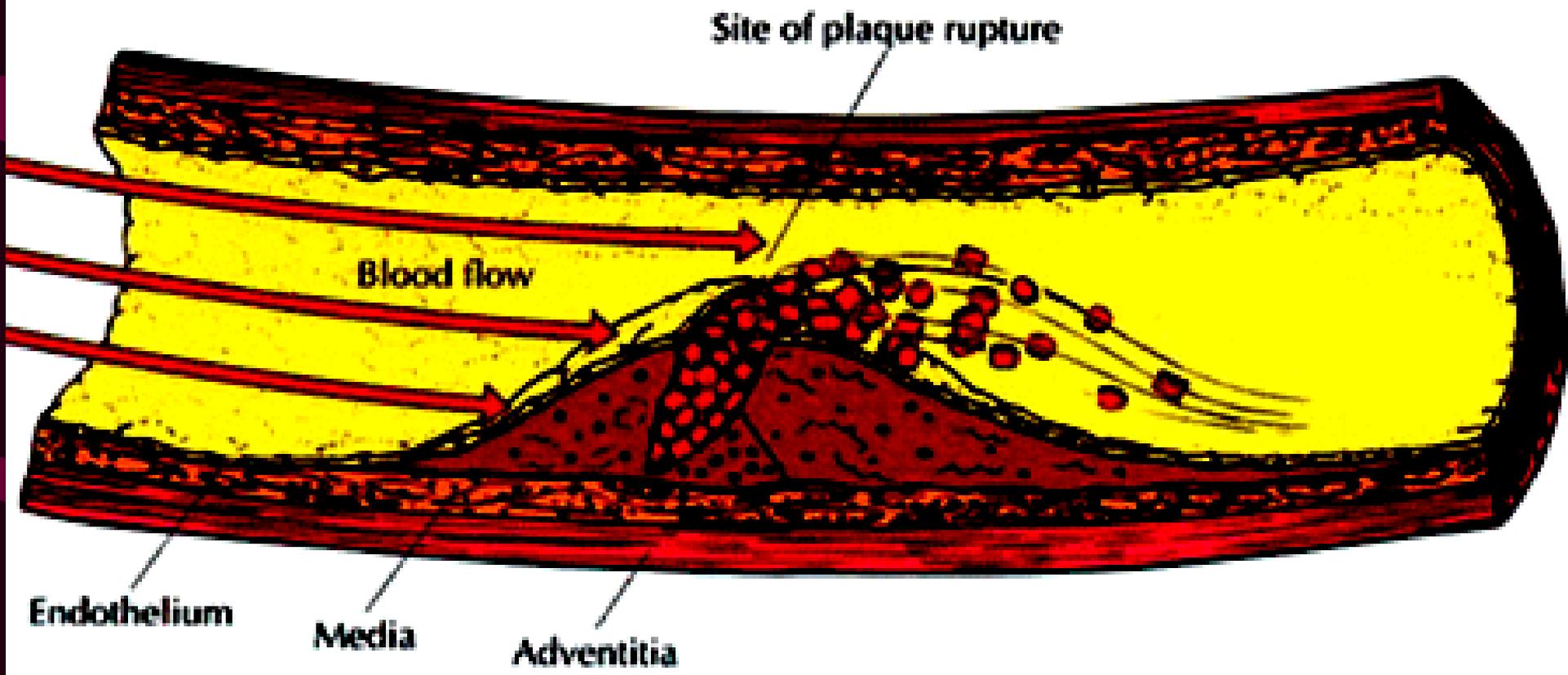


Internal Medicine

Lecture 3. Acute coronary syndrome. Myocardial infarction

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Acute myocardial infarction is an irreversible ischemic myocardial necrosis resulting from abrupt reduction in coronary blood flow to a segment of myocardium. This results from an imbalance of oxygen supply and demand.

Pathophysiology

Myocardial infarction generally occurs when there is an abrupt decrease in coronary blood flow following a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis.

Plaque rupture is the major trigger of coronary thrombosis.

Plaque rupture lead to platelet activation and aggregation, coagulation pathway activation, endothelial induced vasoconstriction, coronary thrombosis and occlusion.

Activated platelets exert procoagulant effects and the soluble coagulation cascade is activated.

Fibrin strands and erythrocytes predominate within the lumen of the vessel and downstream in the "body" and "tail" of the thrombus.

Nonatherosclerotic causes of acute MI

in younger patients or if no evidence of atherosclerosis include:

- coronary artery **embolization** from an infected cardiac valve (in mitral or aortic stenosis and infective endocarditis),
- hypercoagulability and intracardiac thrombi or masses can produce coronary emboli,**
- coronary occlusion** secondary to vasculitis,
- primary coronary vasospasm** (variant angina),
- congenital abnormalities of coronary arteries,**
- cocaine** use intense coronary arterial spasm,
- other factors leading to mismatch of oxygen supply and demand, as may occur with a significant GI bleeding.

Q-wave myocardial infarction involve the whole thickness of myocardium from epicardium to endocardium and are characterized by abnormal Q waves on the ECG.

Non-Q-wave infarction do not extend through the ventricular wall and cause only ST segment and T wave abnormalities.

Precipitating factors of myocardial infarction:

- physical exercise,
- emotional stress,
- medical or surgical illness.

Hypothetical steps in triggering of coronary thrombosis

Triggering activities of patients

Acute risk factors of an arterial pressure surge or vasoconstriction lead to plaque disruption

Acute risk factors of a coagulability increase or vasoconstriction lead to complete occlusion by thrombus

Minor plaque disruption

Nonocclusive thrombus

Occlusive thrombus



Nonvulnerable atherosclerotic plaque

Vulnerable atherosclerotic plaque

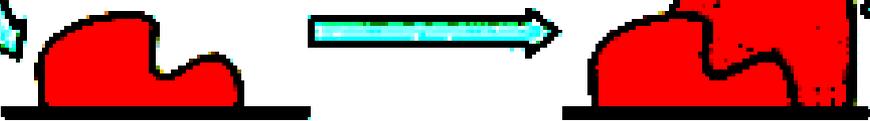


Asymptomatic unstable angina or non-Q MI

MI or sudden cardiac death

Major plaque disruption

Occlusive thrombus



Clinical picture of myocardial infarction

History (complaints):

- Chest pain is deep and visceral, may be severe enough to be described as the worst pain the patient has ever felt. The pain involves the central portion of the chest. A sense of impending death accompany it.
 - Substernal pressure sensation that also may be described as squeezing, aching, burning, crushing or even sharp pain.
- Prolonged chest discomfort lasting longer than 30 minutes.
 - Radiation to the left arm or neck. Less common sites of radiation: the abdomen, back, lower jaw.
 - The sensation is precipitated by exertion and relieved by rest and nitroglycerin.
 - Chest pain may be associated with weakness, nausea, vomiting, sweating, diaphoresis, dyspnea, fatigue, or palpitations.
- Atypical chest pain is common, especially, in patients with diabetes and the elderly (***painless MI***), and it increases with age. However, any patient may present with atypical symptoms. These symptoms are considered the anginal equivalent for that patient.

▪ Shortness of breath

- Shortness of breath may be the patient's anginal equivalent or a symptom of heart failure.
- It is due to elevated end-diastolic pressures secondary to ischemia, which then lead to elevated pulmonary pressures.
- Atypical presentations (frequently lead to misdiagnoses)
 - abdominal discomfort or jaw pain as his or her anginal equivalent.
 - altered mental status, sudden loss of consciousness (more common in elderly).
- In the elderly, MI may present as sudden-onset breathlessness, which may progress to pulmonary edema.
- arrhythmia
- sensation of profound weakness,
- unexplained drop in arterial pressure.

Physical:

Physical examination findings can vary enormously; one patient may be comfortable in bed, with normal examination results, while another may be in severe pain with significant respiratory distress requiring ventilatory support.

- Pallor associated with cool, clammy skin and diaphoresis occur commonly.
- Patients have a normal pulse rate and blood pressure. Hypotension or hypertension can be observed depending on the extent of the MI.
- Low-grade fever may be present. Sometimes temperature elevations up to 38°C may be observed during the first week after acute MI.
- Fourth heart sound (S₄) may be heard in patients with ischemia.
- Dyskinetic cardiac bulge (in anterior wall MI) occasionally can be palpated.
- Systolic murmur can be heard if mitral regurgitation (MR), mitral valve dysfunction or ventricular septal defect (VSD) develops.
- A pericardial friction rub is heard in patients with MI at same time in the course of the disease.
- Signs of congestive heart failure (CHF) may be found, including the following:
 - Third heart sound (S3) gallop,
 - Pulmonary rales,
 - Lower extremity edema,
 - Elevated jugular venous pressure.

Causes

Atherosclerosis with occlusive or partially occlusive thrombus formation.

- Nonmodifiable risk factors for atherosclerosis: age, gender and family history of premature coronary heart disease.
- Modifiable risk factors for atherosclerosis: smoking, diabetes mellitus, hypertension, dyslipidemia, obesity
- New and other risk factors for atherosclerosis: elevated homocysteine levels, male pattern baldness, sedentary lifestyle and/or lack of exercise, psychosocial stress, presence of peripheral vascular disease, poor oral hygiene
- Nonatherosclerotic causes: vasculitis , coronary emboli , congenital coronary anomalies, coronary trauma, coronary spasm, drug use (cocaine)
 - Factors that increase oxygen requirement, such as heavy exertion, fever, or hyperthyroidism.
 - Factors that decrease oxygen delivery, such as hypoxemia of severe anemia.

Laboratory Studies:

Serum cardiac markers are released into the blood in large quantities from necrotic heart muscle after myocardial infarction.

In patients with suspected MI, obtain serum cardiac markers at regular intervals, starting upon admission and serially for as long as 24 hours.

Creatine kinase

Creatine kinase comprises 3 isoenzymes:

- creatine kinase with **muscle subunits** (CK-MM), which is found mainly in skeletal muscle;
- creatine kinase with **brain subunits** (CK-BB), predominantly found in the brain;
- and **myocardial muscle creatine kinase** (CK-MB), which is found mainly in the heart.

Serial measurements of CK-MB isoenzymes were previously the standard criterion for diagnosis of MI.

CK-MB levels increase within 3-12 hours of onset of chest pain, reach peak values within 24 hours, and return to baseline after 48-72 hours.

Levels peak earlier (wash out) if reperfusion occurs.

Sensitivity is approximately 95%.

Troponins

Troponins are now considered the criterion standard in defining and diagnosing MI, according to the American College of Cardiology (ACC)/American Heart Association (AHA) "consensus statement" on MI (Braunwald et al, 2000).

Cardiac troponins T and I (cTnT and cTnI) have a greater sensitivity and specificity than CK-MB levels in detecting MI.

Serum levels increase within 3-12 hours from the onset of chest pain, peak at 24-48 hours, and return to baseline over 5-14 days.

Thus, measurement of cTnT or cTnI is preferable in patients with suspected myocardial infarction who come to medical attention more than 24 to 48 h after the onset of symptoms.

Myoglobin

Urine myoglobin levels rise within 1-4 hours from the onset of chest pain.

Myoglobin is highly sensitive but not very specific, and may be useful within the context of other studies and in early detection of MI.

AST

AST starts to rise about 12 hours after infarction and reaches a peak on the first or second day, returning to normal within 48-72 hours.

Complete blood cell count

Obtain a CBC count if MI is suspected to rule out anemia as a cause of decreased oxygen supply and prior to giving thrombolytics.

Leukocytosis is also common, but not universal, in the setting of acute MI. The *nonspecific reaction* to myocardial injury is associated with polymorphonuclear leukocytosis, which appears within a few hours after the onset of pain, persists for 3 to 7 days, and often reaches levels of 12,000 to 15,000 leukocytes per microliter.

A platelet count is necessary if a IIb/IIIa agent is considered.

The ESR rises more slowly than the white blood cell count, peaking during the first week and sometimes remaining elevated for 1 or 2 weeks.

Chemistry profile

In the setting of MI, closely monitor *potassium* and *magnesium* levels. *Creatinine* level also is needed prior to initiating treatment with an angiotensin-converting enzyme (ACE) inhibitor.

Lipid profile: This may be helpful if obtained upon presentation because levels can change after 12-24 hours of an acute illness.

C-reactive protein (CRP): Measure CRP and other markers of inflammation upon presentation if an ACS is suspected.

ECG

The electrocardiogram (ECG) is the most important tool in the initial evaluation and triage of patients in whom an ACS is suspected.

Obtain an ECG immediately if MI is considered or suspected.

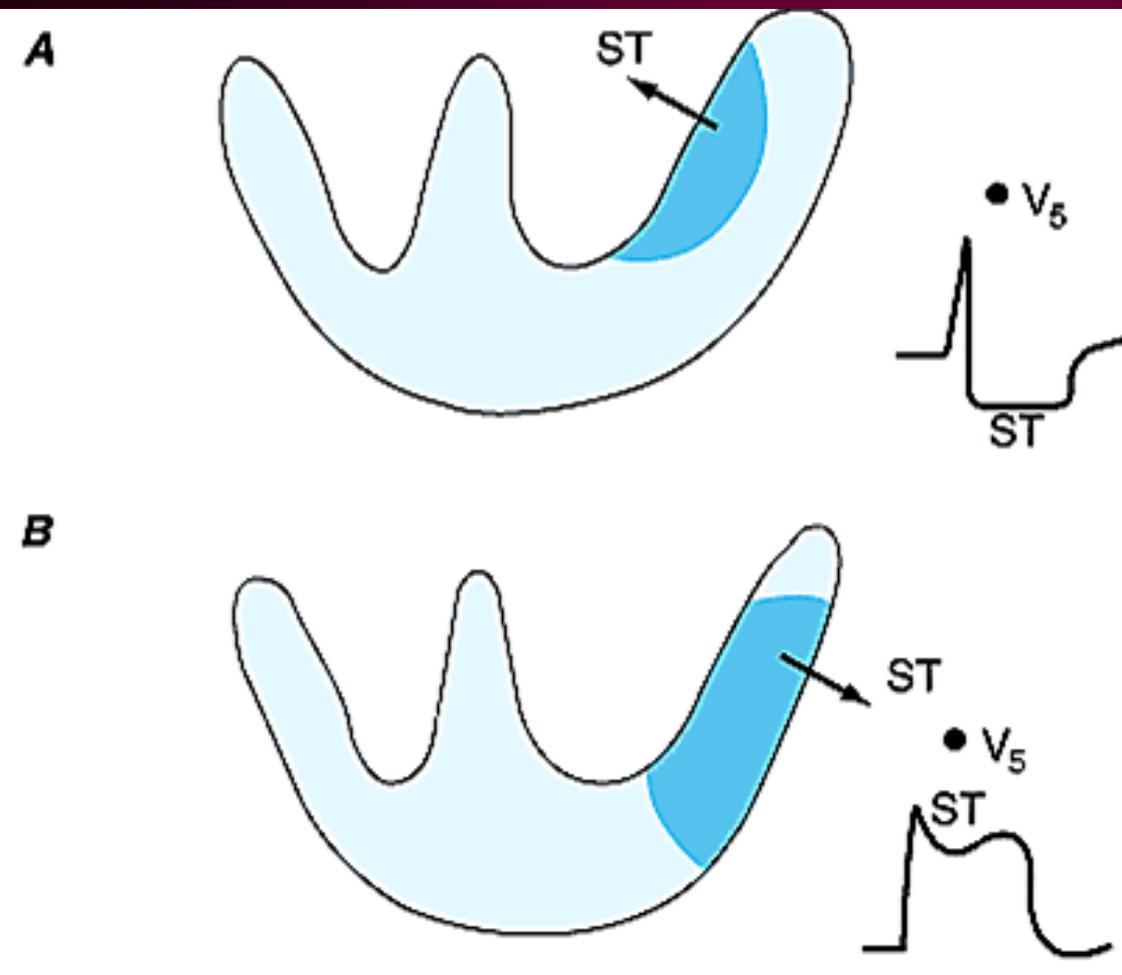
Qualified personnel should review the ECG as soon as possible.

Obtain daily serial ECGs for the first 2-3 days and additionally as needed.

Perform ECGs serially upon presentation to evaluate progression and assess changes with and without pain.

Convex ST-segment elevation with upright or inverted T waves generally is indicative of MI.

ST depression and T-wave changes also may indicate evolution of NQWMI.



NGWMI may be present if the electrocardiogram shows only transient ST-segment and T-wave changes or if the electrocardiogram shows ST-segment depression (with ST elevation in lead aVR).

QWMI is often present if the ECG demonstrates Q waves or loss of R waves and ST elevation.

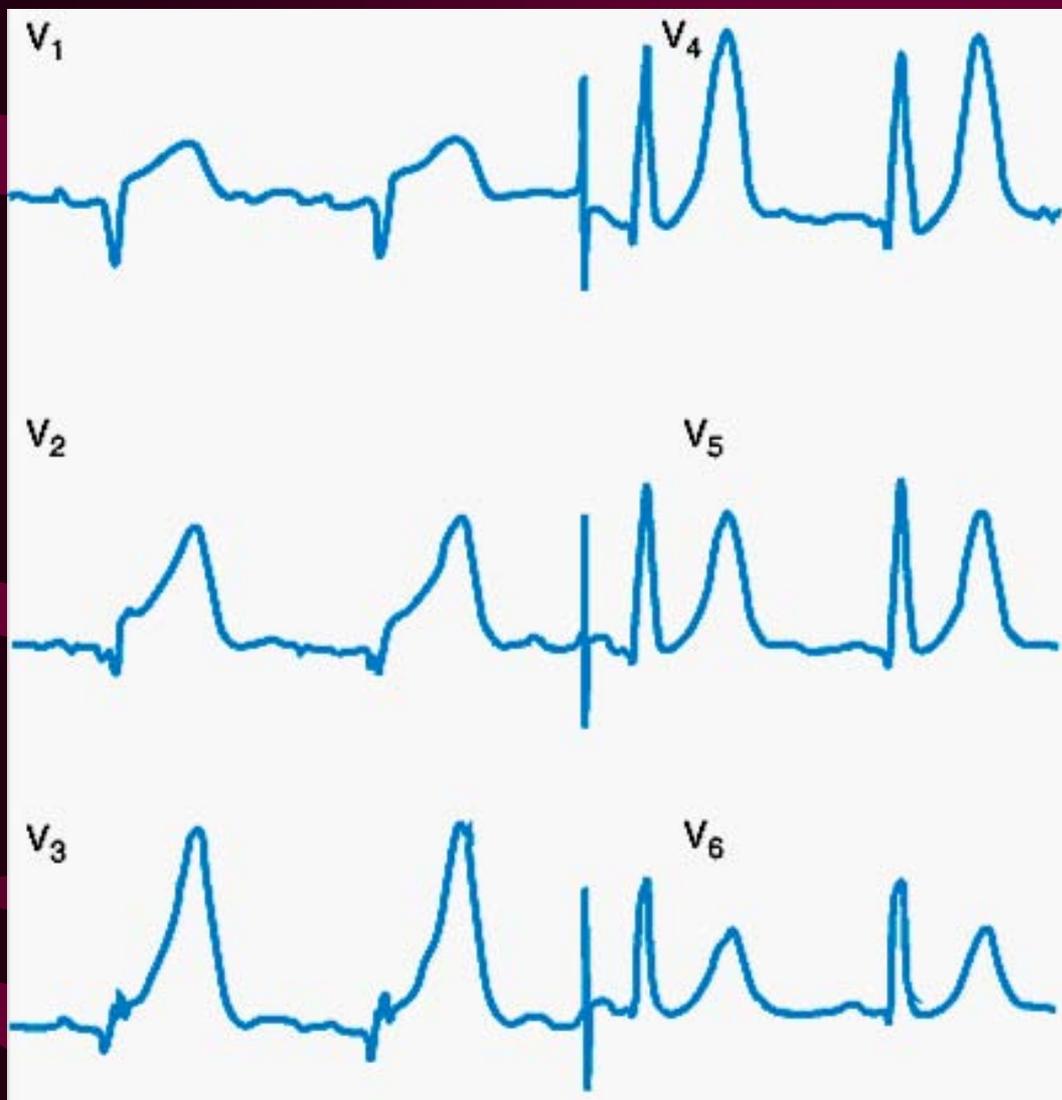
Q-wave myocardial infarction

Acute anterior wall ischemia leading to Q-wave infarction is reflected by ST elevations or increased T-wave positivity in one or more of the precordial leads (V_1 to V_6) and leads I and aVL.

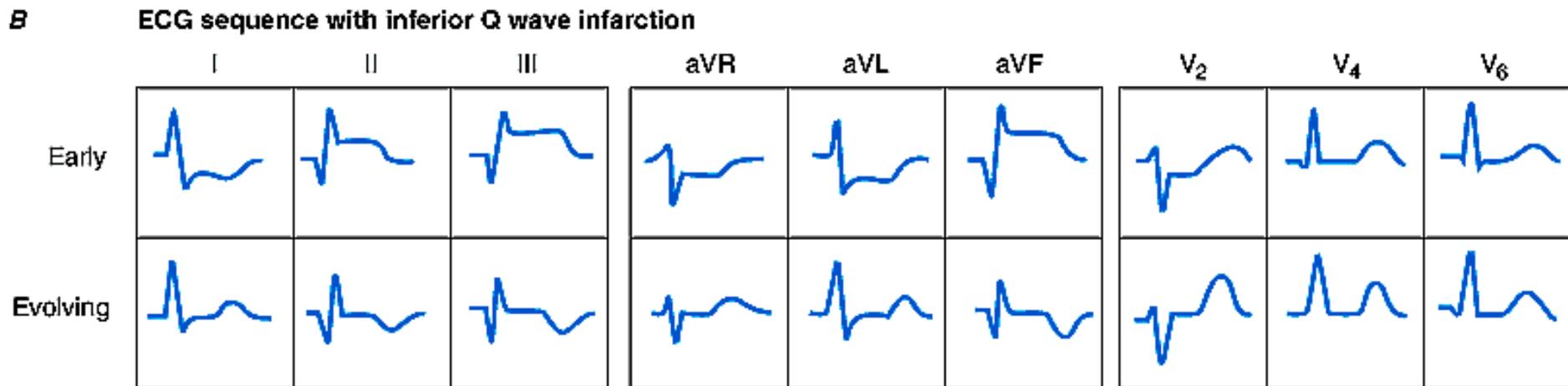
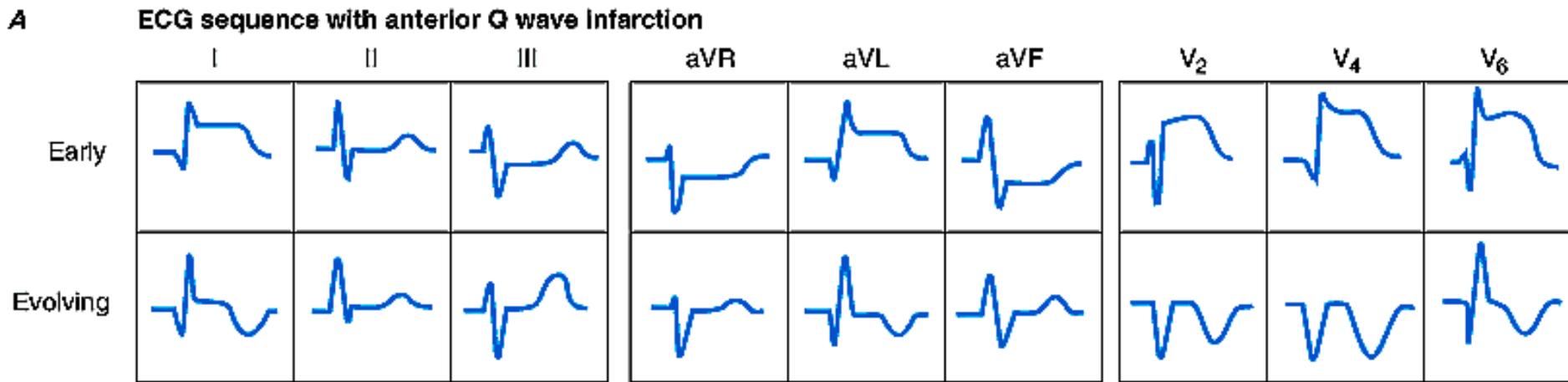
Anteroseptal ischemia produces these changes in leads V_1 to V_3 ; apical or lateral ischemia in leads V_4 to V_6 .

Inferior wall ischemia produces changes in leads II, III, and aVF.

Posterior wall ischemia may be indirectly recognized by **reciprocal** ST depressions in leads V_1 to V_3 .



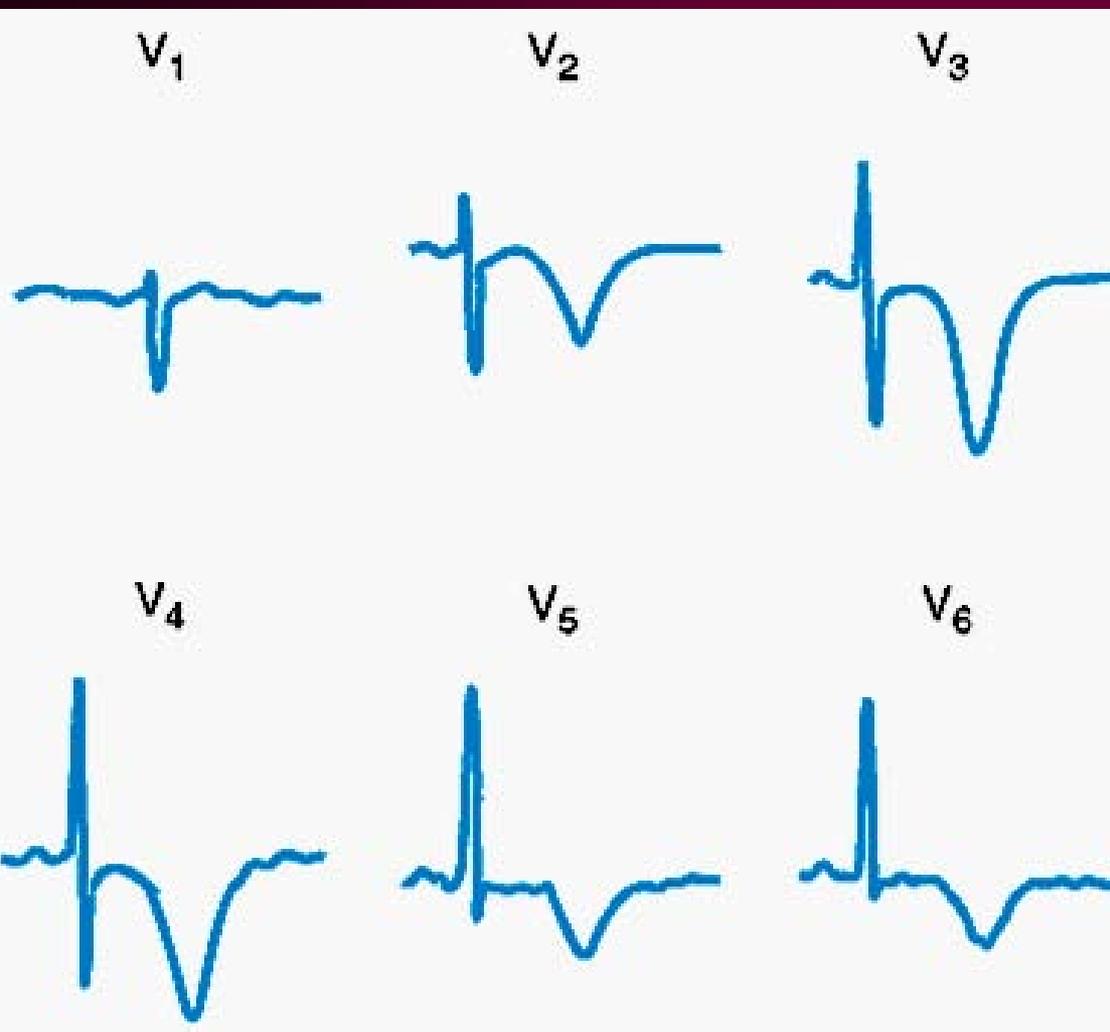
Hyperacute phase of anteroseptal QWMI. Note the tall positive T waves (V_2 to V_3) along with ST-segment elevations and Q waves (V_1 to V_3).



Sequence of depolarization and repolarization changes with (A) acute anterior and (B) acute inferior wall Q-wave myocardial infarctions.

With anterior infarcts, ST elevation in leads I, aVL, and the precordial leads may be accompanied by reciprocal ST depressions in leads II, III, and aVF.

Conversely, acute inferior (or posterior) infarcts may be associated with reciprocal ST depressions in leads V₁ to V₃.

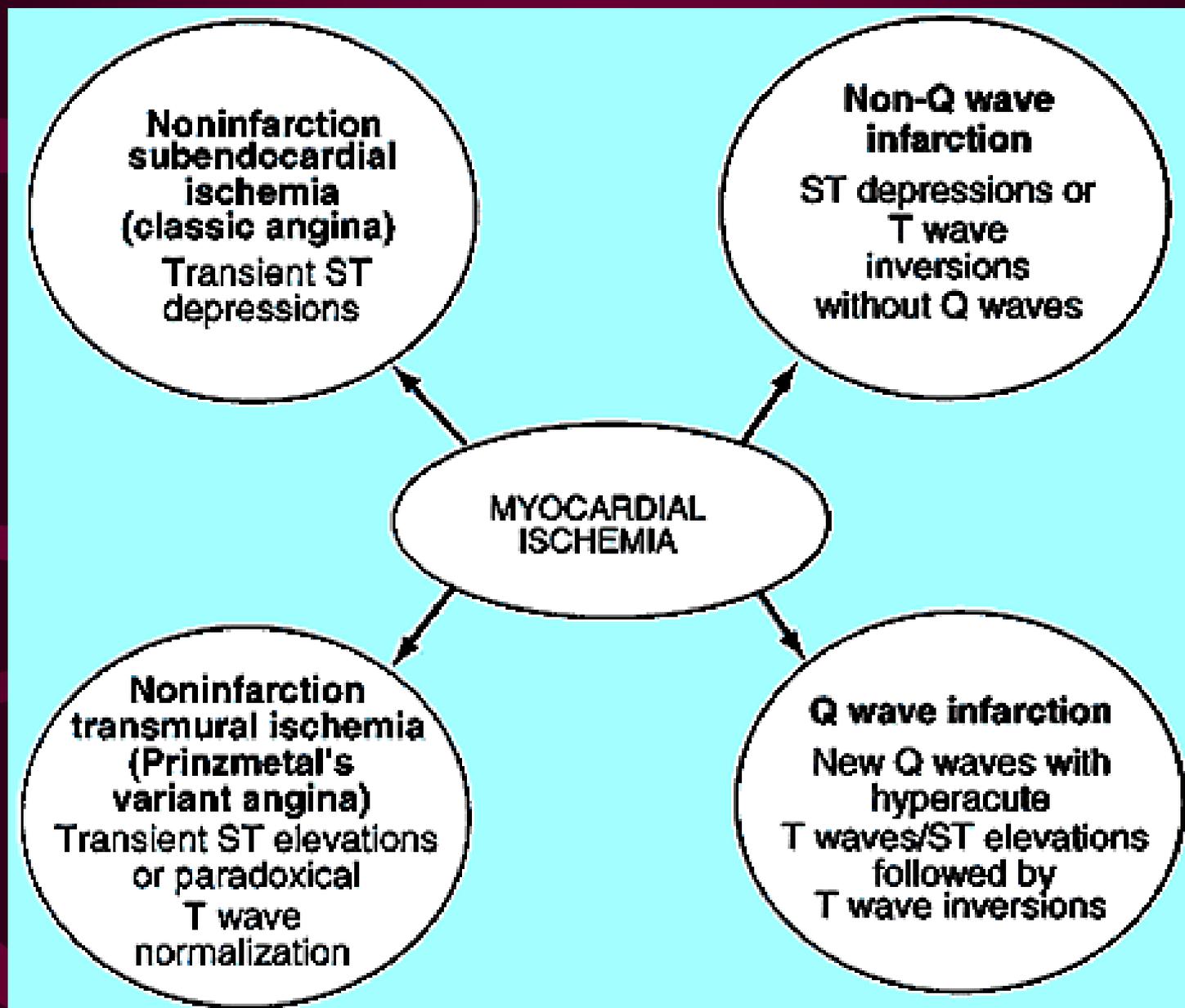


Non-Q-wave infarction

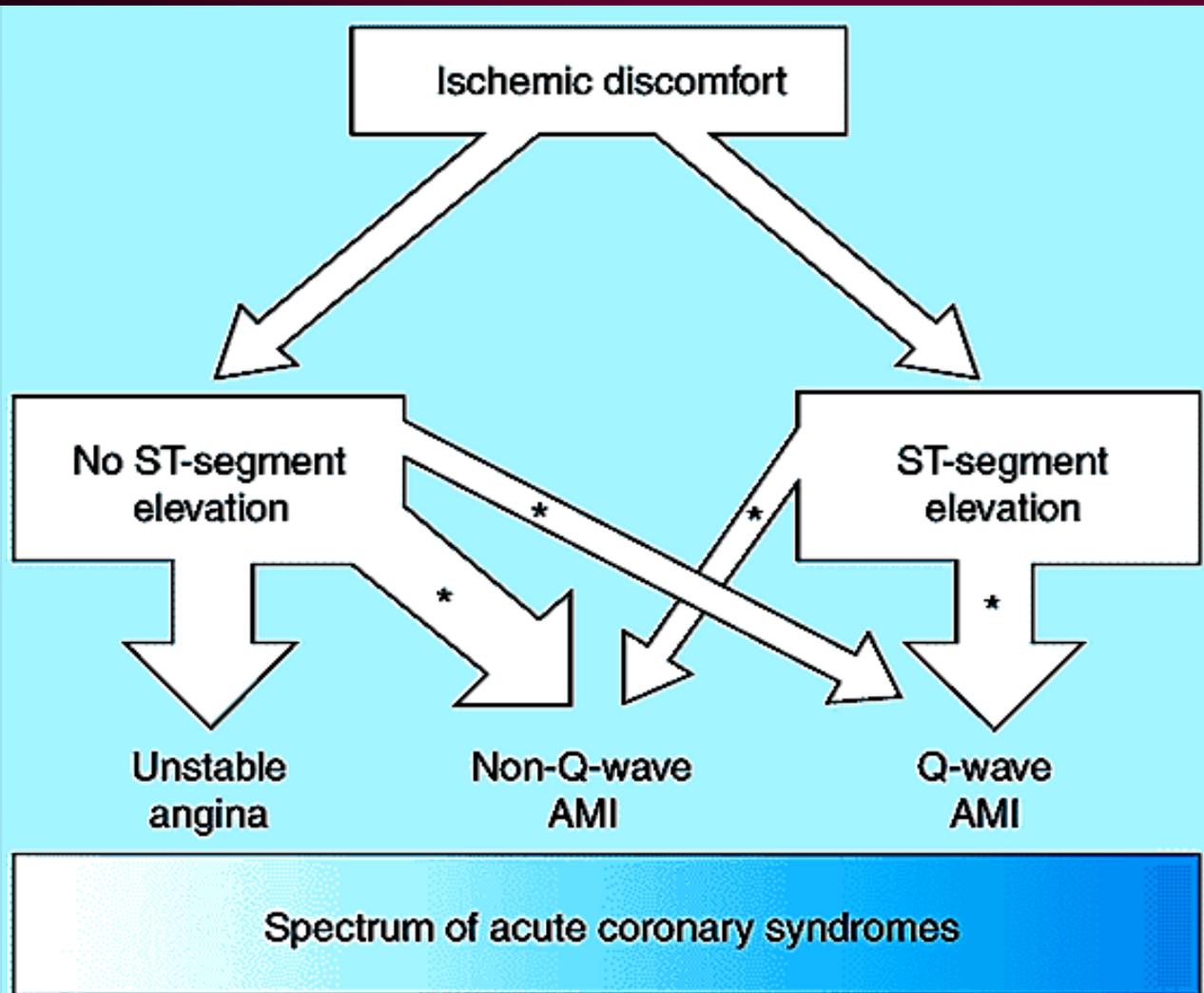
myocardial

Patients with ischemic chest pain who present with deep T-wave inversions in multiple precordial leads (V₁ to V₄) with or without cardiac enzyme elevations we can put diagnosis of NQWMI.

Severe anterior wall ischemia (*Non-Q-wave myocardial infarction*) cause prominent T-wave inversions in the precordial leads.



Variability of ECG patterns with acute myocardial ischemia. All of that pathological states names ***acute coronary syndromes***.



* = Positive serum cardiac marker.

Of the patients who present without ST-segment elevation, most (large arrows) are diagnosed as having unstable angina or NQMI on the basis of the presence or absence of a cardiac marker such as CKMB detected in the serum; a minority of such patients ultimately develop a QWMI.

The clinical conditions in the spectrum ranging from unstable angina through NQWMI to QWMI are referred to as the **acute coronary syndromes**.

Acute coronary syndromes. Patients with ischemic discomfort may present with or without ST-segment elevation on the electrocardiogram. Of patients with ST-segment elevation, most (large arrow) ultimately develop a QWMI, while a minority (small arrow) develop a NQWMI.

Imaging Studies:

Chest radiographs

Upon presentation, obtain a chest film to assess patient's heart size and the presence or absence of decompensated CHF with or without pulmonary edema.

It also may assist in diagnosing concomitant disease, such as pneumonia in an elderly patient, as a precipitating cause for MI.

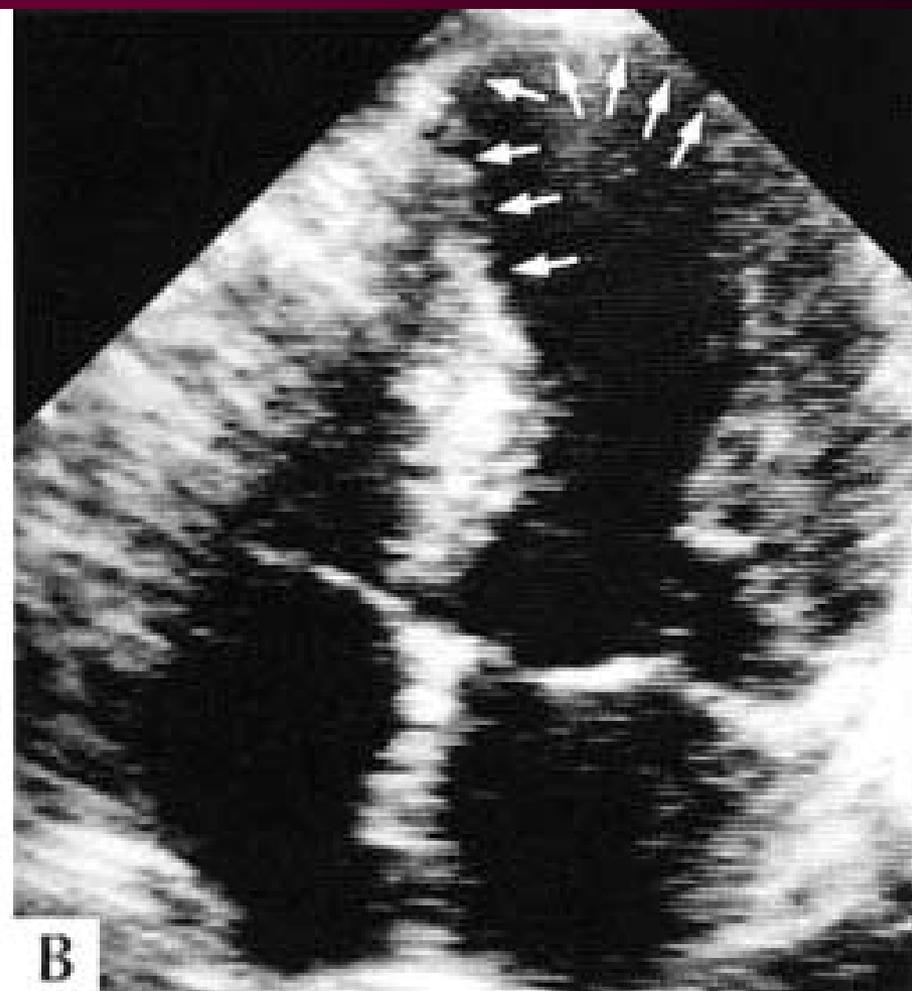
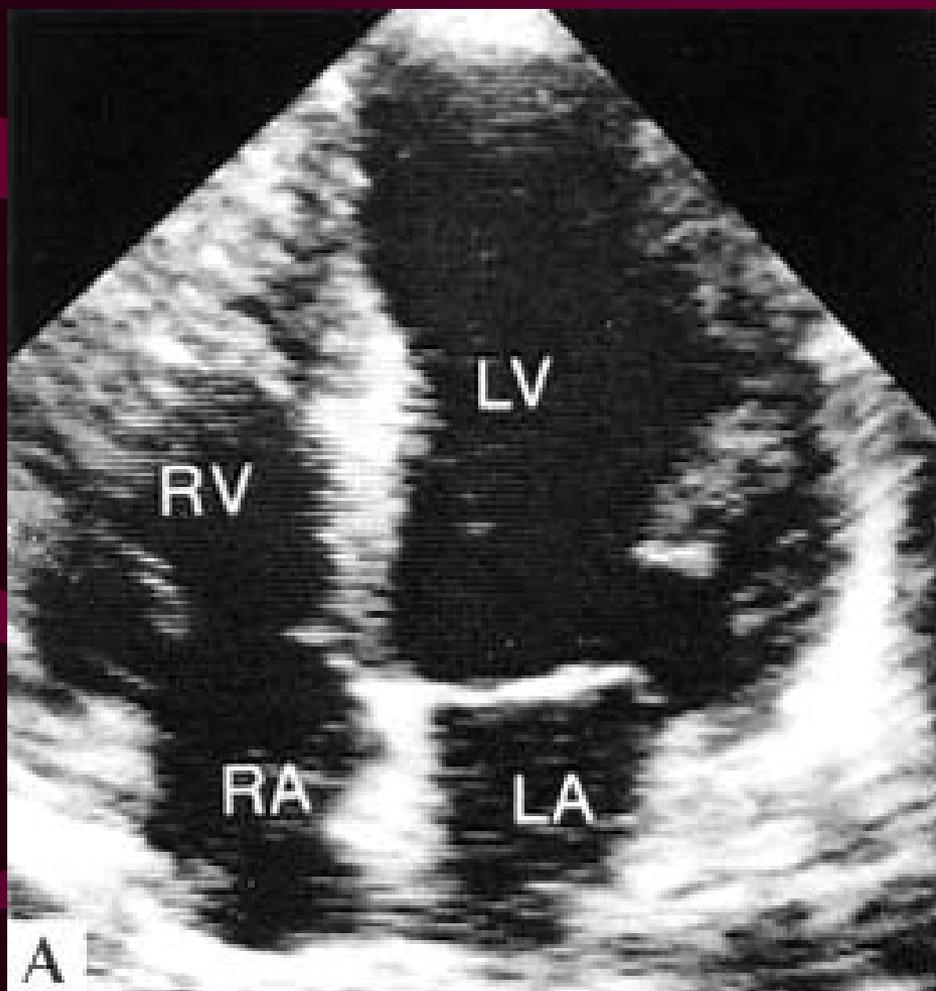
Echocardiography

An echocardiogram may play an important role in the setting of MI.

Regional wall motion abnormalities can be identified, which are especially helpful if the diagnosis is questionable.

An echocardiogram also can define the extent of the infarction and assess overall left ventricle (LV) and right ventricle (RV) function.

An echocardiogram can identify complications, such as acute MR, LV aneurysm, LV rupture, or pericardial effusion.



Echocardiographic wall motion abnormality coronary artery disease.
A, Two-dimensional echocardiographic apical four-chamber view at end-diastole.
B, Two-dimensional echocardiographic apical four-chamber view at end-systole.
The right ventricle (RV) and the septal and lateral walls at the base of the left ventricle (LV) demonstrate normal inward motion from diastole through systole; however, the distal septum and apex demonstrate akinesia (arrows in B). The wall motion abnormality demonstrated in this frame was caused by ischemia from a lesion in the mid-left anterior descending artery.
LA - left atrium; RA - right atrium.

Myocardial perfusion imaging

Prior to discharge, obtain myocardial perfusion imaging to assess the extent of residual ischemia if the patient has not undergone cardiac catheterization. The extent of ischemia can guide further therapy as to whether to proceed with catheterization or to continue conservative therapy.

Myocardial perfusion has been shown to be a valuable method for triage of patients with chest pain in the ED.

Cardiac angiography

Cardiac catheterization defines the patient's coronary anatomy and the extent of the disease.

At this time, the ACC and AHA recommend the conservative approach, which is to proceed to catheterization only if indicated by variables such as recurrent chest pain or significant ischemia shown by perfusion imaging.

Patients with cardiogenic shock, intractable angina despite medications, or severe pulmonary congestion should undergo cardiac catheterization immediately.

Medical Care

Initial therapy for acute MI is directed toward restoration of perfusion in order to salvage as much of the jeopardized myocardium as possible.

This may be accomplished through medical or mechanical means, such as angioplasty or coronary artery bypass grafting.

Further treatment is based on

- (1) restoration of the balance between the oxygen supply and demand to prevent further ischemia,
- (2) pain relief, and
- (3) prevention and treatment of any complications that may arise.

Pain control

Pain control is essential to quality patient care. Analgesics ensure patient comfort, have sedating properties, which are beneficial for patients who experience pain.

Nitroglycerin (Nitro-Bid) - Causes relaxation of vascular smooth muscle via stimulation of intracellular cGMP production, causing decrease in BP.

Dose 400 mcg SL or spray q 5 min, repeat up to 3 times; if symptoms persist, 5-10 mcg/min IV infusion; titrate to 10% reduction in MAP or symptom relief, limiting adverse effects of hypotension.

Contraindications - Documented hypersensitivity; severe anemia; shock; postural hypotension; head trauma; closed-angle glaucoma; cerebral hemorrhage; known history of RV MI.

Precautions - Exercise caution in patients with CAD or low systolic BP.

Thrombolytic therapy

Thrombolytic therapy has been shown to improve survival rates in acute MI if administered in a timely fashion in the appropriate group of patients.

The optimal approach is to administer thrombolytics within 12 hours of onset of symptoms in patients with ST-segment elevation greater than 0.1 mV in two or more contiguous ECG leads, new left bundle-branch block (LBBB).

Recent trials show an even greater patency rate if a IIb/IIIa receptor antagonist, such as abciximab, is combined with a half dose of a thrombolytic agent as the initial reperfusion strategy.

Alteplase (Activase) (tissue plasminogen activator, t-PA) - Fibrin-specific agent with brief half-life of 5 min. Adjunctive therapy with IV heparin necessary to maintain patency of arteries recanalized by t-PA, especially during first 24-48 h.

Dose - 15 mg IV initial bolus, followed by 50 mg IV over next 30 min, and then 35 mg IV over next h; total dose not to exceed 100 mg.

Contraindications - Documented hypersensitivity; active internal bleeding; recent intracranial or intraspinal surgery or trauma; intracranial neoplasm; AV malformation or aneurysm; history of cerebrovascular accident within last 2 mo; seizure at onset of stroke; suspicion of subarachnoid hemorrhage; bleeding diathesis; serious head trauma; severe uncontrolled hypertension; do not administer to patients with history of intracranial hemorrhage.

Streptokinase (Kabikinase, Streptase) - Acts with plasminogen to convert plasminogen to plasmin. Plasmin degrades fibrin clots, as well as fibrinogen and other plasma proteins. Increase in fibrinolytic activity that degrades fibrinogen levels for 24-36 h occurs with IV infusion of streptokinase. Adjunctive therapy with heparin not needed.

Dose - 1.5 million IU in 50 cc D5W IV over 60 min

Contraindications - Documented hypersensitivity; active internal bleeding; intracranial neoplasm; aneurysm; bleeding diathesis; severe uncontrolled arterial hypertension.

Precautions - Use with caution in patients with severe hypertension, those receiving medication via IM administration, and those who had trauma or surgery in previous 10 d; measure hematocrit, platelet count, aPTT, TT, PT, or fibrinogen levels before therapy initiated; either TT or aPTT should be less than twice normal control value following infusion and before instituting heparin; do not take BP in lower extremities, it may dislodge possible deep vein thrombus; monitor PT, aPTT, TT, or fibrinogen 4 h after initiation of therapy.

Aspirin and/or antiplatelet therapy

Aspirin has been shown to decrease mortality and re-infarction rates after MI.

Administer aspirin immediately, which the patient should chew if possible upon presentation. Continue aspirin indefinitely unless an obvious contraindication, such as a bleeding tendency or an allergy, is present.

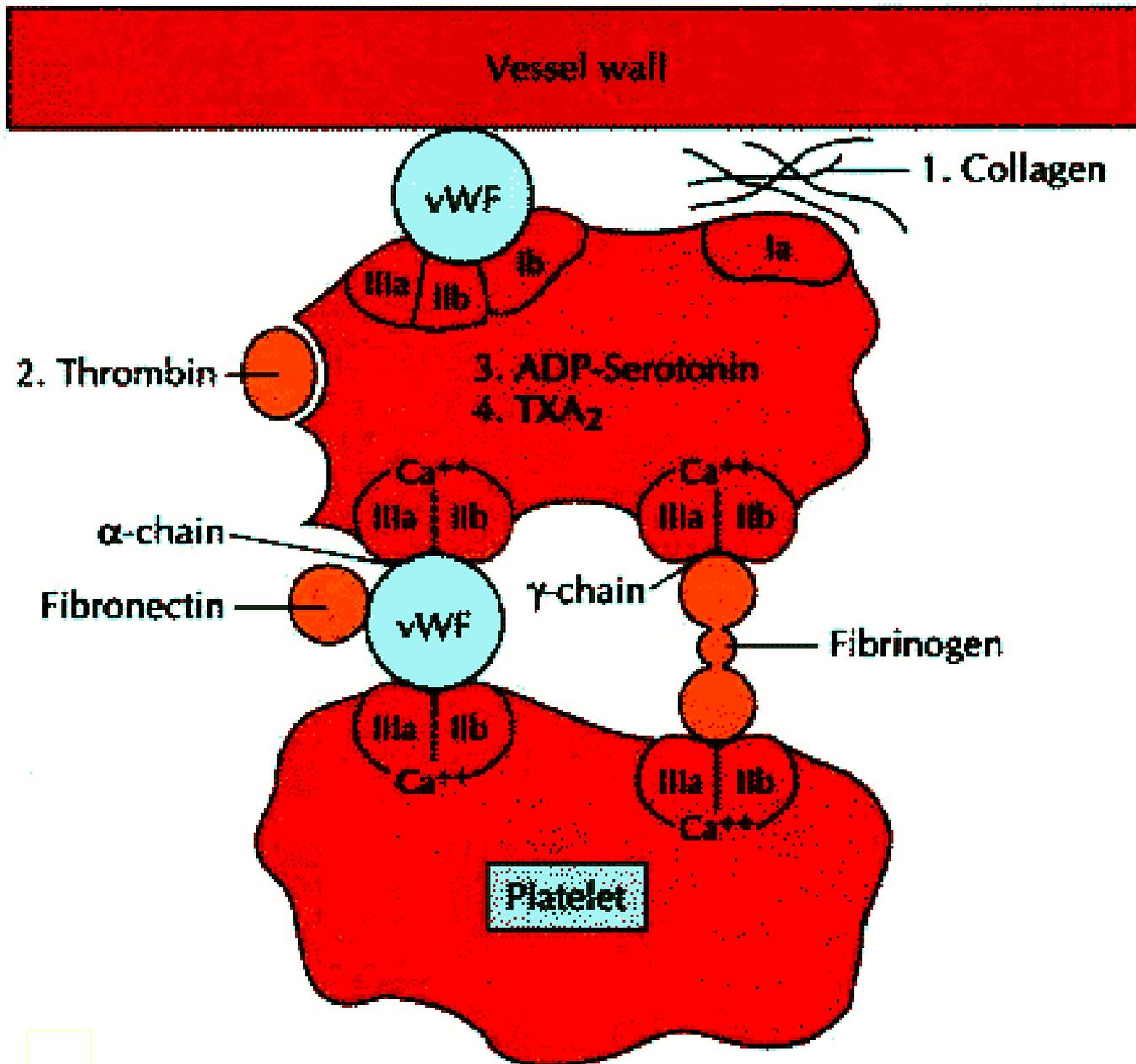
Clopidogrel may be used as an alternative to aspirin in cases of aspirin resistance or allergy.

Administer a platelet glycoprotein (GP) IIb/IIIa-receptor antagonist, in addition to acetylsalicylic acid and unfractionated heparin (UFH), to patients with continuing ischemia or with other high-risk features and to patients in whom a percutaneous coronary intervention (PCI) is planned.

Eptifibatide and **tirofiban** are approved for this use.

Abciximab also can be used for 12-24 hours in patients with unstable angina or non-ST-segment elevation MI in whom a PCI is planned within the next 24 hours.

GP IIb/IIIa blockade at the platelet surface



Abciximab (ReoPro) - Chimeric human-murine monoclonal antibody. Binds to receptor with high affinity and reduces platelet aggregation by 80%. Inhibition of platelet aggregation persists for as long as 48 h after infusion stopped.

Dose - 0.25 mcg/kg bolus, followed by 0.125 mcg/kg/min infusion for 12 h

Contraindications - Documented hypersensitivity; bleeding diathesis; thrombocytopenia (<100,000 platelets/mL); recent trauma; intracranial tumor; severe uncontrolled hypertension; history of vasculitis; cerebrovascular accident within 2 y.

Precautions - Bleeding complications are rare and usually related to use of standard-dose heparin instead of weight-based dosing; severe thrombocytopenia has been associated with abciximab within first 24 h of use.

Eptifibatide (Integrilin) - Cyclic peptide that reversibly inhibits platelet aggregation by binding to IIb/IIIa receptor.

Dose - Unstable angina: 180 mcg/kg IV bolus, followed by 2 mcg/kg/min continuous infusion until discharge or surgery

Patients undergoing PCI: 135 mcg/kg IV bolus before PCI, followed by 0.5 mcg/kg/min continuous infusion.

Measure ACT and maintain aPTT at 50-70 s unless PCI necessary; maintain ACT at 250-300 s during PCI; if platelets decrease to $<100,000/\text{mL}$, discontinue GP IIb/IIIa inhibitors and heparin and appropriately monitor and treat condition.

Clonidogrel (Plavix) - Selectively inhibits adenosine diphosphate (ADP) binding to platelet receptor and subsequent ADP-mediated activation of glycoprotein IIb/IIIa complex, thereby inhibiting platelet aggregation.

This agent is used as an alternative to aspirin or in addition to aspirin after coronary stenting.

Dose CURE protocol for unstable angina patients within 24 h of symptom onset: 300 mg loading dose followed by 75 mg PO qd for 3-12 mo (mean = 9 mo) in conjunction with aspirin 75-325 mg/d PO.

Contraindications - Documented hypersensitivity; active pathological bleeding, such as peptic ulcer, or intracranial hemorrhage.

Precautions - Caution in patients at increased risk of bleeding from trauma, surgery, or other pathological conditions; caution in patients with lesions with propensity to bleed (ulcers).

Heparin

Heparin (and other anticoagulant agents) has an established role as an adjunctive agent in patients receiving t-PA but not with streptokinase. Heparin also is indicated in patients undergoing primary angioplasty. Little data exist with regard to efficacy in patients not receiving thrombolytic therapy in the setting of acute MI.

Dose - 70 IU/kg IV bolus, followed by 15 mcg/kg/h infusion, adjust to maintain aPTT 1.5-2 times control.

Contraindications - Documented hypersensitivity, subacute bacterial endocarditis; active bleeding; history of heparin-induced thrombocytopenia.

Precautions - Observe for prolonged or excessive bleeding at venipuncture sites; some preparations contain benzyl alcohol as preservative, and benzyl alcohol used in large amounts has been associated with fetal toxicity (gasping syndrome); use of preservative-free heparin recommended in neonates; use with caution in patients with shock or severe hypotension

Low-molecular-weight heparins

Low-molecular-weight heparins (LMWHs) have been shown to be superior to UFHs in patients with unstable angina or NQWMI.

Low-molecular-weight heparins augments activity of antithrombin III and prevents conversion of fibrinogen to fibrin. Does not actively lyse but is able to inhibit further thrombus formation. Prevents reaccumulation of clot after spontaneous fibrinolysis.

Enoxaparin (Lovenox) -- Enhances inhibition of factor Xa and thrombin by increasing antithrombin III activity. In addition, preferentially increases inhibition of factor Xa.

Dose - 1 mg/kg SC bid.

Contraindications - Documented hypersensitivity; major bleeding; history of heparin-induced thrombocytopenia.

Enoxaparin

Precautions - Caution in recent surgery, GI lesions that may be prone to bleeding, hematologic conditions, uncontrolled hypertension, diabetic retinopathy, or vitreous hemorrhage; caution in patients with renal insufficiency because elimination delayed, increasing anticoagulant effect; if thromboembolic event occurs despite LMWH prophylaxis, discontinue drug and initiate appropriate therapy; reversible elevation of hepatic transaminases seen occasionally; heparin-induced thrombocytopenia has been seen with LMWH; for significant bleeding complications, 1 mg of protamine sulfate reverses effect of approximately 1 mg of enoxaparin.

Nitrates

Nitrates have no apparent impact on mortality rate in patients with ischemic syndromes.

Their utility is in symptomatic relief and preload reduction. Administer to all patients with acute MI within the first 48 hours of presentation, unless contraindicated (ie, in RV infarction).

Nitroglycerin (Nitro-Bid) -- Causes relaxation of vascular smooth muscle via stimulation of intracellular cyclic guanosine monophosphate production, causing decrease in BP.

Dose - 400 mcg SL or spray q5min, repeat up to 3 times; if symptoms persist, 5-10 mcg/min IV infusion; titrate to 10% reduction in MAP or symptom relief, limiting adverse effects of hypotension.

Contraindications - Documented hypersensitivity; severe anemia; shock; postural hypotension; head trauma; closed-angle glaucoma; cerebral hemorrhage; known history of RV MI.

Interactions - calcium channel blockers may cause marked symptomatic orthostatic hypotension (dose adjustment of either agent may be necessary).

Precautions - Exercise caution in patients with CAD or low systolic BP.

Beta-blockers

Beta-blockers reduce the rates of reinfarction and recurrent ischemia and possibly reduce mortality rate if administered within 12 hours after MI. Administer routinely to all patients with MI unless a contraindication is present.

Metoprolol (Lopressor) -- selective beta₁-adrenergic receptor blocker that decreases automaticity and contractions. Goals of treatment are reduction in heart rate to 60-80 bpm. During IV administration, carefully monitor BP, heart rate, and ECG.

Dose - 5 mg IV slow infusion q5min; not to exceed 15 mg or desired heart rate. 25 mg PO bid usual initial dose, up to 100 mg bid; titrate to desired effect.

Contraindications - Documented hypersensitivity; decompensated CHF; bradycardia; bronchial asthma; cardiogenic shock; AV conduction abnormalities.

Precautions - Do not use in cocaine-related ischemia; beta-adrenergic blockade may reduce signs and symptoms of acute hypoglycemia and may decrease clinical signs of hyperthyroidism; abrupt withdrawal may exacerbate symptoms of hyperthyroidism, including thyroid storm, monitor patient closely and withdraw drug slowly; during IV administration, carefully monitor BP, heart rate, and ECG.

ACE inhibitors

ACE inhibitors reduce mortality rates after MI.

Administer ACE inhibitors as soon as possible as long as the patient has no contraindications and remains in stable condition.

ACE inhibitors have the greatest benefit in patients with ventricular dysfunction.

Continue ACE inhibitors indefinitely after MI.

Angiotensin-receptor blockers may be used as an alternative in patients who develop adverse effects, such as a persistent cough, although initial trials need to be confirmed.

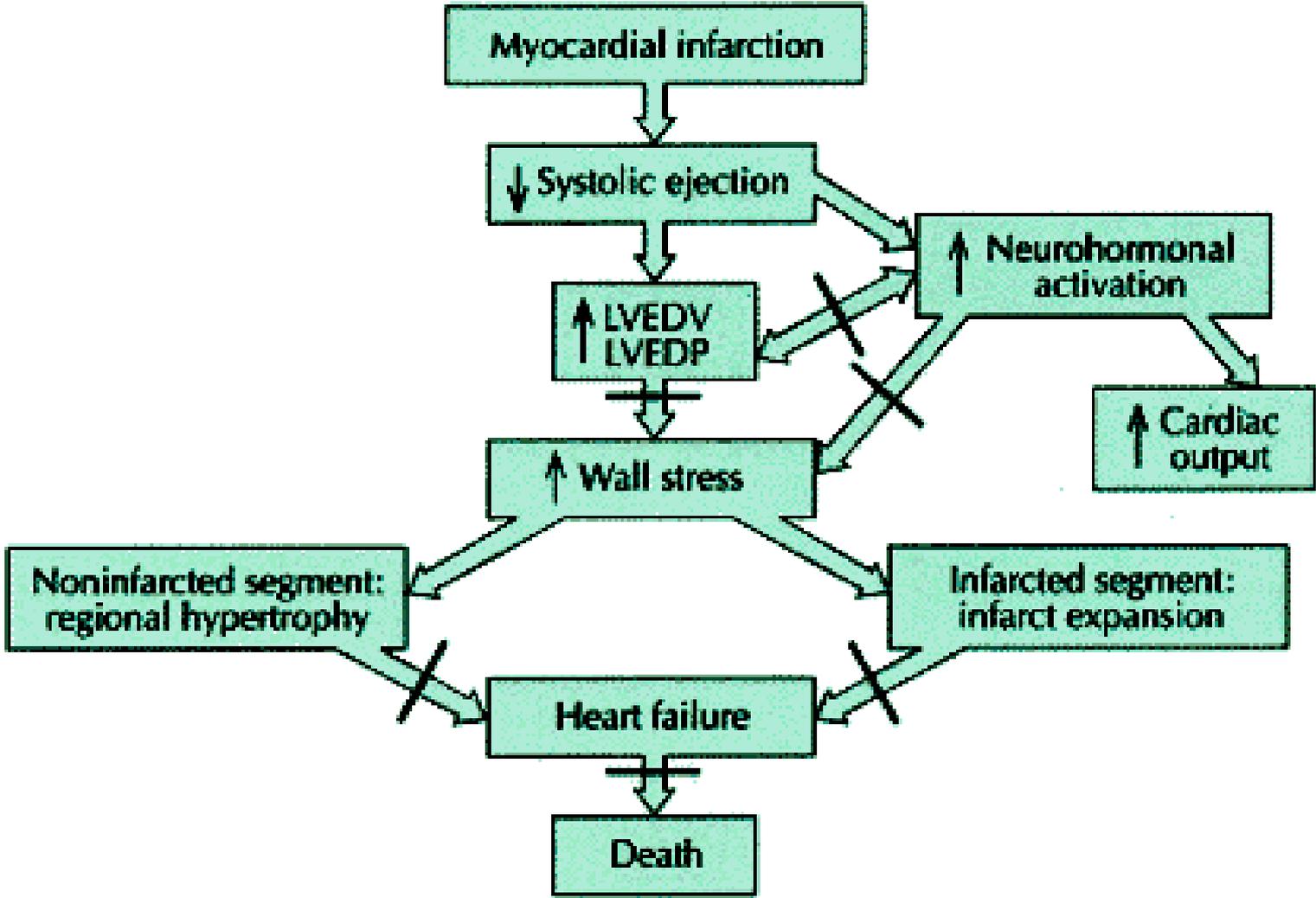
Captopril (Capoten) - Has short half-life, which makes it important drug for initiation of ACE inhibitor therapy. Can be started at low dose and titrated upward as needed and as patient tolerates.

Dose - 6.25 mg PO tid initially; may titrate to total 450 mg/d.

Contraindications - Documented hypersensitivity.

Precautions - Administer with caution in patients with renal insufficiency and those with borderline low BP; may worsen renal function, especially in patients with bilateral renal artery stenosis; administer cautiously in patients with aortic stenosis because afterload reduction may worsen coronary perfusion.

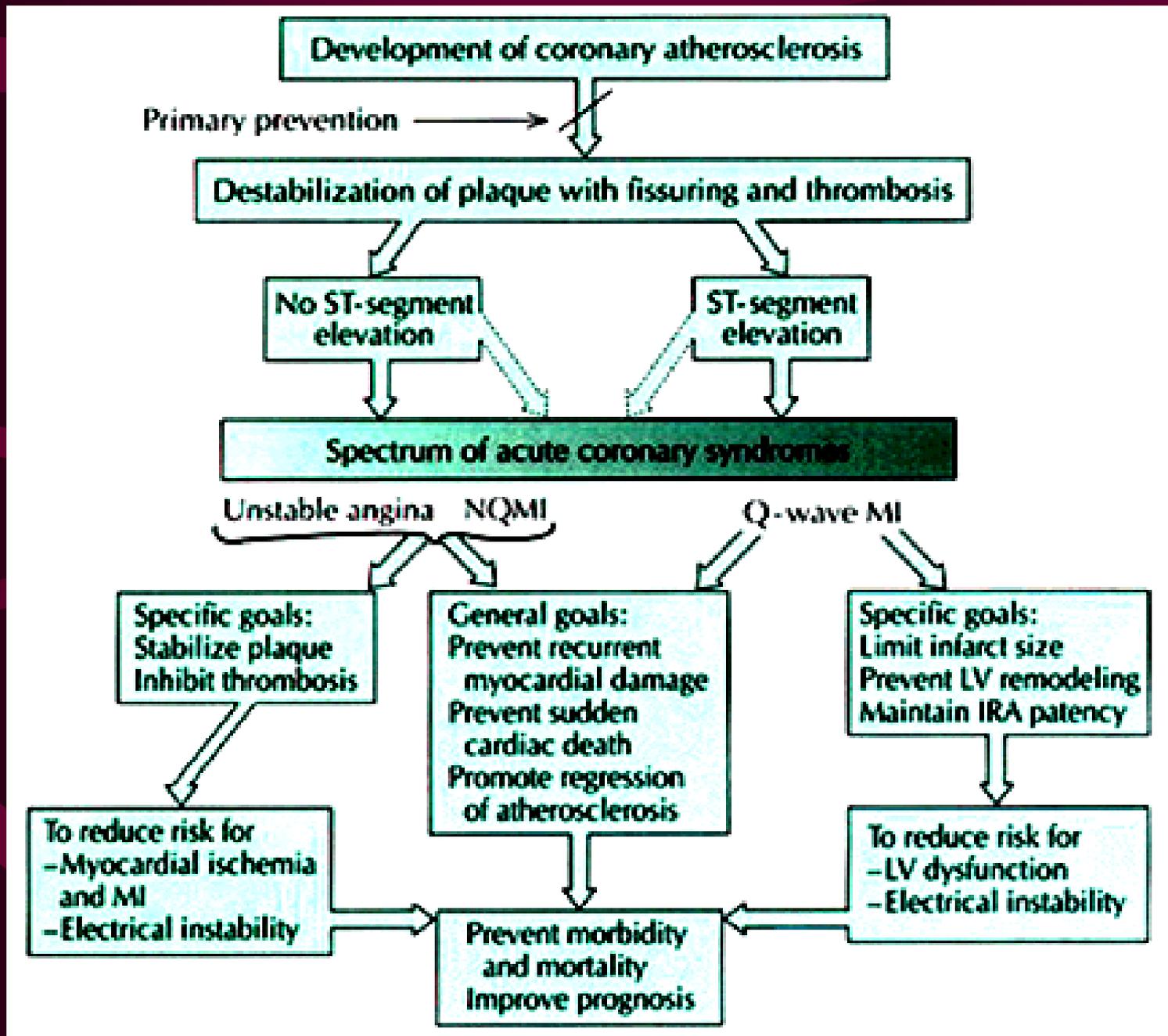
Potential role of ACE inhibitors in left ventricular remodeling



LVEDPs left ventricular end-diastolic pressure;
LVEDVs left ventricular end-diastolic volume.

Shown with intersecting bars are sites at which an ACE inhibitor may interrupt an adverse consequence of myocardial infarction that would contribute to heart failure or death.

Major goals of medical therapy for acute coronary syndromes



ST elevation: Suspected acute Q-wave MI

ASA
 β -Blockade
heparin

≤ 12 h

> 12 h

Eligible for
thrombolytic
therapy

Thrombolytic
therapy
contraindicated

Not a candidate
for reperfusion
therapy

Persistent
symptoms?

Thrombolytic
therapy:
Front-loaded
t-PA or SK

Primary
PTCA

No

Yes

Other medical therapy:
ACE inhibitors
? Nitrates
? Magnesium

Consider
reperfusion
therapy

A. All patients suspected of having a Q-wave myocardial infarction (MI) (i.e., ST-segment elevation on ECG) should receive aspirin (ASA), beta blockers, and an antithrombin [particularly if tissue-type plasminogen activator (t-PA) is used for thrombolytic therapy]. Heparin is probably not required in patients receiving streptokinase (SK). Patients treated within 12 h who are eligible for thrombolytic therapy should expeditiously receive either t-PA or SK or be considered for primary percutaneous transluminal coronary angioplasty (PTCA). Immediate, primary PTCA is also to be considered when lytic therapy is contraindicated. Patients treated after 12 h should receive the initial medical therapy noted above and, on an individual basis, may be candidates for β -blockers and ACE inhibitors.

**ST depression/T-wave inversion:
Suspected AMI**

**Heparin+ASA
Nitrates for recurrent angina**

Patients without prior beta
blocker/therapy or who are
inadequately treated on
current dose of beta blocker

Persistent symptoms in
patients with prior beta
blocker/therapy or
who cannot tolerate

Establish adequate
beta blockade

Add calcium
antagonist

Assess clinical status

High-risk patient:
1. Recurrent ischemia
2. Depressed LV function
3. Widespread ECG changes
4. Prior MI

Clinical stability

Anatomy suitable
for revascularization

Yes

No

Continued observation
in hospital
Consideration of
stress testing

Revascularization
(PTCA, CABG)

Medical therapy

B. All patients without ST elevation should be treated with an antithrombin and aspirin.

Nitrates should be administered for recurrent episodes of angina. Adequate beta blockade should then be established; when that is not possible or contraindications exist, a calcium antagonist can be considered. Patients at high risk should be triaged to cardiac catheterization with plans for revascularization if clinically suitable, while patients who are clinically stable can be treated more conservatively with continued observation in the hospital and consideration of a stress test to screen for any provokable myocardial ischemia. (CABG, coronary artery bypass grafting; LV, left ventricular.)

Surgical Care:

Primary angioplasty

Primary percutaneous transluminal coronary angioplasty (PTCA) is an attractive alternative to thrombolytic therapy. PTCA provides greater coronary patency (>96% thrombolysis in myocardial infarction [TIMI] 3 flow), lower risk of bleeding, and instant knowledge about the extent of the underlying disease.

The widespread use of stenting and adjunctive IIb/IIIa therapy are improving the results of primary PTCA.

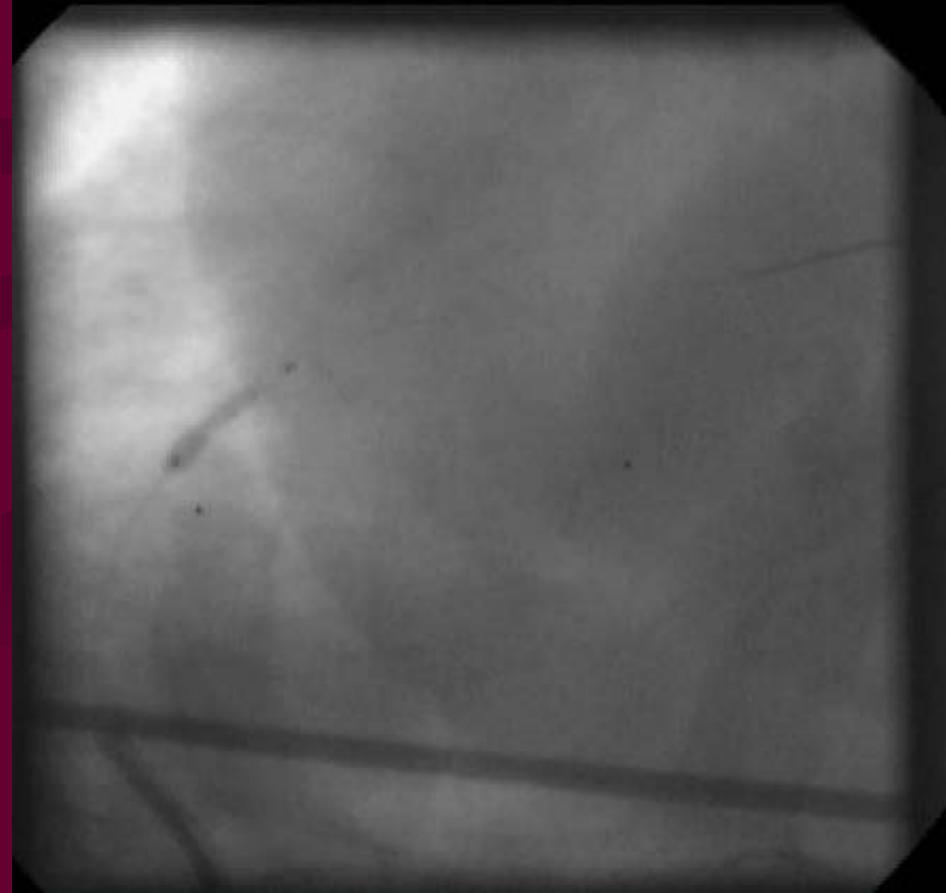
A recently published trial showed that, in patients with acute MI, coronary stenting plus abciximab leads to a greater degree of myocardial salvage and a better clinical outcome than does fibrinolysis with a t-PA.

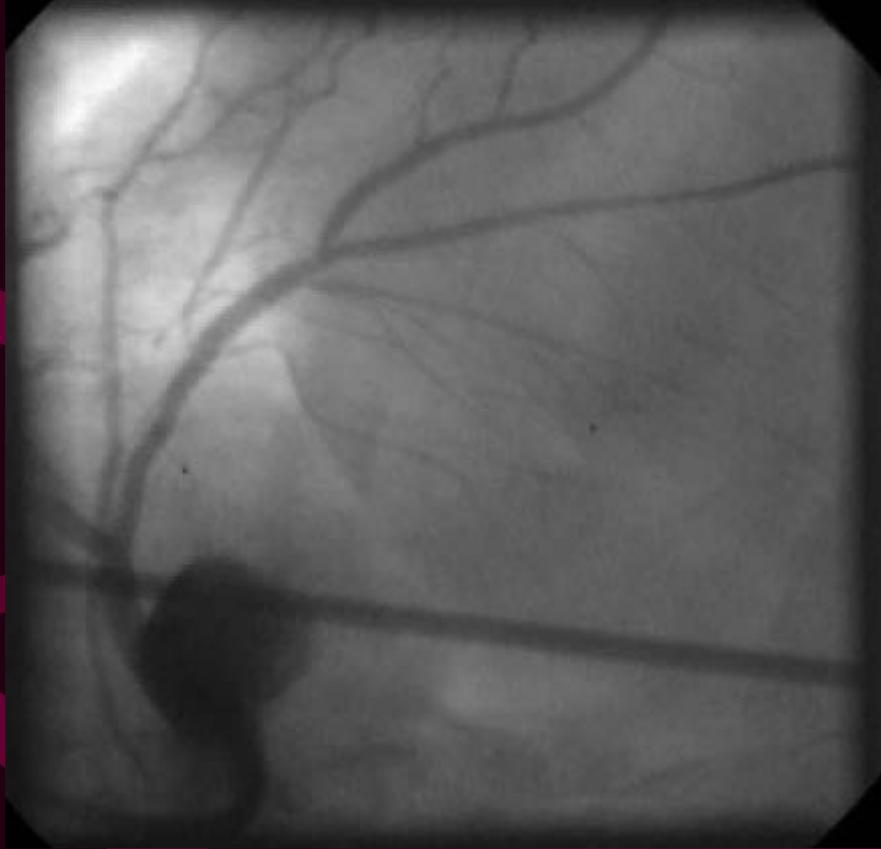
Cardiac catheterization and angioplasty are indicated in patients who do not fit the above-mentioned criteria for thrombolytic therapy or have persistent ischemia.

Primary angioplasty also is the treatment of choice in patients with cardiogenic shock, patients in whom thrombolysis failed, and those with high risk of bleeding or contraindications to thrombolytic therapy.

Emergent or urgent coronary artery graft bypass surgery is indicated in patients in whom angioplasty fails and in patients who develop mechanical complications such as a VSD, LV rupture, or a papillary muscle rupture.

Drug-Eluting Stents (DES)





The Problem of Restenosis



Drug Coated Stents

Potential benefits

- Can be used as initial therapy
- Less expensive
- Less risk of subacute thrombosis

Major challenge: Appropriate delivery

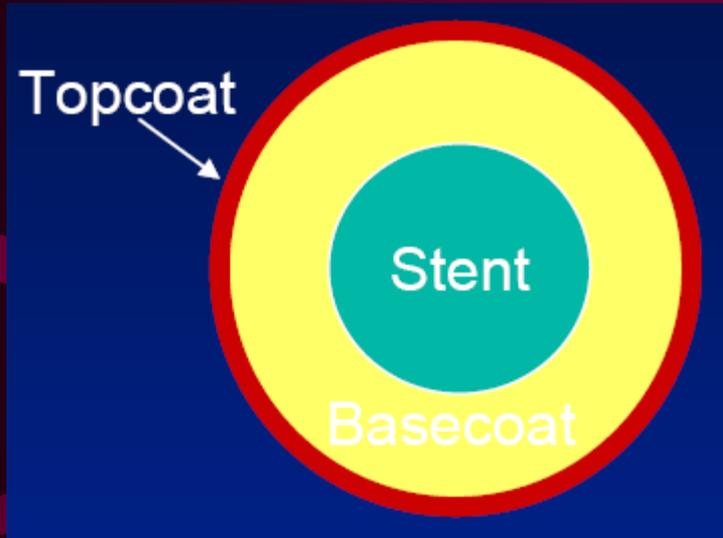
Medium

Potential Drugs

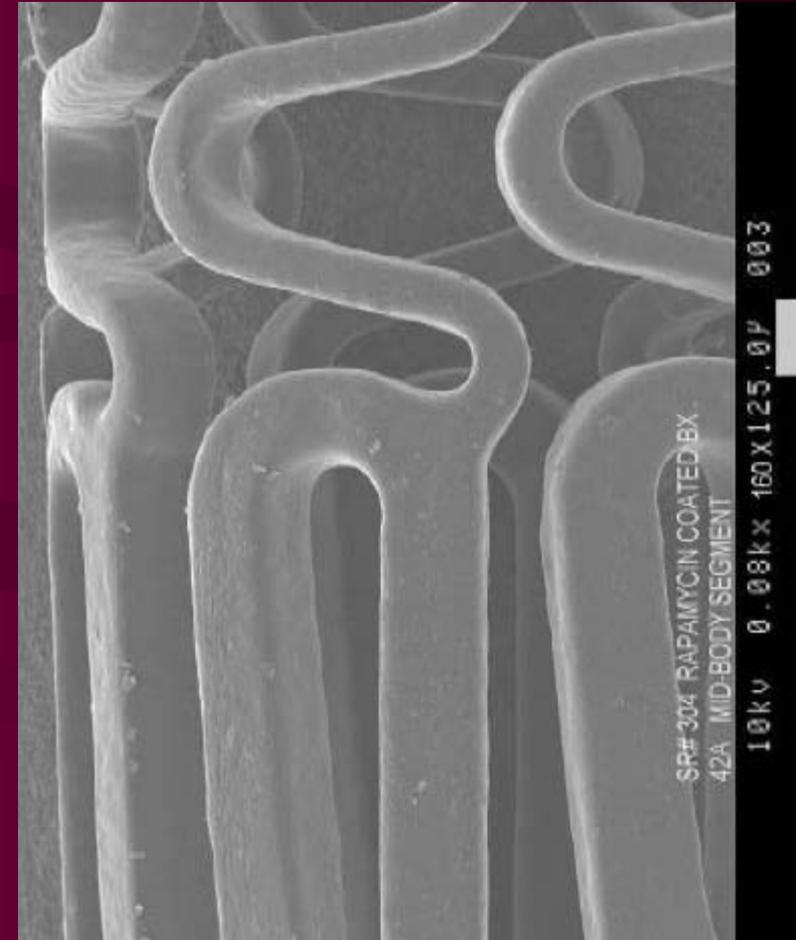
- Rapamycin (Sirolimus)
- Taxol
- Many others

Sirolimus-Coated Bx Velocity™ Stent

1X-TC Formulation



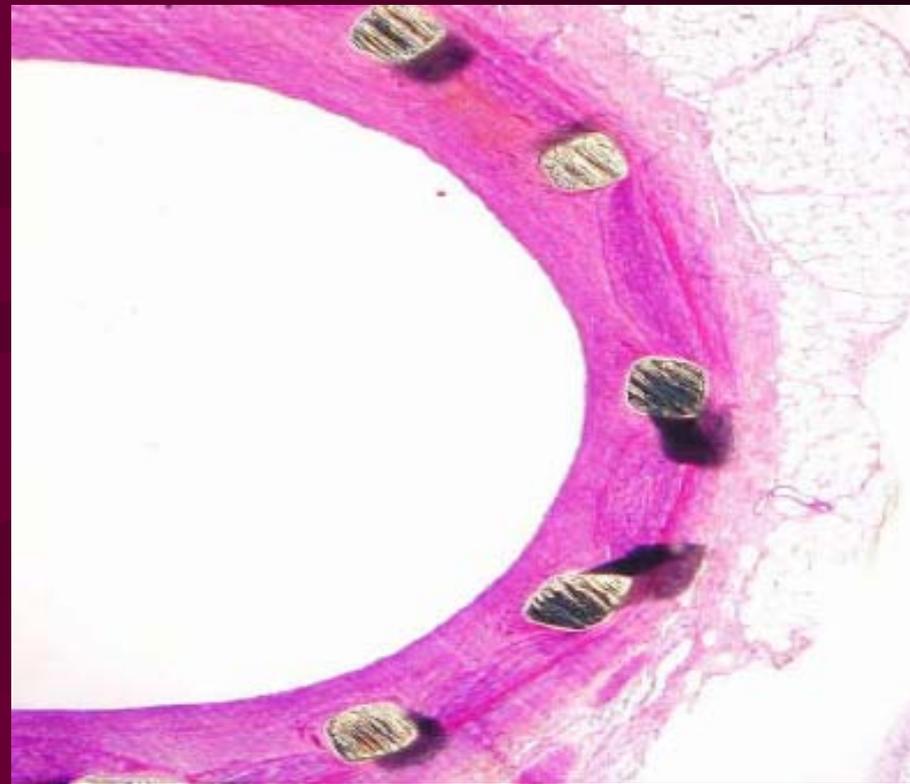
- Basecoat
 - A + B + Sirolimus
 - Contains fixed dose sirolimus/cm²
- Topcoat
 - B only



Sirolimus Coating Modulates Neointima in 30-Day Porcine Coronary Model



Control



+ Sirolimus

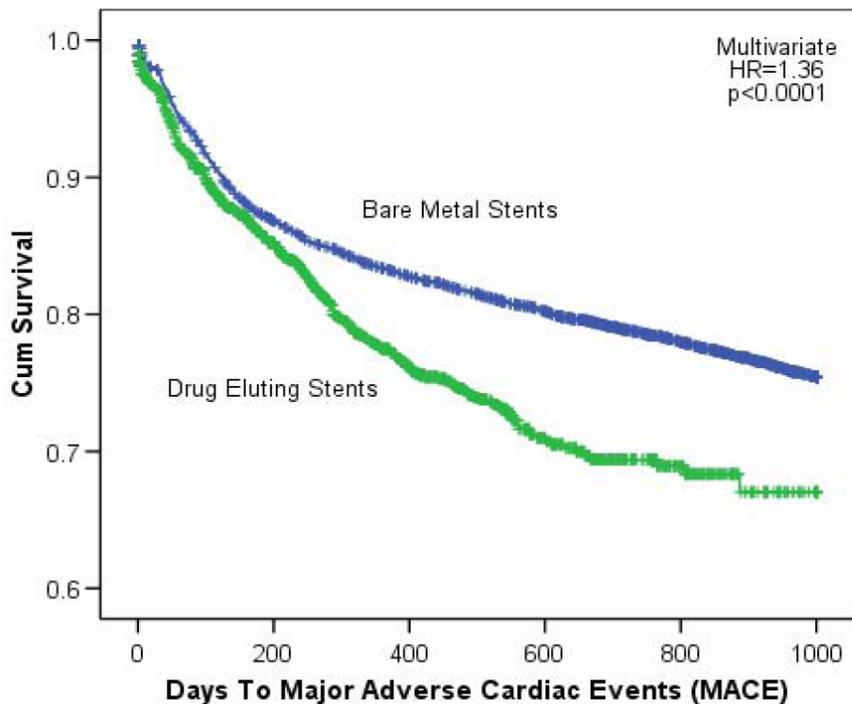
Reendothelialization of Sirolimus-Coated Stent in 30-day Porcine Coronary Model

Endothelial Monolayer

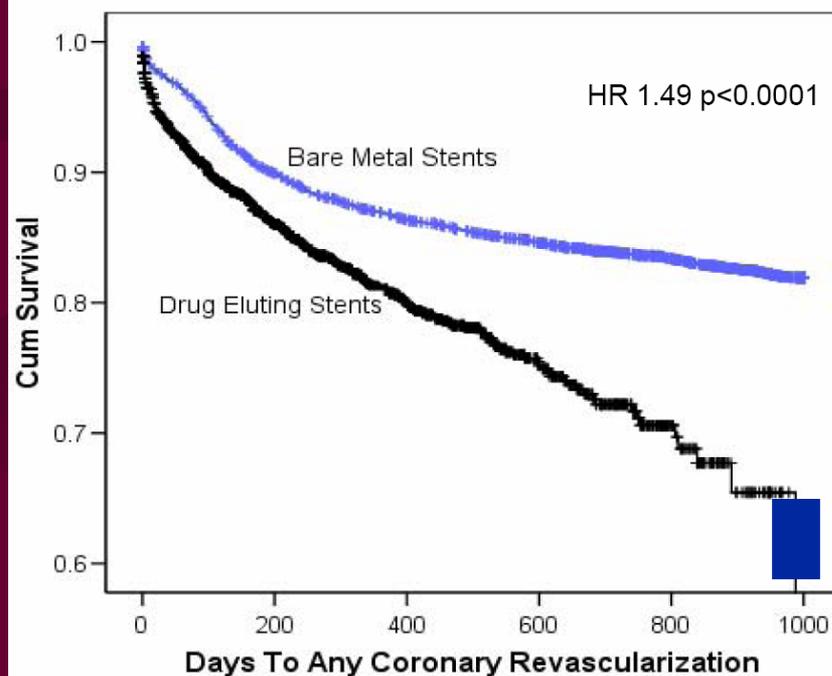


40x

Outcomes: 3 Year MACE



Any Revascularization



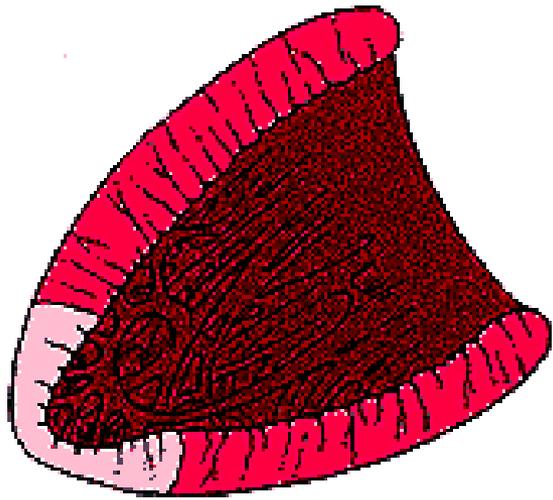
Diet

A low-salt, low-fat, and low-cholesterol diet generally is recommended.

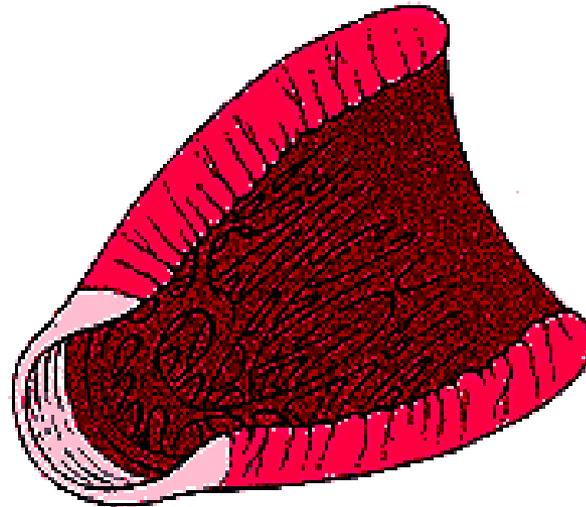
Activity:

Confine patients to bed rest to minimize oxygen consumption until reperfusion and initial therapy are complete.

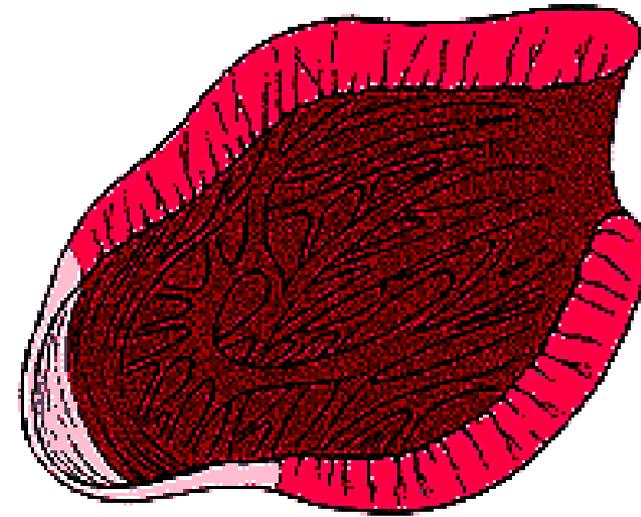
This usually lasts about 24-48 hours; after that, the patient's activity may be accelerated slowly as tolerated and as the clinical situation allows.



Acute infarction
(hours)



Infarct expansion
(hours to days)



Global remodeling
(days to months)

Left ventricular remodeling after myocardial infarction (MI).

The Classification of Left Ventricular Pump Failure Proposed by Killip (1967):

Class I, no signs of pulmonary or venous congestion;

Class II, moderate heart failure as evidenced by rales at the lung bases, gallop rhythm, tachypnea, or signs of failure of the right side of the heart, including venous and hepatic congestion;

Class III, severe heart failure, pulmonary edema;

Class IV, shock with systolic pressure less than 90 mmHg and evidence of peripheral vasoconstriction, peripheral cyanosis, mental confusion, and oliguria.

The expected hospital mortality rate of patients in these clinical classes when this classification was established in 1967 was as follows: class I, 0 to 5 percent; class II, 10 to 20 percent; class III, 35 to 45 percent; and class IV, 85 to 95 percent. With advances in management, the mortality rate has fallen, perhaps by as much as one-third to one-half, in each class.

CARDIOGENIC SHOCK

Cardiogenic shock is characterized by marked hypotension with systolic arterial pressure of <80 mmHg and a marked reduction of cardiac index [<1.8 L/(min/m²)] in the face of an elevated left ventricular filling (pulmonary capillary wedge) pressure (>18 mmHg). Cardiogenic shock is generally associated with a mortality rate of >70 percent.

Risk factors for the in-hospital development of shock include advanced age, a depressed left ventricular ejection fraction on admission, a large infarct, previous myocardial infarction, and a history of diabetes mellitus.

Patients with several of these risk factors should be considered for cardiac catheterization and mechanical reperfusion *before* the development of shock.

Clinical picture of cardiogenic shock

Patients in shock usually appear ashen or cyanotic and have cool skin and mottled extremities.

Peripheral pulses are rapid and faint and may be irregular if arrhythmias are present.

Jugular venous distention and crackles in the lungs are usually present.

Peripheral edema also may be present.

Heart sounds are distant, and third and fourth heart sounds may be present.

The pulse pressure may be low, and patients are usually tachycardic.

Patients show signs of hypoperfusion, such as altered mental status and decreased urine output.

A systolic murmur is generally heard in patients with acute mitral regurgitation or ventricular septal rupture.

Treatment of cardiogenic shock

Initial management includes fluid resuscitation to correct hypovolemia and hypotension, unless pulmonary edema is present.

Central venous lines are often required. Swan-Ganz catheterization and continuous percutaneous oximetry are routine.

Oxygenation and airway protection are critical; intubation and mechanical ventilation are commonly required.

Correction of electrolyte and acid-base abnormalities, such as hypokalemia, hypomagnesemia, and acidosis, are essential.

The relief of pain is important, as some vasodepressor reflex activity may be a response to severe pain.

Dopamine, norepinephrine, and epinephrine are vasoconstricting drugs that help maintain adequate blood pressure and help preserve perfusion pressure for optimizing flow in various organs.

Hemodynamic support

Dopamine is a precursor of norepinephrine and epinephrine and has varying effects according to the doses infused. A dose of less than 5 mcg/kg/min causes vasodilation of renal, mesenteric, and coronary beds. At a dose of 5-10 mcg/kg/min, beta₁-adrenergic effects induce an increase in cardiac contractility and heart rate. At doses of approximately 10 mcg/kg/min, alpha-adrenergic effects lead to arterial vasoconstriction and an elevation in blood pressure. Systolic arterial blood pressure should be maintained at approximately 90 mmHg.

Norepinephrine is a potent alpha-adrenergic agonist with minimal beta-adrenergic agonist effects. The dose of norepinephrine may vary from 0.2-1.5 mcg/kg/min, and large doses, as high as 3 mcg/kg/min.

Epinephrine can increase the MAP by increasing the cardiac index and stroke volume, along with an increase in SVR and heart rate. The use of epinephrine is recommended only in patients who are unresponsive to traditional agents.

Inotropic supportive therapy

Dobutamine 2.5 to 10 $\mu\text{g}/\text{kg}$ per min IV.

Amrinone should be started at an initial loading dose of 0.75 mg/kg is given over 2 to 3 min. If effective, it is followed by an infusion of 5 to 10 $\mu\text{g}/\text{kg}$ per min. If necessary, the dose may then be increased up to 15 $\mu\text{g}/\text{kg}$ per min for short periods.

Milrinone is given as a loading dose of 50 $\mu\text{g}/\text{kg}$ over 10 min followed by a maintenance infusion of 0.375 to 0.75 $\mu\text{g}/\text{kg}$ per min.

Intra-aortic balloon pump - the use of the IABP reduces systolic left ventricular afterload and augments diastolic coronary perfusion pressure, thereby increasing cardiac output and improving coronary artery blood flow.

Ventricular assist devices - the Pierce-Donachy left ventricular assist device has been used as a bridge to cardiac transplantation. Insertion of this device has allowed survival to transplant in 75% of 29 patients.

Free wall rupture

Myocardial rupture is a complication of myocardial infarction that is most likely to occur during the first week after the onset of symptoms; its frequency increases with the age of the patient.

The clinical presentation typically is a sudden loss of pulse, blood pressure and consciousness while the electrocardiogram continues to show sinus rhythm (*apparent* electromechanical dissociation).

The myocardium continues to contract, but forward flow is not maintained as blood escapes into the pericardium.

Cardiac tamponade ensues, and closed-chest massage is ineffective.

This condition is almost universally fatal, although dramatic cases of urgent pericardiectomy followed by successful surgical repair have been reported.

Ventricular septal defect

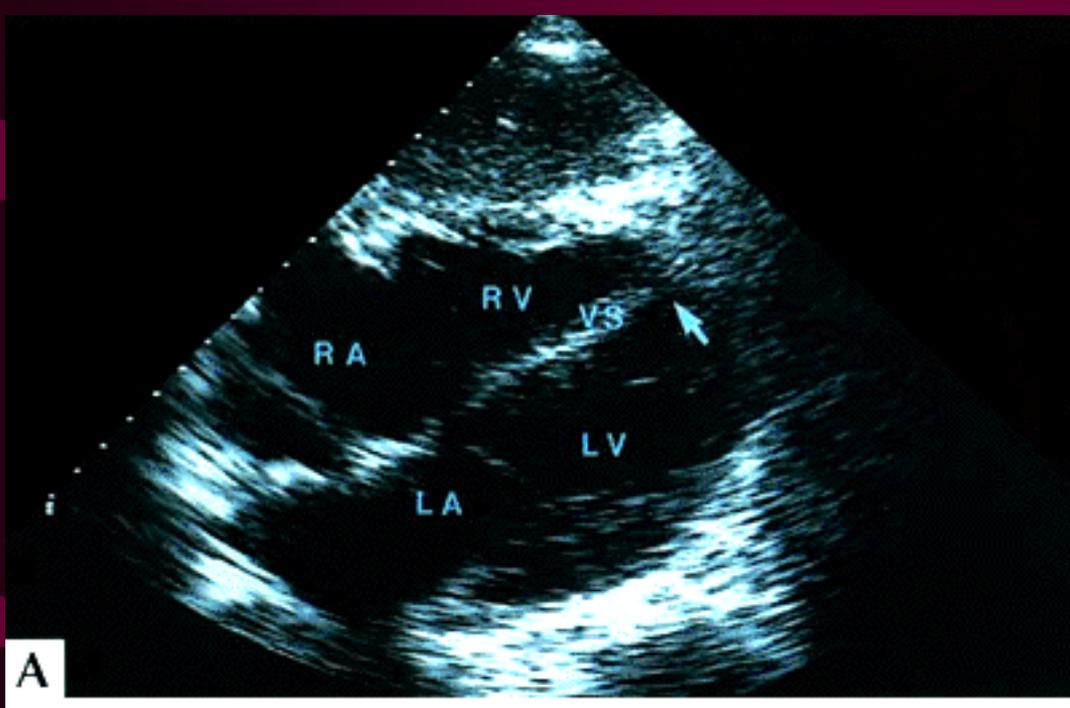
The pathogenesis of perforation of the ventricular septum is similar to that of free wall rupture, but the chance of successful therapy is greater.

Patients with ventricular septal rupture present with sudden, severe left ventricular failure in association with the appearance of a pansystolic murmur, often accompanied by a parasternal thrill.

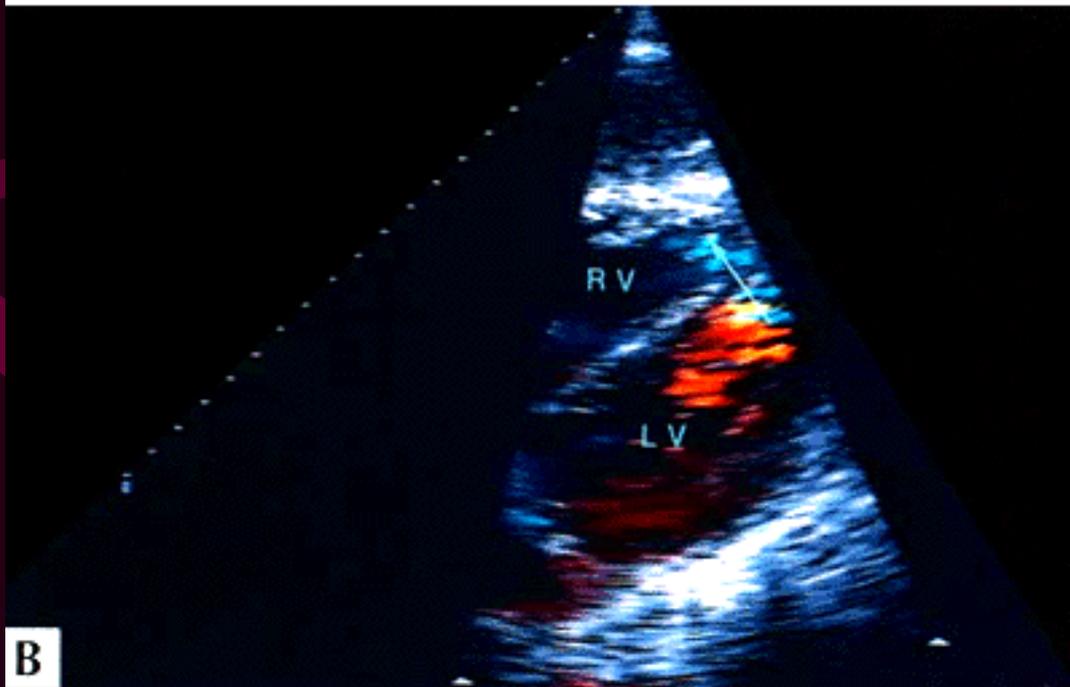
The diagnosis of ventricular septal defect can be established by the demonstration of a left-to-right shunt (i.e., an oxygen step-up at the level of the right ventricle) by means of limited cardiac catheterization performed at the bedside using a flow-directed balloon catheter.

Color flow Doppler echocardiography can also be extremely useful for making this diagnosis at the bedside.

A prolonged period of hemodynamic compromise may produce end-organ damage and other complications that can be avoided by early intervention, including nitroprusside infusion and intraaortic balloon counterpulsation.



A, Two-dimensional echocardiogram demonstrating ventricular septal (VS) rupture (VSR) following acute myocardial infarction. The arrow indicates the defect in the apical portion of the VS.



B, Color Doppler flow through the VSR. The arrow shows systolic flow from the left ventricle (LV) to the right ventricle (RV) across the VSR. LA as left atrium; RA as right atrium.

Mitral Regurgitation

The reported incidence of apical systolic murmurs of mitral regurgitation during the first few days after the onset of a MI varies widely (from 10 to 50 percent of patients).

Left ventricular dilatation or alteration in the size or shape of the ventricle due to impaired contractility or to aneurysm formation causes disordered contraction of the papillary muscles, their rupture. Left ventricular function may deteriorate dramatically.

Intraaortic balloon counterpulsation, which lowers the aortic systolic pressure mechanically, and the infusion of nitroglycerin or sodium nitroprusside, which reduce systemic vascular resistance, have been used with success in the management of patients with severe mitral regurgitation in the setting of acute myocardial infarction. Ideally, definitive operative treatment should be postponed until pulmonary congestion has cleared and the infarct has had time to heal.

Ventricular premature beats

Infrequent, sporadic ventricular premature depolarizations occur in almost all patients with MI and do not require therapy.

Close monitoring and immediate treatment of arrhythmias may be the most important part of the treatment of a post-MI patient within the first 48 hours.

Pharmacologic therapy is reserved for patients with **sustained ventricular arrhythmias**. *Prophylactic antiarrhythmic therapy is indicated* for patients with clinically important ventricular tachyarrhythmias.

Beta-blockers are effective in abolishing ventricular ectopic activity in infarct patients and in the prevention of ventricular fibrillation. Hypokalemia and hypomagnesemia are risk factors for ventricular fibrillation in patients with acute MI; the serum potassium concentration should be adjusted to 4.5 and magnesium to about 2.0 mmol/L.

Ventricular tachycardia and fibrillation

Within the first 24 h of MI, ventricular tachycardia and fibrillation can occur without prior warning arrhythmias.

The occurrence of ventricular fibrillation can be reduced by prophylactic administration of intravenous lidocaine.

Lidocaine use may predispose to an excess risk of bradycardia and asystole. For these reasons, and with earlier treatment of active ischemia, more frequent use of beta-blocking agents, and the nearly universal success of electrical cardioversion or defibrillation.

Prophylactic antiarrhythmic drug therapy should be reserved for patients who cannot reach a hospital or for those treated in hospitals that lack the constant presence in the coronary care unit of a physician or nurse trained in the recognition and treatment of ventricular fibrillation.

Ventricular tachycardia should be treated with an intravenous regimen of:

- *lidocaine* [bolus of 1.0 to 1.5 mg/kg; infusion of 20 to 50 µg/kg per min],
- *procainamide* (bolus of 15 mg/kg over 20 to 30 min; infusion of 1 to 4 mg/min), or
- *amiodarone* (bolus of 75 to 150 mg over 10 to 15 min followed by infusion of 1.0 mg/min for 6 h and then 0.5 mg/min);

if it does not stop promptly,

- ***electroversion*** should be used.

Electroshock (an unsynchronized discharge of 200 to 300 J) is used immediately in patients with ventricular fibrillation or when ventricular tachycardia causes hemodynamic deterioration.

Ventricular tachycardia or fibrillation that is refractory to electroshock may be more responsive after treatment with:

- *epinephrine* (1 mg intravenously or 10 mL of a 1:10.000 solution via the intracardiac route),
- *bretylum* (a 5-mg/kg bolus), or
- *amiodarone* (a 75 to 150-mg bolus).

The long-term survival is good in patients who survive *after primary* ventricular fibrillation, i.e., ventricular fibrillation that is a primary response to acute ischemia and is not associated with predisposing factors such as congestive heart failure, shock, bundle branch block, or ventricular aneurysm.

The long-term prognosis is poor for patients who develop ventricular fibrillation *secondary* to severe pump failure.

Recurrent angina

Recurrent angina develops in approximately $\frac{1}{4}$ of patients hospitalized for acute MI.

Since recurrent or persistent ischemia often heralds ***extension*** of the original infarct or ***reinfarction*** in a new myocardial zone and is associated with a doubling of risk following acute MI.

Patients with these symptoms should be considered for repeat thrombolysis or referred for prompt coronary arteriography and mechanical revascularization.

Repeat administration of a thrombolytic agent is an alternative to early mechanical revascularization.

Pericarditis

Pericardial friction rubs and/or pericardial pain are frequently encountered in patients with acute transmural MI.

This complication can usually be managed with non steroid anti-inflammatory drugs: aspirin (650 mg qid), diclofenac (50 mg qid), meloxicam (15 mg bid) or celecoxib 30 mg bid).

Dressler's syndrome

Dressler's syndrome (post-MI syndrome), characterized by fever and pleuropericardial chest pain, is thought to be due to an autoimmune pericarditis, pleuritis, and/or pneumonitis.

It may begin from a few days to 6 weeks after MI and usually responds promptly to therapy with non steroid anti-inflammatory drugs.

Pulmonary artery and another site thromboembolism

Thromboembolism complicates acute MI in approximately 10 % of cases and one is an important contributing cause of death in 25 % of infarct patients.

Arterial emboli originate from left ventricular mural thrombi, while most pulmonary emboli arise in the leg veins.

Thromboembolism typically occurs in association with large infarcts (especially anterior), heart failure, and a left ventricular thrombus detected by echocardiography.

When a thrombus has been clearly demonstrated by echocardiographic or when a large area of regional wall motion abnormality is seen even in the absence of a detectable mural thrombus, systemic anticoagulation should be undertaken, as the incidence of embolic complications appears to be markedly lowered by such therapy.

The appropriate duration of therapy 3 to 6 months.

Acute and chronic left ventricular aneurysm

The term *ventricular aneurysm* is used to describe *dyskinesis* or local expansive paradoxical wall motion.

Normally functioning myocardial fibers must shorten more if stroke volume and cardiac output are to be maintained in patients with ventricular aneurysm; if they cannot, overall ventricular function is impaired.

True aneurysms are composed of scar tissue.

The complications of left ventricular aneurysm include congestive heart failure, arterial embolism, and ventricular arrhythmias.

Ventricular aneurysms are readily detected by echocardiography, which may also reveal a mural thrombus in an aneurysm.

Left ventricle aneurysm is detected in period of first massive MI names acute LV aneurysm, after that period – chronic LV aneurysm.