ACUTE CORONARY SYNDROMES

DEFINITIONS

- Acute coronary syndromes (ACSs) include all clinical syndromes compatible with acute myocardial ischemia resulting from an imbalance between myocardial oxygen demand and supply.
- In contrast to stable angina, an ACS results primarily from diminished myocardial blood flow secondary to an occlusive or partially occlusive coronary artery thrombus.
- ACSs are classified according to electrocardiographic (ECG) changes into.

(1) ST-segment-elevation ACS (STE ACS or STEMI) .

(2) non–ST segment- elevation ACS (NSTE ACS), which includes non–ST-segment elevation myocardial infarction (NSTE MI) and unstable angina (UA).

PATHOPHYSIOLOGY

- The formation of atherosclerotic plaques is the underlying cause of coronary artery disease (CAD) and ACS in most patients.
- Endothelial dysfunction leads to the formation of fatty streaks in the coronary arteries and eventually to atherosclerotic plaques.
- The cause of ACS in more than 90% of patients is rupture, fissuring, or erosion of an unstable atheromatous plaque.

CLINICAL PRESENTATION

- The predominant symptom of ACS is midline **anterior chest discomfort** (most often occurring at rest), severe new-onset angina, or increasing angina that lasts at least 20 minutes.
- The discomfort may radiate to the shoulder, down the left arm, to the back, or to the jaw.
- Accompanying symptoms may include nausea, vomiting, diaphoresis, or shortness of breath. Elderly patients, patients with diabetes, and women are less likely to present with classic symptoms.
- There are no specific features indicative of ACS on physical examination.

DIAGNOSIS

- A 12-lead ECG should be obtained within 10 minutes of patient presentation. Key findings indicating myocardial ischemia or MI are ST-segment elevation, ST-segment depression, and T-wave inversion.
- Biochemical markers of myocardial cell death are important for confirming the diagnosis of MI. An evolving MI is defined as a typical rise and gradual fall in troponin I or T or a more rapid rise and fall of CK-MB.

DESIRED OUTCOME

- Short-term goals of therapy include:

  (1) early restoration of blood flow to the infarct-related artery to prevent infarct expansion (in the case of MI) or prevent complete occlusion and MI (in UA),

  (2) prevention of complications and death,

  (3) prevention of coronary artery reocclusion,

  (4) relief of ischemic chest discomfort, and

  (5) maintenance of normoglycemia.

TREATMENT

- GENERAL APPROACH

  General treatment measures include hospital admission, oxygen administration if saturation is less than 90%, continuous multilead ST-segment monitoring for arrhythmias and ischemia, glycemic control, frequent measurement of vital signs, bedrest for 12 hours in hemodynamically stable patients, use of stools softeners to avoid Valsalva maneuver, and pain relief.

NONPHARMACOLOGIC THERAPY

- For patients with STE ACS, either fibrinolysis or primary PCI (precutaneous coronary artery intervention) (with either balloon angioplasty or stent placement) is the treatment of choice for reestablishing coronary artery blood flow when the patient presents within 3 hours of symptom onset.
- Primary PCI may be associated with a lower mortality rate than fibrinolysis, possibly because PCI opens more than 90% of coronary arteries compared with less than 60% opened with fibrinolytics. The risks of intracranial hemorrhage (ICH) and major bleeding are also lower with PCI than with fibrinolysis.

EARLY PHARMACOTHERAPY FOR ST–SEGMENT ELEVATION ACUTE CORONARY SYNDROME

- According to the American College of Cardiology / American Heart Association (ACC/AHA) practice guidelines, early pharmacologic therapy should include:

  (1) intranasal oxygen (if oxygen saturation is less than 90%); (2) sublingual (SL) nitroglycerin (NTG); (3) aspirin; (4) a β-blocker; (5) unfractionated heparin (UFH) or enoxaparin; and (6) fibrinolysis in eligible candidates.

EARLY PHARMACOTHERAPY FOR ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME

- Morphine is administered to patients with refractory angina as an analgesic and venodilator that lowers preload. These agents should be administered early, while the patient is still in the emergency department.
- An angiotensin-converting enzyme (ACE) inhibitor should be started within 24 hours of presentation, particularly in patients with left ventricular ejection fraction (LVEF) ≤40%, signs of heart failure, or an anterior wall MI, if there are no contraindications.
- IV NTG and β-blockers should be administered to selected patients without contraindications.

Fibrinolytic Therapy

- A fibrinolytic agent is indicated in patients with STE ACS presenting within 12 hours of the onset of chest discomfort who have at least 1 mm of STE in two or more contiguous ECG leads or a new left bundle-branch block.
- It should also be considered in patients with those findings and persistent symptoms of ischemia who present within 12 to 24 hours of symptom onset. Fibrinolysis is preferred over primary PCI in patients presenting within 3 hours of symptom onset when there would be a delay in performing primary PCI.
- It is not necessary to obtain the results of biochemical markers before initiating fibrinolytic therapy.

Fibrinolytic Therapy

- Absolute contraindications to fibrinolytic therapy include:
  (1) active internal bleeding;
  (2) previous ICH at any time;
  (3) ischemic stroke within 3 months;
  (4) known intracranial neoplasm;
  (5) known structural vascular lesion;
  (6) suspected aortic dissection; and
  (7) significant closed head or facial trauma within 3 months.
- Primary PCI is preferred in these situations.

Fibrinolytic Therapy

- Patients with relative contraindications to fibrinolytics may receive therapy if the perceived risk of death from MI is higher than the risk of major hemorrhage.
- These situations include: (1) severe, uncontrolled hypertension (blood pressure [BP] greater than 180/110 mm Hg); (2) history of prior ischemic stroke longer than 3 months prior, dementia, or known intracranial pathology not considered an absolute contraindication; (3) current anticoagulant use; (4) known bleeding diathesis; (5) traumatic or prolonged cardiopulmonary resuscitation or major surgery within 3 weeks; (6) noncompressible vascular puncture; (7) recent (within 2 to 4 weeks) internal bleeding; (8) pregnancy; (9) active peptic ulcer; (10) history of severe, chronic poorly controlled hypertension; and (11) for streptokinase, prior administration (>5 days) or prior allergic reactions.

Aspirin

- *Aspirin* should be administered to all patients without contraindications within the first 24 hours of hospital admission. It provides an additional mortality benefit in patients with STE ACS when given with fibrinolytic therapy.
- In patients experiencing an ACS, non–enteric-coated aspirin, 162 to 325 mg, should be chewed and swallowed as soon as possible after the onset of symptoms or immediately after presentation to the emergency department regardless of the reperfusion strategy being considered.

Thienopyridines

- *Clopidogrel* is recommended for patients with an aspirin allergy. A 300- to 600-mg loading dose is given on the first hospital day, followed by a maintenance dose of 75 mg daily. It should be continued indefinitely.
- For patients treated with fibrinolytics and in those receiving no revascularization therapy, clopidogrel either 75 mg or 300 mg on day 1 followed by 75 mg once daily should be given for at least 14 to 28 days in addition to aspirin.

Glycoprotein IIb/IIIa Receptor Inhibitors

- ***Abciximab*** is a first-line GP IIb/IIIa inhibitor for patients undergoing primary PCI who have not received fibrinolytics. It should not be administered to STE ACS patients who will not be undergoing PCI.
- ***Abciximab*** is preferred over ***eptifibatide*** **and** ***tirofiban*** **in this setting** because it is the most widely studied agent in primary PCI trials.
- GP IIb/IIIa inhibitors may increase the risk of bleeding, especially if given in the setting of recent (<4 hours) administration of fibrinolytic therapy.
- An immune-mediated thrombocytopenia occurs in about 5% of patients.

Anticoagulants

- ***Unfractionated Heparin (UFH)*** is a first-line anticoagulant for STE ACS, both for medical therapy and PCI.
- UFH should be initiated in the emergency department and continued for at least 48 hours in patients who will receive chronic warfarin after acute MI. If apatient undergoes PCI, UFH is discontinued immediately after the procedure.
- If a fibrinolytic agent is administered, UFH is given concomitantly with alteplase, reteplase, and tenecteplase, but UFH is not administered with streptokinase because no benefit of combined therapy has been demonstrated.

Anticoagulants

- **Low-molecular-weight heparins (LMWHs)** may be an alternative to UFH in STE ACS.
- **Enoxaparin** may produce a modest benefit over UFH in reducing the risk of death or nonfatal MI. Enoxaparin has not been studied in the setting of primary PCI.

Nitrates

- Immediately upon presentation, one SL **NTG** tablet should be administered every 5 minutes for up to three doses to relieve chest pain and myocardial ischemia.
- Intravenous NTG should be initiated in all patients with an ACS who do not have a contraindication and who have persistent ischemic symptoms, heart failure, or uncontrolled high BP.

β-Adrenergic Blockers

- If there are no contraindications, a β-blocker should be administered early in the care of patients with STE ACS (within the first 24 hours) and continued indefinitely.
- The benefits result from blockade of β1 receptors in the myocardium, which reduces heart rate, myocardial contractility, and BP, thereby decreasing myocardial oxygen demand. The reduced heart rate increases diastolic time, thus improving ventricular filling and coronary artery perfusion.
- Because of these effects, β-blockers reduce the risk for recurrent ischemia, infarct size, risk of reinfarction, and occurrence of ventricular arrhythmias.

Calcium Channel Blockers

- In the setting of STE ACS, calcium channel blockers are reserved for patients who have contraindications to β-blockers. They are used for relief of ischemic symptoms only.
- Patients who had been prescribed calcium channel blockers for hypertension who are not receiving β-blockers and who do not have a contraindication should have the calcium channel blocker discontinued and a β-blocker initiated.

EARLY PHARMACOTHERAPY FOR NON–ST–SEGMENT ELEVATION ACUTE CORONARY SYNDROME

- Early pharmacotherapy for NSTE ACS is similar to that for STE ACS except that: (1) fibrinolytic therapy is not administered; (2) GP IIb/IIIa receptor blockers are administered to high-risk patients; and (3) there are no standard quality performance measures for patients with NSTE ACS with UA.
- According to ACC/AHA practice guidelines, early pharmacotherapy should include: (1) *intranasal oxygen (if oxygen saturation is <90%); (2) SL NTG (IV therapy for selected patients); (3) aspirin; (4) an oral β-blocker (IV therapy optional); and (5) an anticoagulant (UFH, LMWH [enoxaparin], fondaparinux, or bivalirudin)*.