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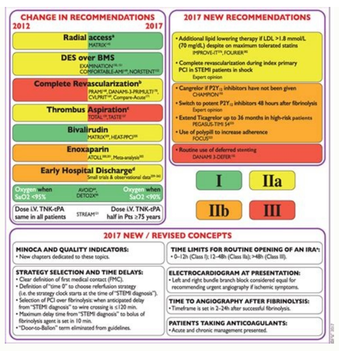


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Achieved diastolic blood pressure and pulse pressure at target systolic blood pressure (120–140 mmHg) and cardiovascular outcomes in high-risk patients: results from ONTARGET and TRANSCEND trials. See Figure legend on page 2913.

Focus Issue on Hypertension

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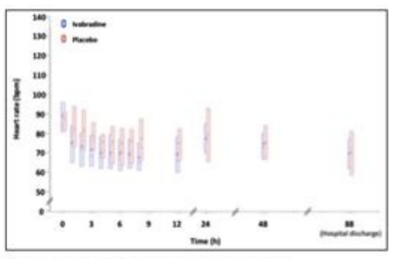

Figure 3. Heart rate from bolus to discharge (12-lead electrocardiographic recordings).

prasugrel in the study. With respect to glycoprotein IIb/IIIa blockers, 59% (48/82) of the patients received GpIIb/IIIa blockers in the ivabradine group (41 abciximab, 4 tirofiban and 3 eptifibatide) and the proportion was 70% (25/41) in the placebo group (19 abciximab, 4 tirofiban, 2 eptifibatide). The majority of patients received bare metal stents, with 28% of the ivabradine patients and 37% of the placebo patients receiving at least one drug-eluting stent.

Effect on heart rate

The changes in heart rate over the treatment period and up to hospital discharge are shown in Figure 3. Ivabradine reduced heart rate from 88.2±9.8 bpm at baseline to 66.2±10.1 bpm at last value over the 8 h treatment period (E(SE), −22.2 (1.3) bpm, 95% CI, −24.6 to −19.4). Most of the heart rate reduction was achieved by 4 h after starting therapy. Heart rate in the placebo group was reduced from 87.2±8.1 to 78.3±14.6 bpm over the same time period (E(SE), −8.9 (1.8) bpm, 95% CI, −12.6 to −5.2). This difference at 8 h between groups was significant ($p<0.001$). Similar changes in heart rate were found by continuous heart rate monitoring (−19.3±10.9 bpm from baseline to last value over 12 h with ivabradine versus −8.4±11.6 bpm with placebo ($p<0.001$). After the infusion, heart rate returned to placebo levels by 48 h, and remained similar in both groups at hospital discharge.

As expected in STEMI patients, there were increases in plasma concentrations of all cardiac markers (troponin I, troponin T, and CK-MB) up to 5 h after bolus, declining towards normal values at 24 h (Figure 4). Throughout the study period, there was no difference between groups in the levels of biomarkers.

Echocardiographic results

Echocardiographic measurements were made at baseline and last post-treatment (mean: 1.16±0.98 days) for 23 patients (28%) in the ivabradine group versus 11 patients (28%) in the placebo group (Table 2). There were no differences between ivabradine and placebo in baseline left ventricular volumes. However, final volumes were lower in the ivabradine group both for LVEDV (87.1±28.2 versus 117.8±21.4 ml for ivabradine versus placebo, $p=0.01$) and LVESV (42.5±19.0 versus 59.1±11.3 ml, $p=0.03$). There were no significant differences in the changes in volumes between groups, nor was there a difference in baseline or final LVEF (Table 2).

MRI results

Based upon feasibility in the AMI setting, a subset of 37 patients underwent MRI. The MRI results at hospital discharge and at four months are presented in Table 3. The area of delayed hyperenhancement, which is indicative of the infarcted volume as a percentage of LV mass, was 12.7% with ivabradine versus 17.2% placebo at hospital discharge. The inter–group difference was −4.6% (95% CI −11.4 to 2.3, $p=0.190$). Microvascular obstruction was found in 8/26 patients in the ivabradine group (31%) and 6/14 patients in the placebo group (43%) at discharge. The inter-group difference (in grams of myocardium with obstruction) was 2.6 (95% CI −8.8 to 3.7, $p=0.315$). In patients with obstruction, the mean size of the area of microvascular obstruction was similar in both groups (3.6% vs 4.6% of the LV mass at discharge, for the ivabradine and placebo groups respectively, with a

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REVIEW

Clinical update

Management of cardiogenic shock

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Cardiogenic shock (CS) remains the most common cause of death in patients with acute myocardial infarction although mortality could be reduced from formerly ~80% to 40–50%. In addition to percutaneous coronary intervention or coronary artery bypass grafting, catecholamines, fluids, intraaortic balloon pumping (IABP), and also active assist devices are widely used for CS management. However, there is only limited evidence for any of the above treatments except for early revascularization and the relative ineffectiveness of IABP. This updated review will therefore outline the management of CS complicating acute myocardial infarction with major focus on evidence-based revascularization techniques, intensive care unit treatment including ventilation, transfusion regimens, adjunctive medication, and mechanical support devices.

Keywords Shock • Heart failure • Treatment • Percutaneous coronary intervention • Myocardial infarction • Assist device

Introduction

Cardiogenic shock (CS) is defined as a state of critical endorgan hypoperfusion due to reduced cardiac output. Notably, CS forms a spectrum that ranges from mild hypoperfusion to profound shock. Established criteria for the diagnosis of CS are: (i) systolic blood pressure <90 mmHg for >30 min or vasopressors required to achieve a blood pressure ≥90 mmHg; (ii) pulmonary congestion or elevated left-ventricular filling pressures; (iii) signs of impaired organ perfusion with at least one of the following criteria: (a) altered mental status; (b) cold, clammy skin; (c) oliguria; (d) increased serum-lactate. The diagnosis of CS can usually be made on the basis of easy-to-assess clinical criteria without advanced haemodynamic monitoring although it has previously been recommended to assess cardiac index and pulmonary capillary wedge pressure.[1]

Acute myocardial infarction (AMI) with subsequent ventricular dysfunction is the most frequent cause of CS accounting for ~80% of cases. Mechanical complications such as ventricular septal (4%) or free wall rupture (2%), and acute severe mitral regurgitation (7%) are less frequent causes of CS after AMI.[2] Non-AMI-related CS may be caused by decompensated valvular heart disease, acute myocarditis, arrhythmias, etc. with heterogeneous treatment options.

Cardiogenic shock complicating AMI occurs in the range from 5 to 15%.[3–5] This translates in ~40 000 to 50 000 patients per year in the USA and ~60 000 to 70 000 in Europe.[6] Despite advances in treatment, mainly by early revascularization with subsequent mortality reduction, CS remains the leading cause of death in AMI with mortality rates still approaching 40–50% according to recent registries and randomized trials.[3–5,7]

The underlying causes, the pathophysiology, and treatment of CS complicating AMI have been reviewed previously.[1,8] This update will outline evidence-based therapeutic management of CS complicating AMI with major focus on revascularization techniques, intensive care unit treatment including ventilation, transfusion regimens, adjunctive medication, and mechanical support devices.

Pathophysiology and prognosis assessment

The pathophysiology of CS is complex and has been summarized previously.[1,8] In brief, ischaemia induces profound depression of myocardial contractility, which initiates a vicious spiral of reduced cardiac index and low blood pressure which in combination impair cardiac power index and further promote coronary ischaemia. The reduction in cardiac index causes severe tissue hypoperfusion which is most sensitively measured by serum lactate and may finally lead to death if the circle is not successfully interrupted by adequate treatment measures. It has been recognized that CS cannot only be attributed to the loss of left-ventricular function but is rather the result of derangements in the entire circulatory system. Initial compensatory vasoconstriction is subsequently counteracted by pathological vasodilation. Among others, development of systemic

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PDF Split View Article contents Figures & tables Video Audio Supplementary Data Guidelines, Acute coronary syndromes, Acute myocardial infarction, Antithrombotic therapy, Antithrombotics, Emergency medical system, Evidence, Fibrinolysis, Ischaemic heart disease, Primary percutaneous coronary intervention, Quality indicators, MINOCA, Reperfusion therapy, Risk assessment, Secondary prevention, ST-segment elevationThe disclosure forms of all experts involved in the development of these guidelines are available on the ESC website www.escardio.org/guidelines For the Web Addenda which include background information and detailed discussion of the data that have provided the basis for the recommendations see ��Click here to access the web addenda Table of Contents Abbreviations and acronyms 31. Preamble 52. Introduction 6 2.1 Definition of acute myocardial infarction 6 2.2 Epidemiology of ST-segment elevation myocardial infarction 63. What is new in the 2017 version? 74. 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Global Registry of Acute Coronary Events Grupo de Análisis de la Cardiopatía Isquémica Aguda high-density lipoprotein cholesterol Heart Failure Association intra-aortic balloon pump intensive cardiac care unit implantable cardioverter defibrillator Improved Reduction of Outcomes: Vytorin Efficacy International Trial low-density lipoprotein cholesterol late gadolinium enhancement left ventricle/ventricular Left ventricular assist device left ventricular ejection fraction major adverse cardiac event Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX Effect of Metoprolol in Cardioprotection During an Acute Myocardial Infarction myocardial infarction with non-obstructive coronary arteries mineralocorticoid receptor antagonist microvascular obstruction non-ST-segment elevation myocardial infarction N-terminal pro B-type natriuretic peptide Organization for the Assessment of Strategies for Ischemic Syndromes Second Primary Angioplasty in Myocardial Infarction partial pressure of oxygen percutaneous coronary intervention proprotein convertase subtilisin/kexin type 9 Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin–Thrombolysis in Myocardial Infarction 54 positron emission tomography Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects with Atrial Fibrillation who Undergo Percutaneous Coronary Intervention Preventive Angioplasty in Acute Myocardial Infarction PROlonging Dual Antiplatelet Treatment After Grading stent-induced Intimal hyperplasia studY right bundle branch block A Double-Blind, Randomized, Placebo-Controlled Trial Evaluating The Safety And Efficacy Of Early Treatment With Eplerenone In Patients With Acute Myocardial Infarction Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome Radial Versus Femoral Access for Coronary intervention right ventricle/ventricular arterial oxygen saturation sodium-glucose co-transporter-2 single-photon emission computed tomography ST-segment elevation myocardial infarction STrategic Reperfusion Early After Myocardial infarction Thrombolysis In Myocardial Infarction Tenecteplase tissue plasminogen activator Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI tissue plasminogen activator VALsartan In Acute myocardial iNfarcTion 24 h a day, seven days a week 1. Preamble Guidelines summarize and evaluate available evidence with the aim of assisting health professionals in selecting the best management strategies for an individual patient with a given condition. Guidelines and their recommendations should facilitate decision making of health professionals in their daily practice. However, the final decisions concerning an individual patient must be made by the responsible health professional(s) in consultation with the patient and caregiver as appropriate.A great number of guidelines have been issued in recent years by the European Society of Cardiology (ESC), as well as by other societies and organisations. 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 can be found on the ESC website (. ESC Guidelines represent the official position of the ESC on a given topic and are regularly updated.Members of this Task Force were selected by the ESC, including representation from its relevant ESC sub-specialty groups, in order to represent professionals involved with the medical care of patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for management of a given condition according to ESC Committee for Practice Guidelines (CPG) policy. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessment of the risk–benefit ratio. The level of evidence and the strength of the recommendation of particular management options were weighed and graded according to predefined scales, as outlined in Tables 1 and 2. Table 1Classes of recommendations Table 2 The experts of the writing and reviewing panels provided declaration of interest forms for all relationships that might be perceived as real or potential sources of conflicts of interest. These forms were compiled into one file and can be found on the ESC website (. Any changes in declarations of interest that arise during the writing period were notified to the ESC and updated. The Task Force received its entire financial support from the ESC without any involvement from the healthcare industry.The ESC CPG supervises and coordinates the preparation of new ESC Guidelines. The Committee is also responsible for the endorsement process of these Guidelines. The ESC Guidelines undergo extensive review by the CPG and external experts. After appropriate revisions the Guidelines are approved by all the experts involved in the Task Force. The finalized document is approved by the CPG for publication in the European Heart Journal. The Guidelines were developed after careful consideration of the scientific and medical knowledge and the evidence available at the time of their dating.The task of developing ESC Guidelines also includes the creation of educational tools and implementation programmes for the recommendations including condensed pocket guideline versions, summary slides, booklets with essential messages, summary cards for non-specialists and an electronic version for digital applications (smartphones, etc.). These versions are abridged and thus, if needed, one should always refer to the full text version, which is freely available via the ESC website and hosted on the EHJ website. The National Societies of the ESC are encouraged to endorse, translate and implement all ESC Guidelines. 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.Surveys and registries are needed to verify that real-life daily practice is in keeping with what is recommended in the guidelines, thus completing the loop between clinical research, writing of guidelines, disseminating them and implementing them into clinical practice.Health professionals are encouraged to take the ESC Guidelines fully into account when exercising their clinical judgment, as well as in the determination and the implementation of preventive, diagnostic or therapeutic medical strategies. However, the ESC Guidelines do not override in any way whatsoever the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient or the patient's caregiver where appropriate and/or necessary. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription. 2. Introduction Updates on the management of patients presenting with ST-segment elevation myocardial infarction (STEMI) should be based on sound evidence, derived from well-conducted clinical trials whenever possible, or motivated expert opinion when needed. It must be recognized that, even when excellent clinical trials have been undertaken, the results are open to interpretation and treatments may need to be adapted to take account of clinical circumstances and resources.The present Task Force has made an important effort to be as aligned as possible with the other ESC Guidelines1–6 and consensus documents, including the simultaneously published update on dual antiplatelet therapy (DAPT),7 for consistency in the ESC Guidelines strategy. The levels of evidence and the strengths of recommendation of particular treatment options were weighed and graded according to pre-defined scales, as outlined in Tables 1 and 2. Despite recommendations with a level of evidence being based on expert opinion, this Task Force decided to add references to guide the reader regarding data that were taken into consideration for these decisions in some cases. 2.1 Definition of acute myocardial infarction The term acute myocardial infarction (AMI) should be used when there is evidence of myocardial injury (defined as an elevation of cardiac troponin values with at least one value above the 99th percentile upper reference limit) with necrosis in a clinical setting consistent with myocardial ischaemia.8 For the sake of immediate treatment strategies such as reperfusion therapy, it is usual practice to designate patients with persistent chest discomfort or other symptoms suggestive of ischaemia and ST-segment elevation in at least two contiguous leads as STEMI. In contrast, patients without ST-segment elevation at presentation are usually designated as having a non-ST-segment elevation myocardial infarction (MI) (NSTEMI) and separate guidelines have recently been developed for these.2 Some patients with MI develop Q-waves (Q-wave MI), but many do not (non-Q-wave MI).In addition to these categories, MI is classified into various types, based on pathological, clinical, and prognostic differences, along with different treatment strategies (see the Third Universal Definition of MI document,8 which will be updated in 2018). Despite the fact that the majority of STEMI patients are classified as a type 1 MI (with evidence of a coronary thrombus), some STEMIs fall into other MI types.8 MI, even presenting as STEMI, also occurs in the absence of obstructive coronary artery disease (CAD) on angiography.9–12 This type of MI is termed ‘myocardial infarction with non-obstructive coronary arteries’ (MINOCA) and is discussed in Chapter 9 of this document. 2.2 Epidemiology of ST-segment elevation myocardial infarction Worldwide, ischaemic heart disease is the single most common cause of death and its frequency is increasing. However, in Europe, there has been an overall trend for a reduction in ischaemic heart disease mortality over the past three decades.13 Ischaemic heart disease now accounts for almost 1.8 million annual deaths, or 20% of all deaths in Europe, although with large variations between countries.14The relative incidences of STEMI and NSTEMI are decreasing and increasing, respectively.15,16 Probably the most comprehensive European STEMI registry is found in Sweden, where the incidence rate of STEMI was 58 per 100 000 per year in 2015.17 In other European countries, the incidence rate ranged from 43 to 144 per 100 000 per year.18 Similarly, the reported adjusted incidence rates from the USA decreased from 133 per 100 000 in 1999 to 50 per 100 000 in 2008, whereas the incidence of NSTEMI remained constant or increased slightly.19 There is a consistent pattern for STEMI to be relatively more common in younger than in older people, and more common in men than in women.17,20The mortality in STEMI patients is influenced by many factors, among them advanced age, Killip class, time delay to treatment, presence of emergency medical system (EMS)-based STEMI networks, treatment strategy, history of MI, diabetes mellitus, renal failure, number of diseased coronary arteries, and left ventricular ejection fraction (LVEF). Several recent studies have highlighted a fall in acute and long-term mortality following STEMI in parallel with greater use of reperfusion therapy, primary percutaneous coronary intervention (PCI), modern antithrombotic therapy, and secondary prevention.14,21,22 Nevertheless, mortality remains substantial; the in-hospital mortality of unselected patients with STEMI in the national registries of the ESC countries varies between 4 and 12%,23 while reported 1-year mortality among STEMI patients in angiography registries is approximately 10%.24,25Although ischaemic heart disease develops on average 7–10 years later in women compared with men, MI remains a leading cause of death in women. Acute coronary syndrome (ACS) occurs three to four times more often in men than in women below the age of 60 years, but after the age of 75, women represent the majority of patients.26 Women tend to present more often with atypical symptoms, up to 30% in some registries,27 and tend to present later than men.28,29 It is therefore important to maintain a high degree of awareness for MI in women with potential symptoms of ischaemia. Women also have a higher risk of bleeding complications with PCI. There is an ongoing debate regarding whether outcomes are poorer in women, with several studies indicating that a poorer outcome is related to older age and more comorbidities among women suffering MI.26,30,31 Some studies have indicated that women tend to undergo fewer interventions than men and receive reperfusion therapy less frequently.26,32,33 These guidelines aim to highlight the fact that women and men receive equal benefit from a reperfusion strategy and STEMI-related therapy, and that both genders must be managed in a similar fashion. 3. What is new in the 2017 version? Open in new tabDownload slideWhat is new in 2017 STEMI Guidelines. BMS = bare metal stent; DES = drug eluting stent; IRA = infarct related artery; i.v. = intravenous; LDL = low-density lipoprotein; PCI = percutaneous coronary intervention; SaO2 = arterial oxygen saturation; STEMI = ST-elevation myocardial infarction; TNK-tPA = Tenecteplase tissue plasminogen activator. For explanation of trial names, see list of.aOnly for experienced radial operators.bBefore hospital discharge (either immediate or staged).cRoutine thrombus aspiration (bailout in certain cases may be considered).dIn 2012 early discharge was considered after 72h, in 2017 early discharge is 48–72h.eIf symptoms or haemodynamic instability IRA should be opened regardless time from symptoms onset.In left and mid panels, below each recommendation, the most representative trial (acronym and reference) driving the indication is mentioned. 4. Emergency care 4.1 Initial diagnosis Management—including diagnosis and treatment—of STEMI starts from the point of first medical contact (FMC, defined in Table 4). It is recommended that a regional reperfusion strategy should be established to maximize efficiency.A working diagnosis of STEMI (called the ‘STEMI diagnosis’ throughout this document) must first be made. This is usually based on symptoms consistent with myocardial ischaemia (i.e. persistent chest pain) and signs [i.e. 12-lead electrocardiogram (ECG)]. Important clues are a history of CAD and radiation of pain to the neck, lower jaw, or left arm. Some patients present with less-typical symptoms such as shortness of breath, nausea/vomiting, fatigue, palpitations, or syncope.34 A reduction in chest pain after nitroglycerin (glyceryl trinitrate) administration can be misleading and is not recommended as a diagnostic manoeuvre.35 In cases of symptom relief after nitroglycerin administration, another 12-lead ECG must be obtained. A complete normalization of the ST-segment elevation after nitroglycerin administration, along with complete relief of symptoms, is suggestive of coronary spasm, with or without associated MI. In these cases, an early coronary angiography (within 24 h) is recommended. In cases of recurrent episodes of ST-segment elevation or chest pain, immediate angiography is required.It is recommended to initiate ECG monitoring as soon as possible in all patients with suspected STEMI in order to detect life-threatening arrhythmias and allow prompt defibrillation if indicated. When a STEMI is suspected, a 12-lead ECG must be acquired and interpreted as soon as possible at the time of FMC to facilitate early STEMI diagnosis and triage.36–40In patients with a clinical suspicion of myocardial ischaemia and ST-segment elevation, reperfusion therapy needs to be initiated as soon as possible.41 If the ECG is equivocal or does not show evidence to support the clinical suspicion of MI, ECGs should be repeated and, when possible compared with previous recordings. If interpretation of pre-hospital ECG is not possible on-site, field transmission of the ECG is recommended.42ECG criteria are based on changes of electrical currents of the heart (measured in millivolts). Standard calibration of the ECG is 10mm/mV. Therefore 0.1 mV equals to 1 mm square on the vertical axis. For simplicity, in this document ECG deviations are expressed in mm following the standard calibration.In the proper clinical context, ST-segment elevation (measured at the J-point) is considered suggestive of ongoing coronary artery acute occlusion in the following cases: at least two contiguous leads with ST-segment elevation ≥ 2.5 mm in men < 40 years, ≥2 mm in men ≥ 40 years, or ≥ 1.5 mm in women in leads V2–V3 and/or ≥ 1 mm in the other leads [in the absence of left ventricular (LV) hypertrophy or left bundle branch block LBBB)].8 In patients with inferior MI, it is recommended to record right precordial leads (V3R and V4R) seeking ST-segment elevation, to identify concomitant right ventricular (RV) infarction.8,43 Likewise, ST-segment depression in leads V1–V3 suggests myocardial ischaemia, especially when the terminal T-wave is positive (ST-segment elevation equivalent), and confirmation by concomitant ST-segment elevation ≥ 0.5 mm recorded in leads V7–V9 should be considered as a means to identify posterior MI.8 The presence of a Q-wave on the ECG should not necessarily change the reperfusion strategy decision. Recommendations for initial diagnosis The ECG diagnosis may be more difficult in some cases, which nevertheless deserve prompt management and triage. Among these:Bundle branch block. In the presence of LBBB, the ECG diagnosis of AMI is difficult but often possible if marked ST-segment abnormalities are present. Somewhat complex algorithms have been offered to assist the diagnosis,50,51 but they do not provide diagnostic certainty.52 The presence of concordant ST-segment elevation (i.e. in leads with positive QRS deflections) appears to be one of the best indicators of ongoing MI with an occluded infarct artery.53 Patients with a clinical suspicion of ongoing myocardial ischaemia and LBBB should be managed in a way similar to STEMI patients, regardless of whether the LBBB is previously known. It is important to remark that the presence of a (presumed) new LBBB does not predict an MI per se.54Patients with MI and right bundle branch block (RBBB) have a poor prognosis.55 It may be difficult to detect transmural ischaemia in patients with chest pain and RBBB.55 Therefore, a primary PCI strategy (emergent coronary angiography and PCI if indicated) should be considered when persistent ischaemic symptoms occur in the presence of RBBB.Ventricular pacing. Pacemaker rhythm may also prevent interpretation of ST-segment changes and may require urgent angiography to confirm diagnosis and initiate therapy. Reprogramming the pacemaker—allowing an evaluation of ECG changes during intrinsic heart rhythm—may be considered in patients who are not dependent on ventricular pacing, without delaying invasive investigation.56,57Non-diagnostic ECG. Some patients with an acute coronary occlusion may have an initial ECG without ST-segment elevation, sometimes because they are seen very early after symptom onset (in which case, one should look for hyper-acute T-waves, which may precede ST-segment elevation). It is important to repeat the ECG or monitor for dynamic ST-segment changes. In addition, there is a concern that some patients with acute occlusion of a coronary artery and ongoing MI, such as those with an occluded circumflex coronary artery,58,59 acute occlusion of a vein graft, or left main disease, may present without ST-segment elevation and be denied reperfusion therapy, resulting in a larger infarction and worse outcomes. Extending the standard 12-lead ECG with V7–V9 leads may identify some of these patients. In any case, suspicion of ongoing myocardial ischaemia is an indication for a primary PCI strategy even in patients without diagnostic ST-segment elevation.8,38,46–49Table 3 lists the atypical ECG presentations that should prompt a primary PCI strategy in patients with ongoing symptoms consistent with myocardial ischaemia. Table 3Atypical electrocardiographic presentations that should prompt a primary percutaneous coronary intervention strategy in patients with ongoing symptoms consistent with myocardial ischaemia Table 4Definitions of terms related to reperfusion therapy Isolated posterior MI. In AMI of the inferior and basal portion of the heart, often corresponding to the left circumflex territory, isolated ST-segment depression ≥ 0.5 mm in leads V1–V3 represents the dominant finding. These should be managed as a STEMI. The use of additional posterior chest wall leads [elevation V7–V9 ≥ 0.5 mm (≥1 mm in men, 40 years old)] is recommended to detect ST-segment elevation consistent with inferior and basal MI.Left main coronary obstruction. The presence of ST depression ≥ 1 mm in eight or more surface leads (inferolateral ST depression), coupled with ST-segment elevation in aVR and/or V1, suggests multivessel ischemia or left main coronary artery obstruction, particularly if the patient presents with haemodynamic compromise.60Blood sampling for serum markers is routinely carried out in the acute phase. This is indicated, but should not delay the reperfusion strategy/treatment.If in doubt regarding the possibility of acute evolving MI, emergency imaging aids the provision of timely reperfusion therapy to these patients. Recommendations for the use of echocardiography for initial diagnosis are described in section 6.6.2. If echocardiography is not available or if doubts persist after echo, a primary PCI strategy is indicated (including immediate transfer to a PCI centre if the patient is being treated in a non-PCI centre).In the STEMI emergency setting, there is no role for routine computed tomography (CT). Use of CT should be confined to selected cases where acute aortic dissection or pulmonary embolism is suspected, but CT is not recommended if STEMI diagnosis is likely.Some non-AMI conditions can present with symptoms and ECG findings similar to STEMI. An emergency coronary angiography is therefore indicated in these cases (Chapter 9 expands on this topic). 4.2 Relief of pain, breathlessness, and anxiety Relief of pain is of paramount importance, not only for comfort reasons but because the pain is associated with sympathetic activation, which causes vasoconstriction and increases the workload of the heart. Titrated intravenous (i.v.) opioids (e.g. morphine) are the analgesics most commonly used in this context. However, morphine use is associated with a slower uptake, delayed onset of action, and diminished effects of oral antiplatelet agents (i.e. clopidogrel, ticagrelor, and prasugrel), which may lead to early treatment failure in susceptible individuals.61–63Relief of hypoxaemia and symptoms Oxygen is indicated in hypoxic patients with arterial oxygen saturation (SaO2) < 90%. There is some evidence suggesting that hyperoxia may be harmful in patients with uncomplicated MI, presumably due to increased myocardial injury.64–67 Thus, routine oxygen is not recommended when SaO2 is ≥ 90%.Anxiety is a natural response to the pain and the circumstances surrounding an MI. Reassurance of patients and those closely associated with them is of great importance.A mild tranquillizer (usually a benzodiazepine) should be considered in anxious patients. 4.3 Cardiac arrest Many deaths occur very early after STEMI onset due to ventricular fibrillation (VF).68 As this arrhythmia frequently occurs at an early stage, these deaths usually happen

out of hospital. It is indicated that all medical and paramedical personnel caring for patients with suspected MI have access to defibrillation equipment and are trained in cardiac life support, and that, at the point of FMC, ECG monitoring must be implemented immediately for all patients with suspected MI.Patients with chest pain suggestive of MI should be directed through public awareness programmes to contact the EMS and wait to be transferred to the hospital by the EMS.In patients following cardiac arrest and ST-segment elevation on the ECG, primary PCI is the strategy of choice.69–74Given the high prevalence of coronary occlusions and the potential difficulties in interpreting the ECG in patients after cardiac arrest, urgent angiography (within 2 h)2 should be considered in survivors of cardiac arrest, including unresponsive survivors, when there is a high index of suspicion of ongoing infarction (such as the presence of chest pain before arrest, a history of established CAD, and abnormal or uncertain ECG results).73,74 However, in patients without ST-segment elevation, a quick evaluation at the emergency department or intensive cardiac care unit (ICCU) to exclude non-coronary causes (cerebrovascular event, respiratory failure, non-cardiogenic shock, pulmonary embolism, and intoxication), and to perform urgent echocardiography, is reasonable. The decision to perform urgent coronary angiography and PCI if indicated should also take into account factors associated with poor neurological outcome. Unfavourable pre-hospital settings indicating a remote likelihood for neurological recovery [i.e. unwitnessed cardiac arrest, late arrival of a pre-hospital team without lay basic life support (>10 min), presence of an initial non-shockable rhythm, or more than 20 min of advanced life support without return to spontaneous circulation]75 should be taken strongly into consideration to argue against an invasive coronary strategy.73Unconscious patients admitted to critical care units after out-of-hospital cardiac arrest are at high risk for death, and neurologic deficits are common among those who survive.76 Targeted temperature management (also called therapeutic hypothermia), aiming for a constant temperature between 32 and 36 °C for at least 24 h, is indicated in patients who remain unconscious after resuscitation from cardiac arrest (of presumed cardiac cause).73,77–82 However, hypothermia conditions are associated with slow uptake, delayed onset of action, and diminished effects of oral antiplatelet agents (i.e. clopidogrel, ticagrelor, and prasugrel). Moreover, metabolic conversion of clopidogrel in the liver may be reduced in hypothermia conditions.83 Cooling should not delay primary PCI and can be started in parallel in the catheterization laboratory. Close attention to anticoagulation needs to be paid in patients reaching low temperatures.84Prevention and improved treatment of out-of-hospital cardiac arrest is crucial to reduce the mortality related to CAD. For a more detailed discussion of these issues, refer to the recent European Resuscitation Council Guidelines for resuscitation.74 4.4 Pre-hospital logistics of care 4.4.1 Delays Treatment delays are the most easily audited index of quality of care in STEMI; they should be recorded in every system providing care to STEMI patients and be reviewed regularly, to ensure that simple quality of care indicators are met and maintained over time (see Chapter 10). If projected target times are not met, then interventions are needed to improve performance of the system. Components of the ischaemic time, delays of initial management, and selection of reperfusion strategy are shown in Figure 2. Open in new tabDownload slideModes of patient presentation, components of ischaemia time and flowchart for reperfusion strategy selection. EMS = Emergency Medical System; FMC = First Medical Contact; PCI = Percutaneous Coronary Intervention; STEMI = ST-segment elevation myocardial infarction.The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the decision for choosing reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when EMS arrives to the scene (see Table 4). ´denotes minutes. aPatients with fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.To minimize patient delay, it is recommended to increase public awareness of how to recognize common symptoms of AMI and to call the emergency services. All components of the system delay represent the quality of care and it is recommended to measure them as quality indicators (see Chapter 10).In hospitals and EMS participating in the care of STEMI patients, the goal is to reduce the delay between FMC and STEMI diagnosis to ≤ 10 min. STEMI diagnosis refers to the time when the ECG is interpreted as ST-segment elevation or equivalent and it is the time zero to guide appropriate therapy.System delay is more readily modifiable by organizational measures than is patient delay, and it is a predictor of outcomes.87When STEMI diagnosis is made in the pre-hospital setting (EMS), immediate activation of the catheterization laboratory not only reduces treatment delays but may also reduce patient mortality.88–91 When a STEMI diagnosis is made by the EMS in the pre-hospital setting and the patient is triaged for a primary PCI strategy, it is indicated to bypass the emergency department and bring the patient straight to the catheterization laboratory. Bypassing the emergency department is associated with a 20 min saving in the time from FMC to wire crossing.92 For patients presenting in a non-PCI centre, door-in to door-out time, defined as the duration between arrival of the patient at the hospital to discharge of the patient in an ambulance en route to the PCI centre, is a new clinical performance measure, and ≤30 min is recommended to expedite reperfusion care.93 4.4.2 Emergency medical system An EMS with an easily recalled and well publicized unique medical dispatching number (112 for most medical emergencies across Europe) is important to speed up activation. Parallel circuits for referral and transport of patients with a STEMI that bypass the EMS should be avoided. The ambulance system has a critical role in the early management of STEMI patients and it is not only a mode of transport but also a system to enhance early initial diagnosis, triage, and treatment.87,94It is indicated that all ambulances in the EMS are equipped with ECG recorders, defibrillators, and at least one person trained in advanced life support. The quality of the care provided depends on the training of the staff involved. It is indicated that all ambulance personnel are trained to recognize the symptoms of an AMI, administer oxygen when appropriate, relieve pain, and provide basic life support.95 Ambulance staff should be able to record an ECG for diagnostic purposes and either interpret or transmit it, so that it can be reviewed by experienced staff in a coronary care unit (CCU)/ICCU or elsewhere and establish a STEMI diagnosis. Paramedics trained to administer fibrinolytics do so safely and effectively.96 As pre-hospital fibrinolysis is indicated in patients presenting early when anticipated STEMI diagnosis to PCI-mediated reperfusion time is > 120 min,97–99 ongoing training of paramedics to undertake these functions is recommended, even in the current setting of primary PCI. 4.4.3 Organization of ST-segment elevation myocardial infarction treatment in networks Optimal treatment of STEMI should be based on the implementation of networks between hospitals (‘hub’ and ‘spoke’) with various levels of technology, linked by a prioritized and efficient ambulance service. The goal of these networks is to provide optimal care while minimizing delays, thereby improving clinical outcomes. Cardiologists should actively collaborate with all stakeholders, particularly emergency physicians, in establishing such networks. The main features of such a network are: ■ Clear definition of geographic areas of responsibility.■ Shared written protocols, based on risk stratification and transportation by a trained physician, nurse, or paramedic staff in appropriately equipped ambulances or helicopters.■ Pre-hospital triage of STEMI patients to the appropriate institution, bypassing non-PCI hospitals or hospitals without a 24 h a day, 7 days a week (24/7) primary PCI programme.■ On arrival at the appropriate hospital, the patient should immediately be taken to the catheterization laboratory, bypassing the emergency department.■ Patients presenting to a non-PCI-capable hospital and awaiting transportation for primary or rescue PCI must be attended in an appropriately monitored and staffed area.■ If the diagnosis of STEMI has not been made by the ambulance crew and the ambulance arrives at a non-PCI-capable hospital, the ambulance should await the diagnosis and, if a STEMI diagnosis is made, should continue to a PCI-capable hospital.To maximize staff experience, primary PCI centres should perform the procedure systematically on a 24/7 basis for all STEMI patients. Other models, although not ideal, may include weekly or daily rotation of primary PCI centres or multiple primary PCI centres in the same region. Hospitals that cannot offer a 24/7 service for primary PCI should be allowed to perform primary PCI in patients already admitted for another reason who develop STEMI during their hospital stay. However, these hospitals should be discouraged from initiating a service limited to daytime- or within-hours primary PCI, as this may generate confusion with the EMS operators and may affect the STEMI diagnosis-to-reperfusion time and the quality of intervention of focused 24/7 true primary PCI centres. Therefore, it is indicated that the EMS transports STEMI patients to hospitals with an established interventional cardiology programme available 24/7, if necessary bypassing a non-PCI-capable hospital (if the transfer time is within the recommended time-windows for primary PCI; see Figure 3). Open in new tabDownload slideMaximum target times according to reperfusion strategy selection in patients presenting via EMS or in a non-PCI centre. ECG = electrocardiogram; PCI = Percutaneous Coronary Intervention; STEMI = ST-segment elevation myocardial infarction. STEMI diagnosis is the time 0 for the strategy clock. The decision for choosing reperfusion strategy in patients presenting via EMS (out-of-hospital setting) or in a non-PCI centre is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion. Target times from STEMI diagnosis represent the maximum time to do specific interventions.aif fibrinolysis is contra-indicated, direct for primary PCI strategy regardless of time to PCI.b10 min is the maximum target delay time from STEMI diagnosis to fibrinolytic bolus administration, however, it should be given as soon as possible after STEMI diagnosis (after ruling out contra-indications).Geographic areas where the expected transfer time to the primary PCI centre makes it impossible to achieve the maximal allowable delays indicated in the recommendations (Figure 2) should develop systems for rapid fibrinolysis, at the place of STEMI diagnosis, with subsequent immediate transfer to primary PCI centres. Such networks increase the proportion of patients receiving reperfusion with the shortest possible treatment delay.100–102 The quality of care, time delays, and patient outcomes should be measured and compared at regular intervals for improvement. 4.4.3.1. General practitioners In some countries, general practitioners play a role in the early care of patients with AMI and are often the first to be contacted by the patients.If general practitioners respond quickly they can be very effective, as they usually know the patient and can perform and interpret the ECG. Their first task after the STEMI diagnosis should be to alert the EMS. In addition, they can administer opioids and antithrombotic drugs (including fibrinolytics, if that management strategy is indicated), and can undertake defibrillation if needed. However, in most settings, consultation with a general practitioner—instead of a direct call to the EMS—will increase pre-hospital delay. Therefore, in general, the public should be educated to call the EMS rather than the primary care physician for symptoms suggestive of MI. Logistics of pre-hospital care 5. Reperfusion therapy 5.1 Selection of reperfusion strategies Table 4 lists the definitions of terms relating to reperfusion therapy.Primary PCI is the preferred reperfusion strategy in patients with STEMI within 12 h of symptom onset, provided it can be performed expeditiously (i.e. 120 min from STEMI diagnosis, Figures 2 and 3) by an experienced team. An experienced team includes not only interventional cardiologists but also skilled support staff. Lower mortality rates among patients undergoing primary PCI are observed in centres with a high volume of PCI procedures.111 Real-life data confirm that primary PCI is performed faster and results in lower mortality if performed in high-volume centres.112 Randomized clinical trials in high-volume, experienced centres have repeatedly shown that, if delay to treatment is similar, primary PCI is superior to fibrinolysis in reducing mortality, reinfarction, or stroke.113–116 However, in some circumstances, primary PCI is not an immediate option and fibrinolysis could be initiated expeditiously. The extent to which the PCI-related time delay diminishes the advantages of PCI over fibrinolysis has been widely debated. Because no specifically designed study has addressed this issue, caution is needed when interpreting available data from post hoc analyses. A PCI-related time delay potentially mitigating the benefits of PCI has been calculated as 60 min117, 110 min,118 and 120 min119 in different studies. Registry data estimated this time limit as 114 min for in-hospital patients107 and 120 min in patients presenting in a non-PCI centre.120 All these data are old and patients undergoing fibrinolysis did not undergo routine early angiography, which improves outcomes in patients receiving fibrinolysis. The recent STrategic Reperfusion Early After Myocardial infarction (STREAM) trial randomized early STEMI presenters without the possibility of immediate PCI to immediate fibrinolysis (followed by routine early angiography) or transfer to primary PCI.121 The median PCI-related delay in this trial was 78 min, and there were no differences in clinical outcomes. This Task Force recognizes the lack of contemporaneous data to set the limit to choose PCI over fibrinolysis. For simplicity, an absolute time from STEMI diagnosis to PCI-mediated reperfusion [i.e. wire crossing of the infarct-related artery (IRA)] rather than a relative PCI-related delay over fibrinolysis has been chosen. This limit is set to 120 min. Given the maximum limit of 10 min from STEMI diagnosis to bolus of fibrinolytics (see below), the 120 min absolute time would correspond to a PCI-related delay in the range of 110–120 min, being in the range of the times identified in old studies and registries as the limit delay to choose PCI.107,117–120If the reperfusion strategy is fibrinolysis, the goal is to inject the bolus of fibrinolytics within 10 min from STEMI diagnosis. This time is selected based on the median time from randomization to bolus recorded in the STREAM trial, which was 9 min.121 In previous ESC STEMI guidelines,122 the target time was 30 min, but this was calculated from FMC (as opposed to STEMI diagnosis). STEMI diagnosis should occur within 10 min from FMC.Figure 3 summarizes target times for patients presenting in the pre-hospital setting or in a non-PCI centre.To shorten time to treatment, fibrinolysis should be administered in the pre-hospital setting if possible98,121,123 (Figures 2 and 3). Patients should be transferred to a PCI-capable facility as soon as possible after bolus of lytics administration. Rescue PCI is indicated in the case of failed fibrinolysis (i.e. ST-segment resolution < 50% within 60–90 min of fibrinolytic administration), or in the presence of haemodynamic or electrical instability, worsening ischaemia, or persistent chest pain,121,124 while a routine early PCI strategy is indicated after successful fibrinolysis (preferably 2–24 h after fibrinolysis) (see section 5.3).125–130Patients with a clinical presentation compatible with AMI and a non-interpretable ST-segment on the ECG, such as those with bundle branch block or ventricular pacing,55,131,132 should undergo a primary PCI strategy.There is general agreement that a primary PCI strategy should also be followed for patients with symptoms lasting >12 h in the presence of: (1) ECG evidence of ongoing ischaemia; (2) ongoing or recurrent pain and dynamic ECG changes; and (3) ongoing or recurrent pain, symptoms, and signs of heart failure, shock, or malignant arrhythmias. 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 asymptomatic patients without persistent symptoms 12–48 h after symptom onset, a small (n = 347) randomized study showed improved myocardial salvage and 4 year survival in patients treated with primary PCI compared with conservative treatment alone.133,134 However, in stable patients with persistent occlusion of the IRA 3–28 days after MI, the large (n = 2166) Occluded Artery Trial (OAT) revealed no clinical benefit from routine coronary intervention with medical management, beyond that from medical management alone.135,136 A meta-analysis of trials testing whether late recanalization of an occluded IRA is beneficial showed no benefit of reperfusion.137 Therefore, routine PCI of an occluded IRA in asymptomatic patients >48 h after onset of symptoms is not indicated. These patients should be managed like all patients with chronic total occlusion, in which revascularization should be considered in the presence of symptoms or objective evidence of viability/ischaemia in the territory of the occluded artery.1 Recommendations for reperfusion therapy Table 5 summarizes the important time targets in acute STEMI. Table 5Summary of important time targets 5.2 Primary percutaneous coronary intervention and adjunctive therapy 5.2.1 Procedural aspects of primary percutaneous coronary intervention 5.2.1.1 Access route Over recent years, several studies have provided robust evidence in favour of the radial approach as the default access site in ACS patients undergoing primary PCI by experienced radial operators. The Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX (MATRIX)143 trial recruited 8404 ACS patients (48% STEMI) who were randomly allocated to transradial or transfemoral access. Radial access was associated with lower risks of access site bleeding, vascular complications, and need for transfusion. Importantly, there was a significant mortality benefit in patients allocated to the transradial access site, which reinforced previous observations from the Radial Versus Femoral Access for Coronary Intervention (RIVAL) access for coronary intervention trial,144 and the Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome (RIFLE-STEACS) trial.145 No significant interaction was observed in the MATRIX trial between the type of ACS and treatment benefit, suggesting that the results of this investigation can be extended with confidence to the treatment of patients with STEMI. 5.2.1.2 Stenting in primary percutaneous intervention Coronary stenting is the technique of choice during primary PCI. Compared with balloon angioplasty alone, stenting with a bare-metal stent (BMS) is associated with a lower risk of reinfarction and target vessel revascularization but is not associated with a reduction in the mortality rate.146,147 In primary PCI, drug-eluting stents (DES) reduce the risk of repeated target vessel revascularization compared with BMS.148New-generation DES have shown superior safety and preserved or even improved efficacy compared with first-generation DES, in particular with respect to lower risks of stent thrombosis and recurrent MI. In two recent trials—the Effect of biolimus-eluting stents with biodegradable polymer vs. bare-metal stents on cardiovascular events among patients with AMI (COMFORTABLE AMI) trial149 and the Everolimus-Eluting Stents Versus Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction (EXAMINATION) trial150—new-generation DES have been shown to be superior to BMS in patients with AMI, mostly in terms of need for reintervention. In the latter trial, the recently released 5 year follow-up results showed a reduction in all-cause mortality by DES as compared to BMS.151 In the Norwegian Coronary Stent (NORSTENT) trial,152 9013 patients undergoing PCI (26% with STEMI) were randomized to DES or BMS. There were no differences in the incidence of the primary endpoint (composite of death from any cause or non-fatal spontaneous MI) after a median follow-up of 5 years. However, DES were associated with lower rates of definite stent thrombosis (0.8% vs. 1.2%; P = 0.0498) and of target lesion and any repeat revascularization (16.5% vs. 19.8%; P < 0.001).152Deferring stenting in primary PCI has been investigated as an option to reduce microvascular obstruction (MVO) and preserve microcirculatory function. Two small studies recently found opposite results in the effect of deferred stenting on cardiac magnetic resonance (CMR) imaging-measured MVO.153,154 In the larger DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction – Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER) trial,155 in 1215 STEMI patients, deferred stenting (48 h after the index procedure) had no effect on the primary clinical outcome (composite of all-cause mortality, non-fatal MI, or ischaemia-driven revascularization of non-IRA lesions). Routine deferred stenting was associated with a higher need for target vessel revascularization. Based on these findings, routine use of deferred stenting is not recommended. 5.2.1.3 Thrombus aspiration A number of small-scale or single-centre studies and one meta-analysis of 11 small trials156 suggested that there could be benefits from routine manual thrombus aspiration during primary PCI. Recently, two large (>10 000 and >7000 patients) randomized controlled trials, which were adequately powered to detect superiority of routine manual thrombus aspiration versus conventional PCI, showed no benefit on clinical outcomes of routine aspiration strategy overall.157–160 A safety concern emerged in the Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL) trial (n = 10 732), with an increase in the risk of stroke.161 In the subgroup with high thrombus burden [TIMI (Thrombolysis in Myocardial Infarction) thrombus grade ≥ 3], thrombus aspiration was associated with fewer cardiovascular deaths [170 (2.5%) vs. 205 (3.1%); hazard ratio (HR) 0.80, 95% confidence interval (CI) 0.65–0.98; P = 0.03] and with more strokes or transient ischaemic attacks [55 (0.9%) vs. 34 (0.5%); odds ratio 1.56, 95% CI 1.02–2.42, P =0.04]. However, the interaction P values were 0.32 and 0.34, respectively.162In the Taste157 and TOTAL trials159, 1–5% of randomized patients crossed over from PCI alone to thrombus aspiration. Based on these data and the results of a recent meta-analysis,162 routine thrombus aspiration is not recommended, but in cases of large residual thrombus burden after opening the vessel with a guide wire or a balloon, thrombus aspiration may be considered. 5.2.1.4 Multivessel coronary revascularization Multivessel disease is common (in approximately 50%) in patients with STEMI.163,164 While it is recommended to always treat the IRA, evidence supporting immediate (preventive) revascularization of additional significant coronary stenoses is conflicting. It has been reported that patients with extensive CAD in vessels remote from the IRA have lower rates of ST-segment recovery and an adverse prognosis following primary PCI.163 Data from the US National Cardiovascular Data Registry and New York State’s Percutaneous Coronary Interventions Reporting System suggested an increase in adverse events, including mortality, in patients treated with immediate multivessel revascularization versus IRA PCI only, while patients in cardiogenic shock were excluded from the analysis.165,166Randomized clinical trials addressing this issue have been small (each of them included from 69 to 885 patients). One study allocated 214 STEMI patients with multivessel disease to three arms: IRA angioplasty-only, simultaneous treatment of non-IRA lesions, and staged revascularization of the non-IRA. At a mean follow-up of 2.5 years, patients allocated to IRA angioplasty-only had more major adverse cardiac events (MACE) (i.e. death, reinfarction, rehospitalization for ACS, and repeat coronary revascularization) than the patients treated with other strategies.167 After this study, four randomized clinical trials have compared PCI of the IRA only vs. complete revascularization: the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial (n = 465, 23 months follow-up),168 the Complete Versus Lesion-Only Primary PCI Trial (CvLPRIT) (n = 296, 12 months follow-up),169 the Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3–PRIMULTI) trial (n = 627, 27 months follow-up),170 and the Comparison Between FFR Guided Revascularization Versus Conventional Strategy in Acute STEMI Patients With Multivessel disease (Compare-Acute, n = 885, 12 months follow-up) trial.171 PCI of non-IRA was done either during the index procedure (PRAMI and Compare-Acute), staged during hospital admission (DANAMI-3–PRIMULTI), or any time before discharge (immediate or staged) (CVLPRIT). Indication for PCI in non-IRA was angiography-guided in lesions with ≥50% stenosis (PRAMI), >70% stenosis (CVLPRIT), or fractional flow reserve (FFR)-guided (DANAMI-3–PRIMULTI and Compare-Acute). Primary outcome (composite of different endpoints) was significantly reduced in the complete revascularization group in all four trials. Total mortality was not statistically different in any of the four trials. Repeat revascularization was significantly reduced in the complete revascularization arm in the PRAMI, DANAMI-3–PRIMULTI, and Compare-Acute trials. Non-fatal MI was reduced in the non-IRA PCI group only in PRAMI. The lack of significant treatment effect of non-IRA lesion intervention on death or MI was confirmed by three meta-analyses included the Compare-Acute trial, and one173 did not include the DANAMI-3–PRIMULTI). Based on these data, revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease before hospital discharge. As the optimal timing of revascularization (immediate vs. staged) has not been adequately investigated, no recommendation in favour of immediate vs. staged multivessel PCI can be formulated. 5.2.1.5 Intra-aortic balloon pump The Counterpulsation to Reduce Infarct Size Pre-PCI-Acute Myocardial Infarction (CRISP AMI) trial showed no benefit from a routine intra-aortic balloon pump (IABP) in anterior MI without shock,175 but there was increased bleeding, which is consistent with previous data regarding the role of IABP in high-risk STEMI without cardiogenic shock.176 In addition, a recent randomized trial showed that IABP did not improve outcomes in MI with cardiogenic shock.177 Haemodynamic support in patients with cardiogenic shock is discussed in Chapter 8. Procedural aspects of the primary percutaneous coronary intervention strategy 5.2.2 Periprocedural pharmacotherapy 5.2.2.1 Platelet inhibition Patients undergoing primary PCI should receive DAPT, a combination of aspirin and a P2Y12 inhibitor, and a parenteral anticoagulant. Aspirin can be given orally including chewing, or i.v. to ensure complete inhibition of thromboxane A2-dependent platelet aggregation. The oral dose of plain aspirin (non-enteric-coated formulation) should preferably be 150–300 mg. There are few clinical data on the optimal i.v. dosage. Given a 50% oral bioavailability of oral aspirin, a corresponding dose is 75–150 mg. Pharmacological data suggest that this lower dose range avoids inhibition of cyclooxygenase-2-dependent prostacyclin. A recent randomized study showed that a single dose of 250 or 500 mg acetylsalicylic acid i.v. compared to 300 mg orally was associated with a faster and more complete inhibition of thromboxane generation and platelet aggregation at 5 min, with comparable rates of bleeding complications.181There is limited evidence with respect to when the P2Y12 inhibitor should be initiated in STEMI patients. The Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST Elevation Myocardial Infarction to Open the Coronary Artery (ATLANTIC) trial182 is the only randomized study testing the safety and efficacy of different timings of P2Y12 inhibitor initiation in STEMI. In this trial, patients were randomized to receive ticagrelor either during transfer to a primary PCI centre or immediately before angiography.182 The median difference between the two tested loading treatment strategies was only 31 min. This study failed to meet the pre-specified primary endpoint in terms of improved ST-segment elevation resolution or TIMI flow before intervention. Rates of major and minor bleeding events were identical in both treatment arms. While the evidence of a clinical benefit of P2Y12 inhibitor pre-treatment in this setting is lacking, early initiation of a P2Y12 inhibitor while the patient is being transported to a primary PCI centre is common practice in Europe and is consistent with the pharmacokinetic data. Furthermore, early treatment with high-dose clopidogrel was superior to in-catheterization laboratory treatment in observational studies and one small randomized trial.183–185 In all, the data suggest that the earliest administration may be preferable to achieve early efficacy, particularly for long delays. However, in cases in which the STEMI diagnosis is not clear, delaying P2Y12 inhibitor loading until the anatomy is known should be considered.The preferred P2Y12 inhibitors are prasugrel [60 mg loading dose and 10 mg maintenance dose once daily per os (p.o.)] or ticagrelor (180 mg p.o. loading dose and 90 mg maintenance dose twice daily). These drugs have a more rapid onset of action, greater potency, and are superior to clopidogrel in clinical outcomes.186,187 Prasugrel is contraindicated in patients with previous stroke/transient ischaemic attack, and its use is generally not recommended in patients aged ≥75 years or in patients with lower body weight (

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