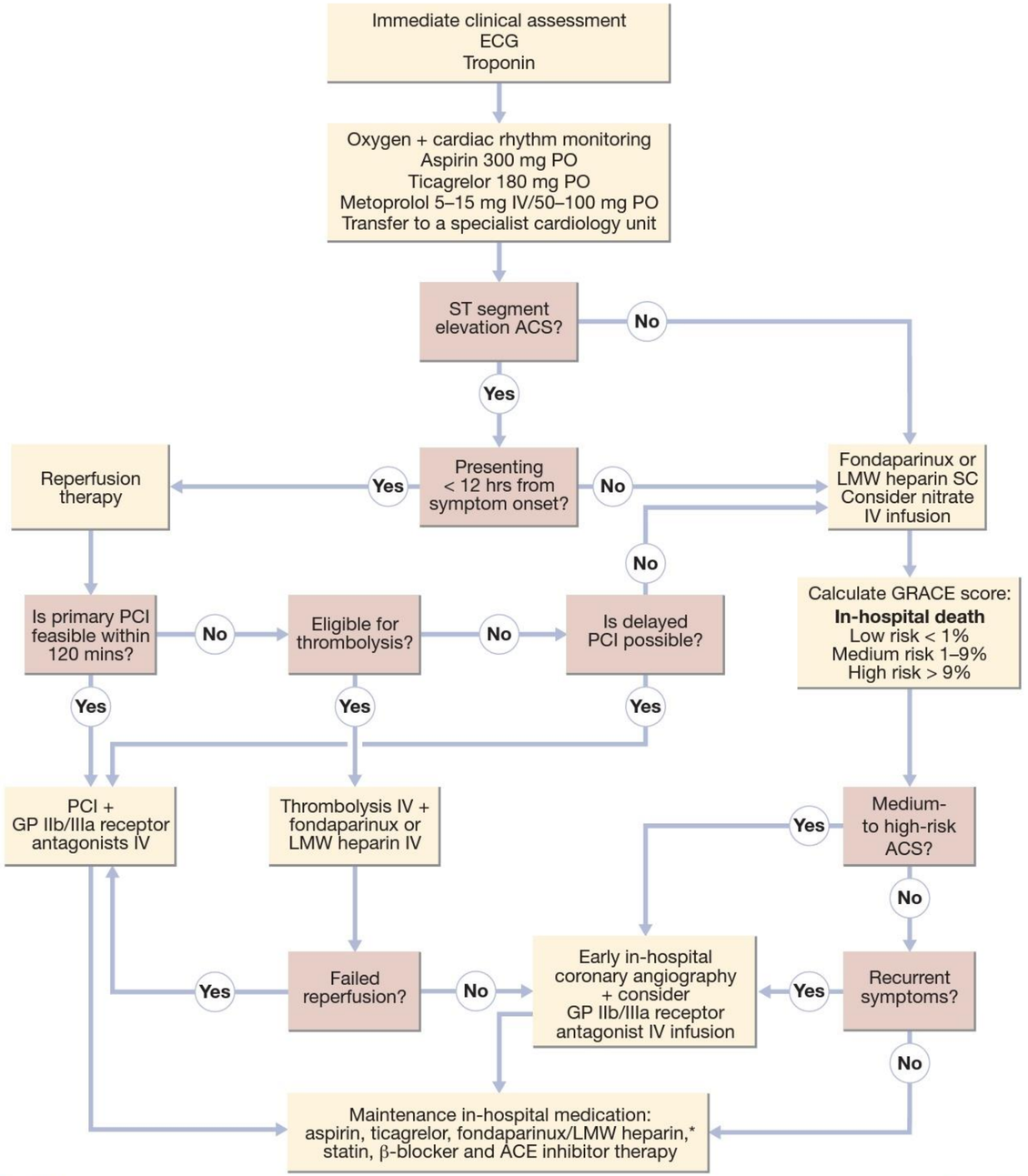


Fig. 16.70 **Summary of treatment for acute coronary syndrome (ACS).** *Not required following PCI. For details of the GRACE score, see Figure 16.62. (ACE = angiotensin-converting enzyme; ECG = electrocardiogram; GP = glycoprotein; IV = intravenous; LMW = low-molecular-weight; PCI = percutaneous coronary intervention; PO = by mouth; SC = subcutaneous) *Adapted from SIGN 93, Feb 2007, and updated in SIGN 148, April 2016.*

16.52 Relative contraindications to thrombolytic therapy

- Active internal bleeding
- Previous subarachnoid or intracerebral haemorrhage
- Uncontrolled hypertension
- Recent surgery (within 1 month)
- Recent trauma (including traumatic resuscitation)
- High probability of active peptic ulcer
- Pregnancy

Antithrombotic therapy

Oral administration of 75–325 mg aspirin daily improves survival, with a 25% relative risk reduction in mortality. The first tablet (300 mg) should be given orally within the first 12 hours and therapy should be continued indefinitely if there are no side-effects. A P2Y12 receptor antagonist (ticagrelor (180 mg, followed by 90 mg twice daily), prasugrel (60 mg, followed by 10 mg daily) or clopidogrel (300 mg, followed by 75 mg daily)) should be given in combination with aspirin for up to 12 months. Glycoprotein IIb/IIIa receptor antagonists, such as tirofiban and abciximab, block the final common pathway of platelet aggregation and are potent inhibitors of platelet-rich thrombus formation. They are of particular benefit in highrisk patients with acute coronary syndromes who undergo PCI, especially those with a high thrombus burden at angiography or who have received inadequate prior antiplatelet therapy. These intravenous agents should be administered in addition to oral aspirin and a P2Y12 receptor antagonist. Anticoagulation further reduces the risk of thromboembolic complications, and prevents re-infarction in the absence of reperfusion therapy or after successful thrombolysis. Anticoagulation can be achieved using unfractionated heparin, fractioned (low-molecular-weight) heparin or a pentasaccharide, such as subcutaneous fondaparinux (2.5 mg daily). Comparative clinical trials show that the pentasaccharides have the best safety and efficacy profile but low-molecular-weight heparin, such as subcutaneous enoxaparin (1 mg/kg twice daily), is a reasonable alternative. Anticoagulation should be continued for 8 days or until discharge from hospital or coronary revascularisation has been completed. A period of treatment with an oral anticoagulant should be considered if there is persistent AF or evidence of extensive anterior infarction with mural thrombus because these patients are at increased risk of systemic thromboembolism.

Anti-anginal therapy

Sublingual glyceryl trinitrate (300–500 μg) is a valuable first-aid measure in unstable angina or threatened infarction, and intravenous nitrates (glyceryl trinitrate 0.6–1.2 mg/hr or isosorbide dinitrate 1–2 mg/hr) are useful for the treatment of left ventricular failure and the relief of recurrent or persistent ischaemic pain. Intravenous β-blockade (atenolol 5–10 mg or metoprolol 5–15 mg given over 5 min) relieves pain, reduces arrhythmias and improves short-term mortality in patients who present within 12 hours of symptom onset . However, they should be avoided if there is heart failure (pulmonary oedema), hypotension (systolic BP < 105 mmHg) or bradycardia (heart rate < 65/min). Nifedipine or amlodipine can be added if there is persistent chest discomfort but these drugs may cause tachycardia if used alone. Verapamil and diltiazem should be used if β-blockade is contraindicated. In the longer term, treatment with an oral β-blocker reduces long-term mortality by approximately 25% among the survivors of an acute MI, especially those with left ventricular systolic dysfunction. Patients with heart failure, COPD or peripheral arterial disease appear to derive similar secondary preventative benefits from β-blocker therapy and should receive maintenance therapy unless poorly tolerated. Unfortunately, a minority of patients do not tolerate β-blockade because of bradycardia, AV block, hypotension or asthma.

16.51 Late management of myocardial infarction

Risk stratification and further investigation

See text for details

Lifestyle modification

- Diet (weight control, lipid-lowering, 'Mediterranean diet')
- Cessation of smoking
- Regular exercise

Secondary prevention drug therapy

- Antiplatelet therapy (aspirin and/or clopidogrel)
- β-blocker
- ACE inhibitor/ARB
- Statin
- Additional therapy for control of diabetes and hypertension
- Mineralocorticoid receptor antagonist

Rehabilitation

Devices

- Implantable cardiac defibrillator (high-risk patients)

(ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker)

Renin–angiotensin blockade

Long-term treatment with ACE inhibitors such as enalapril (10 mg twice daily) or ramipril (2.5–5 mg twice daily) can counteract ventricular remodelling, prevent the onset of heart failure, improve survival, reduce recurrent MI and avoid rehospitalisation. The benefits are greatest in those with overt heart failure (clinical or radiological) but extend to patients with asymptomatic left ventricular systolic dysfunction and those with preserved left ventricular function. They should be considered in all patients with acute coronary syndrome. Caution must be exercised in hypovolaemic or hypotensive patients because ACE inhibition may exacerbate hypotension and impair coronary perfusion. In patients intolerant of ACE inhibitors, ARBs such as valsartan (40160 mg twice daily) or candesartan (4–16 mg daily) are alternatives that are better tolerated.

Mineralocorticoid receptor antagonists

Patients with acute MI and left ventricular dysfunction (ejection fraction < 35%) and either pulmonary oedema or diabetes mellitus further benefit from additional mineralocorticoid receptor antagonists (eplerenone 25–50 mg daily, or spironolactone 25–50 mg daily).

Lipid-lowering therapy

The benefits of lowering serum cholesterol following acute coronary syndrome have been demonstrated in several large-scale randomised trials. All patients should receive therapy with HMG CoA reductase enzyme inhibitors (statins) after acute coronary syndrome, irrespective of serum cholesterol concentrations. Patients with serum LDL cholesterol concentrations above 3.2 mmol/L (approximately 120 mg/dL) benefit from more intensive therapy, such as atorvastatin (80 mg daily). Other agents, such as ezetimibe, fibrates, anion exchange resins and injectable PCSK9 inhibitors, may be used in cases where total cholesterol or LDL cholesterol cannot be lowered adequately using statins alone.

Smoking cessation

The 5-year mortality of patients who continue to smoke cigarettes is double that of those who quit smoking at the time of their acute coronary syndrome. Giving up smoking is the single most effective contribution a patient can make to their future. The success of smoking cessation can be increased by supportive advice and pharmacological therapy.

Diet and exercise

Maintaining an ideal body weight, eating a **Mediterranean-style diet**, taking regular exercise, and achieving good control of hypertension and diabetes mellitus may all improve the long-term outlook.

Rehabilitation

When there are no complications, the patient can mobilise on the second day, return home in 2–3 days and gradually increase activity, with the aim of returning to work in 4 weeks. The majority of patients may resume driving after 1–4 weeks, although, in most countries, drivers of heavy goods and public service vehicles require special assessment before returning to work. Emotional problems, such as denial, anxiety and depression, are common and must be addressed. Some patients are severely and even permanently incapacitated as a result of the psychological effects of acute coronary syndrome rather than the physical ones, and all benefit from thoughtful explanation, counselling and reassurance. Many patients mistakenly believe that stress was the cause of their heart attack and may restrict their activity inappropriately.

The patient's spouse or partner will also require emotional support, information and counselling. Formal rehabilitation programmes, based on graded exercise protocols with individual and group counselling, are often very successful and, in some cases, have been shown to improve quality of life and long-term outcome.

Implantable defibrillators

These devices are of benefit in preventing sudden cardiac death in patients who have severe left ventricular impairment (ejection fraction $\leq 30\%$) after MI.

Type 2 myocardial infarction

The optimal management and treatment of patients with type 2 MI has yet to be established. There is currently no evidence that treatments for type 1 MI are effective in the setting of type 2 MI. The focus for patients with type 2 MI should be on treating the underlying cause of their presentation and, where applicable, their previously undiagnosed concomitant CAD.

Prognosis

The prognosis of patients who have survived an acute coronary syndrome is related to the extent of residual myocardial ischaemia, the degree of myocardial damage and the presence of ventricular arrhythmias. In almost one-quarter of all cases of MI, death occurs within a few minutes without medical care. Half the deaths occur within 24 hours of the onset of symptoms and about 40% of all affected patients die within the first month. The prognosis of those who survive to reach hospital is much better, with a 28-day survival of more than 85%. Patients with unstable angina have a mortality of approximately half that of patients with MI. Early death is usually due to an arrhythmia and is independent of the extent of MI. However, late outcomes are determined by the extent of myocardial damage, and unfavourable features include poor left ventricular function, AV block and persistent ventricular arrhythmias. The prognosis is worse for anterior than for inferior infarcts. Bundle branch block and high cardiac marker concentrations both indicate extensive myocardial damage. Old age, depression and social isolation are also associated with a higher mortality. Of those who survive an acute attack, more than 80% live for a further year, about 75% for 5 years, 50% for 10 years and 25% for 20 years.

THANK YOU FOR LISTENING