Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology:

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Acute myocardial infarction • ST-segment elevation • Ischaemic heart disease • Reperfusion therapy • Secondary prevention
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## Abbreviations

- **ACE**: angiotensin-converting enzyme
- **ACT**: activated clotting time
- **AF**: atrial fibrillation
- **APTT**: activated partial prothrombin time
- **ARB**: angiotensin receptor blocker
- **AV**: atrio-ventricular
- **BMI**: body mass index
- **bpm**: beats per minute
- **CABG**: coronary artery bypass graft
make all decisions transparent to the user. The recommendations
development of guidelines have been established in order to
Because of the impact on clinical practice, quality criteria for the
ments have been issued in recent years by the European Society
strategies for a typical patient, suffering from a given condition,
taking into account the impact on outcome, as well as the risk/
favourably influenced by the thorough application of clinical
research, writing of guidelines, and implementing them in clinical
programmes for the recommendations. The loop between clinical
translate them into practice, so this is why implementation
becomes aware of the existence of guidelines, or simply do not
Some surveys have shown that the intended end-users are some-
PDA-downloadable versions are useful at the point of care.
importance. Pocket-sized versions and personal digital assistant
(PDA)-downloadable versions are useful at the point of care.
Some surveys have shown that the intended end-users are some-
time not aware of the existence of guidelines, or simply do not
translate them into practice, so this is why implementation
programmes for new guidelines form an important component
of the dissemination of knowledge. Meetings are organized by the
ESC, and directed towards its member National Societies
and key opinion leaders in Europe. Implementation meetings can
also be undertaken at national levels, once the guidelines have
been endorsed by the ESC member societies, and translated into
the national language. Implementation programmes are needed
because it has been shown that the outcome of disease may be
favourably influenced by the thorough application of clinical
recommendations.

Thus, the task of writing Guidelines or Expert Consensus documents
covers not only the integration of the most recent research, but also the creation of educational tools and implementation
programmes for the recommendations. The loop between clinical
research, writing of guidelines, and implementing them in clinical
practice can then only be completed if surveys and registries
are performed to verify that real-life daily practice is in keeping
with what is recommended in the guidelines. Such surveys
and registries also make it possible to evaluate the impact of
implementation of the guidelines on patient outcomes. Guidelines

A. Preamble

Guidelines and Expert Consensus Documents summarize and
evaluate all currently available evidence on a particular issue with
the aim of assisting physicians in selecting the best management
strategies for a typical patient, suffering from a given condition,
taking into account the impact on outcome, as well as the risk/
benefit ratio of particular diagnostic or therapeutic means. Guide-
lines are no substitutes for textbooks. The legal implications of
medical guidelines have been discussed previously.

A great number of Guidelines and Expert Consensus Docu-
ments have been issued in recent years by the European Society
of Cardiology (ESC) as well as by other societies and organizations.
Because of the impact on clinical practice, quality criteria for the
development of guidelines have been established in order to
make all decisions transparent to the user. The recommendations

for formulating and issuing ESC Guidelines and Expert Consensus
Documents can be found on the ESC website (http://www.
escardio.org/knowledge/guidelines/rules).

In brief, experts in the field are selected and undertake a
comprehensive review of the published evidence for management
and/or prevention of a given condition. Unpublished clinical trial
results have not been taken into account. A critical evaluation of
diagnostic and therapeutic procedures is performed including
assessment of the risk/benefit ratio. Estimates of expected health
outcomes for larger societies are included, where data exist. The
level of evidence and the strength of recommendation of particular
treatment options are weighed and graded according to predefined
scales, as outlined in Tables 1 and 2.

The experts of the writing panels have provided disclosure state-
ments of all relationships they may have which might be perceived
as real or potential sources of conflicts of interest. These disclosure
forms are kept on file at the European Heart House, headquarters
of the ESC. Any changes in conflict of interest that arise during the
writing period must be notified to the ESC. The Task Force report
was entirely supported financially by the ESC and was developed
without any involvement of the industry.

The ESC Committee for Practice Guidelines (CPG) supervises
and coordinates the preparation of new Guidelines and Expert
Consensus Documents produced by Task Forces, expert groups,
or consensus panels. The Committee is also responsible for the
endorsement process of these Guidelines and Expert Consensus
Documents or statements. Once the document has been finalized
and approved by all the experts involved in the Task Force, it is
submitted to outside specialists for review. The document is
revised, and finally approved by the CPG and subsequently
published.

After publication, dissemination of the message is of paramount
importance. Pocket-sized versions and personal digital assistant
(PDA)-downloadable versions are useful at the point of care.
and recommendations should help the physicians to make decisions in their daily practice; however, the ultimate judgement regarding the care of an individual patient must be made by the physician in charge of his/her care.

In order to keep this document surveyable and useful for the practising physician, the results of the studies on which the guidelines are based are not discussed in detail, especially those that have been published some time ago. For details, readers are referred to the publications in the reference list.

It must be recognized that even when excellent clinical trials have been undertaken, their results are open to interpretation, and that treatment options may be limited by resources. The Task Force realizes that the recommended diagnostic examinations and treatment options may not be available or affordable in all countries. Even in rich countries cost-effectiveness is becoming an increasingly important issue when deciding upon therapeutic strategies. 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 judgement, experience, and common sense.

When compared with the 2003 guidelines, the most significant changes made in the current document relate to antithrombotic therapies and the choice between mechanical vs. pharmacological reperfusion.

B. Introduction

1. The definition of acute myocardial infarction

Acute myocardial infarction can be defined from a number of different perspectives related to clinical, electrocardiographic (ECG), biochemical, and pathological characteristics. The present guidelines pertain to patients presenting with ischaemic symptoms and persistent ST-segment elevation on the ECG (STEMI). The great majority of these patients will show a typical rise of biomarkers of myocardial necrosis and progress to Q-wave myocardial infarction. Separate guidelines have been developed by another Task Force of the ESC for patients presenting with ischaemic symptoms but without persistent ST-segment elevation.
2. The pathogenesis of ST-segment elevation acute myocardial infarction

Most cases of STEMI are caused by an occlusion of a major coronary artery. Coronary occlusion and reduction in coronary blood flow are usually due to physical disruption of an atherosclerotic plaque with subsequent formation of an occluding thrombus. Concomitant coronary vasoconstriction and microembolization may be involved to some extent. Less commonly a thrombus may form from a superficial erosion of the endothelial surface.

The risk of plaque disruption depends on plaque composition and vulnerability (plaque type) and degree of stenosis (plaque size).3 As many as three-quarters of all infarct-related thrombi appear to evolve over plaques causing only mild to moderate stenosis. Even portions of the coronary arterial tree that appear normal by angiographic criteria often harbour a substantial burden of atherosclerosis. In particular, plaques with substantial outward remodelling, or ‘compensatory enlargement’, can have thin, fibrous caps and large lipid pools without encroachment of the lumen.4 However, severe stenoses are as likely to undergo plaque events leading to infarction as mild ones.5 There is frequently a delay (up to 2 weeks) between the rupture of a plaque and its clinical consequences.6 Inflammation plays an important role in plaque instability, and therefore in the pathogenesis of acute coronary syndromes. Circulating levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 are correlating with the clinical course and outcome of an acute coronary syndrome.7–9

The circadian variation of STEMI with a higher incidence in the early morning hours can be explained by the combination of β-adrenergic stimulation (increased vascular tone and blood pressure), hypercoagulability of the blood, and hyper-reactivity of platelets. Activities associated with increased sympathetic stimulation and vasoconstriction, such as physical or emotional stress, may also trigger plaque disruption and coronary thrombosis.10

Myocardial necrosis caused by complete coronary artery occlusion begins to develop after 15–30 min of severe ischaemia (no forward or collateral flow) and progresses from the subendothelium to the subepicardium in a time-dependent fashion (‘the wave-front phenomenon’). Reperfusion, including recruitment of collaterals, may save myocardium at risk from undergoing necrosis, and subcritical but persistent forward flow may extend the time window for achieving myocardial salvage.

The thrombotic response to plaque disruption is dynamic: thrombosis and clot lysis, often associated with vasospasm, occur simultaneously, and may cause intermittent flow obstruction and distal embolization.11 The absence of healing of an ageing plaque (incomplete re-endothelialization) and thrombus formation play an important role in the occurrence of sudden occlusive coronary thrombosis. In ~25–30% of patients undergoing primary percutaneous intervention (PCI), initial angiography shows a patent infarct-related artery.12 In these patients, it is presumed that spontaneous, endogenous lysis occurred before angiography.

Both platelets and fibrin are involved in the evolution of a persisting coronary thrombus. Whereas platelet adhesion and aggregation initiate mural thrombus formation, fibrin is important for the subsequent stabilization of the early and fragile platelet thrombus.

3. The natural history of STEMI

The true natural history of STEMI is hard to establish for a number of reasons: the common occurrence of silent infarction, the frequency of sudden death outside the hospital, and the varying methods and definitions used in the diagnosis of the condition. Community studies have consistently shown that the overall case fatality rate of patients with presumed myocardial infarction or acute coronary syndrome in the first month is ~50%, and of these deaths about half occur within the first 2 h.13 This high initial mortality seems to have altered little over the last years in contrast to hospital mortality.14 In contrast to community mortality, there has been a profound fall in the fatality of patients treated in hospital. Prior to the introduction of coronary care units in the 1960s, the in-hospital mortality seems to have averaged ~25–30%. A systematic review of mortality studies in the pre-reperfusion era of the mid-1980s showed an average in-hospital fatality of ~16%. With the widespread use of coronary interventions, fibrinolytic agents, antithrombotic therapy, and secondary prevention, the overall 1-month mortality has since been reduced to 4–6%, at least in those who participated in the latest randomized large-scale trials and qualified for fibrinolysis and/or coronary interventions.15,16 However, mortality rates in registry studies are much higher, suggesting that the patients included in the randomized studies17 are at a lower risk when compared with those seen in the real world.

C. First medical contact and emergency care flow

Optimal treatment of STEMI should be based on the implementation of an emergency medical system (EMS) supervising a network between hospitals with various levels of technology, connected by an efficient ambulance (or helicopter) service (Figure 1).
The main features of such a network are: clear definition of geographical areas of interest, shared protocols based on risk stratification, and transportation with appropriately equipped and staffed ambulances (or helicopters). The logistics of such a network are discussed in section I. A well-functioning regional system of care based on pre-hospital diagnosis and triage and fast transport to the most appropriate facility is key to the success of the treatment, and significantly improves outcome.18,19 For selection of the reperfusion strategy see Figure 2.

1. Initial diagnosis and early risk stratification

Rapid diagnosis and early risk stratification of patients presenting with acute chest pain are important to identify patients in whom early interventions can improve outcome. On the other hand, when the diagnosis of STEMI has been ruled out, attention can be focused on the detection of other cardiac or non-cardiac causes of the presenting symptoms such as aortic dissection, pulmonary embolism, and pericarditis. A working diagnosis of STEMI must first be made (Table 3). This is usually based on the history of chest pain/discomfort lasting for 10–20 min or more (not responding fully to nitroglycerine). Other locations such as epigastric or intercapsular are possible. Important clues are a previous history of coronary artery disease and radiation of the pain to the neck, lower jaw, or left arm. The pain may not be severe and, in the elderly particularly, other presentations such as fatigue, dyspnoea, faintness, or syncope are common. There are no individual physical signs diagnostic of STEMI, but many patients have evidence of autonomic nervous system activation (palor, 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 ECG should be obtained as soon as possible. Even at an early stage, the ECG is seldom normal. In the case of STEMI or new or presumed left bundle-branch block, reperfusion therapy needs to be given, and measures to initiate this treatment must be taken as soon as possible. However, the ECG can be equivocal in the early hours, and even in proven infarction it may never show the classical features of ST-segment elevation and new Q-waves. Repeated ECG recordings should be obtained and, when possible, the current ECG should be compared with previous records. Additional recordings of lead V1–V8 or V4R are helpful to make the diagnosis in selected cases (true posterior infarction or right ventricular infarction, respectively). ECG monitoring should be initiated as soon as possible in all patients to detect life-threatening arrhythmias. In patients with slowly evolving or stuttering myocardial infarction, serial ECGs should be taken to detect evolving infarction. Blood sampling for serum markers of necrosis is routinely done in the acute phase, but one should not wait for the results to initiate reperfusion treatment. The finding of elevated markers of necrosis may sometimes be helpful in deciding to perform coronary angiography (e.g. in patients with left bundle-branch block). Two-dimensional echocardiography has become a useful bedside technique in the triage of patients with acute chest pain. Regional wall motion abnormalities occur within seconds after coronary occlusion, well before necrosis. However, wall motion abnormalities are not specific for STEMI and may be due to ischaemia or an old infarction. Two-dimensional echocardiography is of particular value when the diagnosis of STEMI is uncertain, and other causes of chest pain such as acute aortic dissection, pericardial effusion, or pulmonary embolism are being considered. The performance of echocardiography should not delay the initiation of treatment. The absence of wall motion abnormalities excludes major myocardial ischaemia.

Older age, higher Killip class, elevated heart rate, lower systolic blood pressure, and anterior location of the infarct have been identified as the most important independent predictors of early mortality in clinical trials20 and registries.17,21 These characteristics contain most of the prognostic information in the clinical data available at the time of the first medical contact. Other independent predictors are previous infarction, height, time to treatment, diabetes, weight, and smoking status20.

2. Relief of pain, breathlessness, and anxiety

Relief of pain is of paramount importance, not only for humane reasons but also because the pain is associated with sympathetic activation, which causes vasoconstriction and increases the workload of the heart. I.v. opioids are the analgesics most commonly used in this context (e.g. 4–8 mg of morphine with additional doses of 2 mg at intervals of 5–15 min until the pain is relieved); intramuscular injections should be avoided (Table 4). Side effects include nausea and vomiting, hypotension with bradycardia, and respiratory depression. Antiemetics (e.g. metoclopramide 5–10 mg i.v.) may be administered concurrently with opioids.

### Table 3 Initial diagnosis

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of chest pain/discomfort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent ST-segment elevation or (presumed) new left bundle-branch block. Repeated ECG recordings often needed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated markers of myocardial necrosis (CK-MB, troponin). One should not wait for the results to initiate reperfusion treatment. 2-D echocardiography to rule out major acute myocardial ischaemia or other causes of chest pain/discomfort.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CK-MB** = creatine kinase MB form.

### Table 4 Relief of pain, breathlessness, and anxiety

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.v. opioids (4–8 mg morphine) with additional doses of 2 mg at 5–15 min intervals</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>O₂</strong> (2–4 L/min) if breathlessness or other signs of heart failure</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Tranquillizer—in very anxious patients</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

*Class of recommendation.

*Level of evidence.*
The hypotension and bradycardia will usually respond to atropine (0.5–1 mg i.v., up to a total dose of 2 mg), and respiratory depression may require ventilatory support. Oxygen (2–4 L/min by mask or nasal prongs) should be administered to those who are breathless or who have any features of heart failure or shock (see also Table 15). Non-invasive monitoring of blood oxygen saturation greatly helps in deciding on the need for oxygen administration or, in severe cases, ventilatory support. Non-steroidal anti-inflammatory drugs (NSAIDs) should not be given for pain relief because of possible prothrombotic effects.

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 tranquillizer, but opioids are all that is required in many cases.

3. Cardiac arrest
Many deaths occur in the very first hours after STEMI due to ventricular fibrillation (VF). The implementation of an organization to cope with out-of-hospital cardiac arrest is pivotal to provide prompt cardiopulmonary resuscitation, early defibrillation if needed, and effective advanced cardiac life support. Availability of automated external defibrillators is a key factor in increasing survival. Readers are referred to the latest guidelines on cardiopulmonary resuscitation provided by the European Resuscitation Council.

D. Pre-hospital or early in-hospital care

1. Restoring coronary flow and myocardial tissue reperfusion
For patients with the clinical presentation of STEMI within 12 h after symptom onset and with persistent ST-segment elevation or new or presumed left bundle-branch block, early mechanical (PCI) or pharmacological reperfusion should be performed.

There is general agreement that reperfusion therapy (primary PCI) should be considered if there is clinical and/or electrocardiographic evidence of ongoing ischaemia, even if, according to the patient, symptoms started >12 h before as the exact onset of symptoms is often unclear. However, there is no consensus as to whether PCI is also beneficial in patients presenting >12 h from symptom onset in the absence of clinical and/or electrocardiographic evidence of ongoing ischaemia. In a randomized study in STEMI patients presenting without persisting symptoms between 12 and 48 h after symptom onset (n = 347), PCI was associated with significant myocardial salvage, lending some support to an invasive strategy in these patients, but clinical outcomes were not better. In the OAT trial including 2166 stable patients with an occluded infarct-related vessel 3 to 28 calendar days after symptom onset, PCI did not improve clinical outcome, including in the subgroup of 331 patients randomized between 24 and 72 h after onset of infarction. No firm recommendations can be made given the limited data currently available (Table 5).

Figure 2 Reperfusion strategies. The thick arrow indicates the preferred strategy.
### Table 5: Reperfusion therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reperfusion therapy is indicated in all patients with history of chest pain/discomfort of &lt;12 h and with persistent ST-segment elevation or (presumed) new left bundle-branch block</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Reperfusion therapy should be considered if there is clinical and/or ECG evidence of ongoing ischaemia even if, according to patient, symptoms started &gt;12 h before</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Reperfusion using PCI may be considered in stable patients presenting &gt;12 to 24 h after symptom onset</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>PCI of a totally occluded infarct artery &gt;24 h after symptom onset in stable patients without signs of ischaemia</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td><strong>Primary PCI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preferred treatment if performed by an experienced team as soon as possible after FMC</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Time from FMC to balloon inflation should be &lt;2 h in any case and &lt;90 min in patients presenting early (e.g., &lt;2 h) with large infarct and low bleeding risk</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Indicated for patients in shock and those with contraindications to fibrinolytic therapy irrespective of time delay</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>Antiplatelet co-therapy</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>NSAID and COX-2 selective inhibitors</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Clopidogrel loading dose</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>GPIIb/IIIa antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abciximab</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>Tirofiban</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td><strong>Antithrombin therapy</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td><strong>Adjunctive devices</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td><strong>Rescue PCI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After failed fibrinolysis in patients with large infarcts if performed within 12 h after onset</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td><strong>Fibrinolytic therapy</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In the absence of contraindications (see Table 7) and if primary PCI cannot be performed within the recommended time (see above and Figure 2)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A fibrin-specific agent should be given</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Pre-hospital initiation of fibrinolytic therapy</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td><strong>Antiplatelet co-therapy</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>if not already on aspirin oral (soluble or chewable/non-enteric-coated) or i.v. dose of aspirin plus clopidogrel oral loading dose if age ≤75 years</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>if age &gt;75 years start with maintenance dose</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>Antithrombin co-therapy</strong>&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with alteplase, reteplase, and tenecteplase: enoxaparin i.v. bolus followed 15 min later by first s.c. dose; if age &gt;75 years no i.v. bolus and start with reduced first s.c. dose</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>if enoxaparin is not available; a weight-adjusted bolus of i.v. heparin followed by a weight-adjusted i.v. infusion with first aPTT control after 3 h</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>with streptokinase: an i.v. bolus of fondaparinux followed by an s.c. dose 24 h later</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>enoxaparin i.v. bolus followed 15 min later by first s.c. dose; if age &gt;75 years no i.v. bolus and start with reduced first s.c. dose</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>or a weight-adjusted dose of i.v. heparin followed by a weight-adjusted infusion</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>For doses see Tables 8, 9, and 10.
Different reperfusion strategies are depicted in Figure 2. In this figure the first medical contact is the place (ambulance or hospital) where, at least in principle, reperfusion therapy could be given. The (increasing) time limits for the different reperfusion strategies are also depicted schematically.

a. Percutaneous coronary interventions

The role of PCIs during the early hours of STEMI can be divided into primary PCI, PCI combined with pharmacological reperfusion therapy (facilitated PCI), and 'rescue PCI' after failed pharmacological reperfusion. Separate ESC Guidelines covering all indications for PCI have been published before.26

Primary PCI and delay times

Primary PCI is defined as angioplasty and/or stenting without prior or concomitant fibrinolytic therapy, and is the preferred therapeutic option when it can be performed expeditiously by an experienced team (Table 5). An experienced team includes not only interventional cardiologists but also skilled supporting staff. This means that only hospitals with an established interventional cardiology programme (24 h/7 days) should use primary PCI as a routine treatment option for patients presenting with the symptoms and signs of STEMI. Lower mortality rates among patients undergoing primary PCI are observed in centres with a high volume of PCI procedures.27,28 Primary PCI is effective in securing and maintaining coronary artery patency and avoids some of the bleeding risks of fibrinolysis. Randomized clinical trials comparing timely performed primary PCI with in-hospital fibrinolytic therapy in high-volume, experienced centres have shown more effective restoration of patency, less reocclusion, improved residual left ventricular (LV), function and better clinical outcome with primary PCI.29 Routine coronary stent implantation in patients with STEMI decreases the need for target vessel revascularization but is not associated with significant reductions in death or reinfarction rates30,31 when compared with primary angioplasty. In addition, several randomized clinical trials with medium-term follow-up, including patients with STEMI, have shown that drug-eluting stents reduce the risk of reintervention compared with bare metal stents, without having a significant impact on the risk of stent thrombosis, recurrent myocardial infarction, and death.32–34 As for other clinical presentations of coronary artery disease, long-term data on the efficacy and safety of drug-eluting stents in patients with STEMI are still needed.

Both randomized studies and registries have indicated that long delay times to primary PCI are associated with a worse clinical outcome.35,36 Several delay times can be defined: time from symptom onset to first medical contact (FMC), time from FMC to arrival in cath lab, time from FMC to sheath insertion, time from FMC to balloon inflation. The ‘PCI-related delay time’ is the theoretical difference between the time of FMC to balloon inflation minus the time from FMC to start of fibrinolytic therapy (= ‘door-to-balloon’ minus ‘door-to-needle’). The extent to which the PCI-related time delay diminishes the advantages of PCI over fibrinolysis has been the subject of many analyses and debates. Because no specifically designed study has addressed this issue, caution is needed when interpreting the results of these post hoc analyses. From randomized trials it was calculated that the PCI-related time delay that may mitigate the benefit of the mechanical intervention varies between 6037 and 110 min38 depending on the fibrinolytic used.39 In another analysis of these trials, a benefit of primary PCI over fibrinolytic therapy up to a PCI-related delay of 120 min was calculated.40 In 192 509 patients included in the NRMI 2-4 registry,41 the mean PCI-related time delay where mortality rates of the two reperfusion strategies were equal was calculated at 114 min. This study also indicated that this time delay varied considerably according to age, symptom duration, and infarct location: from <1 h for an anterior infarction in a patient <65 years presenting <2 h after symptom onset, to almost 3 h for a non-anterior infarction in a patient >65 years presenting >2 h after symptom onset. Although these results were derived from a post hoc analysis of a registry and reported delay times are sometimes inaccurate, this study suggests that an individualized rather than a uniform approach for selecting the optimal reperfusion modality could be more appropriate when PCI cannot be performed within a short delay. Taking into account the studies and registries mentioned above, primary PCI (balloon inflation) should be performed within 2 h after FMC in all cases. In patients presenting early with a large amount of myocardium at risk, the delay should be shorter. Although no specific studies have been performed, a maximum delay of only 90 min after FMC seems to be a reasonable recommendation in these patients.

Patients with contraindications to fibrinolytic therapy have a higher morbidity and mortality than those eligible for this therapy. Primary PCI can be performed with success in these patients.42 Primary PCI is the preferred treatment for patients in shock.43 Except for patients in cardiogenic shock, only the culprit lesion should be dilated in the acute setting. Complete revascularization of the non-culprit lesions may be performed at a later time point depending on the remaining ischaemia.

Facilitated PCI

Facilitated PCI is defined as a pharmacological reperfusion treatment delivered prior to a planned PCI, in order to bridge the PCI-related time delay. Full-dose lytic therapy, half-dose lytic therapy with a glycoprotein (GP)IIb/IIIa inhibitor and GPIIb/IIIa inhibitor alone have been tested for this indication. There is no evidence of a significant clinical benefit with any of these agents.16,12,44,45 In spite of the fact that pre-PCI patency rates were higher with lytic-based treatments, no mortality benefit but more bleeding complications were observed. The pre-PCI patency rates with upfront abciximab or high-bolus dose tirofiban alone were not higher than with placebo. Facilitated PCI as it has been tested in these trials cannot be recommended.

Rescue PCI

Rescue PCI is defined as PCI performed on a coronary artery which remains occluded despite fibrinolytic therapy. The non-invasive identification of failed fibrinolysis remains a challenging issue, but <50% ST-segment resolution in the lead(s) with the highest ST-segment elevations 60–90 min after start of fibrinolytic therapy has increasingly been used as a surrogate. Rescue PCI has been shown to be feasible and relatively safe. In a randomized study of 427 patients (REACT), the event-free survival at
6 months after failed fibrinolysis was significantly higher with rescue PCI than with repeated administration of a fibrinolytic agent or conservative treatment. A recent meta-analysis, including REACT, showed that rescue PCI is associated with a significant reduction in heart failure and reinfarction and a trend towards lower all-cause mortality when compared with a conservative strategy, at the cost, however, of an increased risk of stroke and bleeding complications. Rescue PCI should be considered when there is evidence of failed fibrinolysis based on clinical signs and insufficient ST-segment resolution (<50%), if there is clinical or ECG evidence of a large infarct, and if the procedure can be performed within a reasonable time delay (up to 12 h after onset of symptoms).

Adjunctive antithrombotic treatment and devices (Tables 6 and 9)
Aspirin, NSAID, COX-2 inhibitors. Aspirin should be given to all patients with a STEMI as soon as possible after the diagnosis is deemed probable. There are few contraindications to the use of aspirin, but it should not be given to those with a known hypersensitivity, active gastrointestinal bleeding, known clotting disorders, or severe hepatic disease. Aspirin may occasionally trigger bronchoospasm in asthmatic patients. Aspirin should be started at a dose of 150–325 mg in a chewable form (enteric-coated aspirin should not be given because of slow onset of action). An alternative approach, especially if oral ingestion is not possible, is i.v. administration of aspirin at a dose of 250–500 mg, although no specific data are available on the relative merits of this strategy. A lower dose (75–160 mg) is given orally daily thereafter for life.

Aspirin, NSAID, COX-2 inhibitors have been demonstrated to increase the risk of death, reinfarction, cardiac rupture, and other complications in STEMI patients: discontinuation of these drugs is indicated at the time of STEMI.

Clopidogrel. Although clopidogrel is less studied in patients with STEMI treated with primary PCI, there is abundant evidence on its usefulness as an adjunctive antiplatelet therapy on top of aspirin in patients undergoing PCI. Based on these data, clopidogrel should be given as soon as possible to all patients with STEMI undergoing PCI. It is started with a loading dose of at least 300 mg, but a 600 mg loading dose achieves a more rapid and stronger inhibition of platelet aggregation. This should be followed by a daily dose of 75 mg.

GPIIb/IIIa antagonists. Platelet GPIIb/IIIa inhibitors block the final pathway of platelet aggregation. Most of the studies on the role of GPIIb/IIIa antagonists in STEMI have focused on abciximab rather than on the other two members of the family, tirofiban and epifibatide. Several randomized trials have assessed the value of periprocedural administration of i.v. abciximab in addition to aspirin and heparin in this setting. A systematic review of these trials showed that abciximab reduced 30-day mortality by 32% without affecting the risk of haemorrhagic stroke and major bleeding. Abciximab did not have a significant impact on the patency of infarct-related vessels, and its administration upstream of a planned PCI procedure did not offer advantages compared with the administration in the cath lab. Abciximab is given i.v. as a bolus of 0.25 mg/kg bolus, 0.125 µg/kg/min infusion (maximum 10 µg/min for 12 h). However, it remains to be elucidated whether abciximab provides an additional benefit to STEMI patients who receive an optimal clopidogrel treatment prior to PCI. In the On-TIME 2 trial (n = 984) pre-hospital initiation of high-bolus dose tirofiban in association with aspirin, clopidogrel (600 mg), and heparin improved ST-segment resolution but was not associated with more patency of the infarct vessel or a significant net clinical benefit when compared with placebo.

Heparin. Heparin is standard anticoagulant therapy during PCI. The lack of randomized clinical trials of heparin vs. placebo during PCI in STEMI is due to the strong belief that anticoagulation therapy is a requirement during the procedure. Heparin is given as an i.v. bolus at a usual starting dose of 100 U/kg weight (60 U/kg if GPIIb/IIIa

| Table 6 | Antithrombotic treatment without reperfusion therapy |
|---------------------------------|---------------------------------|---------------------------------|
| Recommendations | Classa | Levelb |
| **Antiplatelet co-therapy** | | |
| If not already on aspirin oral (soluble or chewable/ non-enteric-coated) or i.v. dose of aspirin if oral ingestion is not feasible | I | A |
| Oral dose of clopidogrel | I | B |
| **Antithrombin co-therapy** | | |
| I.v. bolus of fondaparinux followed 24 h later by an s.c. dose | I | B |
| If fondaparinux is not available: enoxaparin i.v. bolus followed 15 min later by first s.c. dose; if age >75 years no i.v. bolus and start with reduced s.c. dose or | I | B |
| I.v. heparin followed by a weight-adjusted i.v. infusion with first aPTT control after 3 h | I | B |

*aClass of recommendation.
*Level of evidence.
*For doses see Tables 9 and 10.
40% reduction in major bleeding (major bleeding, was significantly reduced by bivalirudin due to a composite of 30-day incidence of major adverse cardiac events or parin) plus a GPIIb/IIIa inhibitor.56 The primary end-point, the com-

With provisional use of GPIIb/IIIa inhibitor or heparin (or enoxa-

domly assigned in an unblinded fashion to receive either bivalirudin (HORIZONS-AMI) trial, 3602 patients undergoing PCI were ran-

branches in Acute Myocardial Infarction undergoing PCI. In the Harmonizing Outcomes With Revas-

b. Fibrinolytic treatment

The benefit of fibrinolytic therapy is well established:61 approximately 30 early deaths are prevented per 1000 patients treated, with 20 deaths prevented per 1000 patients treated between 7 and 12 h after symptom onset. Overall, the largest absolute benefit is seen among patients with the highest risk, even though the proportional benefit may be similar. In a subgroup of 3300 patients over the age of 75 presenting within 12 h of symptom onset and with either STEMI or bundle-branch block, mortality rates were significantly reduced by fibrinolytic therapy.62

Time to treatment

Analysis of studies in which >6000 patients were randomized to pre-hospital or in-hospital fibrinolysis has shown a significant reduction (17%) in early mortality with pre-hospital fibrinolytic treatment.63 In a meta-analysis of 22 trials,64 a much larger mortality reduction

antagonists are used). It is recommended to perform the procedure under activated clotting time (ACT) guidance: heparin should be given at a dose able to maintain an ACT of 250–350 s (200–250 s if GPIIb/IIIa antagonists are used).

Low-molecular-weight heparins (LMWHs) have been studied in a limited number of STEMI patients undergoing primary PCI. Thus, there is little evidence to support their use instead of heparin in this setting.

Bivalirudin. The direct thrombin inhibitor, bivalirudin, has been investigated as an adjunct antithrombotic therapy in patients undergoing PCI. In the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial, 3602 patients undergoing PCI were randomly assigned in an unblinded fashion to receive either bivalirudin with provisional use of GPIIb/IIIa inhibitor or heparin (or enoxaparin) plus a GPIIb/IIIa inhibitor.56 The primary end-point, the composite of 30-day incidence of major adverse cardiac events or major bleeding, was significantly reduced by bivalirudin due to a 40% reduction in major bleeding ($P <0.001$). All-cause mortality

at 30 days was 1% lower ($P <0.0047$), but acute stent thrombosis occurred more frequently ($P <0.001$). Bivalirudin is given as an i.v. bolus of 0.75 mg/kg followed by an infusion of 1.75 mg/kg/h not titrated to ACT and usually terminated at the end of the procedure.

Fondaparinux. Fondaparinux, a factor Xa inhibitor, has been com-
pared with heparin or placebo in 12 092 STEMI patients treated with fibrinolytic agents or PCI, or no reperfusion therapy.57 In the PCI subset, fondaparinux was associated with a non-significant 1% higher incidence of death or recurrent infarction at 30 days. These findings together with the occurrence of catheter throm-

bosis do not lend support to the use of fondaparinux as the sole anticoagulant in patients undergoing primary PCI.

Adjunctive devices. Adjunctive devices aiming at the prevention of distal embolization have been investigated in several randomized studies. Formal meta-analyses of these studies show hetero-
genous results with no overall clinical benefit despite a lower rate of distal embolization angiographically.58 In a recent random-
ized study in 1071 patients, aspiration of thrombus prior to PCI was associated with improved tissue reperfusion [myocardial blush grades (MBGs)] and improved survival at 1 year when com-
pared with conventional PCI.68,69 See also section D.1.d. and Table 13.

b. Fibrinolytic treatment

The evidence for benefit

The benefit of fibrinolytic therapy is well established:61 approximately 30 early deaths are prevented per 1000 patients treated, with 20 deaths prevented per 1000 patients treated between 7 and 12 h after symptom onset. Overall, the largest absolute benefit is seen among patients with the highest risk, even though the proportional benefit may be similar. In a subgroup of 3300 patients over the age of 75 presenting within 12 h of symptom onset and with either STEMI or bundle-branch block, mortality rates were significantly reduced by fibrinolytic therapy.62

Time to treatment

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<table>
<thead>
<tr>
<th>Table 8 Doses of fibrinolytic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial treatment</strong></td>
</tr>
<tr>
<td>Streptokinase (SK)</td>
</tr>
<tr>
<td>Alteplase (t-PA)</td>
</tr>
<tr>
<td>1.5 million units over 30–60 min i.v.</td>
</tr>
<tr>
<td>15 mg i.v. bolus</td>
</tr>
<tr>
<td>0.75 mg/kg over 30 min then 0.5 mg/kg over 60 min i.v.</td>
</tr>
<tr>
<td>Total dosage not to exceed 100 mg</td>
</tr>
<tr>
<td>Reteplase (r-PA)</td>
</tr>
<tr>
<td>10 U + 10 U i.v. bolus given 30 min apart</td>
</tr>
<tr>
<td>Tenecteplase (TNK-tPA)</td>
</tr>
<tr>
<td>Single i.v. bolus</td>
</tr>
<tr>
<td>30 mg if &lt;60 kg</td>
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<tr>
<td>35 mg if 60 to &lt;70 kg</td>
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<tr>
<td>40 mg if 70 to &lt;80 kg</td>
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<tr>
<td>45 mg if 80 to &lt;90 kg</td>
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<tr>
<td>50 mg if ≥90 kg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 9 Doses of antiplatelet co-therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With primary PCI</strong></td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Oral dose of 150–325 mg or i.v. dose of 250–500 mg if oral ingestion is not possible</td>
</tr>
<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Oral loading dose of at least 300 mg, preferably 600 mg</td>
</tr>
<tr>
<td>GPIIb/IIIa inhibitors</td>
</tr>
<tr>
<td>Abciximab: i.v. bolus followed by 0.125 μg/kg per min infusion (maximum 10 μg/min for 12 h)</td>
</tr>
<tr>
<td><strong>With fibrinolytic treatment</strong></td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Oral dose of 150–325 mg or i.v. dose of 250 mg if oral ingestion is not possible</td>
</tr>
<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Loading dose of 300 mg if age ≤75 years; 75 mg if age &gt;75</td>
</tr>
<tr>
<td><strong>Without reperfusion therapy</strong></td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Oral dose of 150–325 mg</td>
</tr>
<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Oral dose of 75 mg</td>
</tr>
</tbody>
</table>
or intravascular volume expansion may be required. Streptokinase
lays the patient flat and, elevating the feet. Occasionally atropine
occurs, it should be managed by temporarily halting the infusion,
tration of hydrocortisone is not indicated. When hypotension
occurred, it should be managed by temporarily halting the infusion,
serious allergic reactions are rare. Routine administration of streptokinase
was found in patients treated within the first 2 h than in those
treated later. These data support pre-hospital initiation of fibrino-
lytic treatment if this reperfusion strategy is indicated. More recent
post hoc analyses of several randomized trials and data from regis-
tries have confirmed the clinical usefulness of pre-hospital fibrino-
lysis.16,65–67 Most of these studies reported outcome data similar
to those of primary PCI, provided early angiography and PCI
were performed in those who needed intervention. However,
whether pre-hospital fibrinolysis is associated with a similar or
better clinical outcome than primary PCI in early presenting
cases has not been studied prospectively in an adequately
sized randomized fashion.

Hazard of fibrinolysis
Fibrinolytic therapy is associated with a small but significant excess
of strokes,64 with all of the excess hazard appearing on the first day
after treatment. The early strokes are largely attributable to cer-
ebral haemorrhage; later strokes are more frequently thrombotic
or embolic. Advanced age, lower weight, female gender, prior cer-
ebrovascular disease, and systolic and diastolic hypertension on
admission are significant predictors of intracranial haemorrhage.68
In the latest trials, intracranial bleeding occurred in 0.9–1.0% of the
total population studied.69,70 Major non-cerebral bleeds (bleeding
complications requiring blood transfusion or that are life-
threatening) can occur in 4–13% of the patients treated.69,71 The
most common sources of bleeding are procedure related. Independ-
ent predictors of non-cerebral bleeding are older age, lower
weight, and female gender; also in patients not undergoing PCI.

Administration of streptokinase may be associated with hypo-
tension, but severe allergic reactions are rare. Routine administra-
tion of hydrocortisone is not indicated. When hypotension
occurs, it should be managed by temporarily halting the infusion,
laying the patient flat and, elevating the feet. Occasionally atropine
or intravascular volume expansion may be required. Streptokinase
should never be readministered because of antibodies which can
impair its activity and because of the risk of allergic reactions.

Comparison of fibrinolytic agents
In the GUSTO Trial,72 an accelerated infusion of the fibrin-specific
agent t-PA (tissue plasminogen activator; alteplase) with concomi-
tant aPTT- (activated partial thromboplastin time) adjusted i.v.
heparin resulted in 10 fewer deaths per 1000 patients treated
when compared with streptokinase, at the cost of three additional
strokes. In assessing the net clinical benefit of t-PA (survival
without a neurological deficit), one must take into account that
only one of these additional strokes survived with a residual neuro-
logical deficit. Several variants of t-PA have been studied. Double-
bolus r-PA (reteplase) does not offer any advantage over acceler-
ated t-PA except for its ease of administration.70 Single-bolus
weight-adjusted TNK-tPA (tenecteplase) is equivalent to acceler-
ated t-PA for 30-day mortality and associated with a significantly
lower rate of non-cerebral bleedings and less need for blood trans-
fusion.73 Bolus fibrinolytic therapy is easier to use in the pre-
hospital setting.

Clinical implications
Where appropriate facilities exist, with trained medical or parame-
dical staff able to analyse on-site or to transmit the ECG to the
hospital for supervision, pre-hospital fibrinolysis is recommended
provided that fibrinolytic therapy is the most appropriate reperfu-
sion strategy. The aim is to start fibrinolytic therapy within 30 min
of arrival of the ambulance (Table 5). For patients arriving at the
hospital, a realistic aim is to initiate fibrinolysis within 30 min
(doctor-to-needle time).

Contraindications to fibrinolytic therapy (Table 7)
Absolute and relative contraindications to fibrinolytic therapy are
shown in Table 7. Diabetes (more particularly diabetic retinopathy)
and successful resuscitation are no contraindication to fibrinolytic therapy. Fibrinolytic therapy should not be given to patients refractory to resuscitation.\(^{73}\)

**Readministration of a fibrinolytic agent**

If there is evidence of persistent occlusion, re-occlusion, or reinfarction with recurrence of ST-segment elevation the patient should be immediately transferred to a hospital with PCI capabilities. If rescue PCI is not available, a second administration of a non-immunogenic fibrinolytic agent may be considered, if there is a large infarct and if the risk of bleeding is not high,\(^{74}\) although in the REACT trial readministration of a fibrinolytic agent was not better than a conservative therapy.\(^{46}\)

**Fibrinolytic regimens (Tables 8, 9 and 10)**

**Angiography after fibrinolytic therapy (Table 11)**

If it is likely that fibrinolysis was successful (ST-segment resolution of \(\geq 50\%\) at 60–90 min, typical reperfusion arrhythmia, disappearance of chest pain) angiography is recommended if there are no contraindications. In the CARESS trial, a more conservative strategy with sending patients for angiography only in the case of failed fibrinolysis was associated with a worse clinical outcome when compared with a strategy of referring all patients for angiography and (if indicated) PCI.\(^{75}\) In order to avoid an early PCI during the prothrombotic period following fibrinolysis, on the one hand, and to minimize the risk of reocclusion, on the other hand, a time window of 3–24 h following successful fibrinolysis is recommended.\(^{16,76–78}\)

**Adjunctive anticoagulant and antiplatelet therapy (Tables 5, 9 and 10)**

Convincing evidence of the effectiveness of aspirin was demonstrated by the ISIS-2 trial,\(^{79}\) in which the benefits of aspirin and streptokinase were additive. The first dose of 150–325 mg should be chewed (no enteric-coated aspirin because of slow onset of action) and a lower dose (75–100 mg) given orally daily thereafter. If oral ingestion is not possible, aspirin can be given i.v. (250–500 mg). In the CLARITY trial, patients \(\leq 75\) years were treated with a standard fibrinolytic regimen and randomized to 300 mg clopidogrel loading dose followed by 75 mg per day or placebo on top of aspirin up to and including the day of angiography with a maximum of 8 days (mean duration 3 days). By 30 days, clopidogrel therapy reduced the odds of the composite end-point of death from cardiovascular causes, recurrent myocardial infarction, or recurrent ischaemia, leading to a reduction of the need for urgent revascularization of 20\%. The rates of major bleeding and intracranial haemorrhage were similar in the two groups.\(^{52}\)

In the COMMIT study,\(^{80}\) 45,852 Chinese patients of any age (but \(< 1000\) patients \(> 75\) years) with suspected myocardial infarction (93\% with STEMI) were randomized to clopidogrel 75 mg (no loading dose) or placebo in addition to aspirin. Clopidogrel significantly reduced the odds of the composite of death, myocardial infarction, or stroke, corresponding to nine fewer events per 1000 patients treated for \(\approx 2\) weeks. Accordingly, there is a good case for the routine use of clopidogrel in the acute phase.

A combination of half-dose fibrinolytic therapy and full-dose abciximab did not reduce mortality but was associated with an increased risk of bleeding complications, especially in elderly patients when compared with full dose lytic therapy in two large randomized trials.\(^{81,82}\)

Clopidogrel has been extensively used during and after fibrinolysis, especially with alteplase. Heparin does not improve immediate clot lysis, but coronary patency evaluated in the hours or days following fibrinolytic therapy with alteplase appears to be better with i.v. heparin.\(^{83}\) No difference in patency was apparent in patients treated with either s.c. or i.v. heparin and streptokinase.\(^{84}\) I.v. heparin administration until discharge has not been shown to prevent reocclusion after angiographically proven successful coronary fibrinolysis.\(^{85}\) Heparin infusion after fibrinolytic therapy may be discontinued after 24–48 h. Close monitoring of i.v. heparin therapy is mandatory; aPTT values \(>70\) are associated with higher likelihood of mortality, bleeding, and reinfarction.\(^{86}\)

A full weight adjustment of the heparin dose may decrease the risk of non-cerebral bleeding complications.\(^{87}\)

In the ASSENT-3 trial \((n = 6095)\), a standard dose of the LMWH enoxaparin given in association with tenecteplase for a maximum of 7 days reduced the risk of in-hospital reinfarction or in-hospital refractory ischaemia when compared with heparin. However, in the ASSENT-3 PLUS \((n = 1639)\) trial,\(^{87}\) pre-hospital administration of the same dose of enoxaparin resulted in a significant increase in intracranial haemorrhage rate in elderly patients. In the large ExTRACT trial \((n = 20 506)\), a lower dose of enoxaparin was given to patients \(> 75\) years and to those with impaired renal function (estimated creatinine clearance \(< 30\) mL/min). Enoxaparin treatment was associated with a significant reduction in the risk of death and reinfarction at 30 days when compared with a weight-adjusted heparin dose, however at the cost of a significant increase in non-cerebral bleeding complications. The net clinical benefit (absence of death, non-fatal infarction, or intracranial haemorrhage) favoured enoxaparin. Benefit was observed regardless of the type of fibrinolytic agent and the age of the patient.\(^{88,89}\)

In the large OASIS-6 trial, a low dose of fondaparinux, a synthetic indirect anti-Xa agent, was superior to placebo or heparin in preventing death and reinfarction in 5436 patients who received fibrinolytic therapy.\(^{57}\) In the subgroup of 1021 patients in whom concomitant heparin was felt to be indicated, fondaparinux was

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**Table 11 Angiography during hospital stay after fibrinolytic therapy and in patients who did not receive reperfusion therapy**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class(^a)</th>
<th>Level(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of failed fibrinolysis or uncertainty about success: immediate</td>
<td>Ia</td>
<td>B</td>
</tr>
<tr>
<td>Recurrent ischaemia, reocclusion after initial successful fibrinolysis: immediate</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Evidence of successful fibrinolysis: within 3–24 h after start of fibrinolytic therapy</td>
<td>Ia</td>
<td>A</td>
</tr>
<tr>
<td>In unstable patients who did not receive reperfusion therapy: immediate</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In stable patients who did not receive reperfusion therapy: before discharge</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

\(^{a}\)Class of recommendation.

\(^{b}\)Level of evidence.
not superior to heparin in preventing death, reinfarction, or major bleeding complications.90
In a large trial with streptokinase,91 no mortality reduction at 30 days but significantly fewer reinfarctions were seen with a direct antithrombin, bivalirudin, given for 48 h, as compared with heparin, however at the cost of a modest and non-significant increase in non-cerebral bleeding complications. Bivalirudin has not been studied with fibrin-specific agents. Direct thrombin inhibitors are not recommended as an adjunct to fibrinolysis.

c. Antithrombotic therapy without reperfusion therapy
In patients presenting within 12 h after symptom onset and in whom reperfusion therapy was not given, or in patients presenting after 12 h aspirin, clopidogrel80 and an antithrombin agent (heparin, enoxaparin, or fondaparinux) should be given as soon as possible92–94 (Table 8). In OASIS-6, fondaparinux was superior to heparin in a subgroup of 1641 patients and might be the preferred antithrombin for this indication.95 If coronary angiography/PCI is needed in a patient on fondaparinux, an i.v. bolus of 5000 U of heparin is recommended to avoid catheter thrombosis.
Recommended doses are given in Tables 9 and 10.
In most patients who did not receive reperfusion therapy, angiography before hospital discharge is recommended, similar to patients after successful fibrinolysis (Table 11) if no contraindications are present.

d. Prevention and treatment of microvascular obstruction and reperfusion injury
The ‘no-reflow’ phenomenon in STEMI patients is characterized by inadequate myocardial reperfusion after successful re-opening of the epicardial infarct-related artery.
Depending on the technique used, 10–40% of patients undergoing reperfusion therapy for STEMI may show evidence of no-reflow.96–99

No-reflow may occur as a consequence of downstream microvascular embolization of thrombotic or atheromatous (lipid-rich) debris, reperfusion injury, microvascular disruption, endothelial dysfunction, inflammation, and myocardial oedema.100,101
No-reflow can cause prolonged myocardial ischaemia, may result in severe arrhythmia and critical haemodynamic deterioration, and is associated with a significantly increased risk of clinical complications.97,102 Reversing no-reflow is associated with a favourable effect on LV remodelling even in the absence of significant improvement in regional contractile function.103

Diagnostic techniques104 to detect ‘no-reflow’ after PCI include grading of flow in the infarct vessel and of ‘myocardial blush’ by angiography (see Table 12), and coronary flow velocity measurement with a Doppler wire105 (rapid deceleration of diastolic flow velocity). Non-invasive techniques that have been used are ST-segment resolution analysis, contrast echocardiography, single-photon emission tomography, positron emission tomography (PET), and contrast-enhanced magnetic resonance imaging (MRI). The diagnosis of no-reflow is usually made when post-procedural thrombolysis in myocardial infarction (TIMI) flow is <3 or in the case of a TIMI flow 3 when MBG is 0 or 1 or when ST resolution within 4h of the procedure is <70%.102

Intracoronary administration of vasodilators such as adenosine, verapamil, nicorandil, papaverine, and nitroprusside during and after primary PCI has been shown to improve flow in the infarct-related coronary artery and myocardial perfusion, and/or to reduce infarct size, but large prospective randomized trials with hard clinical outcomes are missing.104,108 High-dose i.v. infusion of adenosine was also associated with a reduction in infarct size, but clinical outcomes were not significantly improved (Table 13).109

The GPIIb/IIIa receptor antagonist abciximab was found to improve tissue perfusion110,111 and is recommended as antithrombotic co-therapy with primary PCI (see section D.1.a.). The use of

| Table 12 Grading of coronary flow and myocardial blush |
|----------------|------------------|
| **TIMI 0** | There is no antegrade flow beyond the point of occlusion. |
| **TIMI 1** | The contrast material passes beyond the area of obstruction, but ‘hangs up’ and fails to opacify the entire coronary bed distal to the obstruction for duration of the cine run. |
| **TIMI 2** | The contrast material passes across the obstruction and opacifies the coronary bed distal to the obstruction. However, the rate of entry of contrast material into the vessel distal to the obstruction or its rate of clearance from the distal bed (or both) are perceptibly slower than its entry into or clearance from comparable areas not perfused by the previously occluded vessel, e.g. the opposite coronary artery or the coronary bed proximal to the obstruction. |
| **TIMI 3** | Antegrade flow into the bed distal to the obstruction occurs as promptly as antegrade flow into the bed proximal to the obstruction, and clearance of contrast material from the involved bed is as rapid as clearance from an uninjured bed in the same vessel or the opposite artery. |
| **MBG 0** | No myocardial blush or staining of blush (due to leakage of dye into the extravascular space) |
| **MBG 1** | Minimal myocardial blush |
| **MBG 2** | Moderate myocardial blush, less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related artery |
| **MBG 3** | Normal myocardial blush, comparable with that obtained during angiography of a contralateral or ipsilateral non-infarct-related artery |

Flow grades in the infarct-related vessel by the TIMI group.106
Myocardial blush grade (MBG) is a densitometric, semi-quantitative parameter which depends on the tissue phase of myocardial perfusion that appears as a ‘blush’ or a ‘ground-glass’ after a sufficiently long, 25 frames/s, X-ray acquisition. MBG is measured on patients with TIMI 3 flow and is based on the principle that a functionally preserved microvascular bed allows the injected contrast to pass easily from the arterial to the venous side of coronary circulation, showing an appreciable ‘blush’ at the myocardial level.107

The ‘no-reflow’ phenomenon in STEMI patients is characterized by inadequate myocardial reperfusion after successful re-opening of the epicardial infarct-related artery.

In most patients who did not receive reperfusion therapy, angiography before hospital discharge is recommended, similar to patients after successful fibrinolysis (Table 11) if no contraindications are present.

No-reflow may occur as a consequence of downstream microvascular embolization of thrombotic or atheromatous (lipid-rich) debris, reperfusion injury, microvascular disruption, endothelial dysfunction, inflammation, and myocardial oedema.

No-reflow can cause prolonged myocardial ischaemia, may result in severe arrhythmia and critical haemodynamic deterioration, and is associated with a significantly increased risk of clinical complications. Reversing no-reflow is associated with a favourable effect on LV remodelling even in the absence of significant improvement in regional contractile function.

Diagnostic techniques to detect ‘no-reflow’ after PCI include grading of flow in the infarct vessel and of ‘myocardial blush’ by angiography (see Table 12), and coronary flow velocity measurement with a Doppler wire (rapid deceleration of diastolic flow velocity). Non-invasive techniques that have been used are ST-segment resolution analysis, contrast echocardiography, single-photon emission tomography, positron emission tomography (PET), and contrast-enhanced magnetic resonance imaging (MRI). The diagnosis of no-reflow is usually made when post-procedural thrombolysis in myocardial infarction (TIMI) flow is <3 or in the case of a TIMI flow 3 when MBG is 0 or 1 or when ST resolution within 4h of the procedure is <70%.

Intracoronary administration of vasodilators such as adenosine, verapamil, nicorandil, papaverine, and nitroprusside during and after primary PCI has been shown to improve flow in the infarct-related coronary artery and myocardial perfusion, and/or to reduce infarct size, but large prospective randomized trials with hard clinical outcomes are missing. High-dose i.v. infusion of adenosine was also associated with a reduction in infarct size, but clinical outcomes were not significantly improved (Table 13).

The GPIIb/IIIa receptor antagonist abciximab was found to improve tissue perfusion and is recommended as antithrombotic co-therapy with primary PCI (see section D.1.a.). The use of...
adjunctive devices for preventing distal embolization is discussed in section D.1.d.

e. Coronary bypass surgery

The number of patients who need a coronary artery bypass graft (CABG) in the acute phase is limited, but CABG may be indicated after failed PCI, coronary occlusion not amenable for PCI, presence of refractory symptoms after PCI, cardiogenic shock, or mechanical complications such as ventricular rupture, acute mitral regurgitation, or ventricular septal defect.\textsuperscript{112,113}

If a patient requires emergency stenting of a culprit lesion in the setting of a STEMI but further surgical revascularization is already predictable in the near future, the use of bare metal stents instead of drug-eluting stents should be recommended to avoid the problem of acute periprocedural stent thrombosis. In patients with an indication for CABG, e.g., multivessel disease, it is recommended to treat the infarct-related lesion by PCI and to perform CABG later in more stable conditions.

2. Pump failure and shock

a. Clinical features

Heart failure is usually due to myocardial damage but may also be the consequence of arrhythmia or mechanical complications such as mitral regurgitation or ventricular septal defect. Heart failure during the acute phase of STEMI is associated with a poor short- and long-term prognosis.\textsuperscript{114} The clinical features are those of breathlessness, sinus tachycardia, a third heart sound, and pulmonary rales, which are basal, but may extend throughout both lung fields. The degree of failure may be categorized according to the Killip classification: class 1, no rales or third heart sound; class 2, pulmonary congestion with rales over <50% of the lung fields or third heart sound; class 3, pulmonary oedema with rales over 50% of the lung fields; class 4, shock. Haemodynamic states that can occur after STEMI are given in Table 14.

General measures include monitoring for arrhythmias, checking for electrolyte abnormalities and for the presence of concomitant conditions such as valvular dysfunction or pulmonary disease. Pulmonary congestion can be assessed by portable chest X-rays. Echocardiography is the key diagnostic tool and should be performed to assess the extent of myocardial damage and possible complications, such as mitral regurgitation and ventricular septal defect.

b. Mild heart failure (Killip class II)

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

Minor degrees of failure often respond quickly to nitrates and diuretics, such as furosemide 20–40 mg given slowly i.v., repeated at 1–4 hourly intervals, if necessary. Higher doses may be required in patients with renal failure or chronic use of diuretics. If there is no hypotension, i.v. nitrates are indicated. The dose of nitrates should be titrated while monitoring blood pressure to avoid hypotension. Angiotensin-converting enzyme (ACE) inhibitors [or an angiotensin receptor blocker (ARB) if ACE-inhibitors are not tolerated] should be initiated within 24 h in the absence of hypotension, hypovolaemia, or significant renal failure (Table 15). See also section D.5.

c. Severe heart failure and shock (Killip class III and IV)

Oxygen should be administered and pulse oximetry is indicated for monitoring of oxygen saturation. Blood gases should be checked regularly, and continuous positive airway pressure or endotracheal intubation with ventilatory support may be required. Non-invasive ventilation should be considered as early as possible in every
Table 15  Treatment of pump failure and cardiogenic shock

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment of mild heart failure</strong> <em>(Killip class II)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$O_2$</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Loop diuretics, i.e. furosemide: 20–40 mg i.v. repeated at 1–4 hourly intervals if necessary</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Nitrates if no hypotension</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>ACE-inhibitor in the absence of hypotension, hypovolaemia or renal failure</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ARB (valsartan) if ACE-inhibitor is not tolerated</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>Treatment of severe heart failure</strong> <em>(Killip class III)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$O_2$</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Ventilatory support according to blood gasses</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Furosemide: see above</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Nitrates if no hypotension</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Inotropic agents: dopamine and/or dobutamine</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Haemodynamic assessment with balloon floating catheter</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Early revascularization</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>*<em>Treatment of shock (Killip class IV)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$O_2$</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Mechanical ventilatory support according to blood gasses</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Haemodynamic assessment with balloon floating catheter</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Inotropic agents: dopamine and dobutamine</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>LV assist devices</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>Early revascularization</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

*aClass of recommendation.  
*bLevel of evidence.

...Patients with acute heart failure may have stunned (reperfused but with delayed contractile recovery) or hypoperfused, viable myocardium. Identification of viable myocardium followed by revascularization can lead to improved LV function. ...

Cardiogenic shock

Cardiogenic shock is a clinical state of hypoperfusion characterized by a systolic pressure <90 mmHg and a central filling pressure (wedge pressure) >20 mmHg, or a cardiac index <1.8 L/min/m² and caused by extensive loss of viable myocardial tissue. Shock is also considered present if i.v. inotropes and/or an intra-aortic balloon pump (IABP) are needed to maintain a systolic blood pressure >90 mmHg and a cardiac index of >1.8 L/min/m².

The diagnosis of cardiogenic shock should be made when other causes of hypotension have been excluded, such as hypovolaemia, vasovagal reactions, electrolyte disturbances, pharmacological side effects, tamponade, or arrhythmias. It is usually associated with extensive LV damage, but may occur in right ventricular infarction (see above). LV function and associated mechanical complications should be evaluated urgently by two-dimensional Doppler echocardiography, Haemodynamic assessment with a balloon floating catheter should be considered. A filling pressure (pulmonary wedge) of at least 15 mmHg should be aimed for, with a cardiac index of >2 L/kg/min. In some cases of cardiogenic shock, inotropic agents may stabilize patients at risk of progressive haemodynamic collapse or serve as a life-sustaining bridge to more definitive therapy. Dopamine <3 µg/kg/min may be given to improve renal function. Dopamine at higher doses or dobutamine 5–20 µg/kg/min may be given to improve or stabilize the haemodynamic state.

Supportive treatment with a balloon pump is recommended as a bridge to mechanical interventions.

Emergency PCI or surgery may be life-saving and should be considered at an early stage. If neither of these are available or can only be provided after a long delay, fibrinolytic therapy should be given.

LV assist devices have been used in patients not responding to standard treatment including IABP and as a bridge to transplantation but the experience is limited.

3. Mechanical complications: cardiac rupture and mitral regurgitation

a. Cardiac rupture

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. Only very rarely is there time to bring the patient to surgery.

Subacute free wall rupture

In ~25% of cases the presentation is subacute (thrombus or adhesions seal the rupture), giving time for intervention. 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. Although echocardiography is not always able to show the site of rupture, it can demonstrate pericardial fluid with or without signs of tamponade. The presence of pericardial fluid alone is not sufficient to diagnose a subacute free wall rupture, because it is relatively common after acute myocardial infarction. The typical finding is an echo-dense mass in the pericardial space consistent with clot (haemopericardium). Immediate surgery should be considered.

Ventricular septal rupture
The diagnosis of ventricular septal rupture, first suspected because of sudden severe clinical deterioration, is confirmed by the occurrence of a loud systolic murmur, by echocardiography and/or by detecting an oxygen step-up in the right ventricle. Echocardiography reveals the location and size of the ventricular septal defect; the left-to-right shunt can be depicted by colour Doppler and further quantified by pulsed Doppler technique. Pharmacological treatment with vasodilators, such as i.v. nitroglycerine, may produce some improvement if there is no cardiogenic shock, but intra-aortic balloon counter pulsation is the most effective method of providing circulatory support while preparing for surgery. Urgent surgery offers the only chance of survival for large post-infarction ventricular septal defect with cardiogenic shock.109,110 Even if there is no haemodynamic instability, early surgery is usually indicated, also because the defect may increase.111 However, there is still no consensus on the optimal timing of surgery as early surgical repair is difficult because of friable necrotic tissue. Successful percutaneous closure of the defect has been reported, but more experience is needed before it can be recommended.

b. Mitral regurgitation
Mitral regurgitation is common and it occurs usually after 2–7 days. There are three mechanisms of acute mitral regurgitation in this setting: (i) mitral valve annulus dilatation due to LV dilatation and dysfunction; (ii) papillary muscle dysfunction usually due to inferior myocardial infarction; and (iii) rupture of the trunk or tip of the papillary muscle. In most patients, acute mitral regurgitation is secondary to papillary muscle dysfunction rather than rupture. The most frequent cause of partial or total papillary muscle rupture is a small infarct of the posteromedial papillary muscle. In most patients, acute mitral regurgitation is typical finding is an echo-dense mass in the pericardial space consistent with clot (haemopericardium). Immediate surgery should be considered.

Ventricular septal rupture
The diagnosis of ventricular septal rupture, first suspected because of sudden severe clinical deterioration, is confirmed by the occurrence of a loud systolic murmur, by echocardiography and/or by detecting an oxygen step-up in the right ventricle. Echocardiography reveals the location and size of the ventricular septal defect; the left-to-right shunt can be depicted by colour Doppler and further quantified by pulsed Doppler technique. Pharmacological treatment with vasodilators, such as i.v. nitroglycerine, may produce some improvement if there is no cardiogenic shock, but intra-aortic balloon counter pulsation is the most effective method of providing circulatory support while preparing for surgery. Urgent surgery offers the only chance of survival for large post-infarction ventricular septal defect with cardiogenic shock.109,110 Even if there is no haemodynamic instability, early surgery is usually indicated, also because the defect may increase.111 However, there is still no consensus on the optimal timing of surgery as early surgical repair is difficult because of friable necrotic tissue. Successful percutaneous closure of the defect has been reported, but more experience is needed before it can be recommended.

a. Ventricular arrhythmias
The incidence of VF occurring within 48 h of the onset of STEMI may be decreasing owing to increased use of reperfusion treatment and β-blockers.129 VF occurring early after STEMI has been associated with an increase in in-hospital mortality, but not with increased long-term mortality. The major determinants of risk of sudden death are related more to the severity of the cardiac disease and less to the frequency or classification of ventricular arrhythmias.127,128

Use of prophylactic β-blockers in the setting of STEMI reduces the incidence of VF.129 Similarly, correction of hypomagnesaemia and hypokalaemia is encouraged because of the potential contribution of electrolyte disturbances to VF. Prophylaxis with lidocaine may reduce the incidence of VF but appears to be associated with increased mortality probably owing to bradycardia and asystole, and has therefore been abandoned. In general, treatment is indicated to prevent potential morbidity or reduce the risk of sudden death. There is no reason to treat asymptomatic ventricular arrhythmias in the absence of such potential benefit.

Ventricular ectopic rhythms
Ventricular ectopic beats are common during the initial phase. Irrespective of their complexity (multiform QRS complex beats, short runs of ventricular beats, or the R-on-T phenomenon) their value as predictors of VF is questionable. No specific therapy is required.

Ventricular tachycardia and ventricular fibrillation
Neither non-sustained VT (lasting <30 s) nor accelerated idioventricular rhythm (usually a harmless consequence of reperfusion with a ventricular rate <120 bpm) occurring in the setting of STEMI serves as a reliably predictive marker of early VF. As such, these arrhythmias do not require prophylactic antiarrhythmic
b. Supraventricular arrhythmias

Atrial fibrillation (AF), which complicates 10–20% of STEMI, is more prevalent in older patients and those with severe LV damage and heart failure. Stroke rates are higher in patients with STEMI and AF compared to those without AF. AF is associated with increased in-hospital mortality. Specific recommendations for management of patients with AF in the setting of STEMI are based primarily on consensus.

In many cases 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 (Table 16). Class IC antiarrhythmic drugs should not be used. Administration of an anti-coagulant is indicated if the patient is not already on such therapy.

Other supraventricular tachycardias are rare and usually self-limited. They may respond to carotid sinus pressure. β-Blockers may be effective, if not contraindicated. If an adenosine may be considered if the haemodynamic status is stable; the ECG should be monitored during administration.

c. Sinus bradycardia and heart block

Sinus bradycardia

Sinus bradycardia is common (9–25%) in the first hour, especially in inferior infarction. In some cases, opioids are responsible. If associated with hemodynamic compromise it should be treated (Table 16).

AV block

Data from four large, randomized trials suggest that AV block occurs in almost 7% and persistent bundle-branch block in up to 5.3% of cases of STEMI. Patients with peri-infarction AV block have a higher in-hospital and late mortality than those with preserved AV conduction. The increased mortality is related to the extensive myocardial damage required to develop heart block rather than to the heart block itself.

While pacing has not been shown to increase long-term survival, it may still be indicated in symptomatic bradyarrhythmias associated with STEMI.

First-degree AV block needs no treatment. AV block associated with inferior wall infarction is usually transient, with a narrow QRS escape rhythm above 40 bpm and low mortality, whereas AV block related to anterior wall infarction is more often located below the AV node and associated with an unstable, wide QRS escape rhythm due to the extensive myocardial necrosis.

A new left bundle-branch block usually indicates extensive anterior infarction with a high likelihood for developing complete AV block and pump failure. The preventive placement of a temporary pacing electrode may be warranted. The subclavian route should be avoided following fibrinolysis or in the presence of antithrombin therapy.

Recommendations for permanent cardiac pacing for persistent conduction disturbances (>14 days) due to STEMI are outlined in the ESC Guidelines for cardiac pacing.
5. Routine prophylactic therapies in the acute phase

Recommendations are summarized in Table 18.

a. Antithrombotic agents: aspirin, clopidogrel, and antithrombins

See reperfusion treatments (Table 5).

b. Antiarrhythmic drugs

Routine prophylactic use is not justified.

c. β-Blockers

The benefit of long-term β-blockers after STEMI is well established (see below); the role of routine early i.v. administration is less firmly established. Two randomized trials of i.v. β-blockade in patients receiving fibrinolysis 138,139 were too small to allow conclusions to be drawn. A post hoc analysis of the use of atenolol in the GUSTO-I trial and a systematic review did not support the routine early i.v. use of β-blockers. 140,141

In the COMMIT CCS 2 trial, i.v. metoprolol followed by oral administration until discharge or up to 4 weeks in 45,852 patients with suspected infarction 142 did not improve survival when compared with placebo. Fewer patients had reinfarction or VF with metoprolol, but this was counterbalanced by a significant increase in cardiogenic shock. Early i.v. use of β-blockers is clearly contraindicated in patients with clinical signs of hypotension or congestive heart failure. Early use may be associated with a modest benefit in low-risk, haemodynamically stable patients. In most patients, however, it is prudent to wait for the patient to stabilize before starting an oral β-blocker.

d. Nitrates

The GISSI-3143 trial tested a strategy of routine transdermal use of nitrates vs. selected administration because of ongoing ischaemia in 19,394 patients. No significant reduction in mortality was observed with the routine administration. The ISIS-4 trial,144 in which oral mononitrate was administered acutely and continued for 1 month, also failed to show a benefit. The routine use of nitrates in the initial phase of a STEMI has not been shown convincingly to be of value and is, therefore, not recommended.

e. Calcium antagonists

A meta-analysis of trials involving calcium antagonists early in the course of a STEMI showed a non-significant adverse trend.145 There is no case for using calcium antagonists for prophylactic purposes in the acute phase.

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Table 17 Intravenous doses of recommended antiarrhythmic/antibradycardia medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bolus</th>
<th>Maintenance Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>150 mg over 10 min. Supplemental boluses of 150 mg may be given over 10–30 min for recurrent arrhythmias, but limited to 6–8 supplemental boluses in any 24-h period</td>
<td>1 mg/min for 6 h and then 0.5 mg/min may be necessary after initial bolus dose</td>
</tr>
<tr>
<td>Esmolol</td>
<td>500 μg/kg over 1 min, followed by 50 μg/kg/min over 4 min</td>
<td>60–200 μg/kg/min</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5–5 mg over 2 min; up to three doses</td>
<td>–</td>
</tr>
<tr>
<td>Atenolol</td>
<td>5–10 mg (1 mg/min)</td>
<td>–</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.15 mg/kg</td>
<td>–</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.25 mg each 2 h, up to 1.5 mg</td>
<td>–</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>0.5–0.75 mg/kg</td>
<td>–</td>
</tr>
<tr>
<td>Sotalol</td>
<td>20–120 mg over 10 min (0.5–1.5 mg/kg). May be repeated after 6 h (maximum 640 mg/24 h)</td>
<td>–</td>
</tr>
<tr>
<td>Verapamil</td>
<td>0.075–0.15 mg/kg over 2 min</td>
<td>–</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>0.25 mg/kg over 2 min</td>
<td>–</td>
</tr>
<tr>
<td>Atropine</td>
<td>Rapid bolus of at least 0.5 mg, repeated up to a total dose of 1.5–2.0 mg (0.04 mg/kg)</td>
<td>–</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>0.05–0.1 μg/kg/min, up to 2 μg/kg/min. Dosage adjusted to heart rate and rhythm</td>
<td>–</td>
</tr>
</tbody>
</table>

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Table 18 Routine prophylactic therapies in the acute phase of STEMI

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin: maintenance dose of 75–100 mg</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Clopidogrel: maintenance dose of 75 mg</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Non-selective and selective COX-2 agents</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>I.v. β-blocker</td>
<td>IIb</td>
<td>A</td>
</tr>
<tr>
<td>Oral β-blocker</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ACE-inhibitor: oral formulation on first day</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>for all patients in whom it is not contraindicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>for high-risk patients</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Nitrates</td>
<td>IIb</td>
<td>A</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Magnesium</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Glucose–insulin–potassium infusion</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

*aClass of recommendation.

*Level of evidence.
with STEMI. The recognition for the routine administration of i.v. magnesium in patients not optimal. The large MAGIC trial confirmed that there is no indication for this therapy in STEMI. 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 LV 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 STEMI. ST-segment elevation in V1–3 is very suggestive of the diagnosis; this lead should certainly be recorded in all cases of inferior STEMI and shock, if not done as a routine. Q-waves and ST-segment elevation in V1–3 also suggest right ventricular infarction. Echocardiography may confirm the diagnosis. Various degrees of right ventricular involvement in inferior STEMI can be found.

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/ARBs. I.v. fluid loading is effective in many cases: initially, it should be administered rapidly. Careful haemodynamic monitoring is required during i.v. fluid loading. Right ventricular infarction is often complicated by AF. 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. Direct PCI should be performed as soon as possible as it may result in rapid haemodynamic improvement. There has been some question of the effectiveness of fibrinolytic therapy in right ventricular infarction, but it certainly seems appropriate in the hypotensive patient if PCI is not available.

### Table 19 Dosages of inhibitors of the renin–angiotensin–aldosterone system in trials after myocardial infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Initial dosage</th>
<th>Target dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>GISSI-3&lt;sup&gt;143&lt;/sup&gt;</td>
<td>5 mg initially</td>
<td>Up to 10 mg daily</td>
</tr>
<tr>
<td>ISIS-4&lt;sup&gt;144&lt;/sup&gt;</td>
<td>6.25 mg initially, 12.5 mg in 2 h, 25 mg at 10–12 h</td>
<td>Up to 50 mg b.i.d.</td>
</tr>
<tr>
<td>CHINESE&lt;sup&gt;146&lt;/sup&gt;</td>
<td>6.25 mg initially, 12.5 mg 2 h later if tolerated</td>
<td>Up to 12.5 mg t.i.d.</td>
</tr>
<tr>
<td>SMILE&lt;sup&gt;144&lt;/sup&gt;</td>
<td>7.5 mg initially, repeated after 12 h and repeatedly doubled if tolerated</td>
<td>Up to 30 mg b.i.d.</td>
</tr>
<tr>
<td>AIR&lt;sup&gt;111&lt;/sup&gt;</td>
<td>2.5 mg b.i.d. increased to 5 mg b.i.d. if tolerated</td>
<td>Up to 5 mg b.i.d.</td>
</tr>
<tr>
<td>SAVE&lt;sup&gt;121&lt;/sup&gt;</td>
<td>Test of 6.25 mg, increased if tolerated to 25 mg t.i.d.</td>
<td>Up to 50 mg t.i.d.</td>
</tr>
<tr>
<td>TRACE&lt;sup&gt;111&lt;/sup&gt;</td>
<td>Test of 0.5 mg</td>
<td>Up to 4 mg daily</td>
</tr>
<tr>
<td>VALIANT&lt;sup&gt;221&lt;/sup&gt;</td>
<td>20 mg initially uptitrated in four steps</td>
<td>Up to 160 mg b.i.d.</td>
</tr>
<tr>
<td>OPTIMAAL&lt;sup&gt;220&lt;/sup&gt;</td>
<td>12.5 mg</td>
<td>Up to 50 mg daily</td>
</tr>
<tr>
<td>EPESUS&lt;sup&gt;222&lt;/sup&gt;</td>
<td>25 mg initially</td>
<td>Up to 50 mg daily</td>
</tr>
</tbody>
</table>

b.i.d = twice daily; t.i.d = three times daily.

f. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

It is now well established that ACE-inhibitors should be given to patients who have an impaired ejection fraction (EF ≤40%) or who have experienced heart failure in the early phase. The GISSI-3,<sup>143</sup> ISIS-4,<sup>144</sup> and the Chinese Study<sup>146</sup> have shown that ACE-inhibitors started on the first day reduce mortality in the succeeding 4–6 weeks by a small but significant amount. A systematic overview of trials of ACE-inhibition early in STEMI indicated that this therapy is safe, well tolerated, and associated with a small but significant reduction in 30-day mortality, with most of the benefit observed in the first week.<sup>144</sup> ACE-inhibitors should be started in the first 24 h if no contraindications are present.<sup>147</sup>

Opinions still differ as to whether to give ACE-inhibitors to all patients or to high-risk patients only. Patients who do not tolerate an ACE-inhibitor should be given an ARB (see Section H). Dosages are given in Table 19.

g. Magnesium

The large ISIS-4 trial<sup>144</sup> does not support the use of magnesium, although it has been argued that the magnesium regimen was not optimal. The large MAGIC trial confirmed that there is no indication for the routine administration of i.v. magnesium in patients with STEMI.<sup>148</sup>

h. Glucose–insulin–potassium

Although smaller studies have shown a favourable effect on the metabolism of the ischaemic myocardium, a high-dose glucose–insulin–potassium infusion had a neutral effect on mortality, cardiac arrest, and cardiogenic shock in >20 000 patients studied in the CREATE-ECLA trial.<sup>94</sup> Therefore, there is no indication for this therapy in STEMI.

### 6. Management of specific types of infarction

**a. Right ventricular infarction**

The recognition of right ventricular infarction is important because it may manifest itself as cardiogenic shock, but the appropriate treatment as non-diabetic patients. This has been shown to be associated with poorer outcome, and is presumably triggered by fear of treatment-related complications.<sup>154,155</sup> Fibrinolysis should not be withheld in patients with diabetes when indicated, even in the...
outcome in diabetic patients with acute coronary syndromes. However, as hypoglycaemia-induced ischaemia might also affect the glycaemic control by use of insulin infusion followed by multiple-dose insulin treatment has been shown to reduce long-term mortality as compared with routine oral antidiabetic therapy in diabetic patients.

In the more recent DIGAMI-2 study (n = 1253 patients), however, mortality did not differ significantly between diabetic patients randomized to either acute insulin infusion followed by insulin-based long-term glucose control, insulin infusion followed by standard glucose control, or standard glucometabolic management, probably reflecting a lack of difference in glucose control among the three groups. Because hyperglycaemia remained one of the most important predictors of outcome in this study, however, it appears to be reasonable to keep glucose levels within normal ranges in diabetic patients. Target glucose levels between 90 and 140 mg/dL (5 and 7.8 mmol/L) have been suggested. Care needs to be taken to avoid blood glucose levels below 80–90 mg/dL (4.4–5 mmol/L), however, as hypoglycaemia-induced ischaemia might also affect outcome in diabetic patients with acute coronary syndromes.

c. Patients with renal dysfunction
The 2-year mortality rate among STEMI patients with end-stage renal disease (creatinine clearance <30 mL/min) is much higher than in the general population, which might be explained on the one hand by a higher proportion of cardiovascular risk factors and on the other hand by the fact that acute reperfusion strategies are offered to these patients less frequently because of fear of higher bleeding rates and contrast medium-induced renal failure.

Although recommendations for STEMI patients with renal dysfunction are essentially the same as for patients without renal disease, the risk of a further deterioration of renal function must be taken into account when administering contrast dye during primary PCI and prescribing drugs such as ACE-inhibitors, ARBs, and diuretics.

E. Management of the later in-hospital course
Management of the later in-hospital phase will be determined by the amount of myocardial necrosis, the demographic characteristics of the patients, and the presence or absence of co-morbidity. While the patient who has become asymptomatic and with minimum myocardial damage may go home after a few days, particularly after a successful PCI, patients with significant LV dysfunction or those who are at risk of new events may require a longer hospitalization.

1. Ambulation
Patients with significant LV damage 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.

2. Management of specific in-hospital complications

a. 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 prophylactic doses of a LMWH and the application of compression stockings. When they occur, they should be treated with therapeutic doses of a LMWH, followed by oral anticoagulation for 3–6 months.

b. Intraventricular thrombus and systemic emboli
These are relatively uncommon complications. It may be treated by high-dose i.v. aspirin (1000 mg/24 h) or NSAIDs. A haemorrhagic effusion with tamponade is uncommon and is particularly associated with antithrombin treatment. It can usually be recognized echocardiographically. Treatment is by pericardiocentesis if haemodynamic compromise occurs. Antithrombin therapy must be interrupted unless there is an absolute indication for its continuous use.

c. Pericarditis
Acute pericarditis may complicate STEMI with transmural necrosis. It gives 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 i.v. aspirin (1000 mg/24 h) or NSAIDs. A haemorrhagic effusion with tamponade is uncommon and is particularly associated with antithrombin treatment. It can usually be recognized echocardiographically. Treatment is by pericardiocentesis if haemodynamic compromise occurs. Antithrombin therapy must be interrupted unless there is an absolute indication for its continuous use.

d. Late ventricular arrhythmias
VT and VF occurring during the first 24–48 h have a low predictive value for recurring risk of arrhythmias over time. Arrhythmias developing later are liable to recur and are associated with an increased risk of sudden death.

Aggressive attempts should be made to treat heart failure and to search for and correct myocardial ischaemia in patients with ventricular tachyarrhythmias. Myocardial revascularization should be performed, when appropriate, to reduce the risk of sudden death in patients experiencing VF or polymorphic VT. No controlled trials, however, have evaluated the effects of myocardial revascularization on VT or VF after STEMI. Observational studies suggest that revascularization is unlikely to prevent recurrent cardiac arrest in patients with markedly
abnormal LV function or sustained monomorphic VT, even if the original arrhythmia appeared to result from transient ischaemia.\textsuperscript{174,175}

Several prospective multicentre clinical trials have documented improved survival with implantable cardioverter–defibrillator (ICD) therapy in high-risk patients with LV dysfunction (EF < 40\%) due to prior infarction.\textsuperscript{176–178} Compared with conventional antiarrhythmic drug therapy, ICD therapy was associated with mortality reductions from 23 to 55\% depending on the risk group studied. The ICD is therefore the primary therapy to reduce mortality in patients with significant LV dysfunction, who present with haemodynamically unstable sustained VT or who are resuscitated from VF that does not occur within the first 24–48 h.\textsuperscript{130} Electrophysiological testing with catheter ablation may occasionally be of benefit if curable arrhythmias, such as bundle-branch re-entry, are revealed.

Patients with sustained monomorphic VT without haemodynamic instability are usually, but not always, at relatively low risk for sudden death (2\% yearly).\textsuperscript{179} If episodes are relatively infrequent, the ICD alone may be the most appropriate initial therapy, in order to avoid the relative ineffectiveness and adverse complications of drug therapy. ICD implantation is in this context also reasonable for treatment of recurrent sustained VT, who present with normal or near normal LV function. Electrophysiologically guided drug testing for assessing antiarrhythmic drug efficacy has largely been abandoned.

Since there is no evidence that suppression of asymptomatic non-sustained VT prolongs life there is no indication to treat non-sustained VT, unless it is associated with haemodynamic instability. Sotalol or amiodarone would then be most appropriate if symptomatic non-sustained VT is unresponsive to β-adrenergic blocking agents.

With the exception of β-blockers, antiarrhythmic drugs have not been shown in randomized clinical trials to be effective in the primary management of patients with life-threatening ventricular arrhythmias or in the prevention of sudden death, and should not be used as primary therapy for such purpose. Amiodarone therapy may be considered in special situations. The SCD-HeFT study showed no benefit of amiodarone in patients with New York Heart Association (NYHA) functional class II heart failure and potential harm in patients with NYHA functional class III heart failure and EF ≤ 35\%.\textsuperscript{176}

e. Post-infarction angina and ischaemia
Angina or recurrent ischaemia or reinfarction in the early post-infarction phase following either successful fibrinolysis or PCI is an absolute indication for urgent (repeated) coronary angiography and, if indicated, (repeated) PCI or CABG.

Although analyses 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 PCI with the sole aim of restoring patency is beneficial. In the OAT trial, PCI of the occluded infarct-related artery 3–28 calendar days after the acute event in 2166 stable patients (no chest pain or signs of ongoing ischaemia) did not reduce death, reinfarction, or heart failure, and was associated with an excess reinfarction during 4 years of follow-up.\textsuperscript{24}

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 LV function.

F. Risk assessment

1. Indications and timing
Several risk scores have been developed based on readily identifiable parameters in the acute phase before reperfusion.\textsuperscript{11,20,180,181} After reperfusion treatment it is important to identify patients at high risk of further events such as reinfarction or death, and hopefully to intervene in order to prevent these events. Because the risk of events decreases with time, early risk assessment is indicated. If not performed by LV angiography in the acute phase, assessment of infarct size and resting LV function by echocardiography will be undertaken within the first 24–48 h. The timing of further investigations will depend on local facilities and on whether or not angiography and PCI have been performed. With the increasing use of primary PCI, risk assessment before discharge has become less important since it can be assumed that the infarct-related coronary lesion has been treated and the presence or absence of significant lesions in other arteries has been assessed.

If in spite of angiography performed in the acute phase at the time of PCI there are concerns about inducible ischaemia in the infarct or non-infarct area, outpatient exercise testing (bicycle or treadmill) or stress imaging (using scintigraphy, echocardiography, or MRI) within 4–6 weeks is appropriate (Table 20). The relative advantages or disadvantages of these stress tests in a post-STEMI population are not well established. If the main concern is arrhythmia, additional electrophysiological testing may be needed before discharge (see below).

All patients should have their metabolic risk markers measured including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol, fasting triglyceride, and plasma glucose, as well as renal function. It has been shown that mean lipid levels vary little in the 4 days after an acute coronary syndrome and can be used for clinical decisions about further therapy.\textsuperscript{181}

2. Assessment of myocardial viability
LV dysfunction after STEMI may be due to necrosis, to stunning of viable myocardium remaining in the infarct territory, to hibernation of viable myocardium, or to a combination of all three.\textsuperscript{181b} Simple stunning should usually recover within 2 weeks of the acute ischaemic insult if reperfusion has been established, but, if ischaemic episodes persist, recurrent stunning may become hibernation and requires revascularization for recovery of function. These concepts are of most relevance in the patient with severely impaired LV function after STEMI when the need for revascularization to improve function is considered.

Several diagnostic techniques can detect myocardial viability. Of these, conventional myocardial perfusion scintigraphy (with thallium-201- or technetium-99 m-labelled agents) or stress echocardiography (usually with dobutamine) are most widely available, whereas MRI and PET are less available.
Table 20 Imaging modalities: timing and usefulness

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>At presentation</th>
<th>Within 48 h</th>
<th>Before or after discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echo at rest</td>
<td>If required for diagnosis</td>
<td>For LV function and presence of thrombus</td>
<td>For LV function, heart failure, shock, or new murmur</td>
</tr>
<tr>
<td>Stress ECG</td>
<td></td>
<td></td>
<td>For ischaemia</td>
</tr>
<tr>
<td>Stress perfusion SPECT</td>
<td></td>
<td></td>
<td>For viability and ischaemia, infarct size</td>
</tr>
<tr>
<td>Stress echo</td>
<td></td>
<td></td>
<td>For viability and ischaemia</td>
</tr>
<tr>
<td>PET (rest)</td>
<td></td>
<td></td>
<td>For viability</td>
</tr>
<tr>
<td>MRI (rest, stress, contrast-enhanced)</td>
<td></td>
<td></td>
<td>For LV function, infarct size, viability, and ischaemia</td>
</tr>
</tbody>
</table>

Echo = transthoracic echocardiography or transoesophageal if required; LV = left ventricular; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

3. Evaluation of risk of arrhythmia for prevention of sudden death

Primary prevention (prophylaxis) refers to treatment of subjects who are at risk but have not yet had a life-threatening ventricular arrhythmia or SCD episode.

Patients without symptomatic arrhythmias and those with EF $\geq 40\%$ are at such low risk of SCD that further testing or prophylactic therapy is not indicated.

Factors that in addition to reduced EF have been demonstrated to contribute to the risk for SCD include the presence of non-sustained VT, symptomatic heart failure, and sustained monomorphic VT inducible by electrophysiological testing. It is important to stress that the clinician’s ability to stratify patients using risk markers other than the ones mentioned is limited related to the lack of large prospective studies. Although T-wave alternans and other ECG techniques (heart rate variability/turbulence, QT dispersion, baroreflex sensitivity, and signal-averaged ECG) may be useful, additional studies are needed to further clarify their role in assessing the risk of SCD in differing clinical settings.

G. Rehabilitation and pre-discharge advice

Rehabilitation is aimed at restoring the patient to as full a life as possible, including return to work. It must take into account physical, psychological, and socio-economic factors. Rehabilitation should be offered to all patients after STEMI. The process should start as soon as possible after hospital admission, and be continued in the succeeding weeks and months. Rehabilitation programmes should be multidisciplinary and aimed at reducing risk factors for coronary artery disease (see also Section H). Home- and hospital-based rehabilitation seem to be similarly beneficial.

The details of the rehabilitation programmes are dealt with in the position paper of the Working Group on cardiac rehabilitation and exercise physiology of the ESC.

1. Psychological and socio-economic aspects

Anxiety is almost inevitable, in both 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 recognized 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. Large studies suggest a role for psychosocial factors as prognostic factors in cardiovascular disease, with the strongest evidence for depression as a negative factor in post-infarction patients. However, whether depression is an independent risk (after adjustment for conventional risk factors) is still unclear and there is, so far, little evidence that any intervention targeting these factors improves prognosis.

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

2. 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 (see Section H).

3. Physical activity

All patients should be given advice with regard to physical activity based upon their recovery from the acute event, taking into account their age, their pre-infarction level of activity, and their physical limitations. In selected cases assessment is aided by a pre-discharge exercise test, which not only provides useful clinical information but can be reassuring to the overanxious patient. A meta-analysis of rehabilitation programmes performed in the pre-reperfusion era which included exercise suggested a significant reduction in mortality, findings recently confirmed in another meta-analysis updated with studies conducted until 2003.

H. Secondary prevention

Coronary heart disease is a chronic condition, and patients who have recovered from a STEMI are at high risk for new events and premature death. Eight to 10% of post-infarction patients have a recurrent infarction within a year after discharge, and mortality after discharge remains much higher than in the general population.
Several evidence-based interventions can improve prognosis. Even though long-term management of this large group of patients will be the responsibility of the general practitioner, these interventions will have a higher chance of being implemented if initiated during hospital stay. In addition, lifestyle changes should be explained and proposed to the patient before discharge. However, habits of a lifetime are not easily changed, and the implementation and follow-up of these changes are a long-term undertaking. In this regard, a close collaboration between the cardiologist and the general practitioner is critically important. Recommendations are given in Tables 21 and 22.

1. Smoking cessation

Unselected acute coronary syndrome patients who are smokers are twice as likely to present as STEMI compared with nonsmokers, indicating a strong prothrombotic effect of smoking. Evidence from observational studies shows that those who stop smoking reduce their mortality in the succeeding years by at least one-third compared with those who continue to smoke. Stopping smoking is potentially the most effective of all secondary prevention measures, and much effort should be devoted to this end. Patients do not smoke during the acute phase of a STEMI, and the convalescent period is ideal for health professionals to help smokers to quit. However, resumption of smoking is common after returning home, and continued support and advice is needed during rehabilitation. Nicotine replacement, bupropione, and antidepressants may be useful. A randomized study has also demonstrated the effectiveness of a nurse-directed programme. A smoking cessation protocol should be adopted by each hospital.

2. Diet, dietary supplements, and weight control

Evidence from systematic reviews of randomized controlled trials on food and nutrition in secondary prevention has recently been published. Current guidelines on prevention recommend (i) to eat a wide variety of foods; (ii) adjustment of calorie intake to avoid overweight; (iii) increased consumption of fruit and vegetables, along with wholegrain cereals and bread, fish (especially oily), lean meat, and low-fat dairy products; (iv) to replace saturated and trans fats with monounsaturated and polyunsaturated fats from vegetable and marine sources and to reduce total fats to <30% of total calorie intake, of which less than one-third should be saturated; and (v) to reduce salt intake if blood pressure is high. Several evidence-based interventions can improve prognosis.

### Table 21 Long-term medical treatment after STEMI

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiplatelets/anticoagulants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin for ever (75–100 mg daily) in all patients without allergy</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Clopidogrel (75 mg daily) for 12 months in all patients irrespective of the acute treatment</td>
<td>Iia</td>
<td>C</td>
</tr>
<tr>
<td>Clopidogrel (75 mg daily) in all patients with contraindication to aspirin</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Oral anticoagulant at INR 2–3 in patients who do not tolerate aspirin and clopidogrel</td>
<td>Iia</td>
<td>B</td>
</tr>
<tr>
<td>Oral anticoagulant at recommended INR when clinically indicated (e.g., atrial fibrillation, LV thrombus, mechanical valve)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Oral anticoagulant (at INR 2–3) in addition to low-dose aspirin (75–100 mg) in patients at high risk of thromboembolic events</td>
<td>Iia</td>
<td>B</td>
</tr>
<tr>
<td>Oral anticoagulant in addition to aspirin and clopidogrel (recent stent placement plus indication for oral anticoagulation)</td>
<td>Iib</td>
<td>C</td>
</tr>
<tr>
<td>Oral anticoagulant in addition to clopidogrel or aspirin (recent stent placement plus indication for oral anticoagulation and increased risk of bleeding)</td>
<td>Iib</td>
<td>C</td>
</tr>
<tr>
<td><strong>β-Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral β-blockers in all patients who tolerate these medications and without contraindications, regardless of blood pressure or LV function</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>ACE-inhibitor and ARB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE-inhibitor should be considered in all patients without contraindications, regardless of blood pressure or LV function</td>
<td>Iia</td>
<td>A</td>
</tr>
<tr>
<td>ARB in all patients without contraindications who do not tolerate ACE-inhibitors, regardless of blood pressure or LV function</td>
<td>Iia</td>
<td>C</td>
</tr>
<tr>
<td><strong>Statins</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins in all patients, in the absence of contraindications, irrespective of cholesterol levels, initiated as soon as possible to achieve LDL cholesterol &lt;100 mg/dL (2.5 mmol/L)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Influenza immunization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In all patients</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

*Class of recommendation.

*Level of evidence.

*If long-term oral anticoagulation is required, use of a bare metal stent rather than a drug-eluting stent will expose the patient to a shorter duration of triple therapy and hence a lower bleeding risk.
is raised. Many processed and prepared foods are high in salt, and in fat of doubtful quality.

There is no evidence for the use of antioxidant supplements of antioxidants, low glycaemic index diets, or homocysteine-lowering therapies post-STEMI. The role of omega-3 fatty acid supplements for secondary prevention is unclear. In the only (open-label) randomized study in patients post-myocardial infarction, the GISSI prevenzione trial, 1 g daily of fish oil on top of a Mediterranean diet significantly reduced total and cardiovascular mortality. However a meta-analysis, including GISSI prevenzione, showed no effect on mortality or cardiovascular events and no evidence that the source or dose affect outcome. Obesity is an increasing problem in patients with STEMI. At least one-third of European women and one in four men with acute coronary syndromes below the age of 65 have a body mass index (BMI) of \( \geq 30 \text{ kg/m}^2 \). Current ESC Guidelines define a

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**Table 22 Long-term management of specific coronary risk factors and LV dysfunction**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class(^a)</th>
<th>Level(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking cessation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assess smoking status and advise to quit and to avoid passive smoking at each visit</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Bupropione and nicotine treatment in patients who keep smoking at follow-up</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Ia</td>
<td>C</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise test-guided moderate intensity aerobic exercise at least five times per week</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Medically supervised rehabilitation programmes for high-risk patients</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>Diabetes management</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifestyle changes and pharmacotherapy to achieve HbA1c &lt; 6.5%</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Intensive modification of other risk factors (hypertension, obesity, dyslipidaemia)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Coordination with a physician specialized in diabetes</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td><strong>Diet and weight reduction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight reduction is recommended when BMI is ( \geq 30 \text{ kg/m}^2 ) and when waist circumference is ( &gt; 102/88 \text{ cm (men/women)} )</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Diet based on low intake of salt and saturated fats, and regular intake of fruit, vegetables, and fish</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Increased consumption of omega-3 fatty acid (oily fish)</td>
<td>Ilb</td>
<td>B</td>
</tr>
<tr>
<td>Supplementation with 1 g of fish oil in patients with a low intake of oily fish</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>Moderate alcohol consumption should not be discouraged</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td><strong>Blood pressure control</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifestyle changes and pharmacotherapy to achieve BP ( &lt;130/80 \text{ mmHg} )</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Lipid management</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins in all patients, in the absence of contraindications, irrespective of cholesterol levels, initiated as soon as possible to achieve LDL cholesterol ( &lt; 100 \text{ mg/dL (2.5 mmol/L)} )</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Further reduction of LDL cholesterol to achieve ( &lt; 80 \text{ mg/dL (2.0 mmol/L)} ) should be considered in high-risk patients</td>
<td>Ilb</td>
<td>A</td>
</tr>
<tr>
<td>Lifestyle change emphasized if TG ( &gt; 150 \text{ mg/dL (1.7 mmol/L)} ) and/or HDL cholesterol ( &lt; 40 \text{ mg/dL (1.0 mmol/L)} )</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Fibrates and omega-3 supplements should be considered in patients who do not tolerate statins, especially if TG ( &gt; 150 \text{ mg/dL (1.7 mmol/L)} ) and/or HDL cholesterol ( &lt; 40 \text{ mg/dL (1.0 mmol/L)} )</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td><strong>Management of heart failure or LV dysfunction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral β-blockers in all patients without contraindications</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ACE-inhibitors in all patients without contraindications</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ARB (valsartan) in all patients without contraindications who do not tolerate ACE-inhibitors</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Aldosterone antagonists if EF ( \leq 40% ) and signs of heart failure or diabetes if creatinine is ( &lt; 2.5 \text{ mg/dL in men and } &lt; 2.0 \text{ mg/dL in women and potassium is } &lt; 5.0 \text{ mmol/L} )</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>CRT in patients with EF ( \leq 35% ) and QRS duration of ( \geq 120 \text{ ms who remain in NYHA class III–VI at least 40 days after STEMI} )</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Prevention of sudden death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD if EF ( \leq 30–40% ) and NYHA ( \geq II ) or III at least 40 days after STEMI</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ICD if EF ( \leq 30–35% ) and NYHA ( I ) at least 40 days after STEMI</td>
<td>Ila</td>
<td>B</td>
</tr>
</tbody>
</table>

\(^a\)Class of recommendation.

\(^b\)Level of evidence.

\(\text{TG} = \text{triglyceride.}\)
Each single-stage increase in physical work capacity is recommended. Exercise therapy at least five times per week is recommended for patients with coronary artery disease. Four mechanisms are considered to be important mediators of a reduced cardiac event rate: (i) improvement of endothelial function; (ii) reduced progression of coronary lesions; (iii) reduced thrombogenic risk; and (iv) improved collateralization. In a large meta-analysis, exercise training as part of coronary rehabilitation programmes was associated with a 26% reduction in cardiac mortality rate in patients with coronary artery disease. It should be appreciated that apart from its influence on mortality, exercise rehabilitation can have other beneficial effects. Exercise capacity, cardiorespiratory fitness, and perception of well-being have also been reported to improve, at least during the actual training period, even in elderly patients. Thirty minutes of moderate intensity aerobic exercise at least five times per week is recommended. Each single-stage increase in physical work capacity is associated with a reduction in all-cause mortality risk in the range of 8–14%.

3. Physical activity
Exercise therapy has long been used for rehabilitation purposes following STEMI, and the benefit of regular physical exercise in stable coronary artery disease patients is also well established. Four mechanisms are considered to be important mediators of a reduced cardiac event rate: (i) improvement of endothelial function; (ii) reduced progression of coronary lesions; (iii) reduced thrombogenic risk; and (iv) improved collateralization. In a large meta-analysis, exercise training as part of coronary rehabilitation programmes was associated with a 26% reduction in cardiac mortality rate in patients with coronary artery disease. It should be appreciated that apart from its influence on mortality, exercise rehabilitation can have other beneficial effects. Exercise capacity, cardiorespiratory fitness, and perception of well-being have also been reported to improve, at least during the actual training period, even in elderly patients. Thirty minutes of moderate intensity aerobic exercise at least five times per week is recommended. Each single-stage increase in physical work capacity is associated with a reduction in all-cause mortality risk in the range of 8–14%.

4. Antiplatelet and anticoagulant treatment
The Antiplatelet Trialists Collaboration 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 evidence that the lower dosages are effective, with fewer side effects. Clinical trials undertaken before the widespread use of aspirin showed that oral anticoagulants (vitamin K antagonists) are effective in preventing reinfarction and death in infarct survivors. Aspirin can be replaced by oral anticoagulants at the recommended international normalized ratio (INR) if there is an indication for oral anticoagulation (e.g. atrial fibrillation, LV thrombus, mechanical valves). In a large meta-analysis of patients with acute coronary syndromes followed for up to 5 years (including >10 000 patients with infarction), the combination of aspirin and oral anticoagulation at INR 2–3 prevented three major adverse events and caused one major bleed per 100 patients treated compared with aspirin alone. This combination therefore seems to be a reasonable treatment in STEMI survivors who have a high risk of thromboembolic events. In some patients, there is an indication for dual antiplatelet therapy and oral anticoagulation (e.g. stent placement and AF). In the absence of prospective randomized studies, no firm recommendations can be given. Triple therapy seems to have an acceptable risk–benefit ratio provided clopidogrel co-therapy is kept short and the bleeding risk is low. Oral anticoagulants plus a short course of clopidogrel might be an alternative in patients with a higher risk of bleeding. Most importantly, drug-eluting stents should be avoided in patients who need oral anticoagulation. Oral anticoagulants may also be considered in patients who do not tolerate aspirin or clopidogrel.

5. β-Blockers
Several trials and meta-analyses have demonstrated that β-blockers reduce mortality and reinfarction by 20–25% in those who have recovered from an infarction. Most of these trials have been performed in the pre-reperfusion era. A meta-analysis of 82 randomized trials provides strong evidence for long-term use of β-blockers to reduce morbidity and mortality after STEMI even if ACE-inhibitors are co-administered. The significant mortality reductions observed with β-blockers in heart failure in general further support the use of these agents after STEMI. Evidence from all available studies suggests that β-blockers should be used indefinitely in all patients who recovered from a STEMI and do not have a contraindication.

6. Calcium antagonists
Trials with verapamil and diltiazem have suggested that they may prevent reinfarction and death. In a trial in 874 patients with STEMI treated with fibrinolytic agents but without heart failure, the 6-month use of diltiazem (300 mg daily) reduced the rate of coronary interventions. The use of verapamil and diltiazem may be appropriate when β-blockers are contraindicated, especially in obstructive Airways disease. Caution must be exercised in the presence of impaired LV function. Trials with dihydro- pyridines have failed to show a benefit in terms of improved prognosis; they should, therefore, only be prescribed for clear clinical indications such as hypertension or angina.

7. Nitrates
There is no evidence that oral or transdermal nitrates improve prognosis. The ISIS-4 and GISSI-3 trials failed to show a benefit at 4–6 weeks after the event. Nitrates continue to be first-line therapy for angina pectoris.
8. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

Several trials have established that ACE-inhibitors reduce mortality after STEMI with reduced residual LV function (<40%). There is a strong case for administering ACE-inhibitors to patients who have experienced heart failure in the acute phase, even if no features of this persist, who have an EF of ≤40%, or a wall motion index of ≥1.2, provided there are no contraindications. Against such a policy is the increased incidence of hypotension and renal failure in those receiving ACE-inhibitors in the acute phase, and the small benefit in those at relatively low risk, such as patients with small inferior infarctions. In favour are observations from studies in populations with stable cardiovascular disease but without LV dysfunction showing beneficial effects, including a reduction in mortality and stroke. Use of ACE-inhibitors should be considered in all patients with atherosclerosis, but, given the relatively modest effect, their long-term use cannot be considered to be mandatory in post-STEMI patients who are normotensive, without heart failure or compromised systolic LV function.

Two trials have evaluated ARBs in the context of STEMI as alternatives to ACE-inhibitors: the OPTIMAAL trial with losartan (50 mg) failed to show superiority or non-inferiority over captopril (50 mg three times daily). Conversely, the VALIANT trial compared valsartan alone (160 mg twice daily), full-dose captopril (50 mg three times daily), or both (80 mg twice daily and 50 mg three times daily). Mortality was similar in the three groups, but discontinuations were more frequent in the groups receiving captopril. Therefore, valsartan in dosages as used in the trial represents an alternative to ACE-inhibitors in patients who do not tolerate ACE-inhibitors and have clinical signs of heart failure and/or an EF ≤40%.

9. Aldosterone blockade

The EPHESUS trial randomized 6642 post-STEMI patients with LV dysfunction (EF ≤40%) and heart failure or diabetes to eplerenone, a selective aldosterone blocker, or placebo. After a mean follow-up of 16 months, there was a 15% relative reduction in total mortality and a 13% reduction in the composite of death and hospitalization for cardiovascular events. However, serious hyperkalaemia was more frequent in the group receiving eplerenone. The results suggest that aldosterone blockade may be considered for post-STEMI patients with an EF <40% and heart failure or diabetes provided that creatinine is <2.5 mg/dL in men and 2.0 mg/dL in women, and potassium is ≤5.0 mEq/L. Routine monitoring of serum potassium is warranted and should be particularly careful when other potential potassium-sparing agents are used.

10. Blood pressure control

According to the ESC Guidelines for the management of arterial hypertension the goal is to achieve a blood pressure <130/80 mmHg in patients with stroke, myocardial infarction, renal disease, and diabetes. Pharmacotherapy recommended post-STEMI (β-blockers, ACE-inhibitors, or ARBs) will help to achieve these goals, in addition to lifestyle modification with respect to physical activity and weight loss. Additional pharmacotherapy may be needed.

11. Management of diabetes

Glucometabolic disturbances are common in patients with coronary disease and should be actively searched for. Since an abnormal glucose tolerance test is a significant risk factor for future cardiovascular events after myocardial infarction, it seems meaningful to perform such a test before or shortly after discharge. In patients with established diabetes, the aim is to achieve HbA1c levels ≤6.5%. This calls for intensive modification of lifestyle (diet, physical activity, weight reduction), usually in addition to pharmacotherapy. Coordination with a physician specialized in diabetes is advisable. In patients with impaired fasting glucose level or impaired glucose tolerance, only lifestyle changes are currently recommended.

12. Interventions on lipid profile

Several trials have unequivocally demonstrated the benefits of long-term use of statins in the prevention of new ischaemic events and mortality in patients with coronary heart disease. The targets established by the Fourth Joint Task Force of the ESC and other societies in patients after infarction are: for total cholesterol, 175 mg/dL (4.5 mmol/L) with an option of 155 mg/dL (4.0 mmol/L) if feasible, and for lower LDL cholesterol 100 mg/dL (2.5 mmol/L) with an option of 80 mg/dL (2.0 mmol/L) if feasible. Although pharmacological treatment is highly efficient in treating dyslipidaemia in heart disease, diet remains a basic requirement for all patients with coronary heart disease. The most recent controversy on lipid-lowering treatment has been focused on intensive, vs. standard lipid-lowering therapy. A recent meta-analysis of randomized controlled trials that compared different intensities of statin therapy identified a total of seven trials, with a total of 29,395 patients with coronary artery disease. Compared with less intensive statin regimens, more intensive regimens further reduced LDL cholesterol levels and reduced the risk of myocardial infarction and stroke. Although there was no effect on mortality among patients with chronic coronary artery disease [odds ratio (OR) 0.96, 95% confidence interval (CI) 0.80–1.14], all-cause mortality was reduced among patients with acute coronary syndromes treated with more intensive statin regimens (OR 0.75, 95% CI 0.61–0.93). All seven trials reported events by randomization arm rather than by LDL cholesterol level achieved. About half of the patients treated with more intensive statin therapy did not achieve an LDL cholesterol level of <80 mg/dL (2.0 mmol/L), and none of the trials tested combination therapies. The analysis supports the use of more intensive statin regimens in patients with established coronary artery disease. There is insufficient evidence to advocate treating to particular LDL cholesterol targets, using combination lipid-lowering therapy to achieve these targets.

In patients who do not tolerate statins, or who have contraindications, other lipid-lowering therapy may be warranted. In a study with gemfibrozil (a fibrate), patients with HDL cholesterol levels...
infarction that occurred at least 40 days earlier when heart
excluded. CRT treatment whenever stunning of viable myocardium can be

reduced. Prophylactic antiarrhythmic drug therapy is not indicated

tification procedures to allow adequate time for recovery of LV

tation should be deferred until at least 3 months after revascular-

ICD implantation should be deferred until at least 40 days after

functional class I on chronic optimal medical therapy. In general,

/ C 20

no clinical data to support its current use in STEMI survivors.

The most critical time of a STEMI is the very early phase, during

1. Pre-hospital care

The most critical time of a STEMI is the very early phase, during

I. Logistics of care

a. Patient delay

The most critical time of a STEMI is the very early phase, during

(13. Influenza vaccination

Influenza immunization is indicated in all patients with coronary

to two patient groups: (i) patients whose EF is

The ICD is the only specific antiarrhythmic treatment proved con-

15. Prophylactic implantation of an

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a. Patient delay

The most critical time of a STEMI is the very early phase, during

I. Logistics of care

1. Pre-hospital care

The most critical time of a STEMI is the very early phase, during

arrest. Furthermore, the earlier that some treatments, notably

reperfusion therapy, are given, the greater the beneficial effect

(time is muscle). Yet, it is often an hour or more after the

onset of symptoms before medical aid is requested. Older patients,

female, diabetic, and congestive heart failure patients are more

likely to delay seeking care.

It should be a normal part of the care of patients with known
coronary heart disease to inform their partners and family about

the symptoms of a heart attack and how to respond to it. The

benefit of education of the general public for reducing delay
times is uncertain. The public must at least be aware of how to
call the EMS.

b. Emergency medical system

An EMS with a well-known unique telephone number for medical

emergencies only is important to avoid further delays.235 Dispatch-

ers have variable degrees of medical training. A tele-consultation

with a reference cardiological centre is ideal but available in a

limited number of countries only. An updated and shared

written management protocol is critically important.236 Although

the use of an EMS decreases delay time,237 it is underutilized238

in many countries.

c. Public education in cardiopulmonary 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 advanced cardiopulmonary resuscitation.

d. The ambulance service

The ambulance (helicopter) service has a critical role in the man-

agement of a STEMI,239 and should be considered not only a mode

of transport but a place for initial diagnosis, triage, and treat-

ment.240 Ambulances should be able to reach the great majority

of chest pain patients within 15 min of the call. 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 recognize the symptoms of a STEMI, administer oxygen,

relieve pain, and provide basic life support. All emergency ambu-

lances (helicopters) should be equipped with 12-lead ECG recor-

ders and defibrillators, and at least one person on board should be

trained in advanced life support.

Ambulance staff should be able to record an ECG for diagnostic

purposes and either interpret it or transmit it so that it can be

reviewed by experienced staff in an Intensive Cardiac Care Unit

(ICCU) or elsewhere. The recording of an ECG prior to hospital

admission can greatly accelerate in-hospital management241,242

and increase the probability of reperfusion therapy.243,244

Physician-manned ambulances, available in only a few countries,
can provide more advanced diagnostic and therapeutic services,

including administration of opioids and fibrinolytic drugs. Since pre-
hospital administration of fibrinolytic therapy is the most effective

way to shorten delay times for this type of reperfusion therapy,245

training of paramedics to undertake these functions is rec-

ommended.246 In specific regions, air ambulance systems further

improve transportation delays and outcomes.247
e. Networks
As indicated above, the implementation of a network of hospitals connected by an efficient ambulance (helicopter) service and using a common protocol is key for an optimal management of patients with STEMI.

With such a network in place, target delay times should be: <10 min for ECG transmission; ≤5 min for tele-consultation; <30 min for ambulance arrival to start fibrinolytic therapy; and <120 min for ambulance arrival to first balloon inflation. Quality of care, appropriateness of reperfusion therapy, delay times, and patient outcomes should be measured and compared at regular times, and appropriate measures for improvement should be taken.

f. General practitioners
In many countries, general practitioners still play a major role in the early care of STEMI. In these countries they are often the first to be called by patients. If they respond quickly, they can be very effective since they usually know the individual patient and can take and interpret the ECG, are able to administer opioids, to take and interpret the ECG, are able to administer opioids, to

2. The Intensive Cardiac Care Unit
STEMI patients should be admitted to ICCUs after the initial reperfusion therapy, which is given in the ambulance, in the emergency room, or in the cath lab. ICCUs should be equipped adequately and staffed with dedicated and properly trained physicians and nurses, due to the increased complexity of older and sicker patients.

a. Non-invasive monitoring
ECG monitoring for arrhythmias and ST-segment deviations should be started immediately in any patient suspected of having sustained a STEMI. This should be continued for at least 24 h. Further ECG monitoring for arrhythmias is dependent upon the perceived risk and upon the equipment available. When a patient leaves the ICCU, monitoring of rhythm may be continued, if necessary, by telemetry. A more prolonged stay at the ICCU is appropriate for those who have sustained heart failure, shock, or serious arrhythmias in the acute phase, as the risk of further events is high.

b. Invasive monitoring
All ICCUs 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. Pulmonary artery catheters have been used for a long time in ICCUs in haemodynamically unstable patients. However, recent studies did not show a benefit of a routine use of these procedures on mortality or on the length of the hospital stay. A restricted use is recommended.

3. The post-discharge period
Multidisciplinary rehabilitation services should be available, and follow-up of the secondary prevention programme should be organized before discharge.

J. Gaps in evidence
There is limited experience with PCI in STEMI patients presenting more than 12 h after onset of symptoms. Transporting patients from a community to a PCI-capable hospital for primary PCI remains a challenge. Even in the best networks many patients are treated with PCI outside the recommended time window. It is unknown whether pre-hospital fibrinolysis during transport to a PCI-capable hospital in patients presenting early to the EMS is beneficial if the intervention cannot be performed within the recommended time window. Cardiologists in community hospitals are still uncertain which pharmacological treatment to start before transport. A number of patients need oral anticoagulation after primary PCI with stenting. Whether aspirin and/or an ADP antagonist added to coumarins are effective and safe in all patients is unknown as is the optimal duration of this antithrombotic regimen. Randomized studies in patients with mechanical complications are lacking.

K. Procedures of the Task Force
This Task Force was created by the ESC in 2006. Individual members were invited to update sections of the 2003 guidelines in their area of expertise. These were discussed at meetings in Frankfurt on March 16, 2007 and January 8, 2008. After several revisions, the final document was submitted to the Committee for Practice Guidelines for approval on August 19, 2008. Invaluable assistance in processing the document was provided by Veronica Dean, Karine Pellard (ESC), Krista Bogaert, Anita Meuris, and Roos Struyven (University of Leuven). The guidelines were developed without any involvement of the industry.

Recommendations of guidelines 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. For instance, large registries have demonstrated that ~30% of all STEMI patients did not receive reperfusion therapy. There is a great need both for continuing medical education and for ongoing audit to ensure the implementation of guidelines. Task Forces should play an active role in this effort.

The electronic version of this document is available on the website of the European Society of Cardiology: www.escardio.org in the section ‘Scientific information’, Guidelines.
The Organizing Committee is responsible for ensuring that all potential conflicts of interest relevant to the programme are declared to the participants prior to the CME activities. In compliance with EBAC/EACCME guidelines, all authors participating in this programme have disclosed potential conflicts of interest that might cause a bias in the article.

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