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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 suspected patients with STEMI in the national registries of the ESC countries is between 4 and 12%,²³ while reported 30-day mortality among STEMI patients in angiography registries is approximately 10%.^{24,25} Although 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.Only for experienced radial operators.b.Before hospital discharge (either immediate or staged).c.Routine thrombus aspiration (bailout in certain cases may be considered).d.In 2012 early discharge was considered after 72h, in 2017 early discharge is 48–72h.e.If symptoms or haemodynamic instability IRA should be opened regardless of time from symptoms onset.In left and mid panels, below each recommendation, the most representative trial (acronym and reference) having 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.^{36–40}In 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 equivalent 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 (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 and bundle branch block 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)¹⁴⁴ and the Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome (RIFLE-STEACS)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)¹⁴⁹ and the Everolimus-Eluting Stents Versus Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction (EXAMINATION)¹⁵⁰—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)¹⁵² 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 = 0.048) 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)¹⁵⁴ 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 >7 000 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)¹⁵⁷ 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 trials^{159, 1–3%} 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.^{165,166}Randomized 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 revascularization 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)¹⁶⁸ trial (n = 465, 23 months follow-up),¹⁶⁸ the Complete Versus Lesion-Only Primary PCI Trial (CvLPRIT)¹⁶⁹ (n = 22, 2 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)¹⁷⁰ 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^{172–174} (none of these 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)¹⁷⁵ 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.¹⁸¹ There 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)¹⁸² 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 intrathecalization 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 patients with STEMI diagnosis that is 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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