Acute Coronary Syndromes (ACS)

Acute coronary syndromes *(ACS) result from acute obstruction of a coronary artery. Consequences depend on degree and location of obstruction and range from **unstable angina** to **non–ST-segment elevation MI** (**NSTEMI**), **ST-segment elevation MI** (**STEMI**), and sudden cardiac death. Symptoms are similar in each of these syndromes (except sudden death) and include chest discomfort with or without dyspnea, nausea, and diaphoresis. Diagnosis is by **ECG** and the presence or absence of serologic markers. Treatment is **antiplatelet drugs**, **anticoagulants**, **nitrates**, **β-blockers**, and, for **STEMI**, emergency reperfusion via **fibrinolytic drugs**, **percutaneous intervention**, or, occasionally, **coronary artery bypass graft surgery**.*

In the US, about 1.5 million MIs occur annually. MI results in death for 400,000 to 500,000 people, with about half dying before they reach the hospital.

Etiology

These syndromes usually occur when an acute thrombus forms in an **atherosclerotic coronary artery**. **Atheromatous** plaque sometimes becomes unstable or inflamed, causing it to rupture or split, exposing **thrombogenic material**, which activates platelets and the **coagulation cascade** and produces an **acute thrombus**. Platelet activation involves a conformational change in **membrane glycoprotein** (GP) IIb/IIIa receptors,

allowing cross-linking (and thus aggregation) of platelets. Even **atheromas** causing minimal obstruction can rupture and result in thrombosis; in > 50% of cases, stenosis is < 40%. The resultant **thrombus** abruptly interferes with blood flow to parts of the **myocardium**. **Spontaneous thrombolysis** occurs in about two thirds of patients; 24 h later, **thrombotic obstruction** is found in only about 30%. However, in virtually all cases, obstruction lasts long enough to cause **tissue necrosis**.

Rarely, these syndromes are caused by arterial embolism (eg, in **mitral** or **aortic stenosis, infective endocarditis, or marantic endocarditis**). Cocaine use and other causes of coronary spasm can sometimes result in **MI**. **Spasm-induced MI** may occur in normal or **atherosclerotic coronary arteries**.

Pathophysiology

Initial consequences vary with size, location, and duration of obstruction and range from transient **ischemia** to **infarction**. Measurement of newer, more sensitive markers indicates that some **cell necrosis** probably occurs even in mild forms; thus, ischemic events occur on a continuum, and classification into subgroups, although useful, is somewhat arbitrary. **Sequelae** of the acute event depend primarily on the mass and type of **cardiac tissue** infarcted.

Myocardial dysfunction: Ischemic (but not infarcted) tissue has impaired contractility, resulting in **hypokinetic** or **akinetic segments**; these segments may expand or bulge during **systole** (called paradoxical motion). The size of the affected area determines effects, which range from minimal to mild heart failure to **cardiogenic shock**. Some degree of heart failure occurs in about two thirds of hospitalized patients with **acute MI**. It is termed **ischemic cardiomyopathy** if low cardiac output and heart failure persist. **Ischemia** involving the papillary muscle may lead to **mitral valve regurgitation**.

MI: **MI** is **myocardial necrosis** resulting from abrupt reduction in **coronary blood flow** to part of the **myocardium**. Infarcted tissue is permanently dysfunctional; however, there is a zone of potentially reversible ischemia adjacent to infarcted tissue.

MI affects predominantly the **left ventricle** (**LV**), but damage may extend into the **right ventricle** (**RV**) or the **atria**. RV infarction usually results from obstruction of the right coronary or a dominant left **circumflex artery**; it is characterized by high RV filling pressure, often with severe tricuspid regurgitation and reduced cardiac output. An **inferoposterior infarction** causes some degree of RV dysfunction in about half of patients and causes **hemodynamic abnormality** in 10 to 15%. RV dysfunction should be considered in any patient who has inferoposterior infarction and elevated **jugular**

venous pressure with hypotension or shock. RV infarction complicating LV infarction may significantly increase mortality risk.
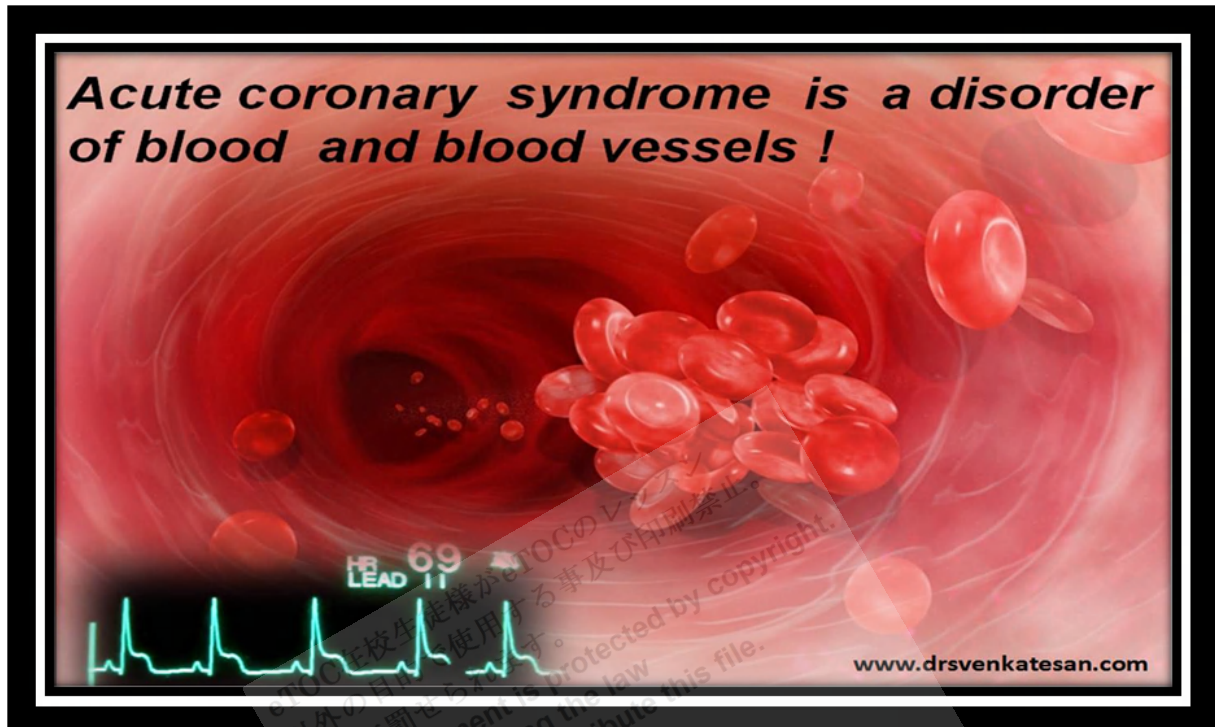
Anterior infarcts tend to be larger and result in a worse prognosis than inferoposterior infarcts. They are usually due to left coronary artery obstruction, especially in the anterior descending artery; inferoposterior infarcts reflect right coronary or dominant left circumflex artery obstruction.

Transmural infarcts involve the whole thickness of **myocardium** from **epicardium** to **endocardium** and are usually characterized by abnormal **Q waves** on **ECG**. **Nontransmural** or **subendocardial infarcts** do not extend through the ventricular wall and cause only ST-segment and T-wave (ST-T) abnormalities. Subendocardial infarcts usually involve the inner one third of myocardium, where wall tension is highest and myocardial blood flow is most vulnerable to circulatory changes. These infarcts may follow prolonged hypotension. Because the **transmural depth** of **necrosis** cannot be precisely determined clinically, infarcts are usually classified by the presence or absence of ST-segment elevation or Q waves on the ECG. Volume of myocardium destroyed can be roughly estimated by the extent and duration of **CK elevation**.

Electrical dysfunction: **Ischemic** and **necrotic cells** are incapable of normal electrical activity, resulting in various ECG changes (predominantly **ST-T abnormalities**), arrhythmias, and conduction disturbances. ST-T abnormalities of ischemia include **ST-segment depression** (often downsloping from the **J point**), **T-wave inversion**, **ST-segment elevation** (often referred to as injury current), and peaked T waves in the hyperacute phase of infarction. Conduction disturbances can reflect damage to the sinus node, the **atrioventricular** (**AV**) node, or specialized conduction tissues. Most changes are transient; some are permanent.

Classification

Classification is based on ECG changes and presence or absence of cardiac markers in blood. Distinguishing **NSTEMI** and **STEMI** is useful because prognosis and treatment are different.

Unstable angina (**acute coronary insufficiency**, **preinfarction angina**, **intermediate syndrome**) is defined as:

- Rest angina that is prolonged (usually > 20 min)
- New-onset angina of at least class III severity in the **Canadian Cardiovascular Society** (**CCS**) classification
- Increasing angina, ie, previously diagnosed angina that has become distinctly more frequent, more severe, longer in duration, or lower in threshold (eg, increased by ≥ 1 CCS class or to at least CCS class III)

Also, ECG changes such as **ST-segment depression**, **ST-segment elevation**, or **T-wave inversion** may occur during unstable angina but are transient. Of cardiac markers, **CK** is not elevated but **troponin I** or **T** may be slightly increased. Unstable angina is clinically unstable and often a prelude to **MI** or **arrhythmias** or, less commonly, to sudden death.

Non–ST-segment elevation MI (**NSTEMI, subendocardial MI**) is **myocardial necrosis** (evidenced by cardiac markers in blood; troponin I or T and CK will be elevated) without acute ST-segment elevation or Q waves. ECG changes such as ST-segment depression, T-wave inversion, or both may be present.

ST-segment elevation MI (**STEMI, transmural MI**) is **myocardial necrosis** with ECG changes showing ST-segment elevation that is not quickly reversed by nitroglycerin or showing new left bundle branch block. **Q waves** may be present. Both troponin and CK are elevated.

Symptoms and Signs

Symptoms of ACS depend somewhat on the extent and location of obstruction and are quite variable. Except when infarction is massive, recognizing the amount of ischemia by symptoms alone is difficult.
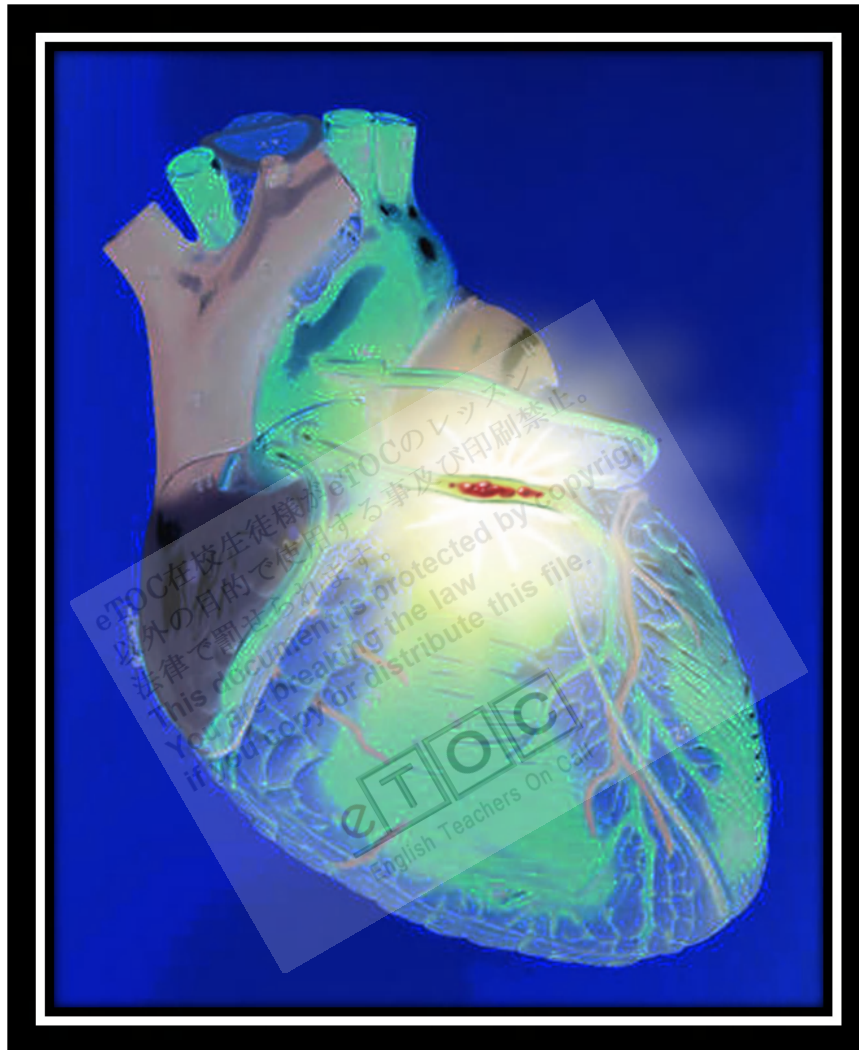
After the acute event, many complications can occur. They usually involve **electrical dysfunction** (eg, **conduction defects**, **arrhythmias**), **myocardial dysfunction** (eg, heart failure, **interventricular septum** or free wall rupture, **ventricular aneurysm**, **pseudoaneurysm**, mural **thrombus formation**, **cardiogenic shock**), or **valvular dysfunction** (typically **mitral regurgitation**). Electrical dysfunction can be significant in any form of ACS, but usually, large parts of myocardium must be ischemic to cause significant myocardial dysfunction. Other complications of ACS include **recurrent**

ischemia and **pericarditis**. Pericarditis that occurs 2 to 10 wk after an MI is known as **post-MI syndrome** or **Dressler's syndrome**.

Unstable angina: Symptoms are those of angina pectoris, except that the pain or discomfort of unstable angina usually is more intense, lasts longer, is precipitated by less exertion, occurs spontaneously at rest (as **angina decubitus**), is progressive (crescendo) in nature, or involves any combination of these features.

NSTEMI and STEMI: Symptoms of NSTEMI and STEMI are the same. Days to weeks before the event, about two thirds of patients experience prodromal symptoms, including unstable or crescendo angina, shortness of breath, and fatigue. Usually, the first symptom of infarction is deep, substernal, visceral pain described as aching or pressure, often radiating to the back, jaw, left arm, right arm, shoulders, or all of these areas. The pain is similar to angina pectoris but is usually more severe and long-lasting; more often accompanied by **dyspnea**, **diaphoresis**, **nausea**, and **vomiting**; and relieved little or only temporarily by rest or nitroglycerin. However, discomfort may be mild; about 20% of acute MIs are silent (ie, **asymptomatic** or causing vague symptoms not recognized as illness by the patient), more commonly in diabetics. Some patients present with **syncope**. Patients often interpret their discomfort as indigestion, particularly because spontaneous relief may be falsely attributed to belching or antacid consumption. Women are more likely to present with atypical chest discomfort. Elderly patients may report dyspnea more than ischemic-type chest pain. In severe ischemic episodes, the patient often has significant pain and feels restless and apprehensive. Nausea and vomiting may occur, especially with inferior MI. **Dyspnea** and weakness due to **LV failure**, **pulmonary edema**, shock, or **significant arrhythmia** may dominate.

Skin may be pale, cool, and **diaphoretic**. **Peripheral** or **central cyanosis** may be present. Pulse may be thready, and BP is variable, although many patients initially have some degree of **hypertension** during pain.

Heart sounds are usually somewhat distant; a 4th heart sound is almost universally present. A soft systolic blowing apical murmur (reflecting **papillary muscle dysfunction**) may occur. During initial examination, a friction rub or more striking murmurs suggest a preexisting heart disorder or another diagnosis. Detection of a friction rub within a few hours after onset of MI symptoms suggests acute **pericarditis** rather than MI. However, friction rubs, usually evanescent, are common on days 2 and 3 **post-STEMI**. The chest wall is tender when palpated in about 15% of patients.

In RV infarction, signs include elevated **RV filling pressure**, **distended jugular veins** (often with **Kussmaul's sign**), clear lung fields, and hypotension.

Diagnosis
- Serial ECGs
- Serial cardiac markers
- Immediate **coronary angiography** for patients with STEMI or complications (eg, persistent chest pain, markedly elevated cardiac markers, unstable arrhythmias)
- Delayed angiography (24 to 48 h) for patients with NSTEMI or unstable angina

ACS should be considered in men > 30 yr and women > 40 yr (younger in patients with diabetes) whose main symptom is chest pain or discomfort. Pain must be differentiated from the pain of **pneumonia**, **pulmonary embolism**, **pericarditis**, **rib fracture**, **costochondral separation**, **esophageal spasm**, **acute aortic dissection**, **renal calculus**, **splenic infarction**, or various abdominal disorders. In patients with previously diagnosed **hiatus hernia**, **peptic ulcer**, or a **gallbladder disorder**, the clinician must be wary of attributing new symptoms to these disorders.

The approach is the same when any ACS is suspected: initial and serial ECG and serial cardiac marker measurements, which distinguish among unstable angina, NSTEMI, and STEMI. Every emergency department should have a triage system to immediately identify patients with chest pain for rapid assessment and ECG. **Pulse oximetry** and chest x-ray (particularly to look for **mediastinal widening**, which suggests **aortic dissection**) is also done.

ECG: ECG is the most important test and should be done within 10 min of presentation. It is the center of the decision pathway because **fibrinolytics** benefit patients with STEMI but may increase risk for those with NSTEMI. Also, urgent cardiac catheterization is indicated for patients with acute STEMI but not for those with NSTEMI.

For STEMI, initial ECG is usually diagnostic, showing ST-segment elevation ≥ 1 mm in 2 or more contiguous leads subtending the damaged area.
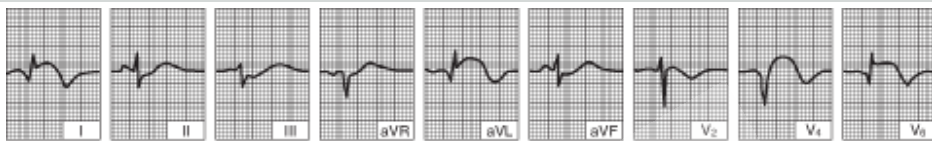
Fig. 1

Acute anterior left ventricular infarction (tracing obtained within a few hours of onset of illness).
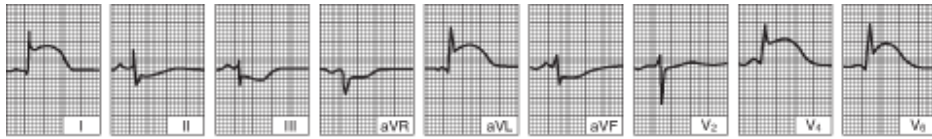
There is striking hyperacute ST-segment elevation in leads I, aVL, V_4, and V_6 and reciprocal depression in other leads.
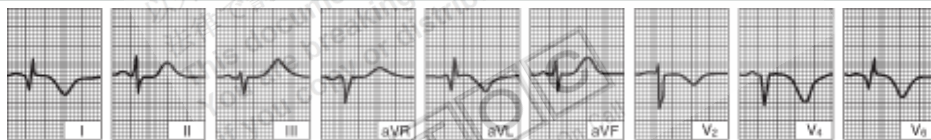
Fig. 2

Acute anterior left ventricular infarction (after the first 24 h).

ST segments are less elevated; significant Q waves develop and R waves are lost in leads I, aVL, V_4, and V_6.

Fig. 3

Acute anterior left ventricular infarction (several days later).

Significant Q waves and loss of R-wave voltage persist. ST segments are now essentially isoelectric. The ECG will probably change only slowly over the next several months.

Fig. 4

Acute inferior (diaphragmatic) left ventricular infarction (tracing obtained within a few hours of onset of illness).
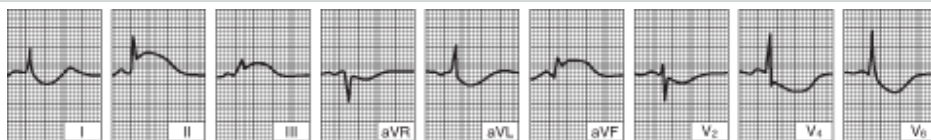
There is hyperacute ST-segment elevation in leads II, III, and aVF and reciprocal depression in other leads.

Fig. 5

Acute inferior (diaphragmatic) left ventricular infarction (after the first 24 h).

Significant Q waves develop with decreasing ST-segment elevation in leads II, III, and aVF.

Fig. 6

Acute inferior (diaphragmatic) left ventricular infarction (several days later).

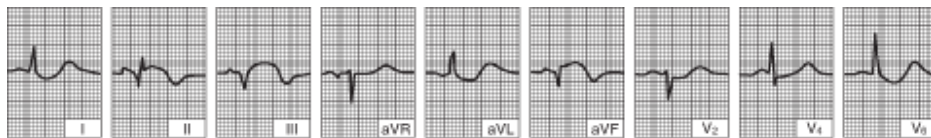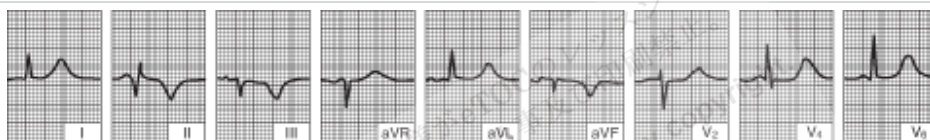ST segments are now isoelectric. Abnormal Q waves in leads II, III, and aVF indicate that myocardial scars persist.

Pathologic Q waves are not necessary for the diagnosis. The ECG must be read carefully because ST-segment elevation may be subtle, particularly in the inferior leads (II, III, aVF); sometimes the reader's attention is mistakenly focused on leads with ST-segment depression. If symptoms are characteristic, ST-segment elevation on ECG has a specificity of 90% and a sensitivity of 45% for diagnosing MI. Serial tracings (obtained every 8 h for 1 day, then daily) showing a gradual evolution toward a stable, more normal pattern or development of abnormal Q waves over a few days tends to confirm the diagnosis.

Because **nontransmural** (non–Q-wave) infarcts are usually in the **subendocardial** or **midmyocardial** layers, they do not produce diagnostic Q waves or distinct ST-segment elevation on the ECG. Instead, they commonly produce only varying degrees of ST-T abnormalities that are less striking, variable, or nonspecific and sometimes difficult to interpret (NSTEMI). If such abnormalities resolve (or worsen) on repeat ECGs, ischemia is very likely. However, when repeat ECGs are unchanged, acute MI is unlikely and, if still suspected clinically, requires other evidence to make the diagnosis. A normal ECG taken when a patient is pain free does not rule out unstable angina; a normal ECG taken during pain, although it does not rule out angina, suggests that the pain is not ischemic.

If RV infarction is suspected, a 15-lead ECG is usually recorded; additional leads are placed at V_4R, and, to detect posterior infarction, V_8 and V_9.

ECG diagnosis of MI is more difficult when a left bundle branch block configuration is present because it resembles STEMI changes. ST-segment elevation concordant with the QRS complex strongly suggests MI as does > 5-mm ST-segment elevation in at least 2 precordial leads. But generally, any patient with suggestive symptoms and new-onset (or not known to be old) left bundle branch block is treated as for STEMI.

Cardiac markers: Cardiac markers are cardiac enzymes (eg, **CK-MB**) and cell contents (eg, **troponin I**, **troponin T**, **myoglobin**) that are released into the bloodstream after myocardial cell necrosis. The markers appear at different times after injury and decrease at different rates.

Fig. 7

Relative timing and levels of cardiac markers in blood after acute MI.
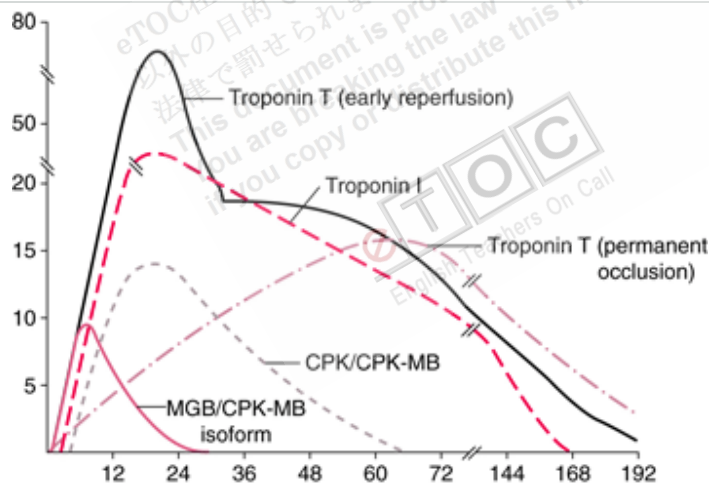
MGB = **myoglobulin**.

Usually, several different markers are measured at regular intervals, typically every 6 to 8 h for 1 day. Newer bedside tests, which are more convenient, can be just as sensitive when done at shorter intervals (eg, time 0, 1, 3, and 6 h after presentation).

Troponins are most specific for MI but can also be elevated by ischemia without infarction; elevated levels (actual number varies with assay used) are considered diagnostic. Borderline elevated **troponin levels** in patients with unstable angina

indicate increased risk of adverse events and thus the need for further evaluation and treatment. False-positives sometimes occur in heart failure and renal failure. CK-MB is slightly less specific. False-positives occur in **renal failure**, **hypothyroidism**, and skeletal muscle injury. Myoglobin is not specific for MI but, because it increases earlier than other markers, may be an early warning sign to assist in triage of patients with nondiagnostic ECGs.

Coronary angiography: Coronary angiography most often combines diagnosis with percutaneous coronary intervention (PCI, ie, **angioplasty**, **stenting**). Angiography is obtained urgently for patients with STEMI, patients with persistent chest pain despite maximal medical therapy, and patients with complications (eg, **markedly elevated cardiac markers, presence of cardiogenic shock, acute mitral regurgitation, ventricular septal defect, unstable arrhythmias**). Patients with uncomplicated NSTEMI or unstable angina whose symptoms have resolved typically undergo **angiography** within the first 24 to 48 h of hospitalization to detect lesions that may require treatment.

After initial evaluation and therapy, coronary angiography may be used in patients with evidence of ongoing ischemia (ECG findings or symptoms), **hemodynamic instability**, recurrent **ventricular tachyarrhythmias**, and other abnormalities that suggest recurrence of ischemic events. Some experts also recommend that angiography be done before hospital discharge in STEMI patients with inducible ischemia on stress imaging or an ejection fraction < 40%.

Other tests: Routine laboratory tests are nondiagnostic but, if obtained, show nonspecific abnormalities compatible with tissue necrosis (eg, increased ESR, moderately elevated WBC count with a shift to the left). A fasting lipid profile should be obtained within the first 24 h for all patients hospitalized with ACS.

Myocardial imaging is not needed to make the diagnosis if **cardiac markers** or ECG is positive. However, in patients with MI, bedside echocardiography is invaluable for detecting mechanical complications. Before or shortly after discharge, patients with symptoms suggesting an ACS but nondiagnostic ECGs and normal cardiac markers should have a stress imaging test (radionuclide or echocardiographic imaging with pharmacologic or exercise stress). Imaging abnormalities in such patients indicate increased risk of complications in the next 3 to 6 mo.

Right heart catheterization using a **balloon-tipped pulmonary artery catheter** can be used to measure **right heart**, **pulmonary artery**, and **pulmonary artery occlusion**

pressures and **cardiac output**. This test is usually done only if patients have significant complications (eg, severe heart failure, **hypoxia**, **hypotension**).

Prognosis

Unstable angina: About 30% of patients with unstable angina have an MI within 3 mo of onset; sudden death is less common. Marked ECG changes with chest pain indicate higher risk of subsequent MI or death.

NSTEMI and STEMI: Overall mortality rate is about 30%, with 50 to 60% of these patients dying before reaching the hospital (typically due to **ventricular fibrillation**). In-hospital mortality rate is about 10% (typically due to **cardiogenic shock**) but varies significantly with severity of LV failure.

Most patients who die of cardiogenic shock have an infarct or a combination of scar and new infarct affecting ≥ 50% of LV mass. Five clinical characteristics predict 90% of the mortality in patients who present with STEMI: older age (31% of total mortality), lower systolic BP (24%), Killip class > 1 (15%), faster heart rate (12%), and anterior location (6%). Mortality rate of diabetics and women tends to be higher.

Mortality rate of patients who survive initial hospitalization is 8 to 10% in the year after acute MI. Most fatalities occur in the first 3 to 4 mo. Persistent **ventricular arrhythmia**, heart failure, poor ventricular function, and recurrent ischemia indicate high risk. Many authorities recommend stress ECG before hospital discharge or within 6 wk. Good exercise performance without ECG abnormalities is associated with a favorable prognosis; further evaluation is usually not required. Poor exercise performance is associated with a poor prognosis.

Cardiac performance after recovery depends largely on how much functioning **myocardium** survives the acute attack. Scars from previous infarcts add to the acute damage. When > 50% of LV mass is damaged, prolonged survival is unusual.

Table 4

Killip Classification and Mortality Rate of Acute MI*

Class	PAO$_2$†	Clinical Description	Hospital Mortality Rate
1	Normal	No clinical evidence of left	3–5%

		ventricular (LV) failure	
2	Slightly reduced	Mild to moderate LV failure	6–10%
3	Abnormal	Severe LV failure, **pulmonary edema**	20–30%
4	Severely abnormal	Cardiogenic shock: **hypotension**, **tachycardia**, **mental obtundation**, **cool extremities**, **oliguria**, **hypoxia**	> 80%

*Determined by repeated examination of the patient during the course of illness.

†Determined while the patient is breathing room air.

Modified from Killip T, Kimball JT: Treatment of myocardial infarction in a coronary care unit. A two-year experience with 250 patients. *The American Journal of Cardiology* 20:457–464, 1967.

Table 5

Mortality Risk at 30 Days in STEMI	
Scoring	
Risk Factor	**Points**
Age ≥ 75	3
Age 65–74	2
Diabetes mellitus, hypertension, or angina	1
Systolic BP < 100 mm Hg	3
Heart rate > 100 beat/min	2

Killip class II–IV	2
Weight < 67 kg	1
Anterior ST-elevation or left branch bundle block	1
Time to treatment > 4 h	1
Total points possible	0–14

Risk

Total Points	Mortality Rate at 30 Days (%)
0	0.8
1	1.6
2	2.2
3	4.4
4	7.3
5	12.4
6	16.1
7	23.4
8	26.8
> 8	35.9

STEMI = ST-segment elevation MI; TIMI =thrombolysis in MI.

Based on data from Morrow DA et al: TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation.*Circulation* 102 (17):2031–2037, 2000 and ACC/AHA guidelines for the management of patients with acute myocardial infarction.

Table 6

Risk of Adverse Events* at 14 Days in NSTEMI

Scoring

Risk Factor	Points
Age > 65	1
CAD risk factors (must have ≥ 3 for 1 point)	1
Family history	
Hypertension	
Current smoker	
High cholesterol	
Diabetes mellitus	
Known CAD (stenosis≥ 50%)	1
Previous chronic use ofaspirin	1

Two episodes of rest angina in past 24 h	1
Elevated cardiac markers	1

Risk level is based on total points: 1–2 = low; 3–4 = intermediate; 5–7 = high.

Absolute risk

Total Points	Risk of Events at 14 Days (%)*
0 or 1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6 or 7	40.9

*Events include all-cause mortality, MI, and recurrent ischemia requiring urgent revascularization.

CAD = coronary artery disease; NSTEMI =non–ST-segment elevation MI; TIMI =thrombolysis in MI.

Based on data from Antman EM et al: The TIMI risk score for

unstable angina/non-ST elevation MI: A method of prognostication and therapeutic decision making. *JAMA* 284:835–42, 2000.

General Treatment

- Monitoring and O_2
- Bed rest initially, with early ambulation
- Low-salt, low-fat diet
- Stool softeners and anxiolytics as needed

Treatment is designed to relieve distress, interrupt thrombosis, reverse ischemia, limit infarct size, reduce cardiac workload, and prevent and treat complications. An ACS is a medical emergency; outcome is greatly influenced by rapid diagnosis and treatment.

Treatment occurs simultaneously with diagnosis. A reliable IV route must be established, O_2 given (typically 2 L by nasal cannula), and continuous single-lead ECG monitoring started. Prehospital interventions by ambulance personnel (including ECG, **chewedaspirin** (325 mg), early thrombolysis when indicated and possible, and triage to the appropriate hospital) can reduce risk of mortality and complications. Early diagnostic data and response to treatment can help determine the need for and timing of **revascularization**.
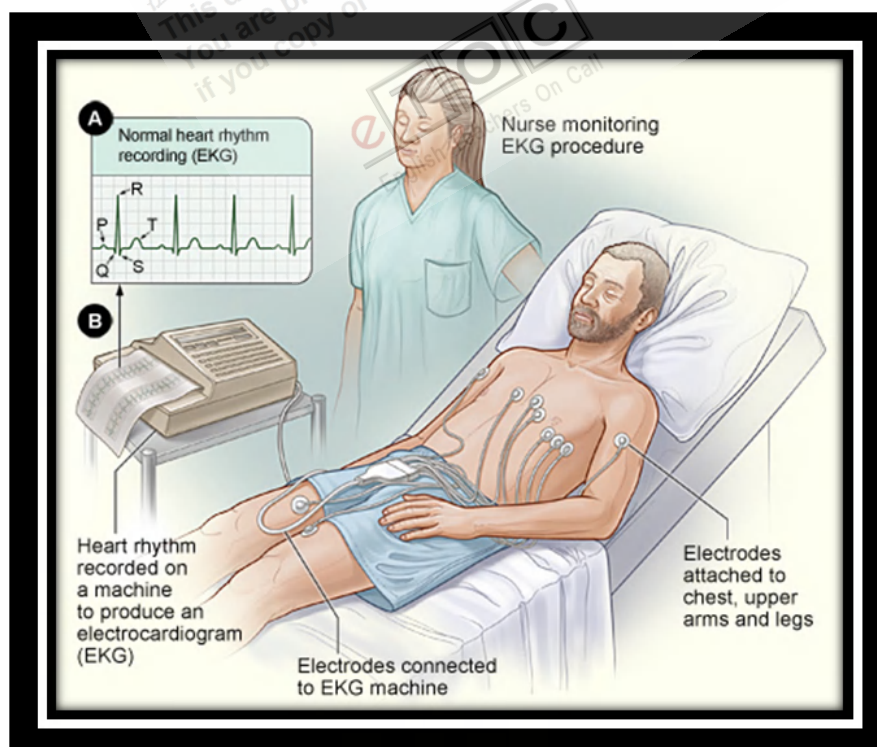
Bedside cardiac marker tests can help identify low-risk patients with a suspected ACS (eg, those with initially negative cardiac markers and nondiagnostic ECGs), who can be managed in 24-h observation units or chest pain centers. Higher-risk patients should be admitted to a monitored inpatient unit or **coronary care unit** (CCU). Several validated tools can help stratify risk. Thrombolysis in MI (TIMI) risk scores may be the most widely used.

Patients with suspected NSTEMI and intermediate or high risk should be admitted to an inpatient care unit. Those with STEMI should be admitted to a CCU.

Only heart rate and rhythm recorded by single-lead ECG are consistently useful for routine, continuous monitoring. However, some clinicians recommend routine **multilead monitoring** with continuous ST-segment recording to identify transient, recurrent ST-segment elevations or depressions. Such findings, even in patients without symptoms, suggest ischemia and identify higher-risk patients who may require more aggressive evaluation and treatment.

Qualified nurses can interpret the ECG for **arrhythmia** and initiate protocols for its treatment. All staff members should know how to do CPR.

Contributing disorders (eg, anemia, heart failure) are aggressively treated.

The care unit should be a quiet, calm, restful area. Single rooms are preferred; privacy consistent with monitoring should be ensured. Usually, visitors and telephone calls are restricted to family members during the first few days. A wall clock, a calendar, and an outside window help orient the patient and prevent a sense of isolation, as can access to a radio, television, and newspaper.

Bed rest is mandatory for the first 24 h. On day 1, patients without complications (eg, **hemodynamic instability**, **ongoing ischemia**), including those in whom reperfusion with **fibrinolytics** or PCI is successful, can sit in a chair, begin passive exercises, and use a commode. Walking to the bathroom and doing nonstressful paperwork is allowed shortly thereafter. Recent studies have shown that patients with successful, uncomplicated primary PCI for acute MI may be ambulated quickly and be safely discharged in 3 to 4 days. If reperfusion is not successful or complications are present, patients require longer bed rest, but they (particularly elderly patients) are mobilized as soon as possible. Prolonged bed rest results in rapid physical deconditioning, with development of **orthostatic hypotension**, decreased work capacity, increased heart

rate during exertion, and increased risk of deep venous thrombosis. Prolonged bed rest also intensifies feelings of depression and helplessness.

Anxiety, mood changes, and denial are common. A mild tranquilizer (usually a **benzodiazepine**) is often given, but many experts believe such drugs are rarely needed.

Reactive depression is common by the 3rd day of illness and is almost universal at some time during recovery. After the acute phase of illness, the most important tasks are often management of depression, rehabilitation, and institution of long-term preventive programs. Overemphasis on bed rest, inactivity, and the seriousness of the disorder reinforces anxiety and depressive tendencies, so patients are encouraged to sit up, get out of bed, and engage in appropriate activities as soon as possible. The effects of the disorder, prognosis, and individualized rehabilitation program should be explained to the patient.

Maintaining normal bowel function with stool softeners (eg, **docusate**) to prevent straining is important. Urinary retention is common among elderly patients, especially after several days of bed rest or if **atropine** was given. A **catheter** may be required but can usually be removed when the patient can stand or sit to void.

Because smoking is prohibited, a hospital stay should be used to encourage smoking cessation. All caregivers should devote considerable effort to making smoking cessation permanent.

Although acutely ill patients have little appetite, tasty food in modest amounts is good for morale. Patients are usually offered a soft diet of 1500 to 1800 kcal/day with Na reduction to 2 to 3 g. Na reduction is not required after the first 2 or 3 days if there is no evidence of heart failure. Patients are given a diet low in cholesterol and saturated fats, which is used to teach healthy eating.

For diabetic patients with STEMI, intensive glucose control is no longer recommended; guidelines call for an insulin-based regimen to achieve and maintain glucose levels <180 mg/dL while avoiding **hypoglycemia**.

Because the chest pain of MI usually subsides within 12 to 24 h, any chest pain that remains or recurs later is investigated. It may indicate such complications as recurrent **ischemia**, **pericarditis**, **pulmonary embolism**, **pneumonia**, **gastritis**, or **ulcer**.

Drugs

- Aspirin, clopidogrel, or both (prasugrel is an alternative toclopidogrel if **fibrinolytic therapy** has not been given)
- β-Blocker
- GP IIb/IIIa inhibitor fconsidered or certain patients undergoing PCI and for some others at high risk (eg, with markedly elevated cardiac markers, TIMI risk score ≥ 4, persistent symptoms)
- A heparin (unfractionated or low molecular weight heparin) orbivalirudin (particularly in STEMI patients at high risk of bleeding)
- IV nitroglycerin (unless low-risk, uncomplicated MI)
- Fibrinolytics for select patients with STEMI when timely PCI unavailable
- ACE inhibitor (as early as possible) and a statin

Antiplatelet and **antithrombotic** drugs, which stop clots from forming, are used routinely. **Anti-ischemic** drugs (eg, **β-blockers**, **IVnitroglycerin**) are frequently added, particularly when chest pain or hypertension is present. **Fibrinolytics** *should be used if not contraindicated* for STEMI if primary PCI is not immediately available but worsen outcome for unstable angina and NSTEMI.

Chest pain can be treated with morphine or nitroglycerin. Morphine 2 to 4 mg IV, repeated q 15 min as needed, is highly effective but can depress **respiration**, can reduce myocardial contractility, and is a potent venous vasodilator. **Hypotension** and **bradycardia** secondary to morphine can usually be overcome by prompt elevation of the lower extremities. Nitroglycerin is initially given sublingually, followed by continuous IV drip if needed.

BP is normal or slightly elevated in most patients on arrival at the emergency department; BP gradually falls over the next several hours. Continued hypertension requires treatment with **antihypertensives**, preferably **IV nitroglycerin**, to lower BP and reduce cardiac workload. Severe hypotension or other signs of shock are ominous and must be treated aggressively with IV fluids and sometimes **vasopressors**.

Antiplatelet drugs: **Aspirin**, **clopidogrel**, **ticlopidine**, and **GP IIb/IIIa inhibitors** are examples. All patients are given aspirin 160 to 325 mg (not enteric-coated), if not contraindicated, at presentation and 81 mg once/day indefinitely thereafter. Chewing the first dose before swallowing quickens absorption. Aspirin reduces short- and long-term mortality risk. If aspirin cannot be taken, **clopidogrel** 75 mg once/day or **ticlopidine** 250 mg bid may be used. Clopidogrel has largely replaced **ticlopidine** for routine use because neutropenia is a risk **withticlopidine** and the WBC count must be monitored regularly. Patients with unstable angina or NSTEMI in whom intervention is not possible or recommended are given both aspirin and clopidogrel for at least 1 mo. The optimal duration of double antiplatelet therapy for these patients is the subject of ongoing investigation.

In patients undergoing PCI, a clopidogrel loading dose (300 to 600 mg po once) improves outcomes, particularly when administered 24 h in advance. However, delaying PCI for 24 h is not appropriate for many patients. Further, such a loading dose increases risk of perioperative bleeding in patients who require coronary artery bypass grafting (CABG) because their coronary anatomy proves unfavorable for PCI. Thus, many clinicians administer a clopidogrel loading dose only in the **catheterization**

laboratory once coronary anatomy and lesions have been proven to be amenable to PCI.

For patients receiving a stent for revascularization, aspirin is continued indefinitely, and clopidogrel should be used for at least 1 mo in patients with a bare-metal stent. Patients with a drug-eluting stent have a prolonged risk of thrombosis and may benefit from 12 mo of clopidogrel treatment, although the recommended duration is still unclear.

GP IIb/IIIa inhibitors (**abciximab**, **tirofiban**, **eptifibatide**) are potent antiplatelet drugs that must be given IV. Although there is some controversy, evidence indicates that patients with ACS undergoing PCI may benefit from a GP IIb/IIIa inhibitor; results appear to be better if the drug is initiated at least 6 h before PCI and continued for 18 to 24 h thereafter. If PCI is not being done, some clinicians give a GP IIb/IIIa inhibitor to all high-risk patients (eg, those with markedly elevated cardiac markers, a TIMI risk score ≥ 4, or persistent symptoms despite adequate drug therapy). The GP IIb/IIIa inhibitor is continued for 24 to 36 h, and **angiography** is done before the infusion period is over. GP IIb/IIIa inhibitors are not recommended for patients receiving **fibrinolytics**. **Abciximab**, **tirofiban**, and **eptifibatide** appear to have equivalent efficacy, and the choice of drug should depend on other factors (eg, cost, availability, familiarity).

Anticoagulant drugs: Either a low molecular weight **heparin** (LMWH), unfractionated heparin, or **bivalirudin** is given routinely to patients with ACS unless contraindicated (eg, by active bleeding or planned use of **streptokinase** or **anistreplase**). Choice of agent is somewhat involved.
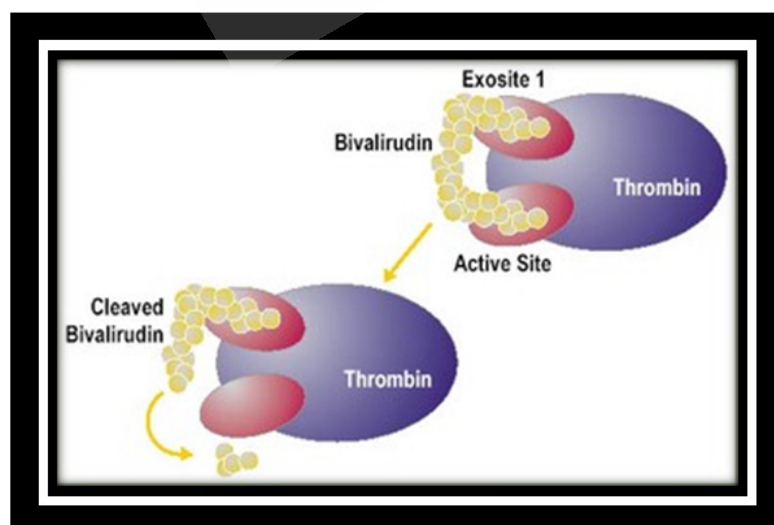
Unfractionated heparin is more complicated to use because it requires frequent (q 6 h) dosing adjustments to achieve an activated PTT (aPTT) 1.5 to 2 times the control value. In patients undergoing **angiography**, further dosing adjustment is done to achieve an activated clotting time (ACT) of 200 to 250 sec if the patient is treated with a GP IIb/IIIa inhibitor and 250 to 300 sec if a GP IIb/IIIa inhibitor is not being given. However, the effects of **unfractionatedheparin** are shorter and can be reversed (with prompt discontinuation of heparin infusion and with administration **ofprotamine sulfate**) if bleeding develops following catheterization.

The LMWHs have better bioavailability, are given by simple weight-based dose without monitoring aPTT and dose titration, and have lower risk of heparin-induced thrombocytopenia. They also may produce an incremental benefit in outcomes relative to unfractionated heparin in patients with ACS. Of the LMWHs, **enoxaparin** appears to be superior to **dalteparin** or **nadroparin**. However, **enoxaparin** may pose a higher bleeding risk in patients with STEMI who are > 75, and its effects are not completely reversible with **protamine**.

Thus, taking all into account, many published guidelines recommend LMWH (eg, enoxaparin) over **unfractionatedheparin** in patients with unstable angina or NSTEMI and in patients < 75 with STEMI who are not undergoing PCI. By contrast, unfractionated heparin is recommended when emergency PCI is done (eg, patients with acute STEMI who proceed to the catheterization laboratory), when CABG is indicated within the next 24 h, and when patients are at high risk of bleeding complications (eg, history of GI bleeding within the last 6 mo) or have creatinine clearance < 30 mL/min. Ongoing studies should help clarify the choice between LMWH and unfractionated heparin.

Bivalirudin is an acceptable **anticoagulant** for patients undergoing primary PCI who are at high risk of bleeding and is recommended for those with a known or suspected history of **heparin-induced thrombocytopenia**. For patients with unstable angina or NSTEMI, dose is an initial bolus of 0.1 mg/kg IV followed by a drip of 0.25 mg/kg/h. For patients with STEMI, initial dose is 0.75 mg/kg IV followed by 1.75 mg/kg/h.

For patients undergoing PCI, **postprocedure heparin** is no longer recommended unless patients are at high risk of thromboembolic events (eg, patients with large anterior MI, known LV thrombus, atrial fibrillation), because **postprocedure ischemic events** have decreased with the use of stents and antiplatelet drugs. For patients not undergoing PCI, heparin is continued for 48 h (or longer if symptoms persist).

The difficulties with the heparins (including bleeding complications, the possibility of **heparin-induced thrombocytopenia**, and, with unfractionated heparin, the need for dosing adjustments) have led to the search for better anticoagulants. The direct **thrombin inhibitors**, **bivalirudin** and **argatroban**, may have a lower incidence of serious bleeding and improved outcomes, particularly in patients with renal insufficiency (**hirudin**, another direct thrombin inhibitor, appears to cause more bleeding than the other drugs). The factor **Xa inhibitor**, **fondaparinux**, reduces mortality and **reinfarction** in patients with NSTEMI who undergo PCI without increasing bleeding but may result in worse outcomes than unfractionated heparin in patients with STEMI. Although routine use of these alternative anticoagulants is thus not currently recommended, they should be used in place of **unfractionatedheparin** or LMWH in patients with a known or suspected history of heparin-induced thrombocytopenia.

Patients at high risk of systemic emboli also require long-term therapy with oral warfarin. Conversion to warfarin should begin 48 h after symptom resolution or PCI.

β-Blockers: These drugs are recommended unless contraindicated (eg, by **bradycardia**, **heart block**, **hypotension**, or **asthma**), especially for high-risk patients. β-Blockers reduce heart rate, arterial pressure, and contractility, thereby reducing cardiac workload and O_2 demand. IV β-blockers given within the first few hours improve prognosis by reducing infarct size, recurrence rate, incidence of **ventricular fibrillation**, and mortality risk. Infarct size largely determines cardiac performance after recovery.

Heart rate and BP must be carefully monitored during treatment with β-blockers. Dosage is reduced if **bradycardia** or hypotension develops. Excessive adverse effects may be reversed by infusion of the β-adrenergic **agonistisoproterenol** 1 to 5 μg/min.

Nitrates: A short-acting nitrate, nitroglycerin, is used to reduce cardiac workload in selected patients.Nitroglycerin dilates veins, arteries, and arterioles, reducing LV preload and afterload. As a result, myocardial O_2demand is reduced, lessening ischemia. IV nitroglycerin is recommended during the first 24 to 48 h for patients with heart failure, large anterior MI, persistent chest discomfort, or hypertension. BP can be reduced by 10 to 20 mm Hg but not to < 80 to 90 mm Hg systolic. Longer use may benefit patients with recurrent chest pain or persistent **pulmonary congestion**. In high-risk patients, nitroglycerin given in the first few hours reduces infarct size and short-term and possibly long-term mortality risk. Nitroglycerin is not routinely given to low-risk patients with uncomplicated MI.

Fibrinolytics: **Tenecteplase** (TNK), **alteplase** (rTPA), **reteplase** (rPA), **streptokinase**, and **anistreplase** (**anisoylated plasminogen activator complex—APSAC**), all given IV, are plasminogen activators. They convert single-chain plasminogen to double-chain plasminogen, which has **fibrinolytic activity**. They have different characteristics and dosing regimens and are appropriate only for selected patients with STEMI.

Tenecteplase and **reteplase** are recommended most often because of their simplicity of administration;tenecteplase is given as a single bolus over 5 sec and reteplase as a double bolus 30 min apart. Administration time and drug errors are reduced compared with other **fibrinolytics**. Tenecteplase, like **alteplase**, has an intermediate risk of intracranial hemorrhage, has a higher rate of recanalization than other fibrinolytics, and is expensive. Reteplase has the highest risk of intracranial hemorrhage and a recanalization rate similar to that **oftenecteplase**, and it is expensive.

Streptokinase may induce allergic reactions, especially if it has been used previously, and must be given by infusion over 30 to 60 min; however, it has a low incidence of **intracerebral hemorrhage** and is relatively inexpensive. **Anistreplase**, related to streptokinase, is similarly allergenic and slightly more expensive but can be given as a single bolus. Neither drug requires concomitant heparin use. For both, **recanalization** rate is lower than that with other **plasminogen activators**. Because of the possibility of allergic reactions, patients who previously **receivedstreptokinase** or **anistreplase** are not given that drug.

Alteplase is given in an accelerated or front-loaded dosage over 90 min. Alteplase with concomitant IV heparin improves patency, is nonallergenic, has a higher recanalization rate than other fibrinolytics, and is expensive.

Table 7

IV Fibrinolytic Drugs Available in the US

Characteristic	Streptokinase	Anistreplase	Alteplase	Reteplase	Tenecteplase
Dosage (IV)	1.5×10^6 U over 30–60 min	30 mg over 5 min	15 mg bolus, then	10 unit bolus over 2	Weight-adjusted single bolus

			0.75 mg/kg over next 30 min (maximum 50 mg), followed by 0.50 mg/kg over 60 min (maximum 35 mg) for total dose of 100 mg	min, repeated once after 30 min	over 5 sec: < 60 kg: 30 mg 60–69 kg: 35 mg 70–79 kg: 40 mg 80–89 kg: 45 mg ≥ 90 kg: 50 mg
Circulating half-life (min)	20	100	6	13–16	Initial half-life of 20–24 min; terminal phase half-life of 90–130 min
Concurrentheparin	No	No	Yes	Yes	Yes
Allergic reactions	Yes	Yes	Rare	Rare	Rare

Other drugs: ACE inhibitors appear to reduce mortality risk in MI patients, especially in those with **anterior infarction**, **heart failure**, or **tachycardia**. The greatest benefit occurs in the highest-risk patients early during convalescence. ACE inhibitors are

given > 24 h after thrombolysis stabilization and, because of continued beneficial effect, may be prescribed long-term.

Angiotensin II receptor blockers may be an effective alternative for patients who cannot tolerate ACE inhibitors (eg, because of cough). Currently, they are not first-line treatment after MI. Contraindications include hypotension, renal failure, bilateral renal artery stenosis, and known allergy.

HMG-CoA **reductase inhibitors** (statins) have long been used for prevention of coronary artery disease and ACS, but there is now increasing evidence that they also have short-term benefits, such as stabilizing plaque, reversing **endothelial dysfunction**, decreasing **thrombogenicity**, and reducing inflammation. Thus, all patients without contraindications to therapy should receive a statin as early as possible following ACS. LDL levels of 70 to 80 mg/dL (1.81 to 2.07 mmol/L) are the recommended ultimate target.

Revascularization Modalities and Indications

Revascularization is the restoration of blood supply to ischemic myocardium in an effort to limit ongoing damage, reduce ventricular irritability, and improve short-term and long-term outcomes. Modes of revascularization include thrombolysis with fibrinolytic drugs, PCI with or without stent placement, and CABG.

The use, timing, and modality of revascularization depend on which ACS is present, timing of presentation, extent and location of anatomic lesions, and availability of personnel and facilities.

Fig. 8

Approach to acute coronary syndromes.

Start drug therapy	**O₂**
	Morphine
	Aspirin 325 mg
	Nitrates
	β-Blockers
	Heparin or another
	anticoagulant
		Consider
		• Clopidogrel 300–600 mg once if
		  PCI is indicated
		• Clopidogrel 75 mg once/day if
		  patients are high risk or intolerant
		  of aspirin
		• Possibly GP IIb/ IIIa inhibitors for
		  patients at high risk

Unstable angina or NSTEMI → Uncomplicated* / Complicated*

STEMI → PCI available within 90 min?

Consider revascularization

Uncomplicated* → Angiography within 24–48 h → Coronary anatomy amenable to PCI?† → No → Consider CABG / Yes → PCI

Complicated* → Urgent or emergency angiography → Coronary anatomy amenable to PCI?† → No → Emergency CABG

PCI available within 90 min? → Yes → (Angiography) / No → Thrombolytic therapy → Persistant ischemia? → Yes → Repeat thrombolytic therapy or do PCI if available / No → Elective PCI within 24–72 h

Post-ACS therapy

• Manage reversible risk factors (eg, hypertension, diabetes, diet, sedentary lifestyle, obesity, smoking)
• ACE inhibitor or angiotension II receptor blocker
• Clopidogrel 75 mg once/day for at least 1 mo for patients with a bare-metal stent and at least 9–12 mo for patients with a drug-eluting stent
• If used, GP IIb/ IIIa inhibitor for at least 18–24 h after PCI, especially with a large clot burden
• Statin (to achieve a target LDL of 70 mg/dL)

* Complicated means that the hospital course was complicated by recurrent angina or infarction, heart failure, or sustained recurrent ventricular arrhythmias. Absence of any of these events is termed uncomplicated.
†CABG is generally preferred to PCI for patients with the following:
  • Left main or left main equivalent disease
  • 2- or 3-vessel disease involving the left anterior descending artery
  • Left ventricular dysfunction
  • Treated diabetes
Also, lesions that are long or near bifurcation points are often not amenable to PCI.
CABG = coronary artery bypass grafting; GP = glycoprotein; LDL = low density lipoprotein; NSTEMI = non-ST-segment elevation MI; PCI = percutaneous intervention; STEMI = ST-segment elevation MI.

Unstable angina and NSTEMI: Immediate **reperfusion** is not as urgent in patients with uncomplicated NSTEMI (in whom a completely occluded infarct-related artery at presentation is uncommon) or in those with unstable angina who respond to medical therapy. Such patients typically undergo angiography within the first 24 to 48 h of hospitalization to identify coronary lesions requiring PCI or CABG. A **noninterventional**

approach and a trial of medical management are used for those in whom angiography demonstrates only a small area of myocardium at risk, lesion morphology not amenable to PCI, anatomically insignificant disease (< 50% **coronary stenosis**), or significant left main disease in patients who are candidates for CABG. Further, angiography or PCI should be deferred in favor of medical management for patients with a high risk of procedure-related morbidity or mortality.

By contrast, patients with persistent chest pain despite maximal medical therapy or complications (eg, markedly elevated cardiac markers, presence of cardiogenic shock, **acute mitral regurgitation**, **ventricular septal defect**, **unstable arrhythmias**) should proceed directly to the cardiac catheterization laboratory to identify coronary lesions requiring PCI or CABG.

As in patients with stable angina, CABG is generally preferred over PCI for patients with left main or left main equivalent disease, for those with 3- or 2-vessel disease involving the left anterior descending artery, and for those with left ventricular dysfunction or diabetes. CABG must also be considered when PCI is unsuccessful, cannot be used (eg, in lesions that are long or near **bifurcation points**), or causes **acute coronary artery dissection**.

Fibrinolytics are not indicated for unstable angina or NSTEMI. Risk outweighs potential benefit.

STEMI: Emergency PCI is the preferred treatment of STEMI when available in a timely fashion (door to balloon-inflation time < 90 min) by an experienced operator. Indications for urgent PCI later in the course of STEMI include hemodynamic instability, malignant arrhythmias requiring transvenous pacing or repeated **cardioversion**, and age > 75. If the lesions necessitate CABG, there is about 4 to 12% mortality and a 20 to 43% morbidity rate.

If there is likely to be a significant delay in availability of PCI, thrombolysis should be done for STEMI patients meeting criteria. Reperfusion using fibrinolytics is most effective if given in the first few minutes to hours after onset of MI. The earlier a fibrinolytic is begun, the better. The goal is a door-to-needle time of 30 to 60 min. Greatest benefit occurs within 3 h, but the drugs may be effective up to 12 h. Used with aspirin, fibrinolytics reduce hospital mortality rate by 30 to 50% and improve ventricular function. Although controversial, prehospital use of fibrinolytics by trained paramedics can significantly reduce time to treatment and should be considered in

situations in which PCI within 90 min is not possible, particularly in patients presenting within 3 h of symptom onset.

Regardless, most patients who undergo thrombolysis will ultimately require transfer to a PCI-capable facility for elective angiography and PCI as necessary prior to discharge. PCI should be considered after fibrinolytics if chest pain or ST-segment elevation persists ≥ 60 min after initiation of fibrinolytics or if pain and ST-segment elevation recur, but only if PCI can be initiated < 90 min after onset of recurrence. If PCI is unavailable, fibrinolytics can be repeated.

Characteristics and selection of fibrinolytic drugs are discussed.

Table 8

Fibrinolytic Therapy for STEMI

Criteria	Specifics
ECG criteria*	ST-segment elevation in ≥ 2 contiguous leads
	Typical symptoms and left bundle branch block not known to be old
	Strictly posterior MI (large R wave in V_1 and ST depression in V_1–V_4
Absolute contraindications	Aortic dissection

	Previous hemorrhagic stroke (at any time)
	Previous ischemic stroke within 1 yr
	Active internal bleeding (not menses)
	Intracranial tumor
	Pericarditis
Relative contraindications	BP > 180/110 mm Hg after initial antihypertensive therapy
	Trauma or major surgery within 4 wk
	Active peptic ulcer
	Pregnancy
	Bleeding diathesis
	Noncompressible vascular puncture

Current anticoagulation (INR > 2)
*Patients presenting in the hyperacute phase of MI with giant T waves do not meet current criteria for fibrinolytics; ECG is repeated in 20 to 30 min to see if ST-segment elevation has developed.

Complications

Electrical dysfunction occurs in > 90% of MI patients. Electrical dysfunction that commonly causes mortality in the first 72 h includes tachycardia (from any focus) rapid enough to reduce cardiac output and lower BP, Mobitz type II block (2nd degree) or complete (3rd degree) AV block, ventricular tachycardia (VT), and ventricular fibrillation (VF). Asystole is uncommon, except as a terminal manifestation of progressive LV failure and shock. Patients with disturbances of cardiac rhythm are checked for hypoxia and electrolyte abnormalities, which can be causative or contributory.

Sinus node disturbances: If the artery supplying the sinus node is affected, sinus node disturbances can occur; they are more likely if there is a preexisting sinus node disorder (common among the elderly). Sinus bradycardia, the most common sinus node disturbance, is usually not treated unless there is **hypotension** or the heart rate is < 50 beats/min. A lower heart rate, if not extreme, means reduced cardiac workload and possibly reduced infarct size. For bradycardia with hypotension (which may reduce myocardial perfusion), atropine sulfate 0.5 to 1 mg IV is used; it can be repeated after several minutes if response is inadequate. Several small doses are best because high doses may induce tachycardia. Occasionally, a temporary **transvenous pacemaker** must be inserted.

Persistent sinus tachycardia is usually ominous, often reflecting LV failure and low cardiac output. Without heart failure or another evident cause, this **arrhythmia** may respond to a β-blocker, given po or IV depending on degree of urgency.

Atrial arrhythmias: **Atrial arrhythmias** (atrial ectopic beats, atrial fibrillation [AF], and, less commonly, atrial flutter) occur in about 10% of MI patients and may reflect LV failure or right atrial infarction. **Paroxysmal atrial tachycardia** is uncommon and usually occurs in patients who have had previous episodes of it. **Atrial ectopy** is usually

benign but if frequency increases, causes, particularly heart failure, are sought. Frequent atrial ectopic beats may respond to a β-blocker.

AF is usually transient if it occurs within the first 24 h. Risk factors include age > 70, heart failure, previous history of MI, **large anterior infarction**, **atrial infarction**, **pericarditis**, **hypokalemia**, **hypomagnesemia**, a **chronic lung disorder**, and **hypoxia**. Fibrinolytics reduce incidence. Recurrent **paroxysmal AF** is a poor prognostic sign and increases risk of **systemic emboli**.

For AF, heparin is usually used because systemic emboli are a risk. IV β-blockers (eg, atenolol 2.5 to 5.0 mg over 2 min to total dose of 10 mg in 10 to 15 min, metoprolol 2 to 5 mg q 2 to 5 min to a total dose of 15 mg in 10 to 15 min) slow the ventricular rate. Heart rate and BP are closely monitored. Treatment is withheld when ventricular rate decreases satisfactorily or systolic BP is < 100 mm Hg. IV digoxin, which is not as effective as β-blockers, is used cautiously and only in patients with AF and LV systolic dysfunction. Usually, digoxin takes at least 2 h to effectively slow heart rate and may rarely aggravate ischemia in patients with recent ACS. For patients without evident LV systolic dysfunction or conduction delay manifested by a wide QRS complex, IV verapamil or IV diltiazem may be considered. Diltiazem may be given as an IV infusion to control heart rate for long periods.

If AF compromises circulatory status (eg, causing LV failure, hypotension, or chest pain), urgent **electrical cardioversion** is done. If AF returns after cardioversion, IV amiodarone should be considered.

For atrial flutter, rate is controlled as for AF, but heparin is not required. Low-energy direct current (DC) cardioversion will terminate atrial flutter.

Conduction defects: Mobitz type I block (**Wenckebach block**, progressive prolongation of PR interval) is relatively common with an **inferior-diaphragmatic infarction**; it is usually self-limited and rarely progresses to higher grade block. Mobitz type II block (dropped beats) usually indicates massive anterior MI, as does complete heart block with wide QRS complexes (atrial impulses do not reach the ventricle); both are uncommon. Frequency of complete (3rd degree) AV block depends on site of infarction. Complete AV block occurs in 5 to 10% of patients with inferior infarction and is usually transient. It occurs in < 5% with uncomplicated anterior infarction but in up to 26% of those with right bundle branch block and left posterior **hemiblock**.

Mobitz Type-2 AV Block(3:1)
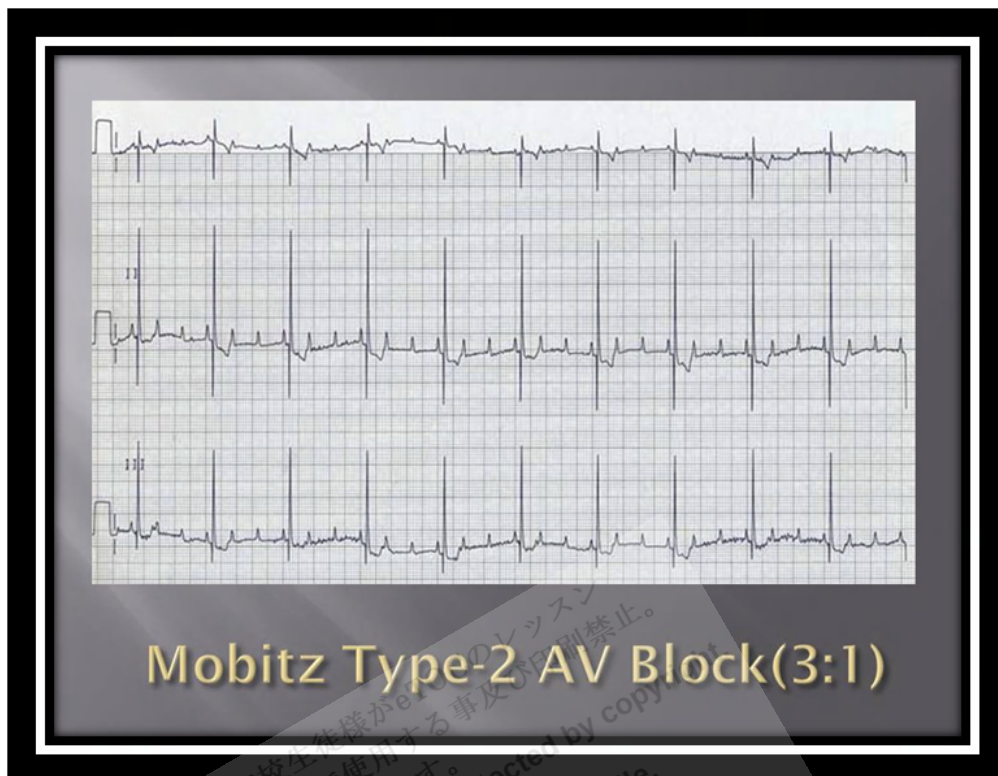
Mobitz type I block usually does not warrant treatment. For true Mobitz type II block with dropped beats or for AV block with slow, wide QRS complexes, **temporary transvenous pacing** is the treatment of choice. External pacing can be used until a temporary **transvenous pacemaker** can be placed. Although isoproterenol infusion may restore rhythm and rate temporarily, it is not used because it increases O_2 demand and risk of rhythm abnormalities.Atropine 0.5 mg IV q 3 to 5 min to a total dose of 2.5 mg may be useful for narrow-complex AV block with a slow ventricular rate but is not recommended for new wide-complex AV block.

Ventricular arrhythmias: These arrhythmias are common and may result from hypoxia, electrolyte imbalance (**hypokalemia**, possibly **hypomagnesemia**), or sympathetic overactivity in ischemic cells adjacent to infarcted tissue (which is not electrically active). Treatable causes of ventricular arrhythmias are sought and corrected. Serum K should be kept above 4.0 mEq/L. IV KCl is recommended; usually, 10 mEq/h can be infused, but for severe hypokalemia (K < 2.5 mEq/L), 20 to 40 mEq/h can be infused through a central venous line.

Ventricular ectopic beats, which are common after MI, do not warrant specific treatment.

Nonsustained VT (ie, < 30 sec) and even sustained slow VT (accelerated **idioventricular** rhythm) without **hemodynamic instability** do not usually require treatment in the first 24 to 48 h. Polymorphic VT, sustained (≥ 30 sec) monomorphic VT, or any VT with symptoms of instability (eg, heart failure, hypotension, chest pain) is treated with **synchronized cardioversion**. VT without hemodynamic instability may be treated with IV lidocaine, procainamide, oramiodarone. Some clinicians also treat complex ventricular arrhythmias with Mg sulfate 2 g IV over 5 min whether or not serum Mg is low. VT may occur months after MI. Late VT is more likely to occur in patients with **transmural infarction** and to be sustained.

VF occurs in 5 to 12% of patients during the first 24 h after MI, usually within 6 h. Late VF usually indicates continued or recurrent **myocardial ischemia** and, when accompanied by **hemodynamic deterioration**, is a poor prognostic sign. VF is treated with immediate unsynchronized. An IV β-blocker early in MI followed by continued oral β-blockers reduces the incidence of **ventricular arrhythmias** (including VF) and mortality in patients who do not have heart failure or **hypotension**. **Prophylaxis** with other drugs (eg,lidocaine) increases mortality risk and is not recommended.

After the acute phase, the presence of complex **ventricular arrhythmias** or **non-sustained VT**, especially with significant **LV systolic dysfunction**, increases mortality risk. An implantable **cardioverter-defibrillator** (ICD) should be considered. Programmed **endocardial stimulation** can help select the most effective **antiarrhythmics** or determine the need for an ICD. Before treatment with an antiarrhythmic or ICD, coronary **angiography** and other tests are done to look for recurrent **myocardial ischemia**, which may require PCI or CABG.

Heart failure: Patients with large infarctions (determined by ECG or serum markers) and those with mechanical complications, hypertension, or **diastolic dysfunction** are more likely to develop heart failure. Clinical findings depend on infarct size, elevation of LV filling pressure, and degree of reduction in cardiac output. Dyspnea, inspiratory rales at the lung bases, and **hypoxemia** are common.

Treatment depends on severity. For mild cases, a **loop diuretic** (eg, furosemide 20 to 40 mg IV once/day or bid) to reduce ventricular filling pressure is often sufficient. For severe cases, **vasodilators** (eg, IV nitroglycerin) are often used to reduce preload and afterload; during treatment, pulmonary artery occlusion pressure is often measured via right heart (**Swan-Ganz**) **catheterization**. ACE inhibitors are used as long as systolic BP remains > 100 mm Hg. A short-acting ACE inhibitor given in low doses (eg, captopril 3.125 to 6.25 mg po q 4 to 6 h, increasing doses as tolerated) is best for

initial treatment. Once the maximum dose is reached (maximum for captopril, 50 mg tid), a longer-acting ACE inhibitor (eg, **fosinopril, lisinopril, ramipril**) is substituted for the long-term. If heart failure remains in New York Heart Association class II or worse, an aldosterone inhibitor (eg, **eplerenone, spironolactone**) should be added. For severe heart failure, an **intraarterial counterpulsation** balloon pump may provide temporary hemodynamic support. When revascularization or surgical repair is not feasible, heart transplantation is considered. Long-term LV or **biventricular implantable assist devices** may be used as a bridge to transplantation; if transplantation is impossible, the LV assist device is occasionally used as permanent treatment. Occasionally, use of such a device results in recovery and can be removed in 3 to 6 mo.

If heart failure causes **hypoxemia**, O_2 is given by **nasal prongs** (to maintain PaO_2 at about 100 mg Hg). It may help oxygenate **myocardium** and limit the **ischemic zone**.

Papillary muscle disorders: Functional **papillary muscle** insufficiency occurs in about 35% of patients during the first few hours of infarction. Papillary muscle ischemia causes incomplete **coaptation** of the **mitral valve leaflets**, which is transient in most patients. But in some patients, papillary muscle or free wall scarring causes permanent **mitral regurgitation**. Functional papillary muscle insufficiency is characterized by an **apical late systolic murmur** and typically resolves without treatment.
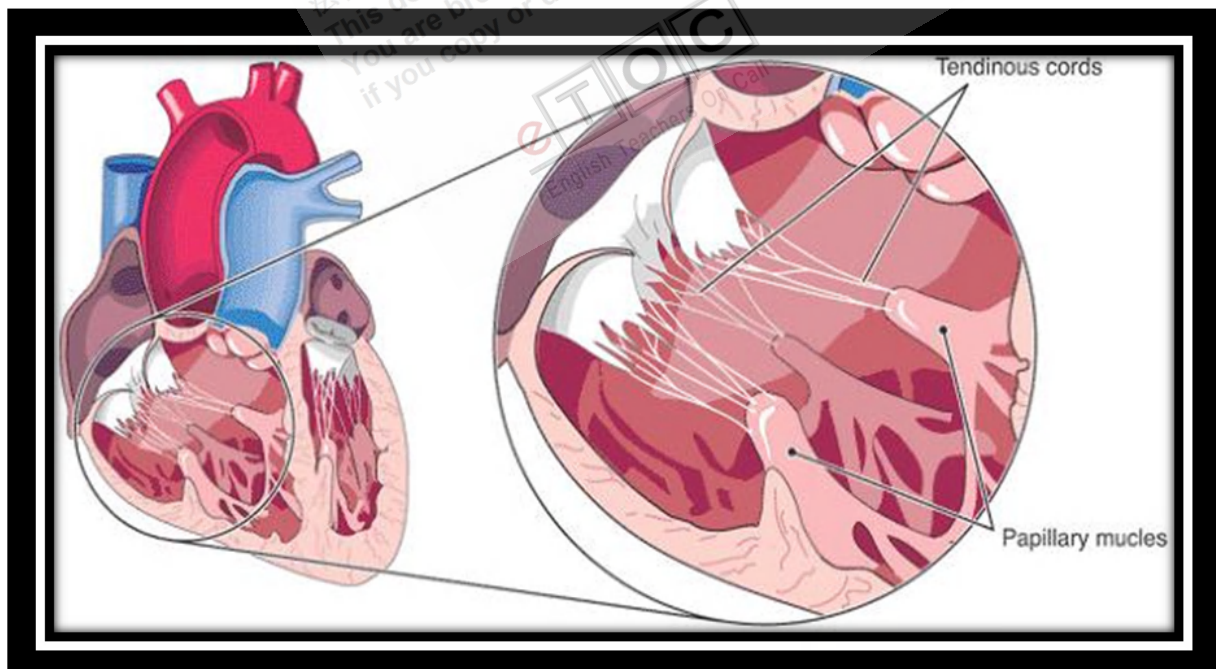
Papillary muscle rupture occurs most often after an **inferoposterior infarct** due to right coronary artery occlusion. It produces acute, severe mitral regurgitation. Papillary muscle rupture is characterized by the sudden appearance of a loud **apical holosystolic murmur** and thrill, usually with **pulmonary edema**. Occasionally, when severe regurgitation is silent but suspected clinically, **echocardiography** is done. Mitral valve repair or replacement is effective.

Myocardial rupture: **Interventricular septum** or free wall rupture occurs in 1% of patients with acute MI. It causes 15% of hospital mortality.

Interventricular septum rupture, although rare, is 8 to 10 times more common than papillary muscle rupture. Intraventricular septum rupture is characterized by the sudden appearance of a loud **systolic murmur** and **thrill medial** to the apex along the left sternal border in the 3rd or 4th intercostal space, accompanied by hypotension with or without signs of LV failure. Diagnosis may be confirmed using a balloon-tipped catheter and comparing blood **O$_2$saturation** or Po$_2$ of right atrial, RV, and pulmonary artery samples. A significant increase in RV Po$_2$ is diagnostic, as is **Doppler echocardiography**, which may demonstrate the actual shunt of blood across the **ventricular septum**. Treatment is surgery, which should be delayed for up to 6 wk after MI so that infarcted myocardium can heal maximally; if **hemodynamic instability** persists, earlier surgery is indicated despite a high mortality risk.

Free wall rupture increases in incidence with age and is more common among women. It is characterized by sudden loss of arterial pressure with momentary persistence of **sinus rhythm** and often by signs of cardiac **tamponade**. Surgery is rarely successful. Rupture of a free wall is almost always fatal.

Ventricular aneurysm: A localized bulge in the **ventricular wall**, usually the LV wall, can occur at the site of a large infarction. **Ventricular aneurysms** are common, especially with a large **transmural infarct** (usually **anterior**). Aneurysms may develop in a few days, weeks, or months. They are unlikely to rupture but may lead to recurrent **ventricular arrhythmias**, low **cardiac output**, and **mural thrombosis** with **systemic embolism**. A ventricular aneurysm may be suspected when **paradoxical precordial movements** are seen or felt. ECG shows persistent ST-segment elevation, and chest x-ray shows a characteristic bulge of the cardiac shadow. **Echocardiography** is done to confirm the diagnosis and determine whether a thrombus is present. Surgical excision may be indicated when LV failure or arrhythmia persists. Use of ACE inhibitors during acute MI modifies LV remodeling and may reduce the incidence of **aneurysm**.

Pseudoaneurysm is incomplete rupture of the free LV wall; it is limited by the pericardium. Pseudoaneurysms almost always contain a thrombus and often rupture completely. They are repaired surgically.

Hypotension and cardiogenic shock: Hypotension may be due to decreased **ventricular filling** or loss of **contractile force** secondary to massive MI. Marked hypotension (eg, systolic BP < 90 mm Hg) with **tachycardia** and symptoms of end-organ **hypoperfusion** (reduced urine output, **mental confusion, diaphoresis, cold extremities**) is termed **cardiogenic shock**. **Pulmonary congestion** develops rapidly in cardiogenic shock.
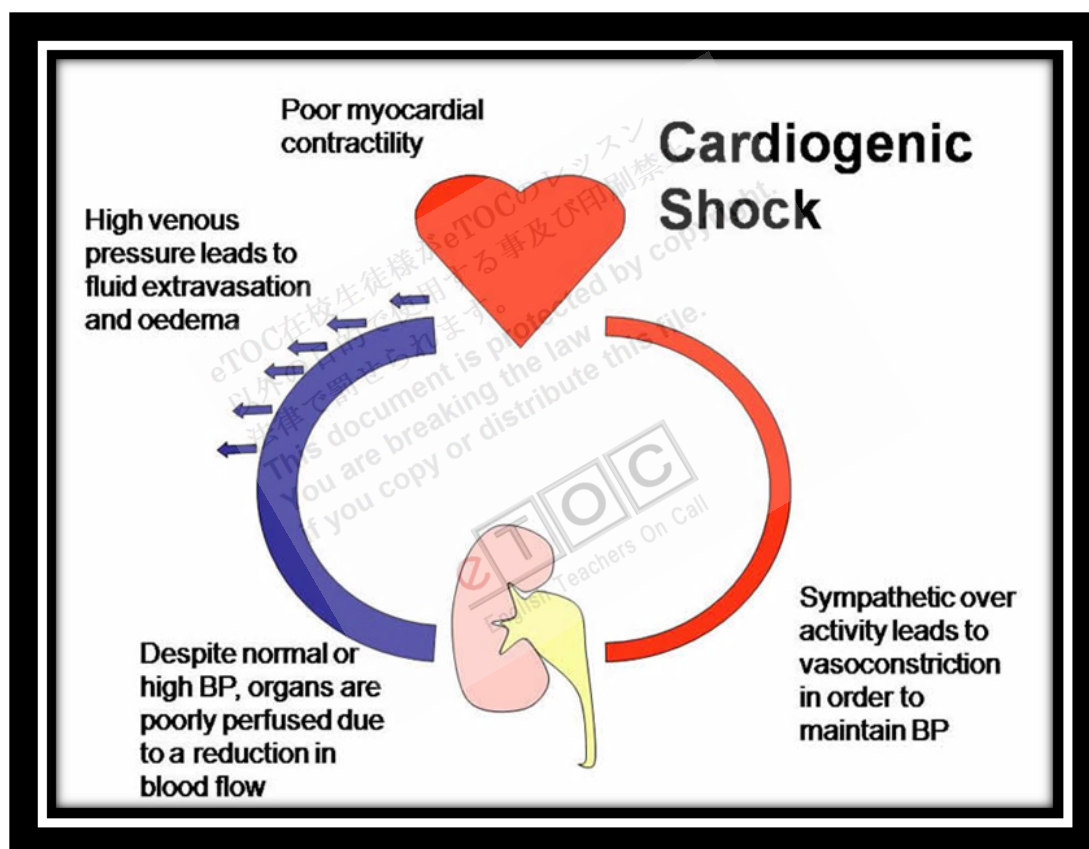
Decreased LV filling is most often caused by reduced venous return secondary to hypovolemia, especially in patients receiving intensive **loop diuretic therapy**, but it may reflect RV infarction. Marked **pulmonary congestion** suggests loss of LV contractile force (LV failure) as the cause. Treatment depends on the cause. In some patients, determining the cause requires use of a pulmonary artery catheter to measure **intracardiac pressures**. If pulmonary artery occlusion pressure is < 18 mm Hg, decreased filling, usually due to **hypovolemia**, is likely; if pressure is > 18 mm Hg, LV

failure is likely. For hypotension due to hypovolemia, cautious fluid replacement with 0.9% saline is usually possible without left heart overload (excessive rise in left atrial pressure). However, sometimes LV function is so compromised that adequate fluid replacement sharply increases pulmonary artery occlusion pressure to levels associated with pulmonary edema (> 25 mm Hg). If left atrial pressure is high, hypotension is probably due to LV failure, and if **diuretics** are ineffective, **inotropic therapy** or **circulatory support** may be required.

In **cardiogenic shock**, an α- or β-agonist may be temporarily effective. Dopamine, a catecholamine with α and β1 effects, is given at 0.5 to 1 μg/kg/min, increased until response is satisfactory or dose is about 10 μg/kg/min. Higher doses induce **vasoconstriction** and **atrial** and **ventricular arrhythmias**. **Dobutamine**, a β-agonist, may be given IV at 2.5 to 10 μg/kg/min or in higher doses. It often causes or exacerbates hypotension; it is most effective when hypotension is secondary to low cardiac output with increased peripheral vascular resistance. **Dopamine** may be more effective than **dobutamine** when a vasopressor effect is also required. In refractory cases, dobutamine **anddopamine** may be combined. An **intraortic counterpulsation** balloon pump can often temporarily support the patient. Definitive treatment for **postinfarction cardiogenic shock** is revascularization by **thrombolysis** of the **clot**, **angioplasty**, or emergency CABG. Revascularization usually greatly improves ventricular function. PCI or CABG may be considered for persistent ischemia, refractory **ventricular arrhythmia**, **hemodynamic instability**, or shock if **coronary anatomy** is suitable.

RV ischemia or infarction: **RV infarction** rarely occurs in isolation; it usually accompanies inferior **LV infarction**, and the first sign may be hypotension developing in a previously stable patient. Right-sided ECG leads may show ST-segment changes. Volume loading with 1 to 2 L of 0.9% saline is often effective. **Dobutamine** may help. Nitrates and diuretics are not used; they reduce preload (and hence cardiac output), causing severe hypotension. Increased right-sided filling pressure should be maintained by IV fluid infusion.

Recurrent ischemia: Any chest pain that remains or recurs 12 to 24 h post-MI may represent recurrent **ischemia**. Post-MI ischemic pain indicates that more **myocardium** is at risk of infarction. Usually, recurrent ischemia can be identified by reversible ST-T changes on the ECG; BP may be elevated. However, because recurrent ischemia may be silent (ECG changes without pain) in up to one third of patients, serial ECGs are routinely done every 8 h for 1 day and then daily. Recurrent ischemia is treated similarly

to unstable angina. Sublingual or IV nitroglycerin is usually effective. Coronary **angiography** and PCI or CABG should be considered to salvage **ischemic myocardium**.

Mural thrombosis: **Mural thrombosis** occurs in about 20% of patients with acute MI. **Systemic embolism** occurs in about 10% of patients with **LV thrombosis**; risk is highest in the first 10 days but persists at least 3 mo. Risk is highest (about 60%) for patients with large **anterior infarctions** (especially involving the distal septum and apex), a dilated and diffusely **hypokinetic LV**, or **chronic AF**. **Anticoagulants** are given to reduce risk of emboli. If not contraindicated, full-dose IV heparin followed by warfarin for 3 to 6 mo is given to maintain INR between 2 and 3. Anticoagulants are continued indefinitely when a dilated diffusely **hypokinetic LV**, **LV aneurysm**, or **chronic AF** is present. Aspirin may also be given indefinitely.

Pericarditis: **Pericarditis** results from extension of **myocardial necrosis** through the wall to the **epicardium**; it develops in about one third of patients with **acute transmural MI**. A friction rub usually begins 24 to 96 h after MI onset. Earlier onset of the friction rub is unusual, although hemorrhagic pericarditis occasionally complicates the early phase of MI. **Acute tamponade** is rare. Pericarditis is diagnosed by ECG, which shows diffuse ST-segment elevation and sometimes PR-interval depression. Echocardiography is frequently done, but results are usually normal. Occasionally, small **pericardial effusions** and even **unsuspected tamponade** are detected.
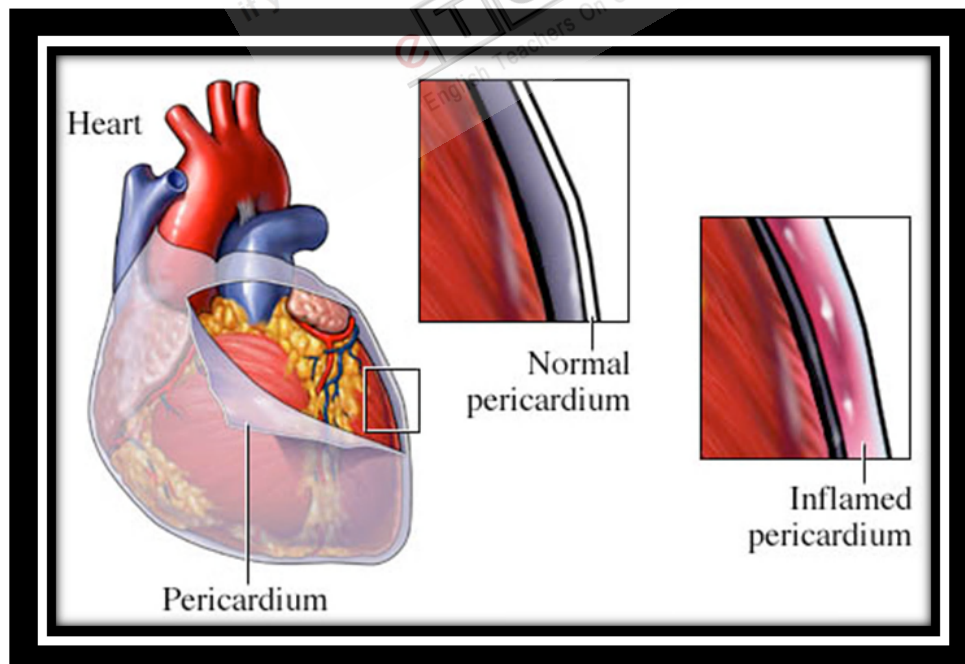
Aspirin or another NSAID usually relieves symptoms. High doses or prolonged use of NSAIDs or corticosteroids may impair infarct healing and should be avoided. Anticoagulation is not contraindicated in early **peri-infarction pericarditis** but is contraindicated in later post-MI (Dressler's) syndrome.

Post-MI syndrome (Dressler's syndrome): Post-MI syndrome develops in a few patients several days to weeks or even months after acute MI; incidence appears to have decreased in recent years. It is characterized by fever, pericarditis with a friction rub, **pericardial effusion**, **pleurisy**, **pleural effusions**, **pulmonary infiltrates**, and joint pain. This syndrome is caused by an autoimmune reaction to material from **necrotic myocytes**. It may recur. Differentiating post-MI syndrome from extension or recurrence of **infarction** may be difficult. However, in post-MI syndrome, cardiac markers do not increase significantly, and ECG changes are nonspecific. NSAIDs are usually effective, but the syndrome can recur several times. In severe cases, a short, intensive course of another NSAID or a **corticosteroid** may be necessary. High doses of an NSAID or a corticosteroid are not used for more than a few days because they may interfere with early ventricular healing after an acute MI.

Rehabilitation and Postdischarge Treatment
- Functional evaluation
- Changes in lifestyle: Regular exercise, diet modification, weight loss, smoking cessation
- Drugs: Continuation of aspirin, β-blockers, ACE inhibitors, and statins

Functional evaluation: Patients who did not have **coronary angiography** during admission, have no high-risk features (eg, **heart failure**, **recurrent angina**, VT or VF after 24 h, mechanical complications such as new **murmurs**, **shock**), and have an ejection fraction > 40% whether or not they received **fibrinolytics** usually should have stress testing of some sort before or shortly after discharge.

Table 9

Functional Evaluation After MI

Exercise Capacity	If ECG Is Interpretable	If ECG Is Not Interpretable
Able to exercise	Submaximal or symptom-limited stress ECG before or after discharge	Exercise echocardiography or nuclear scanning

Unable to exercise	Pharmacologic stress testing (echocardiography or nuclear scanning)	Pharmacologic stress testing (echocardiography or nuclear scanning)

Activity: Physical activity is gradually increased during the first 3 to 6 wk after discharge. Resumption of sexual activity, often of great concern to the patient, and other moderate physical activities may be encouraged. If good cardiac function is maintained 6 wk after acute MI, most patients can return to all their normal activities. A regular exercise program consistent with lifestyle, age, and cardiac status reduces risk of ischemic events and enhances general well-being.

Risk factors: The acute illness and treatment of ACS should be used to strongly motivate the patient to modify risk factors. Evaluating the patient's physical and emotional status and discussing them with the patient, advising about lifestyle (eg, smoking, diet, work and play habits, exercise), and aggressively managing risk factors may improve **prognosis**.

Drugs: Several drugs clearly reduce mortality risk post-MI and are used unless contraindicated or not tolerated.

Aspirin reduces mortality and **reinfarction** rates in post-MI patients by 15 to 30%. **Enteric-coated aspirin** 81 mg once/day is recommended long-term. Data suggest that warfarin with or without aspirin reduces mortality and reinfarction rates. β-Blockers are considered standard therapy. Most available β-blockers (eg, acebutolol, atenolol, metoprolol, propranolol, timolol) reduce post-MI mortality rate by about 25% for at least 7 yr.

ACE inhibitors are given to all post-MI patients. These drugs may provide long-term **cardioprotection** by improving endothelial function. If an ACE inhibitor is not tolerated because of cough or rash (but not **angioedema** or **renal dysfunction**), an angiotensin II receptor blocker may be substituted.

Statins are prescribed. Reducing cholesterol levels after MI reduces rates of recurrent ischemic events and mortality in patients with elevated or normal cholesterol levels. Statins appear to benefit post-MI patients regardless of their initial cholesterol level. Post-MI patients whose primary problem is a low HDL level or an elevated **triglyceride level** may benefit from a **fibrate**, but evidence of benefit is less clear. A lipid-lowering drug should be continued indefinitely, unless significant adverse effects occur, and dose should be increased to achieve an LDL level of 70 to 80 mg/dL (1.81 to 2.07 mmol/L).

Reference: http://www.merckmanuals.com