



# European Resuscitation Council Guidelines for Resuscitation 2005

## Section 5. Initial management of acute coronary syndromes

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### Introduction

The incidence of acute myocardial infarction (AMI) is decreasing in many European countries.<sup>1</sup> Although in-hospital mortality from AMI has been reduced significantly by modern reperfusion therapy and improved secondary prophylaxis,<sup>1</sup> the overall 28-day mortality is virtually unchanged because about two thirds of those that die do so before arrival at hospital.<sup>2</sup> Thus, the best chance of improving survival after AMI is by improving treatment in the early, and particularly the out-of-hospital, phase of the disease.

The term acute coronary syndrome (ACS) encompasses three different entities within the acute manifestation of coronary heart disease: ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina pectoris (UAP) (Figure 5.1). The common pathophysiology of ACS is a ruptured or eroded atherosclerotic plaque.<sup>3</sup> Electrocardiographic characteristics (absence or presence of ST elevation) differentiate STEMI from the other forms of ACS. A NSTEMI or UAP may present with ST segment depression or non-specific ST segment wave abnormalities, or even a normal ECG. In the absence of ST elevation, an increase in the plasma concentration of cardiac markers, particularly troponin T or I as the most specific markers of myocardial cell necrosis, indicates NSTEMI.

Acute coronary syndromes are the commonest cause of malignant arrhythmias leading to sudden cardiac death. The therapeutic goals are to treat acute life-threatening conditions, such as ventricular fibrillation (VF) or extreme bradycardias, and to preserve left ventricular function and prevent heart failure by minimising the extent of any myocardial infarction. These guidelines address the first hours after onset of symptoms. Out-of-hospital treatment and initial therapy in the emergency department may vary according to local capabilities, resources and regulations. The data supporting out-of-hospital treatment are usually extrapolated from studies of initial treatment early after hospital admission; there are only few high-quality out-of-hospital studies. Comprehensive guidelines for the diagnosis and treatment of ACS with and without ST elevation have been published by the European Society of Cardiology and the American College of Cardiology/American Heart Association.<sup>4,5</sup> The current recommendations are in line with these guidelines.

### Diagnostic tests in acute coronary syndromes

Since early treatment offers the greatest benefits, and myocardial ischaemia is the leading precipitant of sudden cardiac death, it is essential that the

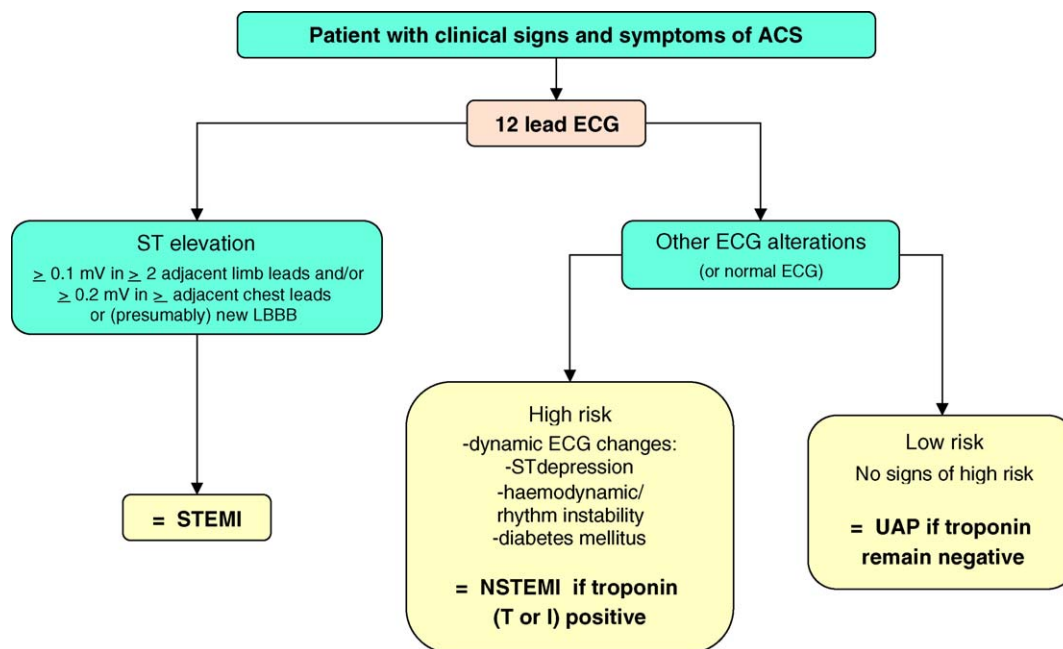


Figure 5.1 Classification of acute coronary syndromes.

public are aware of the typical symptoms associated with ACS. Patients at risk, and their families, should be able to recognise characteristic symptoms such as chest pain, which may radiate into other areas of the upper body, often accompanied by other symptoms including dyspnoea, sweating, nausea or vomiting and syncope. They should understand the importance of early activation of the emergency medical service (EMS) system and, ideally, should be trained in basic life support (BLS).

EMS dispatchers must be trained to recognize ACS symptoms and to ask targeted questions. When an ACS is suspected, an EMS crew trained in advanced life support (ALS) and capable of making the diagnosis and starting treatment should be alerted. The sensitivity, specificity and clinical impact of various diagnostic strategies have been evaluated for ACS/AMI. These include signs and symptoms, the 12-lead electrocardiogram (ECG) and biochemical markers of cardiac risk.

### Signs and symptoms of ACS/AMI

Even though typical symptoms such as radiating chest pain, shortness of breath or sweating may be more intense and generally last longer in patients with AMI, they are not adequately specific for a reliable diagnosis of AMI. A 12-lead ECG, cardiac biomarkers and other diagnostic tests are required before ACS or AMI can be ruled out in the presence of a typical history. Atypical symptoms or unusual

presentations may occur in the elderly, in females, and in people with diabetes.<sup>6,7</sup>

### 12-lead ECG

A 12-lead ECG is the key investigation for assessment of an ACS. In case of STEMI, a 12-lead ECG can indicate the need for immediate reperfusion therapy (e.g., primary percutaneous coronary intervention (PCI) or prehospital thrombolysis). Recording of a 12-lead ECG out-of-hospital enables advanced notification to the receiving facility and expedites treatment decisions after hospital arrival; in many studies, the time from hospital admission to initiating reperfusion therapy is reduced by 10–60 min.<sup>8–10</sup> Recording and transmission of diagnostic quality ECGs to the hospital takes usually less than 5 min. Trained EMS personnel (emergency physicians, paramedics and nurses) can identify STEMI, defined by ST elevation of  $\geq 0.1$  mV elevation in at least two adjacent limb leads or  $> 0.2$  mV in two adjacent precordial leads, with high specificity and sensitivity comparable to diagnostic accuracy in the hospital.<sup>11–13</sup>

### Biomarkers

In the presence of a suggestive history, the absence of ST elevation on the ECG, and elevated concentrations of biomarkers (troponin T and troponin I, CK, CK-MB, myoglobin) characterise non-STEMI

and distinguish it from STEMI and unstable angina, respectively.<sup>3</sup> Elevated concentrations of troponin are particularly helpful in identifying patients at increased risk of adverse outcome.<sup>14</sup> However, the delay in release of biomarkers from damaged myocardium prevents their use in diagnosing myocardial infarction in the first 4–6 h after the onset of symptoms.<sup>15</sup>

## Principles of acute treatment for ACS

### Nitrates

Glyceryl trinitrate is an effective treatment for ischaemic chest pain (Figure 5.2) and has some beneficial haemodynamic effects, e.g., dilation of the venous capacitance vessels, coronary arteries and, to a minor degree, peripheral arteries. Glyceryl trinitrate may be considered if the systolic blood pressure is higher than 90 mmHg and the patient has ongoing ischaemic chest pain. Glyceryl trinitrate can be useful in the treatment of acute pulmonary congestion. Do not use nitrates in patients with hypotension (systolic blood pressure  $\leq 90$  mmHg), particularly if combined with bradycardia, nor in patients with inferior infarction and suspected right ventricular involvement. Use of nitrates under these circumstances may cause a precipitous decrease in blood pressure and cardiac output.

### Morphine

Morphine is the analgesic of choice for nitrate-refractory pain. Being a dilator of venous capacitance vessels, it may have additional benefit in patients with pulmonary congestion. Give morphine in initial doses of 3–5 mg intravenously and repeat every few minutes until the patient is pain free.

### Oxygen

Give supplementary oxygen ( $4\text{--}8\text{ l min}^{-1}$ ) to all patients with arterial oxygen saturation  $<90\%$  and/or pulmonary congestion. Despite lack of proof for long-term benefit of supplementary oxygen,<sup>16</sup> give it to all patients with uncomplicated STEMI; it will benefit patients with unrecognised hypoxia.

### Acetylsalicylic acid

Several large randomised controlled trials indicate decreased mortality when acetylsalicylic acid (ASA), 75–325 mg, is given to patients in hospital with ACS.<sup>17,18</sup> A few studies have suggested reduced mortality if ASA is given earlier.<sup>19</sup> Therefore, give ASA as soon as possible to all patients with suspected ACS unless the patient has a known true allergy to ASA. The initial dose of ASA to be chewed is 160–325 mg. Other forms of ASA (soluble, IV) may be as effective as chewed tablets.<sup>20</sup>

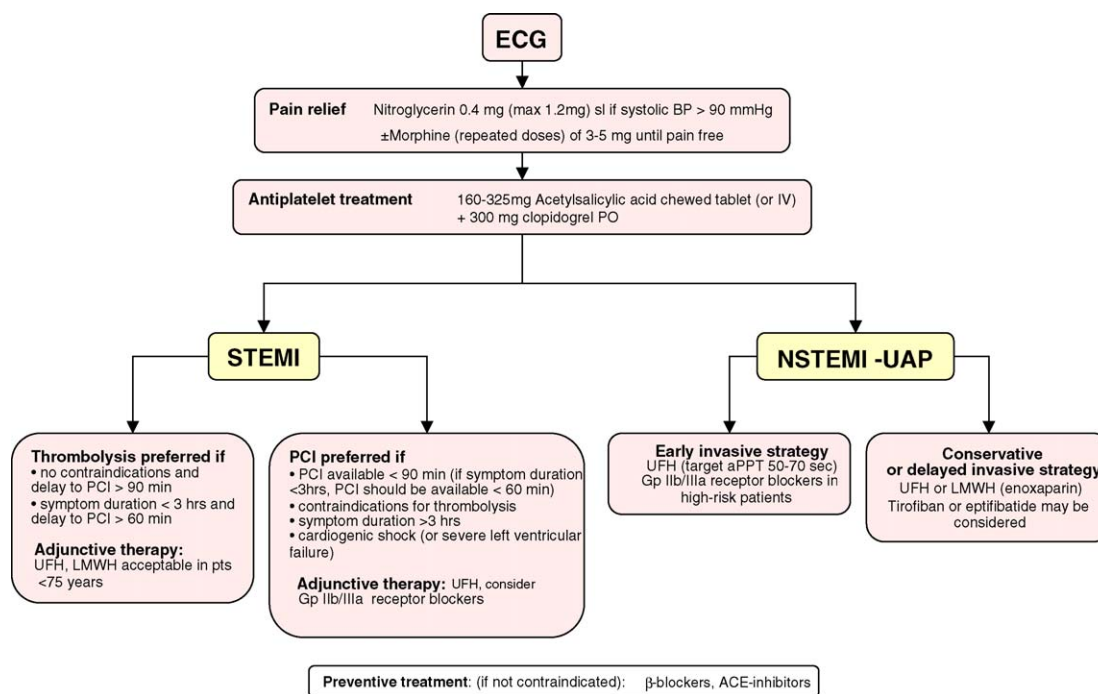


Figure 5.2 Early treatment of patients with signs/symptoms of ACS.

## Reperfusion therapy

Reperfusion therapy is the most important advance in the treatment of AMI in the last 20 years. Large clinical trials have proven that fibrinolytic therapy in ACS patients with STEMI or new or presumed new LBBB, who present within 12 h of onset of symptoms, reduces short- and long-term mortality.<sup>17,21–23</sup> The benefit achieved with fibrinolytic therapy is profoundly time dependent; it is particularly effective if given within the first 3 h of the onset of symptoms.<sup>17,21,22,24</sup> The efficacy of primary PCI is also time-sensitive but less so than fibrinolysis.<sup>25</sup>

### Out-of-hospital fibrinolysis

A meta-analysis of six trials involving 6434 patients documented a 17% decrease in the mortality among patients treated with out-of-hospital fibrinolysis compared with in-hospital fibrinolysis.<sup>26</sup> The average time gained by out-of-hospital fibrinolysis was 60 min, and the results were independent of the experience of the provider. Thus, giving fibrinolytics out-of-hospital to patients with STEMI or signs and symptoms of an ACS with presumed new LBBB is beneficial. Fibrinolytic therapy can be given safely by trained paramedics, nurses or physicians using an established protocol.<sup>27–29</sup> The efficacy is greatest within the first 3 h of the onset of symptoms. An effective and safe system for out-of-hospital thrombolytic therapy requires adequate facilities for the diagnosis and treatment of STEMI and its complications. Ideally, there should be a capability to communicate with experienced hospital doctors (e.g., emergency physicians or cardiologists).

Patients with symptoms of ACS and ECG evidence of STEMI (or presumably new LBBB or true posterior infarction) presenting directly to the emergency department should be given fibrinolytic therapy as soon as possible unless there is immediate access to primary PCI within 90 min.

### Risks of fibrinolytic therapy

Healthcare professionals who give fibrinolytic therapy must be aware of its contraindications (Table 5.1) and risks. Patients with large AMIs (e.g., indicated by extensive ECG changes) are likely to derive the greatest benefit from fibrinolytic therapy. Benefits of fibrinolytic therapy are less impressive in inferior wall infarctions than in anterior infarctions. Older patients have an absolute higher risk of death, but the absolute benefit of fibrinolytic therapy is similar to that of younger patients. Patients over 75 years of age have an increased

**Table 5.1** Contraindications for thrombolysis<sup>a</sup>.

<b>Absolute contraindications</b>	
Haemorrhagic stroke or stroke of unknown origin at any time	
Ischaemic stroke in the preceding 6 months	
Central nervous system damage or neoplasms	
Recent major trauma/surgery/head injury (within the preceding 3 weeks)	
Gastro-intestinal bleeding within the last month	
Known bleeding disorder	
Aortic dissection	
<b>Relative contraindications</b>	
Transient ischaemic attack in preceding 6 months	
Oral anticoagulant therapy	
Pregnancy within 1 week post partum	
Non-compressible punctures	
Traumatic resuscitation	
Refractory hypertension (systolic blood pressure >180 mmHg)	
Advanced liver disease	
Infective endocarditis	
Active peptic ulcer	

<sup>a</sup> According to the guidelines of the European Society of Cardiology.

risk of intracranial bleeding from fibrinolysis; thus, the absolute benefit of thrombolysis is reduced by this complication.<sup>30</sup> The risk of intracranial bleeding in patients with a systolic blood pressure of over 180 mmHg is increased; this degree of hypertension is a relative contraindication to fibrinolytic therapy. The intracranial bleeding risk also depends in part on which fibrinolytic drug is used; the total mortality is lower with the more fibrin-specific thrombolytics (alteplase, tenecteplase, reteplase), but the intracranial bleeding risk is lower with streptokinase. The risk of intracranial bleeding is also increased by the use of antithrombotic therapy, particularly heparin.

### Primary percutaneous intervention

Coronary angioplasty with or without stent placement has become the first-line treatment for patients with STEMI, because it has been shown to be superior to fibrinolysis in the combined endpoints of death, stroke and reinfarction in several studies and meta-analyses.<sup>31,32</sup> This improvement was found when primary PCI was undertaken by a skilled person in a high-volume centre (i.e., >75 procedures per operator per year), with a delay of balloon inflation of not more than 90 min after first contact. In the randomised studies comparing primary PCI and fibrinolytic therapy, the typical delay from decision to the beginning of

treatment with either primary PCI or fibrinolytic therapy was less than 60 min; however, in registries that reflect standard practice more realistically, the delay was often longer. One study<sup>33</sup> and one post hoc analysis<sup>34</sup> comparing fibrinolytic therapy with primary PCI showed no difference in survival if fibrinolytic therapy was initiated within 2 or 3 h of onset of symptoms.

All patients presenting with STEMI and symptoms of ACS and presumably new LBBB presenting within 12 h after onset of symptoms should be evaluated for reperfusion therapy (fibrinolytic therapy or PCI). Primary PCI is preferred in patients with symptom duration of over 3 h, if a skilled team can undertake it within 90 min after first patient contact, and in all patients who have contraindications to fibrinolytic therapy. If the duration of symptoms is less than 3 h, treatment is more time-sensitive and the superiority of out-of-hospital fibrinolytic therapy, immediate in-hospital fibrinolytic therapy or transfer for primary PCI is not yet established clearly.

**Triage and interfacility transfer for primary PCI.** The risk of death, reinfarction or stroke is reduced if patients with STEMI are transferred promptly from community hospitals to tertiary care facilities for primary PCI.<sup>35</sup> It is unclear whether immediate fibrinolytic therapy (in- or out-of-hospital) or transfer for primary PCI is superior for patients presenting with STEMI with a symptom duration of <2–3 h.<sup>33,34</sup> Transfer of STEMI patients for primary PCI is reasonable for those presenting later than 3 h but less than 12 h after onset of symptoms, provided that the transfer can be achieved rapidly. Optimally, primary PCI should occur within 90 min from the first contact with the healthcare provider deciding to treat or transfer.

**Interfacility transfer for early PCI after fibrinolytic therapy.** Older studies, that did not include modern adjunctive drugs and PCI techniques with stenting, do not support a strategy of fibrinolytic therapy combined with early PCI. In contrast, several recent smaller studies support a strategy of in-hospital fibrinolytic therapy in a peripheral hospital followed by transfer for PCI within 24 h of fibrinolytic therapy.<sup>36,37</sup> The timing of PCI after fibrinolytic therapy, the use of coronary stents and control-group interventions differ widely among these trials.

There is insufficient evidence to recommend routine transfer of patients for early PCI after successful fibrinolytic therapy. Transfer for early PCI after is recommended for patients in cardiogenic shock, particularly for those younger than 75 years and for those who are haemodynamically unstable

or have persistent ischaemic symptoms after fibrinolytic therapy.

## Cardiogenic shock

Cardiogenic shock (and to some extent, severe left ventricular failure) is one of the complications of ACS and has a mortality rate of more than 50%. Cardiogenic shock in STEMI is not a contraindication to fibrinolytic therapy, but PCI is preferable. Early revascularisation (i.e., primary or facilitated PCI or surgery) is indicated for those patients who develop shock within 36 h after symptom onset of AMI and are suitable for revascularisation.<sup>38,39</sup>

Suspect right ventricular infarction in patients with inferior infarction, clinical shock and clear lung fields. ST segment elevation  $\geq 1$  mm in lead V4R is a useful indicator of right ventricular infarction. These patients have an in-hospital mortality of up to 30%, and many benefit greatly from reperfusion therapy (fibrinolytic therapy and/or PCI). Avoid nitrates and other vasodilators, and treat hypotension with intravenous fluid.

## Adjunctive treatment in reperfusion therapy in ACS

### Heparin

Heparin is an indirect inhibitor of thrombin, which in combination with ASA is used as an adjunct with fibrinolytic therapy or primary PCI and as an important part of treatment of unstable angina and STEMI. Limitations of unfractionated heparin include its unpredictable anticoagulant effect in individual patients, the need for it to be given intravenously and the need to monitor aPTT. Moreover, heparin can induce thrombocytopenia. Low-molecular-weight heparin has a more predictable anticoagulant effect with lower rates of thrombocytopenia. It can be given subcutaneously in a weight-adjusted dose and does not require laboratory monitoring. Low-molecular-weight heparins may accumulate in patients with impaired renal function.

### Unfractionated heparin versus low-molecular-weight heparin in NSTEMI

In comparison with unfractionated heparin (UFH), low-molecular-weight heparin (LMWH) (enoxaparin) reduces the combined endpoint of mortality, myocardial infarction and the need for urgent revascularisation, if given within the first 24–36 h of onset of symptoms of NSTEMI/UAP.<sup>40–42</sup> Although LMWH increases the incidence of minor bleeding, in comparison with UFH, the incidence of

serious bleeding is not increased. Early treatment with LMWH (enoxaparin) is the preferred therapy for patients with NSTEMI/UAP in addition to ASA, whenever a non-interventional strategy is planned. Consider UFH if reperfusion is planned in the first 24–36 h after symptom onset. Optimal target value of aPPT is 50–70 s. Avoid switching between UFH and LMWH, because it may increase bleeding complications.<sup>43</sup>

### Unfractionated heparin versus low-molecular-weight heparin in STEMI

Two large randomised controlled thrombolysis studies comparing LMWH with UFH demonstrated a reduced frequency of ischaemic complications when given to patients with STEMI within 6 h of the onset of symptoms.<sup>44,45</sup> This must be balanced against the increase in intracranial haemorrhage in patients over 75 years of age who receive LMWH.<sup>45</sup> There is no evidence to support giving LMWH to patients with STEMI proceeding to an invasive strategy. Thus, LMWH is an acceptable alternative to UFH as an ancillary therapy for patients younger than 75 years without significant renal dysfunction who are treated with fibrinolytic therapy. UFH is recommended as an ancillary therapy to fibrinolytic therapy in elderly patients and any STEMI patient for whom revascularisation is planned. The optimal target value of aPPT is 50–70 s. The use of heparin (preferably LMWH) depends partly on which fibrinolytic drug is used. Heparin is needed after shorter-acting drugs because of the rebound hypercoagulable state that occurs after a few hours, but not after streptokinase because the fibrinolytic effect of streptokinase lasts for about 48 h.

### Glycoprotein IIb/IIIa inhibitors

The platelet glycoprotein (Gp) IIb/IIIa receptor is the final common pathway to platelet aggregation. The synthetic substances eptifibatide and tirofiban modulate this receptor activity reversibly, whereas the receptor antibody abciximab blocks it irreversibly.

*Gp IIb/IIIa inhibitors in NSTEMI/unstable angina.* The incidences of death and recurrent ischaemia are reduced when Gp IIb/IIIa inhibitors are added to standard therapy including ASA and heparin in high-risk patients with UAP/NSTEMI treated with mechanical reperfusion.<sup>46</sup> High-risk features include persistent pain, haemodynamic or rhythm instability, diabetes, acute or dynamic ECG changes and any elevation in cardiac troponins. Tirofiban or eptifibatide failed to reduce death or recur-

rent ischaemia in patients with UA/NSTEMI without mechanical perfusion, but showed a reduction in 30-day mortality in a later meta-analysis.<sup>46</sup> In patients with UA/NSTEMI, abciximab, given in addition to standard therapy without mechanical intervention, resulted in a trend towards a worse outcome.<sup>47</sup> Therefore, in high-risk patients, give Gp IIb/IIIa inhibitors in addition to standard therapy in patients for whom revascularisation therapy is planned. If revascularisation therapy is not planned, tirofiban and eptifibatide can be given to high-risk NSTEMI/UAP patients in conjunction with ASA and LMWH. Do not give abciximab if PCI is not planned.

*Gp IIb/IIIa inhibitors in STEMI.* Gp IIb/IIIa receptor blockers in combination with a reduced dose of fibrinolytics do not reduce mortality in patients with STEMI, but increase bleeding risk in patients over 75 years of age.<sup>44,48</sup> Abciximab reduces mortality when given to patients with STEMI and planned primary PCI, but is not beneficial in patients not proceeding to primary PCI.<sup>46</sup> Prehospital use of abciximab may improve the patency of the infarct-related artery with regard to PCI.<sup>49</sup> There is no benefit in giving tirofiban in addition to standard therapy out of hospital or in the emergency department.<sup>50</sup> Abciximab may be helpful in reducing short-term mortality and short-term reinfarction in patients treated with PCI without fibrinolytic therapy. Abciximab is not recommended in combination with fibrinolytics in patients with STEMI.

### Clopidogrel

Clopidogrel inhibits the platelet ADP receptor irreversibly, which further reduces platelet aggregation in addition to that produced by ASA. Compared with ASA, there is no increased risk of bleeding with clopidogrel.<sup>51</sup> If given in addition to heparin and ASA within 4 h of presentation, clopidogrel improves outcome in patients with high-risk ACS.<sup>52,53</sup> There is a significant reduction in adverse ischaemic events at 28 days after elective PCI when clopidogrel is given at least 6 h before intervention.<sup>54</sup> A recent trial documented a significant reduction in the composite endpoint of an occluded infarct-related artery (TIMI flow grade 0 or 1) on angiography or death or recurrent myocardial infarction before angiography, when clopidogrel (300 mg loading dose, followed by 75 mg daily dose up to 8 days in hospital) is given to patients up to 75 years of age with STEMI who are treated with fibrinolytic therapy, ASA and heparin.<sup>55</sup>

Give a 300-mg oral loading dose of clopidogrel early, as well as standard care, to patients with ACS if they have an increase in serum cardiac

biomarkers and/or new ECG changes consistent with ischaemia when a medical approach or PCI is planned. Give clopidogrel to patients with STEMI up to 75 years of age receiving fibrinolytic therapy, ASA and heparin. Clopidogrel, 300 mg, can be given instead of ASA to patients with a suspected ACS who have a true allergy to or gastrointestinal intolerance of ASA.

### Primary and secondary prevention interventions

Start preventive interventions, at the latest, at the initial admission with a confirmed diagnosis of ACS. Give a beta-blocker as soon as possible unless contraindicated or poorly tolerated. Treat all patients with a statin (HMG co-enzyme A reductase inhibitor) unless contraindicated or poorly tolerated. Start an ACE inhibitor in all patients with STEMI, all patients with STEMI and left ventricular systolic impairment, and consider it in all other patients with STEMI unless contraindicated or poorly tolerated. In patients unable to tolerate an ACE inhibitor, an angiotensin receptor blocker may be used as a substitute in those patients with left ventricular systolic impairment.

#### Beta-blockers

Several studies, undertaken mainly in the pre-reperfusion era, indicate decreased mortality and incidence of reinfarction and cardiac rupture as well as a lower incidence of VF and supraventricular arrhythmia in patients treated early with a beta-blocker.<sup>56,57</sup> Intravenous beta-blockade may also reduce mortality in patients undergoing primary PCI who are not on oral beta-blockers.<sup>58</sup>

Haemodynamically stable patients presenting with an ACS should be given intravenous beta-blockers promptly, followed by regular oral therapy unless contraindicated or poorly tolerated. Contraindications to beta-blockers include hypotension, bradycardia, second- or third-degree AV block, moderate to severe congestive heart failure and severe reactive airway disease. Give a beta-blocker irrespective of the need for early revascularisation therapy.

#### Anti-arrhythmics

Apart from the use of a beta-blocker as recommended above, there is no evidence to support the use of anti-arrhythmic prophylaxis after ACS. VF accounts for most of the early deaths from ACS; the incidence of VF is highest in the first

hours after onset of symptoms.<sup>59,60</sup> This explains why numerous studies have been performed with the aim of demonstrating the prophylactic effect of anti-arrhythmic therapy. The effects of anti-arrhythmic drugs (lidocaine, magnesium, disopyramide, mexiletine, verapamil) given prophylactically to patients with ACS have been studied.<sup>61–63</sup> Prophylaxis with lidocaine reduces the incidence of VF but may increase mortality.<sup>58</sup> Routine treatment with magnesium in patients with AMI does not improve mortality.<sup>64</sup> Arrhythmia prophylaxis using disopyramide, mexiletine or verapamil, given within the first hours of an ACS, does not improve mortality.<sup>63</sup> In contrast, intravenous beta-blockers reduced the incidence of VF when given to patients with ACS.<sup>56,57</sup>

#### Angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers

Oral angiotensin-converting inhibitors (ACE) inhibitors reduce mortality when given to patients with acute myocardial infarction with or without early reperfusion therapy.<sup>65,66</sup> The beneficial effects are most pronounced in patients presenting with anterior infarction, pulmonary congestion or left ventricular ejection fraction <40%.<sup>66</sup> Do not give ACE inhibitors if the systolic blood pressure is less than 100 mmHg at admission or if there is a known contraindication to these drugs.<sup>66</sup> A trend towards higher mortality has been documented if an intravenous ACE inhibitor is started within the first 24 h after onset of symptoms.<sup>67</sup> Therefore, give an oral ACE inhibitor within 24 h after symptom onset in patients with AMI regardless of whether early reperfusion therapy is planned, particularly in those patients with anterior infarction, pulmonary congestion or left ventricular ejection fraction below 40%. Do not give intravenous ACE inhibitors within 24 h of onset of symptoms. Give an angiotensin receptor blocker (ARB) to patients intolerant of ACE inhibitors.

#### Statins

Statins reduce the incidence of major adverse cardiovascular events when given within a few days after onset of ACS. Start statin therapy within 24 h of onset of symptoms of ACS. If patients are already receiving statin therapy, do not stop it.<sup>68</sup>

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