Non-ST-Segment Elevation Myocardial Infarction (NSTEMI)

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2.1 Case Report

A 66-year-old man with no previous cardiovascular disease was admitted to the emergency department for worsening chest pain and dyspnea. The patient referred the presence of intermittent chest pain a month ago mainly at rest. No history of fever was present.

Medical History and Cardiovascular Risk Factors

- Cardiovascular risk factors: type II diabetes mellitus, systemic hypertension, and mild renal failure
- Family history: no family history of structural heart disease
- 2013: hospital admission for interstitial pneumonia complicated by respiratory failure

Allergies

None

Medications

Ramipril 5 mg, atorvastatin 20 mg, pantoprazole 20 mg, and insulin

Vital Signs

- Temperature: 36.5 °C
- Heart rate: 95 bpm
- Arterial blood pressure: 150/80 mmHg
- Respiratory rate: 15 breaths/min
- Oxygen saturation: 99 %

Physical Examination

- *General*: alert, awake, and oriented; restless
- *Neck*: no jugular venous distention, no lymphadenopathy, no carotid bruits
- *Cardiovascular*: regular and tachycardic rhythm, apical soft proto-mesosystolic murmur (2/6 at the Levine scale)
- *Lungs*: no rales, rhonchi, or wheezes to auscultation, normal percussion
- *Abdomen*: no hepatomegaly or splenomegaly, no ascites, no masses, normal bowel sounds in

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all four quadrants, soft, non-distended/non-tender, no rebound or guarding, no costovertebral angle tenderness
– *Extremities*: no cyanosis or clubbing, no peripheral edema

Routine Laboratory Tests

– *Complete blood count*: normal
– *Cholesterol* (*total*, *HDL*, *LDL*) *and TG*: total 280 mg/dl, LDL 150 mg/dl
– *Hepatic function* (*GOT*, *GPT*, *γ-GT*, *ALP*, *total bilirubin*, *amylase*, *lipase*): normal
– *Thyroid function* (*TSH*, *FT3*, *FT4*): normal
– *Renal function* (*creatinine*, *BUN*): creatinine 1.5 mg/dl (eGFR 65 ml/min/1.73 mq)
– *Serum electrolytes*: potassium 4.5 mEq/l, sodium 139 mEq/l
– *Biomarkers*: troponin I 5.4 ng/ml, BNP 80 pg/ml, C-reactive protein 0.2 mg/dl, glycosylated hemoglobin 81 mmol/l

Instrumental Examination

An ECG performed at patient's admission revealed a right bundle branch block with left anterior hemiblock and ST depression (>0.1 mv) in V3-6 and DII-avF with ST elevation in aVR (Fig. 2.1).

Echocardiography: moderate concentric hypertrophy (LV mass/BSA 135 g/m^2, relative wall thickness 0.45) with preserved LV global function (estimated ejection fraction of 56 %) and hypokinesia of the middle and apical anterior wall; normal dimension and function of the right ventricle (TAPSE 20 mm, FAC area 40 %); impaired relaxation of the left ventricle (E/A < 0.75, E/E' < 10); mild mitral and tricuspid regurgitation; systolic pulmonary artery pressure of 35 mmHg

Chest x-ray showed the absence of pulmonary congestion, lobe consolidation, or bronchograms.

Clinical Course and Therapeutic Management

Clinical, instrumental, and laboratory data allowed us to make diagnosis of SCA-NSTEMI: ECG changes (ST depression >0.05 in more than two contiguous leads), rise in cardiac biomarker levels, and normal left ventricle global function with regional hypokinesia – no signs of myopericarditis.

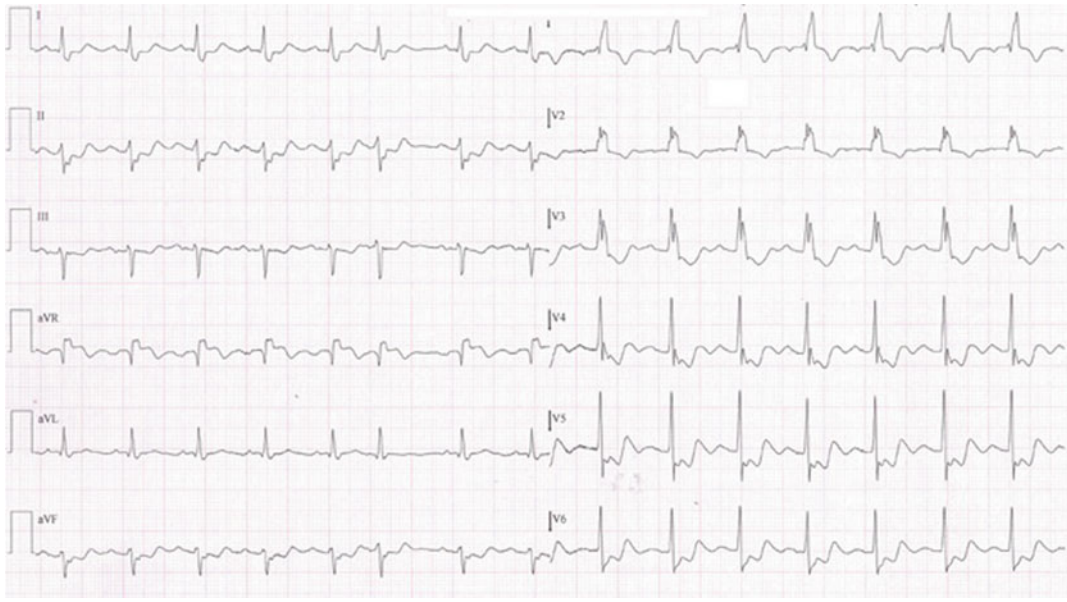

Fig. 2.1 ECG of patients during chest pain

According to guidelines, the patient was assessed with established risk scores for prognosis and bleeding (GRACE 120, intermediate risk; CRUSADE 30, low risk of bleeding). Antiplatelet therapy with aspirin and ticagrelor (P2Y12 inhibitor) with a loading dose of 300 mg and 180 mg, respectively, and anticoagulant therapy with fondaparinux 2.5 mg/die were started. Intravenous nitrate treatment and beta-blocker therapy (metoprolol 2.5 mg ev.) were administered due to persistent angina and tachycardia. ACE inhibitor (ramipril 5 mg) was continued, and high-dose statin therapy (atorvastatin 80 mg) was initiated.

The patient remained asymptomatic in the subsequent hours despite an increase in cardiac biomarkers (troponin I 15 ng/ml) at the laboratory analysis (6 h after patient admission). Given a GRACE score of 120, an ECG suggesting a left main or multivessel coronary artery disease (ST depression in many leads with ST elevation in avR) and the presence of high-risk criteria (significant rise in troponin) an early invasive strategy was performed. Thus, the patient underwent a coronary angiography (<24 h) that showed triple-vessel disease with a SYNTAX score >22 (Fig. 2.2).

Considering the clinical status (asymptomatic patient, progressive lowering in cardiac biomarkers: Tn I 10 ng/ml 12 h after patient admission) and the unfavorable coronary anatomy (SYNTAX score >22), the patient was sent for coronary artery bypass grafting (CABG, class I A). Ticagrelor was then discontinued, and CABG was performed 5 days later without procedural or bleeding complications. The patient was then transferred on day 12 to a postsurgery rehabilitation center with a progressive improvement in functional capacity and subsequently dismissed after 7 days. The therapy at discharge was dual-antiplatelet therapy (aspirin 100 mg and ticagrelor 90 bid), ramipril 5 mg, atorvastatin 80 mg, metoprolol 50 mg bid, pantoprazole 20 mg, and insulin therapy.

2.2 Non-ST-Segment Elevation Myocardial Infarction (NSTEMI)

Definition and Epidemiology

Coronary artery disease (CAD) is one of the major causes of deaths and morbidity in developed countries with a prevalence that increases with age [1]. Nearly 17.3 million deaths in 2013 worldwide were related to cardiovascular disease [2]. Acute coronary syndrome (ACS) represents one of the most frequent and life-threatening clinical presentations of CAD and is related to plaque rupture or an ischemic imbalance between myocardial oxygen supply and demand. The extensive use of high-sensitive troponin assay may have led to more diagnosis of myocardial infarction (MI) hiding a possible reduction in the incidence of MI [3]. According to the most recent guidelines [4], the term myocardial infarction should be used in

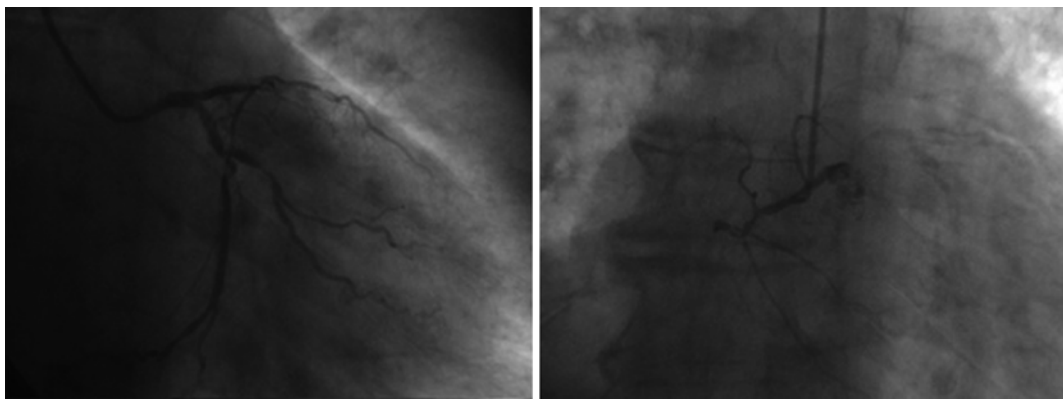

Fig. 2.2 Coronarography showing multivessel disease

the presence of symptoms of ischemia and/or rise in cardiac biomarkers (troponin I or T values above the 99th percentile upper reference limit) with the following criteria: ST-segment or T-wave changes, imaging evidence of loss of viable myocardium or regional motion abnormalities, and intracoronary thrombus by angiography or autopsy. Two different clinical presentations may be encountered based on electrocardiogram (ECG) findings and pathophysiology:

- Myocardial infarction with persistent (>20 min) ST elevation (see Chap. 1).
- Myocardial infarction without persistent ST elevation includes ST-segment depression >0.05 mV in two contiguous leads, T-wave inversion >0.1 mV in two contiguous leads, pseudo-normalization of T wave, or no ECG changes [4]. Two types of non-ST-elevation ACS are recognized: NSTEMI or unstable angina (UA) based on the evaluation of cardiac biomarkers.

In the last years, it has been observed an increase in the rate of non-ST-elevation myocardial infarction (NSTEMI) in relation to ST-elevation myocardial infarction (STEMI) with an annual incidence of ~3 per 1,000 inhabitants [5]. Hospital mortality is higher between STEMI patients, while in the long term death rates are consistently larger in NSTEMI [6]. NSTEMI patients are often older with significant comorbidities. These data suggest the need of significant efforts both in the acute phase and in long-term management to ensure better outcomes.

Pathophysiology

Atherosclerosis is a multifocal disease caused by lipid accumulation that affects large-sized and medium-sized arteries [7]. CAD is a dynamic process that leads to a progressive reduction in the vessel size due to plaque formation. NSTEMI is due to complete or partial occlusion of a coronary artery or a mismatch between oxygen supply and demand. ACS is generally precipitated by a plaque rupture or erosion with acute thrombosis or vasoconstriction leading to a sudden and critical reduction in blood flow. Inflammation plays a determinant role in plaque erosion and subsequent thrombus formation. Rarely ACS may be caused by other mechanisms such as arteritis, trauma, dissection, congenital abnormalities, or drug abuse [8].

Diagnosis

The diagnosis of NSTE is complex and more difficult than STEMI due to less obvious signs and a wider differential diagnosis. Risk stratification should be evaluated during the diagnostic phase guiding the revascularization and treatment strategy.

Clinical Presentation

The more frequent symptom of ACS is retrosternal chest pain irradiating to the left arm or to the neck sometimes described as retrosternal pressure or heaviness. Dyspnea, diaphoresis, or nausea is often associated. Atypical presentation is common in older patients, women, and patients with diabetes and may lead to a missed diagnosis [9]. Exacerbation of symptoms during physical exertion and reduction at rest is common. Relief of pain after administration of nitrates is also quite specific. UA is characterized by the presence of new-onset angina, post-MI angina, or crescendo angina. The presence of risk factors should be carefully evaluated as it significantly increases the probability of CAD diagnosis. The most common risk factors are male sex, family history of CAD, older age, peripheral artery disease, diabetes mellitus, renal failure, previous cardiovascular disease, and dyslipidemia.

Physical Examination

Physical examination shall evaluate the presence of NSTEMI complication such as heart failure with pulmonary or systemic congestion and establish the presence of precipitating factors (i.e., anemia). Extracardiac (pneumonia, pneumothorax, costochondritis) and nonischemic (valvular disease, pericarditis) causes of chest pain may also be excluded.

Electrocardiogram

A 12-lead resting ECG must be obtained in 10 min after the first medical contact. Additional ECG must be obtained if the patient presents symptoms at (3 h) 6-9-24 h and immediately during symptoms [8]. Comparison with previous ECG recordings is recommended especially in patients with known ST alterations (i.e., left ventricular hypertrophy). A completely normal ECG does not exclude the presence of ACS. Typical ECG findings are ST-segment depression or T-wave inversion in at least two contiguous leads.

Cardiac Enzymes

Cardiac troponins are the reference markers of MI because they are more specific and sensitive than other markers [10]. The initial rise in troponins occurs in approximately 4 h and may remain elevated up to 2 weeks. The diagnostic cutoff is a value exceeding the 99th percentile of normal reference population with an assay with an imprecision of <10 % [4]. High-sensitivity assays have been introduced with higher sensitivity and specificity. A single normal test is not sufficient to exclude ACS in the presence of suggestive symptoms and may be repeated. Relevant changes in troponin levels are also important because they allow to make differential diagnosis between a relevant number of possible non-ACS-related troponin elevations (Table 2.1).

Table 2.1 Possible causes of troponin rise

Chronic or acute renal failure
Congestive heart failure
Hypertensive crisis
Arrhythmias
Pulmonary embolism
Myocarditis
Stroke or subarachnoidal hemorrhage
Aortic dissection
Cardiac contusion, ablation, cardioversion
Takotsubo cardiomyopathy
Infiltrative disease (i.e., amyloidosis)
Drug toxicity
Sepsis or respiratory failure
Rhabdomyolysis

Imaging

Noninvasive Imaging

Echocardiography is the tool of choice due to its availability and feasibility. Left and right ventricular systolic function may be assessed and represents a relevant prognostic factor. New-onset regional wall hypokinesia or akinesia is also a typical finding that suggests myocardial ischemia. Echocardiography may also exclude other causes of chest pain such as aortic dissection, pulmonary embolism, aortic stenosis, pericarditis, or hypertrophic cardiomyopathy.

Stress echocardiography and nuclear myocardial perfusion are II° level tests that may lead to myocardial ischemia diagnosis especially in low-risk patients. Multidetector computed tomography (CT) permits visualization of coronary arteries and may be useful in excluding other causes of chest pain such as aortic dissection or pulmonary embolism. Different studies reported high negative predictive value of this technique in intermediate-risk patients [11].

Invasive Imaging

Coronary angiography remains the gold standard as it provides relevant diagnostic informations. Timing of angiography should be evaluated on the basis of risk assessment. It is recommended to prefer radial approach when feasible because it has lower risk of hematomas and bleeding [12]. Angiograms should be obtained after and before the use of nitrates to exclude the vasoconstriction due to ACS. In ambiguous lesions, intravascular ultrasound (IVUS) of fractional flow reserve (FFR) may help in the correct evaluation of stenosis and treatment strategy.

Risk Stratification and Treatment Strategy

To date two alternative approaches have been validated for the treatment of acute coronary syndromes (ACS) without ST-segment elevation (NSTE-ACS), such as unstable angina (UA) and acute myocardial infarction without ST elevation (NSTEMI). The two strategies differ in the timing for cardiac catheterization.

The first option is the early invasive strategy, meaning that the patient is quickly sent to the cath lab for coronary angiography, followed by the eventual PCI or surgical revascularization based on the angiographic results.

The second option, called conservative strategy, consists in medical therapy alone for the initial treatment, reserving cardiac catheterization only to those who have recurrent ischemia or other high-risk features.

Conservative Strategy Versus Invasive Strategy

Currently, the results of these alternative strategies have been analyzed in several randomized trials. A meta-analysis in which seven studies were included showed a significant benefit offered by the early invasive strategy in terms of reduction of 2-year mortality from all causes and myocardial infarction (MI), with no increase in adverse periprocedural events. Patients who have most benefited from an early invasive strategy were those with abnormal troponin values and high-risk features.

These results have been translated into the European Society of Cardiology (ESC) NSTEMI Guidelines published in 2011 that recommend a routine invasive strategy in almost the totality of patients with NSTEMI while highlighting the crucial role of risk stratification.

NSTEMI Patients: Indications in the Light of the Most Recent Guidelines

Although, for ethics and safety reasons, patients with UA/NSTEMI at *very high risk* (refractory angina, severe heart failure, electrical and/or hemodynamic instability) were excluded from randomized clinical trials, it is universally accepted that these patients must be sent within 2 h to the cath lab for an urgent invasive strategy, regardless of risk stratification and the values of troponin (class I, level of evidence C).

Based on randomized clinical trials, patients at *high risk* who have a GRACE score >140 or with at least one of the primary high-risk criteria must be treated with an early invasive strategy, within 24 h from the first medical contact (class I, level of evidence A). Among all other patients with UA/NSTEMI, those who have at least one secondary high-risk criterion or recurrent symptoms should be treated with an invasive strategy within 72 h (class I, level of evidence A).

- *Primary high-risk criteria*:
  - (a) Relevant increase and fall of troponin
  - (b) Dynamic changes of the ST segment and/or T wave
- *Secondary high-risk criteria*:
  - (a) Diabetes mellitus
  - (b) Renal impairment (eGFR <60 mL/min/1.73 m^2)
  - (c) Reduced left ventricular ejection fraction (<40 %)
  - (d) Early postinfarction angina
  - (e) Recent angioplasty (PCI)
  - (f) Previous bypass surgery (CABG)
  - (g) Intermediate- to high-GRACE-risk score (108–140)

From this, it is clear that by definition NSTEMI ACS with elevation of myocardial necrosis markers should be treated with an invasive strategy within 72 h, since the elevation of troponin alone is considered a primary high-risk criterion. Therefore, a conservative strategy is now restricted to a narrow subgroup of patients: basically not to those who have a NSTEMI, but only to patients with unstable angina (then with negative troponin) and without recurrent symptoms.

Moreover, even among patients with UA, only those without high-risk characteristics should be approached with a conservative strategy, that is, nondiabetics, those with normal global contractile function of the left ventricle, those who have not been subjected in the past to PCI or CABG, and those with a GRACE risk score <108. In this small group of patients (low risk and without recurrent symptoms), a noninvasive assessment of inducible ischemia is recommended (class I, level of evidence A), which must be performed before hospital discharge. Coronary angiography

should be performed only if the results of noninvasive tests are positive for inducible ischemia.

Revascularization Strategies

In approximately one-third of patients, angiography will reveal single-vessel disease, allowing ad hoc PCI of the culprit lesion in most cases. In a multivessel disease, the choice has to be made between culprit-lesion PCI, multivessel PCI, CABG, and a combined (hybrid) revascularization [13, 14]. The distribution of PCI versus CABG in patients with multivessel disease suitable for revascularization is approximately 80 % versus 20 % [15]. The revascularization strategy in patients with multivessel CAD should be determined early by the Heart Team and based on the patient's clinical status, as well as the severity and distribution of the CAD and the characteristics of the lesion. The SYNTAX score has proven to be strongly predictive of death, myocardial infarction, and TVR [16]. Culprit-lesion PCI is usually the first choice in most patients with NSTE-ACS and multivessel disease; however, there are no prospective studies comparing culprit-lesion PCI with early CABG. In stabilized patients with multivessel disease and a high SYNTAX score (>22), particularly when there is no clearly identified culprit lesion, a strategy of urgent CABG should be preferred. The strategy of multivessel PCI rather than culprit-lesion PCI has not been evaluated in an appropriate randomized clinical trial. In a large database including 105,866 multivessel CAD patients with NSTE-ACS, multivessel PCI was compared with single-vessel PCI and was associated with lower procedural success but similar in-hospital mortality and morbidity [17]. Complete revascularization at the time of the index procedure did not result in lower mortality rates over 3 years, as compared with a staged procedure strategy. However, incomplete revascularization appears to be associated with more 1-year adverse event rates. In the ACUITY trial, CABG was compared with PCI among patients with multivessel disease [15]. PCI-treated patients had lower rates of stroke, myocardial infarction, bleedings, and renal injury and similar 1-month and 1-year mortality but significantly higher rates of unplanned revascularization at both 1 month and 1 year. However, only 43 % of CABG patients could be matched, and there was a strong trend for a higher rate of major adverse cardiac events (MACE) at 1 year with PCI, compared with CABG (25.0 % vs. 19.5 %, respectively; p 0.05).

Culprit-lesion PCI does not necessarily require a case-by-case review by the Heart Team, when the procedure needs to be performed ad hoc after diagnostic angiography particularly in case of continuing or recurrent ischemia, hemodynamic instability, pulmonary edema, recurrent ventricular arrhythmias, or total occlusion of the culprit coronary artery requiring urgent revascularization. For all other scenarios, revascularization should be discussed in a multidisciplinary setting. After culprit-lesion PCI, patients should be discussed by the Heart Team, in the context of functional evaluation of the remaining lesions, patients' comorbidities, and individual characteristics.

Medical Therapy: The Importance of Balancing the Ischemic and Hemorrhagic Risk

The therapeutic management of NSTEMI includes the use of anti-ischemic and antithrombotic drugs in combination to coronary revascularization. The timing and intensity of these therapeutic interventions must be individualized for each patient in light of both the ischemic and the bleeding risk, since most of the antithrombotic therapies increase the risk of bleeding. Risk assessment is an ongoing process that must begin with the first medical contact, until discharge from the hospital, because it can change the therapeutic strategy at anytime.

Among the main ischemic risk factors, age and the presence of other comorbidity (anemia, diabetes, etc.) have the greatest prognostic impact. Other factors consist in the characteristics and mode of onset of pain (being worse angina at rest and/or relapsing) and hemodynamic conditions. Other prognostic factors recognized and to which attention should be paid are the electrocardiographic changes and the elevation of a series of biomarkers such as troponin, C-reactive protein (CRP), and the N-terminal fragment of the atrial natriuretic peptide (NT-proBNP).

From the integration of all these risk factors, several risk scores have been developed, among which the best known are the TIMI risk score and the Global Registry of Acute Coronary Events (GRACE) score. The TIMI risk score is the most used in the past due to its simplicity, but its discriminating power is significantly lower than that of the GRACE score, basically because it does not take into account parameters of crucial importance as hemodynamics. In contrast, the GRACE score includes the heart rate (HR), blood pressure (BP), and the presence of heart failure, in addition to classical risk factors such as age, any prior MI or previous PCI, creatinine values, myocardial-specific enzymes, and ST changes on ECG. Therefore, it provides a more accurate estimate of the risk both on admission and at discharge. The calculation can be made online at http://www.outcomes-umassmed.org/grace/acs_risk/acs_risk_content.html.

To date, GRACE score remains the only ischemic risk score considered in the ESC Guidelines. At the same time, it is crucial to perform an evaluation of the bleeding risk during the prognostic stratification. The CRUSADE bleeding score is a score that is used to predict the risk of major bleeding in light of eight parameters; patients with an increased risk of bleeding are women, diabetics, and those with low hematocrit, with low values of creatinine clearance, with signs of heart failure, with low (or too high) blood pressure, with high heart rate, and with history of other vascular disease.

A score <21 identifies patients at very low risk, between 21 and 30 configures a low risk, between 31 and 40 the risk is moderate, between 41 and 50 the risk is high, and >50 configures a very high risk. The calculation can be made online at http://www.crusadebleedingscore.org. The execution of both scores is recommended by the ESC Guidelines in class I, level of evidence B.

Anti-ischemic Agents

- Oxygen insufflation: (4–8 L/min) if oxygen saturation is <90 %.
- Nitrate treatment (sublingual, oral, or intravenous) is indicated to relieve angina and/or in patients with signs of heart failure (I; C).
- Morphine 3–5 mg intravenously or subcutaneously, if severe pain.
- Patients who are taking chronic beta-blocker therapy, admitted with ACS, should be continued on beta-blocker therapy if not in Killip class III (I; C).
- Oral beta-blocker treatment is indicated in all patients with LV dysfunction without contraindications (I; B).
- Calcium channel blockers are recommended for symptom relief in patients already receiving nitrates and beta-blockers (dihydropyridine type) and in patients with contraindications to beta-blockers (benzothiazepine or phenylethylamine type) (I; B).
- Calcium channel blockers are recommended in patients with vasospastic angina (I; C).
- Intravenous beta-blocker treatment at the time of admission should be considered for patients in a stable hemodynamic condition (Killip class <III) with hypertension and/or tachycardia (IIa; C).
- Nifedipine or other dihydropyridines are not recommended unless combined with beta-blockers (III; B).

Oral Antiplatelet Agents

- ASA: loading dose of 150–300 mg, maintenance dose of 75–100 mg daily (I; A).
- P2Y12 inhibitor should be added to aspirin and maintained over 12 months (I; A).
- Ticagrelor (180-mg loading dose, 90-mg twice daily maintenance dose) is recommended for all patients at moderate-to-high risk of ischemic events (I; B). Contraindications: previous hemorrhagic stroke, II° or III° degree atrioventricular block, sick sinus syndrome, bradycardia, syncope, and anticoagulant therapy.
- Prasugrel (60-mg loading dose, 10-mg daily maintenance dose) is recommended for patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI (I; B). Contraindications: previous stroke or TIA, oral anticoagulant therapy, trauma or recent surgery, age >75 years, and low body weight <60 kg.

- Clopidogrel (300-mg loading dose, 75-mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel (I; A). A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option (I; B). Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used (IIb; B).
- A proton pump inhibitor (PPI; preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal hemorrhage or peptic ulcer and appropriate for patients with multiple other risk factors (*Helicobacter pylori* infection, age >65 years, anticoagulants, or steroids therapie) (I; B).
- In patients pretreated with P2Y12 inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischemic events, should be considered (IIa; C). Ticagrelor or clopidogrel should be considered to be (re)started after CABG surgery as soon as considered safe (IIa; B).

GP IIb/IIIa Receptor Inhibitors

Among patients who are already treated with DAPT, the addition of a GP IIb/IIIa receptor inhibitor (abciximab, tirofiban, eptifibatide) for high-risk PCI (elevated troponin, visible thrombus) is recommended if the risk of bleeding is low (I; B).

Anticoagulants

Anticoagulation is recommended for all patients (I; A).

- Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favorable efficacy-safety profile (I; A). If the initial anticoagulant is fondaparinux, a single bolus of UFH (85 IU/kg adapted to ACT or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) should be added at the time of PCI (I; B). It is contraindicated in severe renal failure (CrCl <20 mL/min).
- Enoxaparin (1 mg/kg twice daily) is recommended when fondaparinux is not available (I; B). Dose reduction to 1 mg/kg once dialysis is indicated in the case of severe renal failure (CrCl <30 mL/min).
- If fondaparinux or enoxaparin is not available, UFH with a target aPTT of 50–70 s is indicated (I; C). UFH infusion is recommended when CrCl is <30 mL/min or eGFR is <30 mL/min/1.73 m^2 with most anticoagulants (fondaparinux <20 mL/min).

In a purely conservative strategy, anticoagulation should be maintained up to hospital discharge (I; A).

Discontinuation of anticoagulation should be considered after an invasive procedure unless otherwise indicated (IIa; C).

Crossover of heparins (UFH and LMWH) is not recommended (III; B).

Treatment of Anemia and Hyperglycemia

Treatment of elevated blood glucose should avoid both excessive hyperglycemia (>180–200 mg/dL) and hypoglycemia (<90 mg/dL) (I; B).

Blood transfusion may have deleterious effects, so it is recommended only in the case of compromised hemodynamic status or hematocrit <25 % or hemoglobin level <7 g/dL (I; B).

Secondary Prevention

Beta-blockers are recommended in all patients with reduced LV systolic function (LVEF <40 %) (I; A).

ACE inhibitors/ARB are indicated within 24 h in all patients with LVEF <40 % and in patients with heart failure, diabetes, hypertension, or CKD, unless contraindicated (I; A).

ACE inhibitors/ARB are recommended for all other patients to prevent recurrence of ischemic events, with preference given to agents and doses of proven efficacy (I; B).

Aldosterone blockade with eplerenone is indicated in patients after MI who are already being treated with ACE inhibitors and beta-blockers and who have an LVEF <35 % and either diabetes or heart failure, without significant renal dysfunction (serum creatinine >2.5 mg/dL for men and >2.0 mg/dL for women) or hyperkalemia (I; A).

Statin therapy with target LDL-C levels <70 mg/dL initiated early after admission is recommended (I; B).

Patients with NSTE-ACS and severe LV dysfunction should be considered after 1 month for device therapy (CRT and/or ICD) in addition to optimal medical therapy (IIa; B).

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