Treatment of acute coronary syndrome: Part 2: ST-segment elevation myocardial infarction

Jeffrey C. Trost, MD, FACC; Richard A. Lange, MD, FACC

Objective: **Familiarize clinicians with recent information regarding the diagnosis and treatment of ST-segment elevation myocardial infarction.**

Data Sources: **PubMed search and review of relevant medical literature.**

Summary: **Definition, pathophysiology, clinical presentation, diagnosis, and treatment of ST-segment elevation myocardial infarction are reviewed.**

Conclusions: **Patients with ST-segment elevation myocardial infarction benefit from prompt reperfusion therapy. Adjunctive antianginal, antiplatelet, antithrombotic, beta blocker, angiotensin-converting enzyme inhibitor, and statin agents minimize ongoing cardiac ischemia, prevent thrombus propagation, and reduce the risk of recurrent cardiovascular events. (Crit Care Med 2012; 40:1939–1945)**

Key Words: acute coronary syndrome; acute myocardial infarction; coronary artery disease

Acute coronary syndrome (ACS) encompasses three clinical conditions that result from an acute imbalance between myocardial oxygen supply and demand: unstable angina and non-ST-segment elevation myocardial infarction—reviewed in part 1 of this series (1)—and ST-segment elevation myocardial infarction (STEMI). The patient with STEMI has 1) cardiac chest pain; 2) serologic evidence of myonecrosis (i.e., elevation of serum troponin or creatine kinase MB isoenzyme concentration); and 3) persistent (>20 mins) ST-segment elevation or a related electrocardiographic (ECG) abnormality (i.e., an indeterminate or new left bundle branch block, ST depression in the right precordial leads) that suggests the presence of an acutely occluded coronary artery.

Epidemiology

Nearly 1.4 million people are hospitalized annually with ACS in the United States, of whom one quarter to one third have STEMI (2). It is more common in individuals with one or more risk factors for atherosclerosis, peripheral vascular disease, cocaine use, or chronic inflammatory disorders, such as rheumatoid arthritis, psoriasis, or infection.

Pathophysiology

The most common cause of STEMI is rupture of a "vulnerable" atherosclerotic plaque that results in a totally occlusive coronary thrombus. Less commonly, STEMI is due to coronary embolism, coronary vasospasm from focal endothelial dysfunction (e.g., Prinzmetal's angina) or drug ingestion (e.g., cocaine, chemotherapeutic agents, or serotonin receptor agonists), spontaneous coronary dissection (i.e., seen peripartum and in patients with vasculitis), or aortic dissection.

Diagnosis

Prompt diagnosis and treatment is essential for salvaging ischemic myocardium and minimizing infarct-related complications (3). The diagnosis is based on an expeditious assessment of the patient's history, physical examination, and ECG; serologic evidence of myonecrosis occurs hours after the onset of STEMI.

Patient History and Physical Examination

Most patients with STEMI complain of a "dull," "pressure," "heaviness," or "squeezing" chest discomfort at rest. Some, particularly women with diabetes and elderly women, present with atypical symptoms, such as sharp chest pain, indigestion, epigastric discomfort, fatigue, or dyspnea. The onset of pain can be sudden or gradual and either intermittent (i.e., "stuttering") or persistent, with a duration of minutes to hours. Patients may report radiation of the discomfort to the neck, jaw, or either arm. Associated symptoms include nausea, dyspnea, diaphoresis, abdominal pain, and/or syncope.

The physical examination of a patient with STEMI is usually unremarkable. Most patients initially appear uncomfortable from symptoms of chest discomfort, and some are visibly diaphoretic. Patients with extensive myocardial ischemia may have findings consistent with left ventricular dysfunction and/or cardiogenic shock, such as tachycardia, hypotension, an S_3 gallop, and peripheral hypoperfusion, all of which are associated with increased mortality.

Electrocardiogram

ST-segment elevation in two contiguous leads, i.e., inferior limb leads (II, III, and aVF), anterior precordial leads (V1–V4), lateral or anterolateral leads (I, avL, V4–V6), a new or indeterminate left bundle branch block, or isolated ST-segment depression in the right precordial leads (i.e., V1 and V2) indicative of an acute posterior infarct is suggestive of an STEMI. ST-segment elevation incidentally noted in the patient without chest pain suggests the presence of a nonischemic cardiac condition (Table 1) (4).

From the Johns Hopkins School of Medicine (JCT), Baltimore, MD, and the University of Texas Health Science Center at San Antonio (RAL), San Antonio, TX.

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For information regarding this article, E-mail: jtrost2@jhmi.edu

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Cardiac Biomarkers

In the patient suspected of having a STEMI, the presence of elevated serum cardiac biomarkers (serum troponin or CK-MB) confirms the presence of myonecrosis. However, because they are not detectable in the blood until 2–4 hrs after the onset of myocardial infarction (MI), reperfusion therapy should not be delayed in a patient with suspected STEMI until elevated serum concentrations are documented. Although both cTnI and cTnT perform comparably for diagnostic purposes, patients with renal failure are more likely to have an elevation of cTnT compared with cTnI. Persistently elevated troponin levels that do not rise and fall in the temporal pattern typical of MI rarely accompany a variety of other clinical conditions (5).

Table 1. Nonischemic conditions associated with ST-segment elevation on electrocardiogram

Normal variant in young people
Left ventricular hypertrophy
Left bundle branch block
Ventricular paced rhythm
Ventricular pre-excitation (Wolff-Parkinson-White)
Myocarditis
Hyperkalemia
Takotsubo cardiomyopathy
Left ventricular aneurysm
Brugada syndrome
Arrhythmogenic right ventricular dysplasia

Differential Diagnosis

Chest pain with ST-segment elevation can be observed with pericarditis, pulmonary embolism, or aortic dissection with ostial coronary occlusion. Differentiating these from STEMI is important (Table 2) because routine MI therapy may be harmful in these conditions (i.e., fibrinolytic therapy in the patient with pericarditis or aortic dissection may cause tamponade or rupture, and nitrates in the patient with pulmonary embolism may precipitate severe hypotension).

Diagnosing STEMI in Critically Ill Patients

Most patients with STEMI are identified in the hospital emergency room or in the pre-hospital setting by emergency medical personnel. An occasional patient develops STEMI while in-hospital, although the exact occurrence rate is unknown. In a postmortem study of 600 noncardiac intensive care unit (ICU) patients, pathologic evidence of acute MI was found in 75 (12.5%), of whom only ~20% exhibited acute ischemic ECG changes during their ICU stay (6). In a study of 103 consecutive patients admitted to a medical ICU and screened with routine serial troponins and ECGs regardless of the admitting diagnosis, 37 had MI of whom three (8%) had ST-segment elevation (7).

Table 2. Characteristic features of myocardial infarction and its differential diagnoses

	Myocardial Infarction	Pericarditis	Pulmonary Embolism	Acute Aortic Dissection
Chest pain				
Location	Retrosternal	Retrosternal	Anterior, posterior, or lateral	Anterior or posterior
Character	Pressure-like, heavy, squeezing	Sharp, stabbing, occasionally dull	Sharp, stabbing	Severe, tearing ripping
Change with respiration	No	Worse when supine; improved when sitting up or leaning forward	No	No
Radiation	Jaw, neck, shoulder, one or both arms	Jaw, neck, shoulder, one or both arms, trapezius ridge	Shoulder	Follows extension of the dissection
Duration	Mins (ischemia); hrs (infarction)	Hours to days	Hours to days	
Response to nitroglycerin	Improved	No change	No change	No change
Physical examination				
Pulses in upper extremities	Normal	Normal	Normal	Asymmetric or absent
Friction rub	Absent	Present (in 85% of patients)	Rare; pleural friction rub in 3% of patients	Absent
S3, pulmonary congestion	May be present	Absent	Absent	May be present with acute aortic insufficiency
Electrocardiogram				
ST-segment elevation	Convex and localized	Concave and widespread	aVF and V1	With coronary occlusion, convex and localized
PR-segment depression	Rare	Frequent	None	None
Q waves	May be present	Absent	May be present in lead III or aVF or both	Absent
T waves	Inverted when ST-segments are still elevated	Inverted after ST-segments have normalized	Inverted in lead II, aVF, or V1to V4 while ST segments are elevated	Absent
Atrioventricular block, ventricular arrhythmias	May be present	Absent	Absent	Absent

Diagnosing STEMI in critically ill patients can be challenging, because many are unable to verbalize symptoms of chest pain (i.e., respiratory failure requiring mechanical ventilation, altered mental status, analgesic administration). Furthermore, ICU patients are prone to conditions that produce ST-segment elevation in the absence of cardiac ischemia (i.e., hyperkalemia and pulmonary embolism). Although an acute hemodynamic change may suggest the presence of an MI, other etiologies (i.e., hypovolemia, sepsis, and hypoxia) are more often responsible (8).

Several clues may help in diagnosing STEMI in the ICU patient. First, a history obtained from the patient's family or acquaintances may reveal preceding symptoms of unstable or progressive angina. Second, comparison of recent and previous ECG tracings may demonstrate changes suggestive of ischemia and/or infarction. Third, imaging modalities, such as echocardiography, can identify new cardiac wall motion abnormalities suggestive of myocardial ischemia or infarction. Fourth, acute changes in the patient's condition—such as hemodynamic instability, hypoxemia from cardiogenic pulmonary edema, sustained ventricular arrhythmias, or a new mitral regurgitation murmur—may represent clinical manifestations of STEMI.

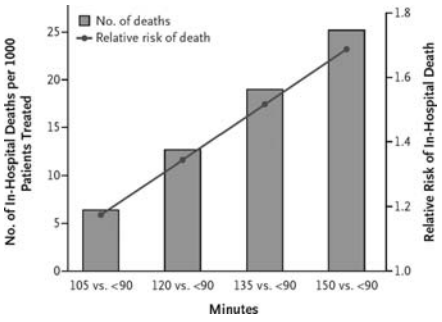

Figure 1. Relative risk of in-hospital death and number of deaths associated with increases in door-to-balloon time. The bars represent the number of in-hospital deaths per 1,000 patients treated, and the line represents the relative risk associated with longer door-to-balloon times with primary percutaneous coronary intervention when compared with treatment within 90 mins. Adapted with permission from Nallamothu et al (11).

Treatment

The primary treatment goal of STEMI is prompt coronary reperfusion, which reduces infarct size and patient mortality. Secondary treatment goals include optimizing myocardial supply and demand and preventing thrombus propagation and recurrent MI.

Reperfusion Therapy

In STEMI patients presenting to a hospital with percutaneous coronary intervention (PCI) capability, primary PCI—in the form of aspiration thrombectomy, balloon angioplasty, and/or stenting—is the preferred reperfusion strategy. The promptness of reperfusion is assessed by the "door-to-balloon" time, with "door" reflecting the time that the patient arrives in the hospital (or, if already hospitalized, when ST-segment elevation is first recognized), and "balloon" reflecting the time at which an intracoronary balloon is initially inflated. A door-to-balloon time of <90 mins is the performance goal for hospitals with primary PCI capability. A direct relationship between door-to-balloon times and in-hospital mortality in STEMI patients (Fig. 1) underscores the importance of prompt reperfusion therapy in these patients (9–11).

At facilities without PCI capability, (approximately 75% of hospitals in the US (12)) patients with STEMI may be 1) treated with fibrinolytic therapy if not contraindicated; or 2) transferred to a facility with PCI capability. In addition, fibrinolysis may be preferable in patients with a relative contraindication to PCI (i.e., absence of suitable arterial access, allergy to contrast agent, and severe renal dysfunction). Fibrinolytic drugs approved for the treatment of STEMI are displayed in Table 3. Patients treated with a fibrinolytic agent should receive anticoagulant therapy for a minimum of 48 hrs and preferably for the duration of the index hospitalization, up to 8 days. High-risk patients should be transferred to a PCI-capable hospital following fibrinolysis with the intent to perform early catheterization and PCI if indicated. In stable patients, routine catheterization can be considered as part of an ischemia evaluation at 24–48 hrs following fibrinolytic therapy.

Patients with a contraindication to fibrinolytic therapy (Table 4) who are at a hospital without PCI capability should be transferred promptly to a hospital where primary PCI can be performed. In addition, STEMI patients with one or more of the following should be considered for transfer for primary PCI rather than fibrinolytic therapy: 1) significant pulmonary edema and/or signs of cardiogenic shock (also referred to as Killip 3 or 4, respectively); 2) time from symptom onset to initial presentation >3 hrs; 3) high-risk features for death; or 4) the diagnosis of STEMI is in doubt (Table 5).

Unfortunately, patients with STEMI requiring interhospital transfer for primary PCI often have prolonged overall door-to-balloon times from first hospital presentation to second hospital PCI (13). Although 30 mins is the benchmark time interval from recognition of STEMI at the first hospital to transfer to a PCI capable facility, this is accomplished in only 11% of patients. Common reasons for transfer delays include delays in transport, delays in diagnosis due to clinical uncertainty or an initially nondiagnostic ECG, and delays caused by cardiac arrest and/or cardiogenic shock (14). In-hospital mortality is significantly higher when transfer is delayed >30 mins compared to when it is accomplished within 30 mins

Table 3. Thrombolytic agents used to treat ST-segment elevation myocardial infarction

Agent	Dose (Intravenous)	Fibrin-Specific	Coronary Patency Rates (at 90 mins)
Alteplase (t-plasminogen activator)	15 mg bolus, then 50 mg given over 30 mins, then 35 mg given over 60 mins	Yes	73%–84%
Reteplase (r-plasminogen activator)	10 units + 10 units boluses, given 30 mins apart	Yes	84%
Tenecteplase[a] (TNKase)	0.5 mg/kg (maximal 50 mg) bolus	Yes	84%
Streptokinase[b]	1.5 million units given over 30–60 mins	No	60%–68%

[a]Most commonly used agent in the intensive care unit setting; [b]streptokinase is antigenic and contraindicated if the patient has previously received it in the preceding 6 months (due to potential of serious allergic reaction).

Table 4. Contraindications to thrombolytic therapy in ST-segment elevation myocardial infarction

Absolute contraindications
Any prior intracranial hemorrhage
Ischemic stroke within 3 months
Known structural cerebral vascular lesion (e.g., arteriovenous malformation)
Known malignant intracranial neoplasm (primary or metastatic)
Intracranial or intraspinal surgery within 2 months
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed-head or facial trauma within 3 months
Severe uncontrolled hypertension (unresponsive to emergent therapy)
For streptokinase, prior treatment within the previous 6 months
Relative contraindications
History of prior ischemic stroke >3 months ago
Significant hypertension on presentation (systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg)
History of chronic, severe, poorly controlled hypertension
Oral anticoagulant therapy with elevated international normalized ratio
Traumatic or prolonged (>10 mins) cardiopulmonary resuscitation
Recent (within 2–4 wks) internal bleeding
Puncture of noncompressible vessel
Major surgery (within past 3 wks)
Pregnancy
Active peptic ulcer
Dementia

Table 5. ST-segment elevation myocardial infarction patients best suited for immediate transfer for percutaneous coronary intervention without fibrinolysis

Patients presenting >3 or 4 hrs after onset of symptoms with short transfer times
Door-to-balloon <90 mins
Emergency medical services to balloon time <120 mins
Patients with high bleeding risk with fibrinolytic therapy
Patients with high risk features
Heart failure or cardiogenic shock (Killip class II-IV)
Hemodynamically compromising ventricular arrthythmias
Age >75 yrs
Hypotension (systolic blood pressure <100 mm Hg)
Tachycardia (heart rate >100 beats/min)
Patients in whom the diagnosis is in question

(5.9% vs. 2.7%, respectively; $p < .001$ (13)). Unfortunately, a delay of >30 mins is encountered in almost 90% of patients transferred for primary PCI (13). For STEMI patients at a facility without PCI capabilities, a rapid transfer plan should be in place to optimize timely treatment.

Optimizing Myocardial Oxygen Supply and Demand

Limiting infarct size can be enhanced by increasing myocardial oxygen supply and reducing myocardial demand with nitroglycerin, morphine, and beta-adrenergic blockers (Table 6). The most recent (2007) American College of Cardiology/American Heart Association guidelines classify administration of supplemental oxygen as a class IIa (i.e., it may be considered) recommendation for all STEMI patients (15). However, data to support routine administration of oxygen for STEMI patients are limited, and administering oxygen in the absence of hypoxemia may worsen mortality in STEMI patients, presumably by increasing coronary resistance (16).

Nitroglycerin increases myocardial oxygen supply by dilating coronary arteries and collaterals. It also reduces myocardial oxygen demand by reducing left ventricular preload and afterload. Nitroglycerin is a first-line agent for treating chest pain due to cardiac ischemia and can be administered sublingually, by spray, or intravenously. Intravenous morphine can be given for chest pain not immediately relieved with nitroglycerin; morphine reduces ventricular preload, which decreases myocardial oxygen demand.

Nitroglycerin and morphine are contraindicated in the patient with right ventricular infarction, in whom a reduction in preload may lead to profound hypotension. A right-sided ECG (e.g., precordial leads positioned on the right side of the chest) should be performed in all patients with an inferior MI to determine if evidence of right ventricular infarction is present (i.e., >1 mm ST elevation in leads V_3R, V_4R, V_5R, or V_6R (17)).

Beta-adrenergic blockers decrease myocardial demand by reducing heart rate, blood pressure, and myocardial contractility. Intravenous administration should be considered in the STEMI patient with persistent chest pain, tachycardia, or hypertension. In the patient without these findings, treatment can be initiated orally. Beta-adrenergic blockers should be avoided in the patient with decompensated heart failure, advanced atrioventricular block, hypotension, or suspected cocaine use due to the risk of unopposed alpha adrenergic receptor stimulation and resultant coronary vasoconstriction (18). In survivors of acute MI, long-term oral beta-blocker use, in comparison with placebo, has been shown to reduce the occurrence rate of all-cause mortality, including sudden cardiac death, by approximately 20%–30%. (19).

Reducing Thrombus Propagation

To reduce thrombus propagation, the patient with STEMI should receive intensive antiplatelet and antithrombotic therapy unless contraindicated (Table 7), regardless of what mode of reperfusion (i.e., thrombolysis or primary PCI) is chosen. Antiplatelet agents used in STEMI patients include aspirin and thienopyridines. Antithrombotic agents used in STEMI patients include unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), fondaparinux, and bivalirudin.

Antiplatelet Therapy. Initiation of two antiplatelet agents, aspirin and a thienopyridine, is recommended in the patient with suspected or confirmed STEMI. Aspirin blocks the synthesis of thromboxane A2, a potent vasoconstrictor and stimulator of platelet aggregation. Compared with placebo, 160 mg of aspirin daily reduces the risk of short-term (i.e., 35-day) death by 23% in STEMI patients (20).

Thienopyridines (i.e., clopidogrel, prasugrel, and ticagrelor) block platelet adenosine diphosphate receptors, thereby reducing platelet activation and aggregation. Combined clopidogrel and aspirin therapy reduces short- (30-day) and long-term (1 yr) cardiovascular events

Table 6. Routine initial therapies for ST-segment elevation myocardial infarction

Therapy	Indication	Dose/Administration	Avoid/Caution
Aspirin	All patients without a contraindication	Initial dose 160–325 mg, then 75–325 mg daily	• Known allergy
Beta blocker	• Oral – all patients without a contraindication • IV – patients with ongoing ischemia or refractory hypertension	• Individualize; begin with oral metoprolol tartrate every 6 hrs and transition to oral metoprolol succinate once daily over 2–3 days (maximum dose 200 mg/24 hrs) • Use IV metoprolol tartrate titrated against heart rate and BP. Standard dose is 5 mg every 5 mins as tolerated up to three doses	• High-grade atrioventricular block • Reactive airway disease • Hypotension • Heart failure • Shock
Nitroglycerin	• Ongoing chest pain • Hypertension and heart failure	• 0.4 mg sublingual every 5 mins up to three doses as BP allows • IV dosing to begin at 10 μg/min; titrate to desired effect	• Avoid in suspected right ventricular infarction • Avoid with systolic BP <90 mm Hg or >30 mm Hg below baseline • Avoid if recent use of 5′-phosphodiesterase inhibitors (24–48 hrs)
Morphine	• Pain • Anxiety • Pulmonary edema	• 4–8 mg IV initially • 2–8 mg IV every 5–15 min if needed	• Lethargic or moribund • Hypotension • Bradycardia • Known hypersensitivity
Oxygen	• Hypoxemia (O_2 saturation <90%) • Heart failure • Dyspnea	• 2–4 L/min • Increase rate or change to face mask as needed	• Chronic obstructive pulmonary disease and CO_2 retention

BP, blood pressure; IV, intravenous.

in ACS patients by 20% in comparison to treatment with aspirin alone (21–23).

Prasugrel and ticagrelor have a greater antiplatelet effect and more rapid onset of action than clopidogrel. In ACS patients treated with aspirin and PCI, prasugrel therapy is associated with a lower risk of cardiovascular death, MI, or stroke at 6 months than clopidogrel therapy (9.9% vs. 12.1%; $p < .001$) and an increased risk for major bleeding (2.4% vs. 1.8%; $p = .03$) (24). Currently, prasugrel is only approved for use in ACS patients managed with PCI. It is not recommended in patients with weights <60 kg, aged >75 yrs, or with histories of transient ischemic attack, stroke, or intracranial bleeding due to excessive bleeding risk. In STEMI patients referred for primary PCI, treatment with ticagrelor when compared with clopidogrel significantly ($p = .02$) reduces the 12-month rate of death from vascular causes, MI, or stroke by 15% (9.3% vs. 11.0%, respectively, without an increase in the rate of major bleeding) (25). Maintenance doses of aspirin >100 mg daily may reduce the effectiveness of ticagrelor and should be avoided (26).

The GPIIb/IIIa inhibitors, abciximab, eptifibatide, and tirofiban, block platelet aggregation and reduce recurrent ischemia and MI in ACS patients who undergo PCI (27). However, data supporting their efficacy and safety in combination with dual antiplatelet therapy in STEMI patients are limited (28). Current guidelines suggest that it is reasonable to use GPIIb/IIIa inhibitors as an adjunctive therapy during primary PCI with administration initiated at the time of revascularization. They are not indicated in the patient who is treated with thrombolytic therapy.

Antithrombotic Therapy. Antithrombotic therapy should be initiated promptly in the patient with STEMI, unless contraindicated. UFH accelerates the inactivation of thrombin and clotting factors IXa and Xa. Its advantages include ease of administration (intravenous) and rapid reversibility with protamine in the patient with bleeding complications. Its disadvantages include a variable anticoagulant effect, the need for frequent monitoring (using anti-factor Xa assay), and associated thrombocytopenia in 1–2% of patients. As with all antithrombotic agents, the most common complication associated with UFH therapy is bleeding, particularly when used in combination with a GPIIb/IIIa inhibitor. The timing and duration of UFH therapy depends on what type of reperfusion strategy is used (Table 7).

In comparison with UFH, LMWH has a more predictable anticoagulant effect, lower occurrence rate of thrombocytopenia, and does not require serum monitoring. In STEMI patients treated with fibrinolytic therapy, LMWH (e.g., enoxaparin) therapy, in comparison with UFH, is associated with a lower, short-term rate of recurrent MI at the expense of a higher risk of major bleeding complications (29). Despite limited data regarding the efficacy and safety of LMWH in STEMI patients receiving primary PCI, LMWH is regarded as an acceptable antithrombotic agent in this setting. The daily LMWH dose can be adjusted based on anti-factor Xa assay results and should be reduced in patients with several renal dysfunction, who are >75 yrs of age, and who are obese (weight >100 kgs) (Table 7).

Fondaparinux is a factor Xa inhibitor that does not cause thrombocytopenia. In a study comparing fondaparinux to enoxaparin in ACS patients (including patients with STEMI receiving either fibrinolytic therapy or primary PCI), short-term (e.g., 9 days) risk of death, MI, or recurrent ischemia was similar for both, but there was a significantly lower rate of major bleeding with fondaparinux therapy (30). Thus, fondaparinux is preferred over UFH or LMWH in patients at high risk of bleeding. In those undergoing PCI, there is an increased rate of catheter-related thrombosis with fondaparinux; therefore, an additional anticoagulant with anti-IIa activity must be used during the procedure.

Bivalirudin is a direct thrombin inhibitor and does not cause thrombocytopenia.

Table 7. Antiplatelet and antithrombotic therapy for ST-segment elevation myocardial infarction

Antiplatelet Therapy (Dual therapy with aspirin and another agent recommended)			
	Loading Dose	Maintenance Dose	Duration
Aspirin	162–325 mg (nonenteric coated)	• 75–162 mg/day • 162–325mg for first month if stent implanted	Indefinitely
Clopidogrel	300–600 mg	75 mg/day	1 yr
Prasugrel[a]	60 mg	10 mg/day	1 yr
Ticagrelor[b]	180 mg	90 mg twice a day	1 yr
GPIIb/IIIa Receptor Antagonists (use reserved for patients undergoing PCI and initiated at the time of cardiac catheterization)			
	Loading Dose (IV)	Maintenance Dose (IV)	Duration
Abciximab	0.25 mg/kg bolus	0.125 μg/kg/min	12 hrs
Eptifibatide	180 μg/kg bolus followed 10 mins later by second IV bolus of 180 μg/kg	2.0 μg/kg/min, started after first bolus (reduce by 50% in patients with creatinine clearance <50 mL/min)	18–24 hrs
Tirofiban	25 μg/kg bolus	0.1 μg/kg/min • reduce rate by 50% with estimated creatinine clearance <30 mL/min	12–24 hrs
Antithrombotic Therapy (initiated before or at the time of reperfusion therapy)			
	Loading Dose	Maintenance Dose	Duration
Unfractionated heparin	• PCI with GPIIb/IIIa: 50–70 U/kg bolus IV • PCI without GPIIb/IIIa: 70–100 U/kg IV • Following fibrinolysis: 60 U/kg (max 4000 U)	• Intermittent bolus to achieve activated clotting time of 200–250 secs • Intermittent bolus to achieve activated clotting time of 250–300 sec • 12 U/kg/min infusion to achieve activated partial thromboplastin time 1.5–2.0 times control	• Discontinue after successful PCI • Discontinue after successful PCI • 48 hrs after fibrinolysis
Bivalirudin[c]	0.75 mg/kg IV bolus	1.75 mg/kg/hr infusion with or without prior treatment with unfractionated heparin	Up to 72 hrs; discontinue after successful PCI
Enoxaparin	30 mg IV bolus (no bolus if age >75 yrs)	1 mg/kg SC every 12 hrs • Age >75 yrs 0.75 mg/kg SC every 12 hrs • If creatinine clearance <30 mL/min, 0.75 mg/kg/d (28)	Duration of hospitalization (up to 8 days); discontinue after successful PCI
Fondaparinux	2.5 mg SC	2.5 mg SC daily	Duration of hospitalization (up to 8 days)

GPIIb/IIIa, glycoprotein IIb/IIIa inhibitor; IV, intravenous; PCI, percutaneous coronary intervention; SC, subcutaneous; U, units.

[a]Avoid use in patients with prior stroke/TIA, age ≥75 yrs or weight <60 kg due to increased risk of bleeding; [b]maintenance doses of aspirin >100 mg daily reduce the effectiveness of ticagrelor and should be avoided; [c]preferred over unfractionated heparin or low-molecular-weight heparin with GPIIb/IIIa receptor inhibitors in patients at high risk of bleeding.

In a study of STEMI patients receiving primary PCI, bivalirudin alone was compared with UFH in combination with a GPIIb/IIIa inhibitor (31). The occurrence rate of all-cause and cardiac death was lower with bivalirudin at 30 days and 1 yr ($p < .05$ for both), and patients treated with bivalirudin had a significantly lower rate of bleeding. Consequently, in STEMI patients undergoing PCI who are at high risk of bleeding, bivalirudin is preferred over UFH or enoxaparin and a GPIIb/IIIa inhibitor.

Complications of MI

Potential complications of STEMI include right and/or left ventricular failure, cardiogenic shock; acute mitral regurgitation from papillary muscle ischemia, infarction and/or rupture; acute ventricular septal rupture; and free wall rupture. In the STEMI patient who develops hemodynamic instability (regardless of whether reperfusion therapy is administered and what type of reperfusion therapy is chosen), one must consider these potential complications, as well as the possibility of complications (i.e., acute bleeding, vessel perforation, and tamponade) from the reperfusion therapy itself.

Preventing Recurrent MI

Before discharge, in addition to antiplatelet and beta blocker therapy, an angiotensin-converting enzyme inhibitor and a high-dose statin should be initiated unless contraindicated. Several large-scale, randomized trials have shown that predischarge initiation of angiotensin-converting enzyme inhibitors and high dose statins in STEMI patients reduce their long-term risk of death and recurrent MI (32–35).

CONCLUSIONS

STEMI is typically caused by total coronary occlusion resulting from acute plaque rupture and thrombus formation. The patient's history and ECG are used to make the initial diagnosis and determine therapy, and the diagnosis is confirmed by either cardiac catheterization and/or cardiac biomarkers. In critically ill patients, diagnosing ACS can be difficult. Treatment goals include prompt reperfusion, relief of ischemia, and prevention of thrombus propagation, recurrent MI, and death.

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