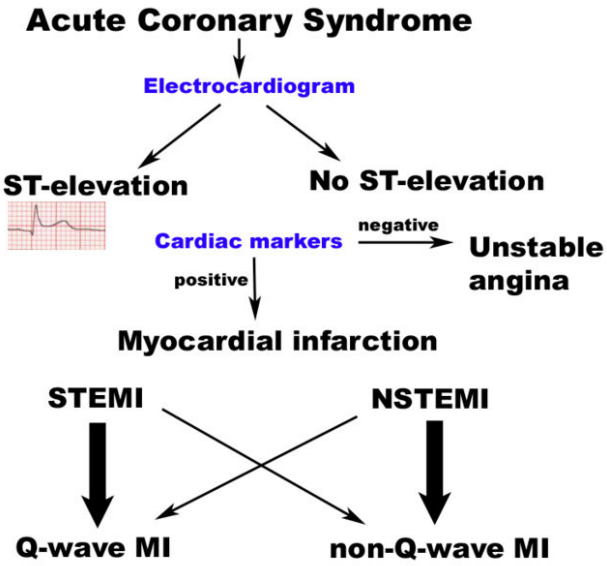
Acute coronary syndromes

Acute coronary syndromes (ACSs) include all syndromes compatible with acute myocardial ischemia resulting from imbalance between myocardial oxygen demand and supply.

Classification

Acute coronary syndromes are classified according to electrocardiographic (ECG) changes into:

- ST-segment-elevation (STE) myocardial infarction (MI)
- non–ST-segment elevation (NSTE) ACS, which includes:
  - NSTE MI
  - Unstable angina (UA).



Pathophysiology

Atherosclerosis is the primary cause of ACS. More than 90% of cases of ACS are resulted from rupture, fissuring, or erosion of an unstable atheromatous plaque.
This will lead to clot formation then promote release of adenosine diphosphate (ADP) and thromboxane A_2 from platelets producing vasoconstriction and platelet activation.
Several steps will lead to formation of a fibrin clot composed of fibrin strands, cross-linked platelets and trapped red blood cells.
Ventricular remodeling occurs after MI and is characterized by left ventricular dilation and reduced pumping function, leading to cardiac failure.

Clinical presentation

Predominant symptom is midline anterior chest discomfort or pain (usually at rest), severe new-onset angina, or increasing angina that lasts at least 20 minutes. Discomfort may radiate to the shoulder, down the left arm, to the back, or to the jaw.
Other signs and symptoms include palpitations, exertional dyspnea that resolves with pain or rest, diaphoresis (sweating), nausea and decreased exercise tolerance.

Complications

Complications of MI include:

- Cardiogenic shock
- Heart failure (HF)
- Valvular dysfunction
- Arrhythmias
- Pericarditis
- Stroke secondary to left ventricular (LV) thrombus embolization
- venous thromboembolism
- LV free-wall rupture.

Diagnosis

Symptoms of ischemia are the most important symptoms in the diagnosis. Patient symptoms and past medical history is taken in mind.

Diagnostic imaging

ECG is very important in the diagnosis of ACS. ST-segment–T-wave changes and pathological Q waves are considered in the differential diagnosis.
Diagnostic imaging modalities that may be useful include the following:

- Chest radiography
- Echocardiography
- Myocardial perfusion imaging
- Cardiac angiography
- Computed tomography, including CT coronary angiography and CT coronary artery calcium scoring

Laboratory studies

Biochemical markers of myocardial cell death (cardiac markers, cardiac troponin is preferred) are important for confirming diagnosis of acute MI.
Laboratory studies that may be helpful include the following cardiac markers:

- Creatine kinase isoenzyme MB (CK-MB) levels
- Cardiac troponin levels
- Myoglobin levels

Other lab. tests such as basic metabolic panel and complete blood count (CBC)

Treatment

Short-term desired outcomes of the treatment in a patient with ACS are:

a. 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)
b. prevention of death and other MI complications
c. prevention of coronary artery reocclusion
d. relief of ischemic chest discomfort
e. resolution of ST-segment and T-wave changes on the ECG.

Long-term desired outcomes of the treatment are control of CV risk factors, prevention of additional CV events, including reinfarction, stroke, and HF, and improvement in quality of life.

Initial therapy for ACS should focus on stabilizing the patient's condition, relieving ischemic pain, and providing antithrombotic therapy to reduce myocardial damage and prevent further ischemia.

In the emergency department (ED)
In absence of contraindications, all patients should be treated with:
• Intranasal oxygen (if low oxygen saturation) • Sublingual nitroglycerine • Aspirin • Anticoagulant (UFH, LMWH, fondaparinux, bivalirudin)
Initial treatment
• Morphine (or fentanyl) for pain control • Oxygen • Sublingual or intravenous (IV) nitroglycerin • ***Dual antiplatelet therapy*** (DAPT) of aspirin 162-325mg + clopidogrel with a 300mg to 600mg loading dose then 75mg.
High-risk patients
They should receive aggressive care which include:
• Aspirin + Clopidogrel • UFH or LMWH • IV platelet glycoprotein IIb/IIIa complex blockers • beta blocker

STE-MI

- For patients with **STE-MI** presenting within 12 hours of symptom onset, the reperfusion treatment of choice is early reperfusion with primary ***percutaneous coronary intervention*** (PCI) of the infarct artery within 90 minutes of first medical contact.
- All patients undergoing PCI should receive aspirin therapy indefinitely. A P2Y12 inhibitor antiplatelet (clopidogrel, prasugrel, or ticagrelor) should be administered concomitantly with aspirin for at least 12 months following PCI for a patient with ACS.
- A ***fibrinolytic agent*** is indicated in patients with STE-MI presenting within 12 hours of the onset of chest pain.
- Although ***PCI*** is the preferred treatment for STEMI, the distance to primary PCI centers and the inherent time delay in delivering primary PCI limits widespread use of this treatment.

NSTE-ACS

- For patients with **NSTE-ACS**, practice guidelines recommend coronary angiography with either ***PCI*** or ***coronary artery bypass graft*** (CABG) surgery revascularization as early treatment.

Summary of Medications

➢ ***Fibrinolytic agents***	
A fibrin-specific agent (**alteplase**, **reteplase**, or **tenecteplase**) is preferred over the non–fibrin-specific agent **streptokinase**. IV fibrinolytic treatment is not recommended in patients with NSTE-ACS.	
➢ ***Antiplatelets***	
Aspirin 160-325 mg	It is to be administered to all patients without contraindications within 24 hours before or after hospital arrival.
$P2Y_{12}$ platelet inhibitor	Oral loading dose of a (ticlopidine, **clopidogrel**, **prasugrel** or **ticagrelor**) is used to reduce platelet aggregation.
Cangrelor	Cangrelor is an IV drug indicated as an adjunct to PCI. Transition patients to oral $P2Y_{12}$ platelet inhibitor is done after discontinuation of cangrelor.
Vorapaxar	A combination of vorapaxar with either aspirin and/or clopidogrel reduces the rate of cardiovascular death, MI, stroke, and urgent coronary.
Glycoprotein IIb/IIIa receptor inhibitors	A glycoprotein IIb/IIIa receptor inhibitor (**Abciximab**, **eptifibatide** or **tirofiban**) may be administered in patients with STE-MI undergoing primary PCI who are treated with unfractionated heparin or patients with NSTE-ACS.
Guidelines recommend using ***dual antiplatelet therapy*** (DAPT) in specific patients with coronary artery disease. Duration of DAPT varies according to different factors.	
➢ ***Anticoagulants***	
Anticoagulants are to be administered in addition to antiplatelet therapy, for all patients, irrespective of the initial treatment strategy.	
Heparins	Unfractionated heparin (UFH)
	LMWH Enoxaparin, bemiparin, dalteparin, tinzaparin
Hirudin	It is indicated only in patients who are unable to receive heparin because of heparin-induced thrombocytopenia.
Bivalirudin	A synthetic analogue of recombinant hirudin. Potential advantages over conventional heparin therapy
factor Xda inhibitor	*Fondaparinux is not currently FDA approved for use in ACS.*
Oral Xa inhibitor	Rivaroxaban and apixaban

Other agents	
I.V. β-blockers ○ *Esmolol* ○ *Metoprolol* ○ *Propranolol* ○ *Atenolol*	• They reduce oxygen demand and ventricular wall tension. • They also decrease mortality and adverse cardiovascular events. • If no contraindications, a β-blocker should be administered early (within the first 24 hours) and continue indefinitely. • Usual doses of β-blockers, with target resting heart rate of 50 to 60 beats/min.
Statins	A high-intensity statin, either atorvastatin 80mg or rosuvastatin 40mg, should be administered to all patients prior to PCI (regardless of prior lipid-lowering therapy).
Nitrates	• Examples: Sublingual and I.V. nitroglycerin • Nitrates do not improve mortality. However, they provide symptomatic relief.
Calcium channel blockers (CCBs)	• After STE MI, CCBs are used for relief of ischemic symptoms in patients who have contraindications to β-blockers. • A CCB that lowers heart rate (**diltiazem** or **verapamil**) is preferred unless the patient has LV systolic dysfunction, bradycardia, or heart block. In those cases, either **amlodipine** or **felodipine** is preferred. Nifedipine should be avoided. • CCBs should not be administered to most patients with NSTE ACS.
Analgesics	Morphine sulfate is the drug of choice for narcotic analgesia because of its reliable and predictable effects, safety profile, and ease of reversibility with naloxone. Morphine sulfate administered intravenously may be dosed in a number of ways and commonly titrated until the desired effect is obtained.
Oxygen	• Supplemental oxygen is administered only when the oxygen saturation falls below 90%, respiratory distress is present, or other high-risk features for hypoxemia are present. • Humidified oxygen may reduce the risk of nosebleeds in patients with ACS who are receiving antiplatelet and antithrombin therapy.

Secondary prevention for patients after a myocardial infarction

ACE inhibitors or ***ARBs***	They are started and continued indefinitely in all patients after MI to reduce mortality, decrease reinfarction, and prevent HF.
β-blockers	Using a **β-blocker** for at least 3 years in patients without HF or an ejection fraction of 40% or less and indefinitely in patients with LV systolic dysfunction or HF symptoms. Patients with HF secondary to reduced LVF should receive one of three β-blockers: bisoprolol, sustained-release metoprolol succinate, or carvedilol. (*Some references add nebivolol*.)
Calcium channel blockers	CCB can be used to prevent anginal symptoms in patients who cannot tolerate or have contraindications to β-blockers.
Aldosterone receptor antagonist	To reduce mortality, a mineralocorticoid (aldosterone) receptor antagonist (***eplerenone*** or ***spironolactone***) should be considered within the first 7 days after MI in all patients already receiving an ACE inhibitor (or ARB) and a β-blocker and have an LVEF of 40% or less and either HF symptoms or diabetes mellitus. The drugs are continued indefinitely.
Antiplatelets	• ***$P2Y_{12}$ inhibitors*** (ticlopidine, clopidogrel, prasugrel or ticagrelor) are continued for at least 12 months for patients undergoing PCI and for patients with NSTE-ACS receiving a medical management strategy. • ***Clopidogrel*** is used for at least 14 days in patients with STE-MI not undergoing PCI.
Nitrates	Short-acting sublingual nitroglycerine or lingual nitroglycerine spray for all patients to relieve anginal symptoms when necessary.