Acute coronary syndrome

Ischemic heart disease (**Coronary Artery Disease (CAD)**

•**Ischemic heart disease (IHD)** is a condition in which there is an **inadequate supply** of blood and oxygen to a portion of the myocardium there is imbalance between **myocardial oxygen supply** and **demand** caused mainly by **Atherosclerosis of Coronary Artery.**

Ischemic heart disease includes:

- **Stable angina** (classical or exertional angina)

It refers to the classic type of angina related to **myocardial ischemia.** A typical presentation of stable angina is the chest discomfort and associated symptoms precipitated by some activity (running, walking, etc.) with minimal or non-existent symptoms at rest or after administration of **sublingual nitroglycerin.**

- **Prinzmetal's or Prinzmetal Angina and Variant Angina**

Unlike typical angina – which is often triggered by exertion or emotional stress – Prinzmetal's angina almost always occurs when a person is at rest, usually between midnight and early morning. These attacks can be very painful. is caused by a spasm in the coronary arteries (which supply blood to the heart muscle).

- **Acute Coronary Syndrome**

Acute coronary syndrome (ACS) refers to a spectrum of clinical presentations ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina. In terms of pathology, ACS is almost always associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct-related artery. In some instances, however, stable coronary artery disease (CAD) may result in ACS in the absence of plaque rupture and thrombosis, when physiologic stress (eg, trauma, blood loss, anemia, infection, tachyarrhythmia) increases demands on the heart.

Pathophysiology

Atherosclerosis is a progressive **inflammatory disorder** of the arterial wall characterized by focal lipid rich deposits of **atheroma.** Starts with any abnormal endothelial function so the inflammatory cells, predominantly **monocytes**, bind to receptors expressed by endothelial cells, migrate into the **intima,** take up oxidized **low-density lipoprotein (LDL)** particles then become **lipid-laden macrophages** or **foam cells**. As Foam cells dies, it releases its lipid pool in intimal space with **cytokines** and **growth factor.** In response, smooth muscle cells migrate from the media of the arterial wall into the intima then the lipid core will be covered by smooth muscle cells and matrix forming **stable atherosclerotic plaque** that will remain asymptomatic until it becomes large enough to obstruct arterial flow. With rupture of an atherosclerotic plaque, exposure of collagen and tissue factor induces platelet adhesion and activation, promoting release of adenosine diphosphate (ADP) and thromboxane A2 from platelets, leading to vasoconstriction and platelet activation. A change in the conformation of the glycoprotein IIb/IIIa surface receptors of platelets occurs that cross-links platelets to each other through fibrinogen bridges. Simultaneously, activation of the extrinsic coagulation cascade occurs as a result of exposure of blood to the thrombogenic lipid core and endothelium, which are rich in tissue factor. This leads to formation of a fibrin clot composed of fibrin strands, cross-linked platelets, and trapped red blood cells.

Risk Factors

Increasing age, Gender (male), Family History, Smoking, Obesity, Diet, Lack of exercise, High serum cholesterol, Hypertension and Diabetes.

Complications

The primary complications can be divided into three major groups: **pump failure**, **arrhythmias**, and **recurrent ischemia and reinfarction.** compensatory mechanisms can eventually worsen the imbalance between myocardial oxygen supply and consumption by increasing the myocardial oxygen demand. If 40% or more of the left ventricle is damaged, cardiogenic shock and death can occur. Ventricular remodeling (**the infracted area may expand as a result of dilatation and thinning of the left ventricular wall)** after MI is characterized by left ventricular (LV) dilation and reduced pumping function, leading to heart failure (HF).

Clinical Presentation

The predominant symptom is chest discomfort (tightness, pressure, heaviness) at rest or for a prolonged period (> 10 minutes, not relieved by sublingual nitrates). Discomfort may radiate to the shoulder, down the left arm, to the back, or to the jaw. Accompanying symptoms may include dyspnoea (shortness of breath), diaphoresis (profuse perspiration), dizziness, nausea or vomiting.

Diagnosis

- The patient's **history and presentation,**
- **ECG** is the first step in management. Patients at risk stratified into two groups: STEMI and suspected NSTE-ACS.
- **Serum cardiac markers**

Creatine kinase (CK-MB)- It is elevated within 3 to 6 hours after myocardial damage, and peak in 12 to 24 hours.

Troponins I and T -most **sensitive markers.** Greater sensitivity and specificity than CK-MB. Levels of troponin T and I start increasing 4 to 9 hours after **acute myocardial infarction**. They peak at 12 to 24 hours. They can remain elevated for up to 14 days.

Myoglobin- Useful in early detection of MI but it returns to normal rapidly.

Other blood tests: erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are also elevated

- **Routine investigations:** blood sugar test, RFT, LFT, lipid profile, CBC.

Therapeutic Objectives

The **immediate therapeutic objectives** are to **minimize the amount of myocardial necrosis** that develops, to **alleviate symptoms**, and to **prevent death**.

The **long-term therapeutic objectives** are to prevent or **minimize recurrent ischemic** symptoms, **reinfarction, heart failure**, and sudden **cardiac death**.

Management of STEMI

Nonpharmacologic Therapy

The therapeutic priority is to **open the occluded artery** as quickly as possible. This is accomplished by **administering a thrombolytic** that **enhances the body's own** fibrinolytic system or by **mechanically reducing the obstruction with PCI (with either balloon angioplasty or stent placement).** 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. A fibrinolytic agent is indicated in patients with STEMI 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. 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.

Absolute contraindications to fibrinolytic therapy include: active internal bleeding; previous ICH at any time; ischemic stroke within 3 months; known intracranial neoplasm; suspected aortic dissection; and facial trauma within 3 months. In these situations, PCI is preferred. 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: severe, uncontrolled hypertension (blood pressure [BP] greater than 180/110 mm Hg); history of prior ischemic stroke longer than 3 months prior; current anticoagulant use; major surgery within 3 weeks; recent (within 2 to 4 weeks) internal bleeding; pregnancy; active peptic ulcer; history of severe, chronic poorly controlled hypertension. The thrombolytics currently used for STEMI: **streptokinase, anistreplase, alteplase (t-PA), reteplase (r-PA), and tenecteplase (TNK).** Treat patients as soon as possible, but preferably within 30 minutes from the time they present to the emergency department, with one of the following regimens:

Alteplase: 15-mg intravenous (IV) bolus followed by 0.75 mg/kg infusion (maximum 50 mg) over 30 minutes, followed by 0.5 mg/kg infusion (maximum 35 mg) over 60 minutes (maximum dose 100 mg)

Reteplase: 10 units IV over 2 minutes, followed 30 minutes later with another 10 units IV over 2 minutes

Tenecteplase: A single IV bolus dose given over 5 seconds based on patient weight: 30 mg if less than 60 kg; 35 mg if 60 to 69.9 kg; 40 mg if 70 to 79.9 kg; 45 mg if 80 to 89.9 kg; and 50 mg if 90 kg or greater.

Streptokinase: 1.5 million units in 50 mL of normal saline or 5% dextrose water IV over 60 minutes

Intracranial hemorrhage (ICH) and major bleeding are the most serious side effects of fibrinolytics. The risk of ICH is higher with fibrin-specific agents than with streptokinase. However, the risk of systemic bleeding other than ICH is higher with streptokinase than with fibrin-specific agents.

EARLY PHARMACOTHERAPY FOR STEMI

Early Pharmacologic Therapy for ST-Segment Elevation Acute Coronary Syndromes include:

- **Intranasal oxygen** (if oxygen saturation is less than 90%), Many patients are modestly **hypoxemic** during the **initial hours** of an AMI**.** Patients with severe hypoxemia or pulmonary edema may require intubation and **mechanical ventilation**.
- **Nitrates:** One sublingual nitroglycerin tablet should be administered every 5 minutes for up to three doses in order to relieve myocardial ischemia. **IV NTG should then be** initiated in all patients with an ACS who have persistent ischemia, HF, or uncontrolled high BP in the absence of contraindications. IV NTG should be continued for approximately 24 hours after ischemia is relieved. nitrates S.E are tachycardia, flushing, headache, and hypotension.
- **Analgesics**

  The pain associated with AMI is **due to continuing tissue ischemia surrounding the area of infarcted tissue. Morphine and meperidine** are the two most commonly prescribed analgesics. By reducing pain and anxiety, the release of circulating catecholamines is diminished, possibly reducing the associated arrhythmias. Morphine also causes peripheral venous and arterial vasodilatation, which reduces preload and afterload, and consequently, the myocardial oxygen demand.

- **Non–enteric-coated aspirin tablet 300 mg, should be chewed and swallowed as soon as possible after the onset of symptoms or immediately after presentation to the emergency department.** aspirin **should be chewed** because it is absorbed more quickly. If patients have a contraindication to aspirin, **clopidogrel can be substituted.** aspirin, initial dose is required to achieve rapid platelet inhibition, long-term therapy with doses of 75 to 100 mg daily.
- **Clopidogrel:** A 600-mg oral loading dose is recommended before primary PCI, except that 300 mg should be given if within 24 hours of fibrinolytic therapy. Avoid loading dose in patients aged 75 years or more.
- **Anticoagulants**

  Unfractionated Heparin (UFH) is a first-line anticoagulant for STEMI, both for medical therapy and PCI. Low-molecular-weight heparins (LMWHs) may be an alternative to UFH in STE ACS.
- **Beta-Blockers**

  If not C.I should be used in the first 24 hrs. Beta-Blockers relieve pain, reduce arrhythmias and improve short-term mortality.
- **PCI** in the first 6-12 hrs if not possible so thrombolytic therapy should be considered.
- **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. Glycoprotein IIb/IIIa inhibitors may increase the risk of bleeding, especially if given in the setting of recent (<4 hours) administration of fibrinolytic therapy.

Early Pharmacotherapy for Non–ST-Segment Elevation Acute Coronary Syndromes

Early pharmacotherapy for NSTE ACS is similar to that for STE ACS except that: (1) fibrinolytic therapy is not administered; and (2) GP IIb/IIIa receptor blockers are administered to high-risk patients. **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]).

SECONDARY PREVENTION FOLLOWING MI

Goals of Treatment: The long-term goals after MI are to: (1) control coronary heart disease (CHD) risk factors; (2) prevent development of systolic HF; (3) prevent recurrent MI and stroke; (4) prevent death, including sudden cardiac death; and (5) prevent stent thrombosis after PCI. Secondary prevention therapy following MI includes:

- For all ACS patients, treat and control modifiable risk factors such as hypertension, dyslipidemia, obesity, smoking, and diabetes mellitus (DM).
- Start pharmacotherapy that has been proven to decrease mortality, HF, reinfarction or stroke, and stent thrombosis prior to hospital discharge for secondary prevention. After an ACS, all patients (in the absence of contraindications) should receive indefinite treatment with **aspirin** (or **clopidogrel** if aspirin contraindications), an ACE inhibitor, and a high-intensity statin for secondary prevention of death, stroke, or recurrent infarction.
- Start an oral ACE inhibitor early (within 24 hours) and continue indefinitely in all patients after MI to reduce mortality, decrease reinfarction, and prevent HF. Use a low initial dose and titrate to the dose used in clinical trials if tolerated. For example:

Captopril: 6.25 to 12.5 mg initially; target dose 50 mg two or three times daily

Enalapril: 2.5 to 5 mg initially; target dose 10 mg twice daily

Lisinopril: 2.5 to 5 mg initially; target dose 10 to 20 mg once daily

Ramipril: 1.25 to 2.5 mg initially; target dose 5 mg twice daily or 10 mg once daily

Trandolapril: 1 mg initially; target dose 4 mg once daily

- An angiotensin receptor blocker may be prescribed for patients with ACE inhibitor cough and a low LVEF and HF after MI:

Candesartan: 4 to 8 mg initially; target dose 32 mg once daily

Valsartan: 40 mg initially; target dose 160 mg twice daily

Losartan: 12.5 to 25 mg initially; target dose 100 mg once daily

- All patients, regardless of LDL-cholesterol level, should ideally be prescribed a high intensity statin. Patients over 75 years of age may be prescribed a moderate-intensity statin.
- Continue a β-blocker for at least 3 years in patients with normal LV function and CCB can be used to prevent anginal symptoms in patients who cannot tolerate or have contraindications to β-blockers but should not be used routinely in the absence of such findings.
- Continue a P2Y12 inhibitor for at least 1 year in most patients with STEMI or NSTEMI. For patients with STEMI managed with fibrinolytics, continue clopidogrel for at least 14 days and ideally 1 year. New guidelines indicate that it is reasonable to continue dual antiplatelet therapy after 12 months in patients with STEMI and NSTEACS who were medically treated, who received fibrinolytics, or who had a PCI if they are not at high risk of bleeding and have not had overt bleeding.
- To reduce mortality, consider an aldosterone antagonist (eplerenone or spironolactone) within the first 7 days after MI.

Eplerenone: 25 mg initially; target dose 50 mg once daily

Spironolactone: 12.5 mg initially; target dose 25 to 50 mg once daily

- Prescribe a short-acting SL NTG or lingual NTG spray for all patients to relieve anginal symptoms when necessary. Chronic long-acting nitrates have not been shown to reduce CHD events after MI and are not used in ACS patients who have undergone revascularization unless the patient has stable ischemic heart disease or significant coronary stenoses that were not revascularized.

EVALUATION OF THERAPEUTIC OUTCOMES

Monitoring parameters for both STEMI and NSTE-ACS include: (1) relief of ischemic discomfort, (2) return of ECG changes to baseline, and (3) absence or resolution of HF signs and symptoms. Monitoring parameters for adverse effects are dependent on the individual drugs used. In general, the most common adverse reactions from ACS therapies include hypotension and bleeding.