

Internal Medicine

**Lecture 4. CHRONIC FORMS OF
ISCHEMIC HEART DISEASE**

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ISCHEMIC HEART DISEASE

Ischemia refers to a lack of oxygen due to inadequate perfusion, which results from an imbalance between oxygen supply and demand.

Angina pectoris – a clinical syndrome due to myocardial ischemia characterized by episodes of precordial discomfort or pressure, typically precipitated by exertion and relieved by rest or sublingual nitroglycerin.

ETIOLOGY AND PATHOPHYSIOLOGY

By reducing the lumen of the coronary arteries, atherosclerosis causes an absolute decrease in myocardial perfusion in the basal state or limits appropriate increases in perfusion when the demand for flow is augmented.

Coronary blood flow can be limited by arterial thrombi or spasm.

Congenital abnormalities of the left coronary artery may cause myocardial ischemia and infarction in infancy.

Myocardial ischemia can occur if myocardial oxygen demands are abnormally increased, as in severe ventricular hypertrophy due to hypertension or aortic stenosis.

A reduction in the oxygen-carrying capacity of the blood, as in severe anemia or in the presence of carboxyhemoglobin, is a rare cause of myocardial ischemia.

Two or more causes of ischemia will coexist, such as an increase in oxygen demand due to left ventricular hypertrophy and a reduction in oxygen supply secondary to coronary atherosclerosis.

CORONARY ATHEROSCLEROSIS

Risk factors for coronary atherosclerosis and CAD:

Family history of premature CAD

- Hyperlipidemia, including hypercholesterolemia (elevated low-density lipoprotein [LDL] level), low high-density lipoprotein (HDL) cholesterol level, and elevated triglyceride level
- Hypertension
- Cigarette smoking
- Diabetes mellitus
- Hypoalphalipoproteinemia
- Dysmetabolic syndrome

Nontraditional risk factors

- Hyperhomocystinemia
- High Lp(a) level
- High iron level.

Risk factors for atherosclerosis are thought to disturb the normal functions of the vascular endothelium. Dysfunction of vascular endothelium and an abnormal interaction with blood monocytes and platelets lead to subintimal collections of abnormal fat, cells, and debris (i.e., atherosclerotic plaques), which develop at irregular rates in different segments of the epicardial coronary tree and lead to segmental reductions in cross-sectional area

Syndromes of accelerated atherosclerosis

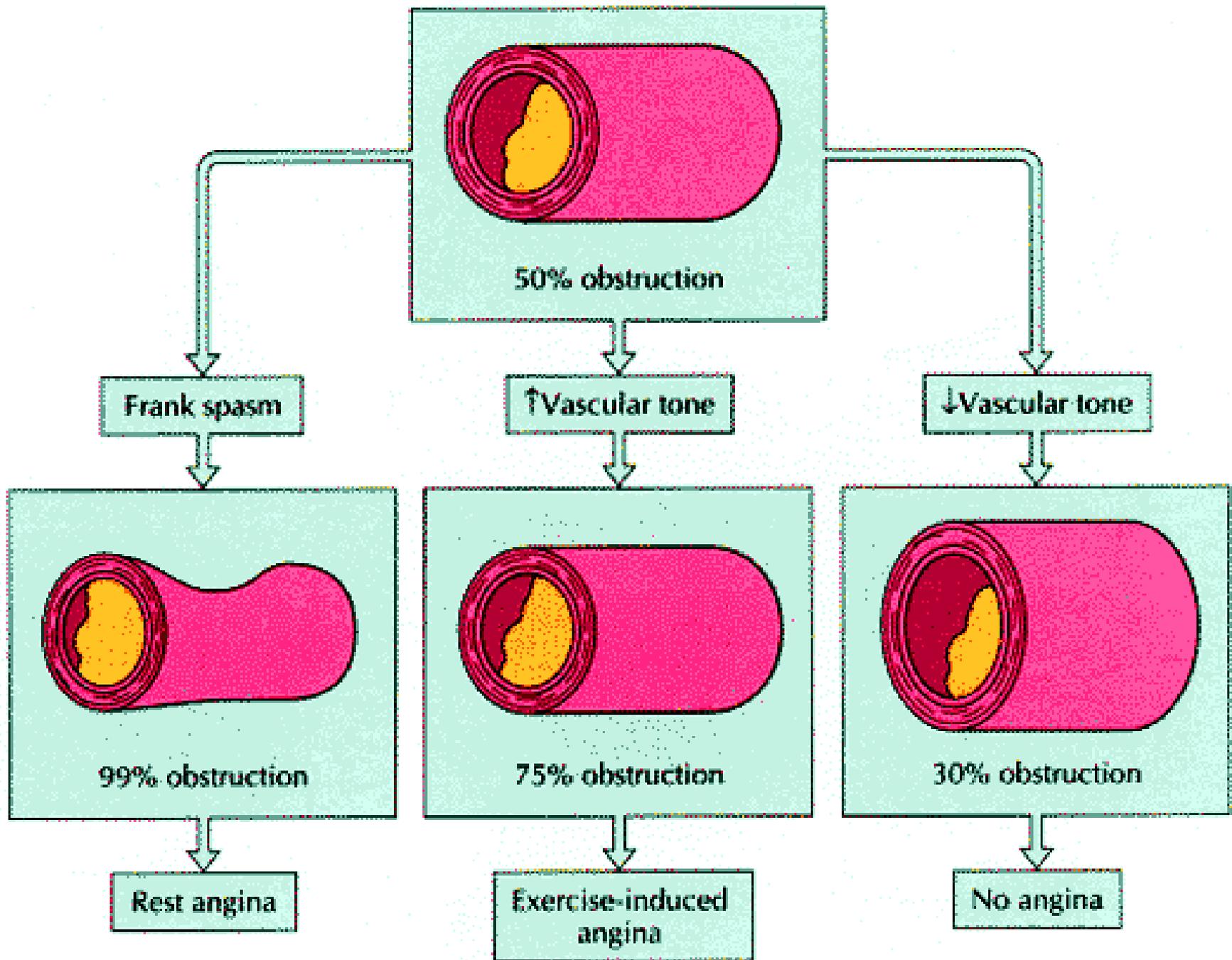
- Graft atherosclerosis
- Postcardiac transplant CAD
- Restenosis

Infections implicated in development of atherosclerosis

- *Chlamydia pneumoniae*
- *Helicobacter pylori*
- Herpes simplex virus

The relationship between pulsatile flow and luminal stenosis is complex, but were shown that when a stenosis reduces the cross-sectional area by approximately 75 percent, a full range of increases in flow to meet increased myocardial demand is not possible.

When the luminal area is reduced by more than approximately 80 percent, blood flow at rest may be reduced, and further minor decreases in the stenotic orifice can reduce coronary flow dramatically and cause myocardial ischemia.



Vulnerable Versus Stable Atherosclerotic Plaques



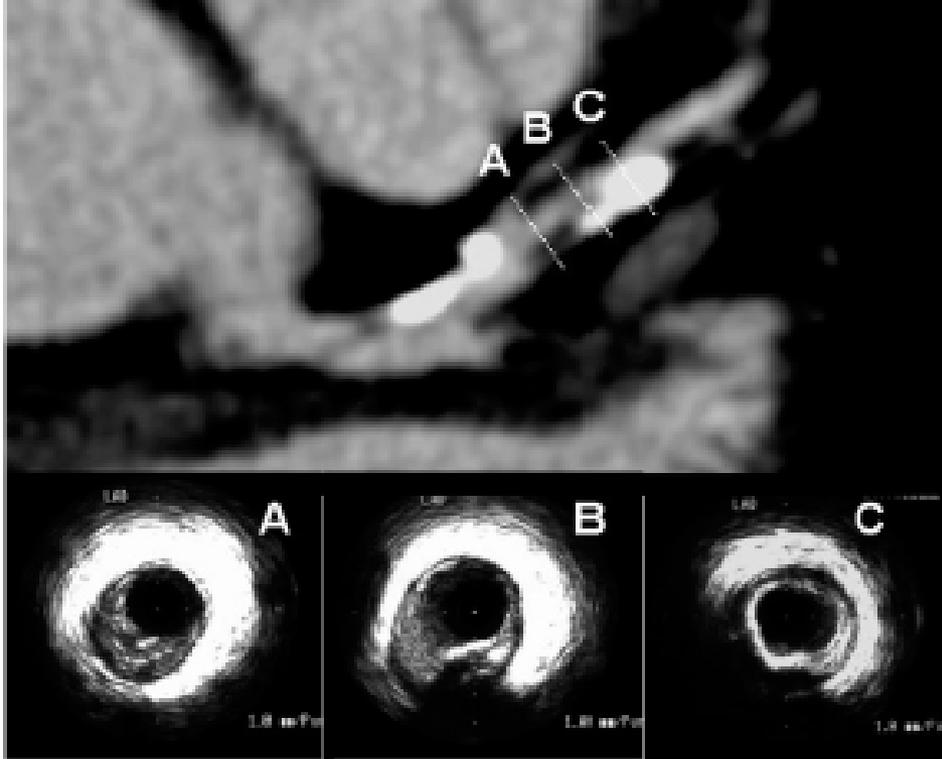
Vulnerable Plaque

- Thin fibrous cap
- Inflammatory cell infiltrates: proteolytic activity
- Lipid-rich plaque



Stable Plaque

- Thick fibrous cap
- Smooth muscle cells: more extracellular matrix
- Lipid-poor plaque

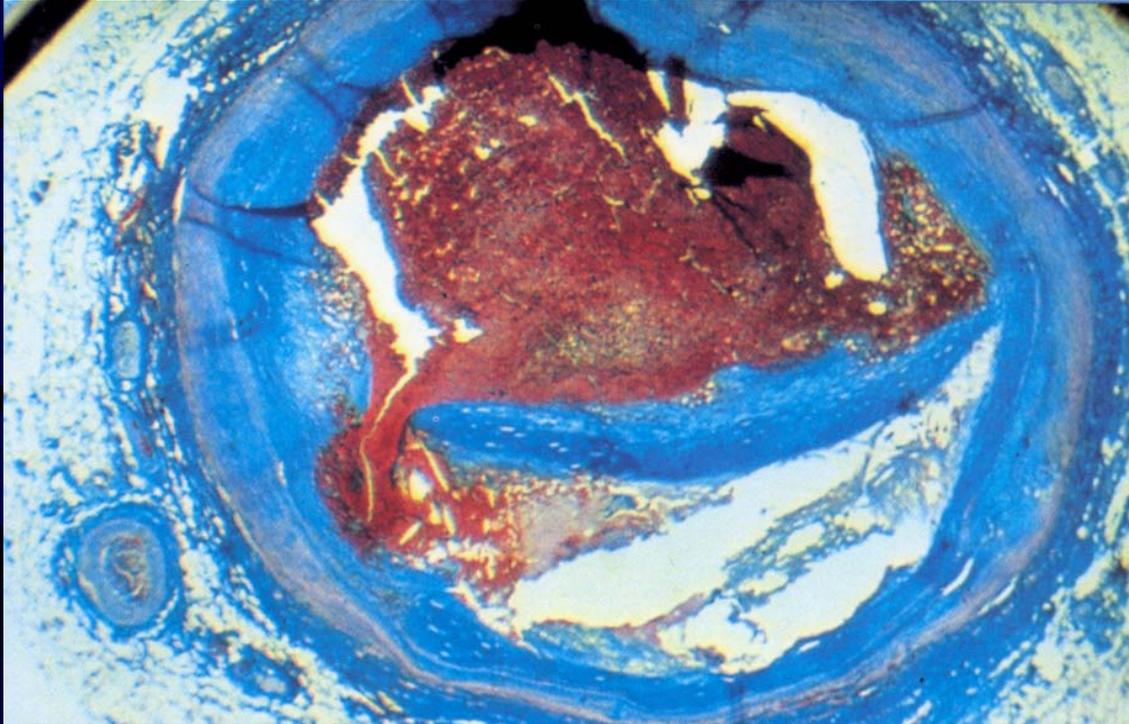


Correlation of CT angiography of the coronary arteries with intravascular ultrasound illustrates the ability of MDCT to demonstrate calcified and non-calcified coronary plaques (Becker et al., Eur J Radiol 2000)



Non-calcified, soft, lipid-rich plaque in left anterior descending artery (arrow) (Somatom Sensation 4, 120 ml Imeron 400). The plaque was confirmed by intravascular ultrasound (Kopp et al., Radiology 2004)

Features of a Ruptured Atherosclerotic Plaque



- Eccentric, lipid-rich
- Fragile fibrous cap
- Prior luminal obstruction < 50%

Segmental atherosclerotic narrowing of epicardial coronary arteries is caused by the formation of a plaque, which is subject to fissuring, hemorrhage, and thrombosis. Any of these events can temporarily worsen the obstruction, reduce coronary blood flow, and cause clinical manifestations of myocardial ischemia.

Severe coronary narrowing and myocardial ischemia are frequently accompanied by the development of collateral vessels, especially when the narrowing develops gradually.

EFFECTS OF ISCHEMIA

The relatively poor perfusion of the subendocardium causes ischemia of this portion of the wall.

Ischemia of large portions of the ventricle will cause transient left ventricular failure, mitral regurgitation can complicate this event.

Transient ischemia is associated with angina pectoris.

Prolonged ischemia can lead to myocardial necrosis and scarring with or without the clinical picture of acute myocardial infarction.

Electrical instability as a result of myocardial ischemia, may lead to ventricular tachycardia, ventricular fibrillation and sudden death from ischemic heart disease as a result of ischemia-induced ventricular tachyarrhythmia.

Patients can present with cardiomegaly and heart failure secondary to ischemic damage of the left ventricular myocardium that caused to the development of heart failure (***ischemic cardiomyopathy***).

Clinical syndromes (conditions) of Ischemic heart disease and myocardial ischemia presentation:

- **Asymptomatic state (subclinical phase)**
- **Stable angina pectoris**
- **Unstable angina (acute coronary syndrome)**
- **Acute MI**
- **Chronic ischemic cardiomyopathy**
- **CHF**
- **Sudden cardiac arrest**

STABLE ANGINA PECTORIS

Characteristics of the pain syndrome

- **Location:** anginal pain is centrally located in the chest. Patients typically press on the sternum, sometimes with a clenched fist, to indicate a squeezing, central, substernal discomfort.
- **Character of the pain:** anginal pain is described as dull, constricting, heaviness, pressure, squeezing, smothering, or choking and only rarely as frank pain. It may be appreciated as troublesome or frightening chest or substernal discomfort, and the constricting sensation can be described as breathlessness.
- **Pattern of onset:** angina is usually crescendo-decrescendo in nature and lasts 1 to 5 min.

STABLE ANGINA PECTORIS

Characteristics of the pain syndrome

- **Radiation:** to the left shoulder, both arms, ulnar surfaces of the forearm and hand, back, neck, jaw, teeth, and epigastrium.
- **Provocation:** anginal pain is precipitated by exertion or emotion and is relieved by resting. With deteriorating or unstable angina, similar pain may be brought on by minimal exertion and may also occur at rest and at night (nocturnal angina) while the patient is recumbent (angina decubitus). The patient may be awakened at night distressed by typical chest discomfort and dyspnea.
- **Associated features:** the typical patient with angina is a 50- to 60-year-old man or 65- to 75-year-old woman. Patients report a fixed threshold for angina, which occurs predictably at a certain level of activity.

The Canadian Cardiovascular Society grading scale classification of angina severity:

Class I - Angina only during strenuous or prolonged physical activity;

Class II - Slight limitation, with angina only during vigorous physical activity;

Class III - Symptoms with everyday living activities, ie, moderate limitation;

Class IV - Inability to perform any activity without angina or angina at rest, ie, severe limitation.

The physical examination is often normal in the patient with stable angina.

The general examination may reveal signs of risk factors associated with coronary atherosclerosis such as xanthelasma, xanthomas, or diabetic skin lesions.

There may also be signs of anemia, thyroid disease, and nicotine stains on the fingertips from cigarette smoking.

Palpation can reveal thickened or absent peripheral arteries, signs of cardiac enlargement, and abnormal contraction of the cardiac impulse (left ventricular akinesia or dyskinesia).

While auscultation can uncover arterial bruits, a third and/or fourth heart sound, and, if acute ischemia or previous infarction has impaired papillary muscle function, an apical systolic murmur due to mitral regurgitation.

Examination during an anginal attack can cause transient left ventricular failure with the appearance of a third and/or fourth heart sound, a dyskinetic cardiac apex, mitral regurgitation, and even pulmonary edema.

Examination of the blood should include measurements of lipids (cholesterol—total, low density, and high density), glucose, creatinine, hematocrit, and, if indicated based on the physical examination, thyroid function.

The urine should be examined for evidence of diabetes mellitus and renal disease, since both these conditions may accelerate atherosclerosis.

A chest x-ray may show the consequences of ischemic heart disease, i.e., *cardiac enlargement, ventricular aneurysm, or signs of heart failure.*

Electrocardiogram *at rest is normal* in about half the patients with angina pectoris, but there may be signs of an old myocardial infarction.

Ischemia causes electrocardiogram (ECG) changes such as repolarization abnormalities, inversion of the T wave, ST segment displacement.

Typical ST-segment and T-wave changes that accompany episodes of angina pectoris and disappear thereafter are specific. ***The ST segment is usually depressed to 2 mm during angina*** but may be ***elevated*** in Prinzmetal's angina. Transient ST-segment depression reflects subendocardial ischemia, transient ST-segment elevation is thought to be caused by more severe transmural ischemia.

Stress Testing involves recording the **ECG** before, during, and after exercise on *a treadmill* or using a *bicycle ergometer*.

Exercise treadmill ECG consists of a standardized incremental increase in external workload while the patients **ECG**, symptoms, and blood pressure are monitored.

The test is discontinued upon evidence of chest discomfort, severe shortness of breath, dizziness, fatigue, ST-segment depression of greater than 0.2 mV (2 mm), a fall in systolic blood pressure exceeding 10 mm hg, or the development of a ventricular tachyarrhythmia.

This test seeks to discover any limitation in exercise performance and establish the relationship between chest discomfort and the typical **ECG** signs of myocardial ischemia.

The ischemic ST-segment response is generally defined as flat depression of the ST segment of more than 0.1 mV below the baseline and lasting longer than 0.08 s.

Negative exercise tests in which the target heart rate (85 percent of maximal heart rate for age and sex) is not achieved are considered to be nondiagnostic.

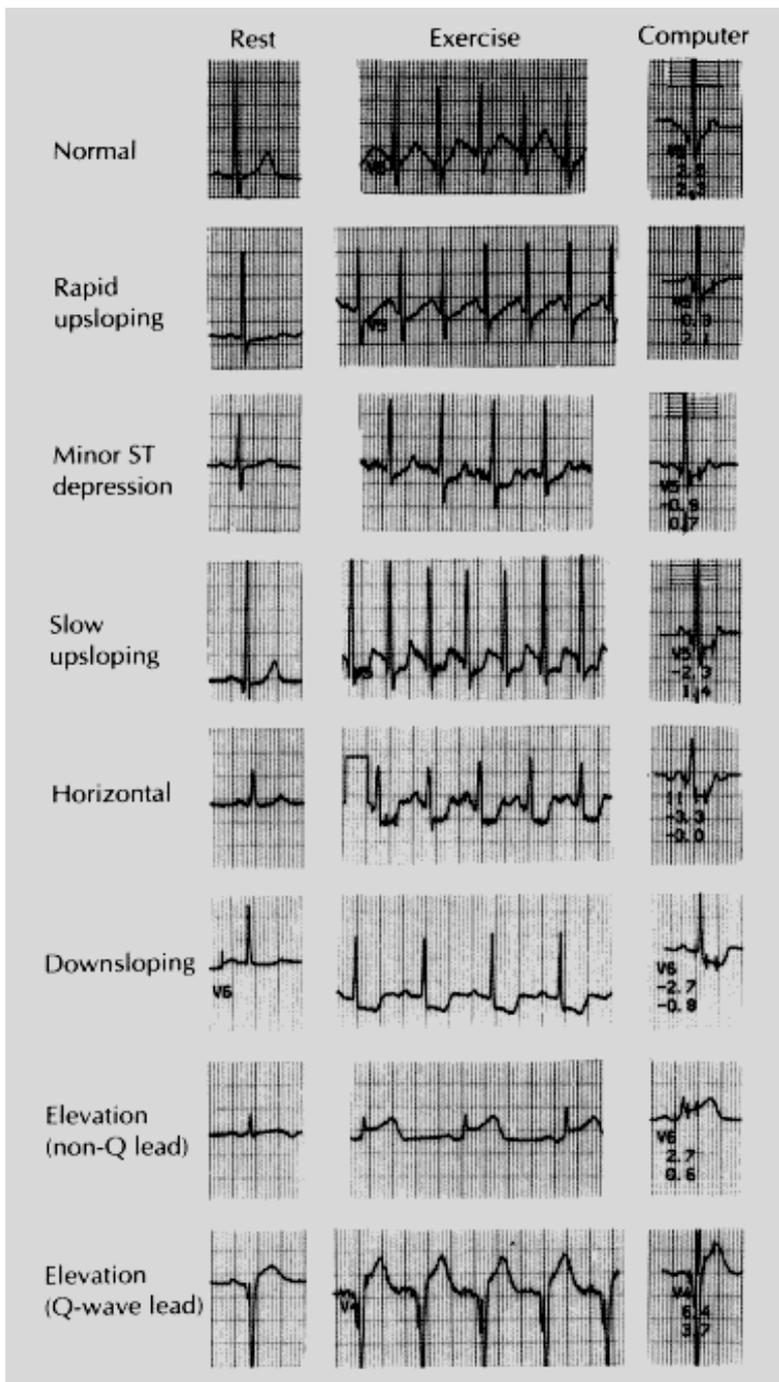
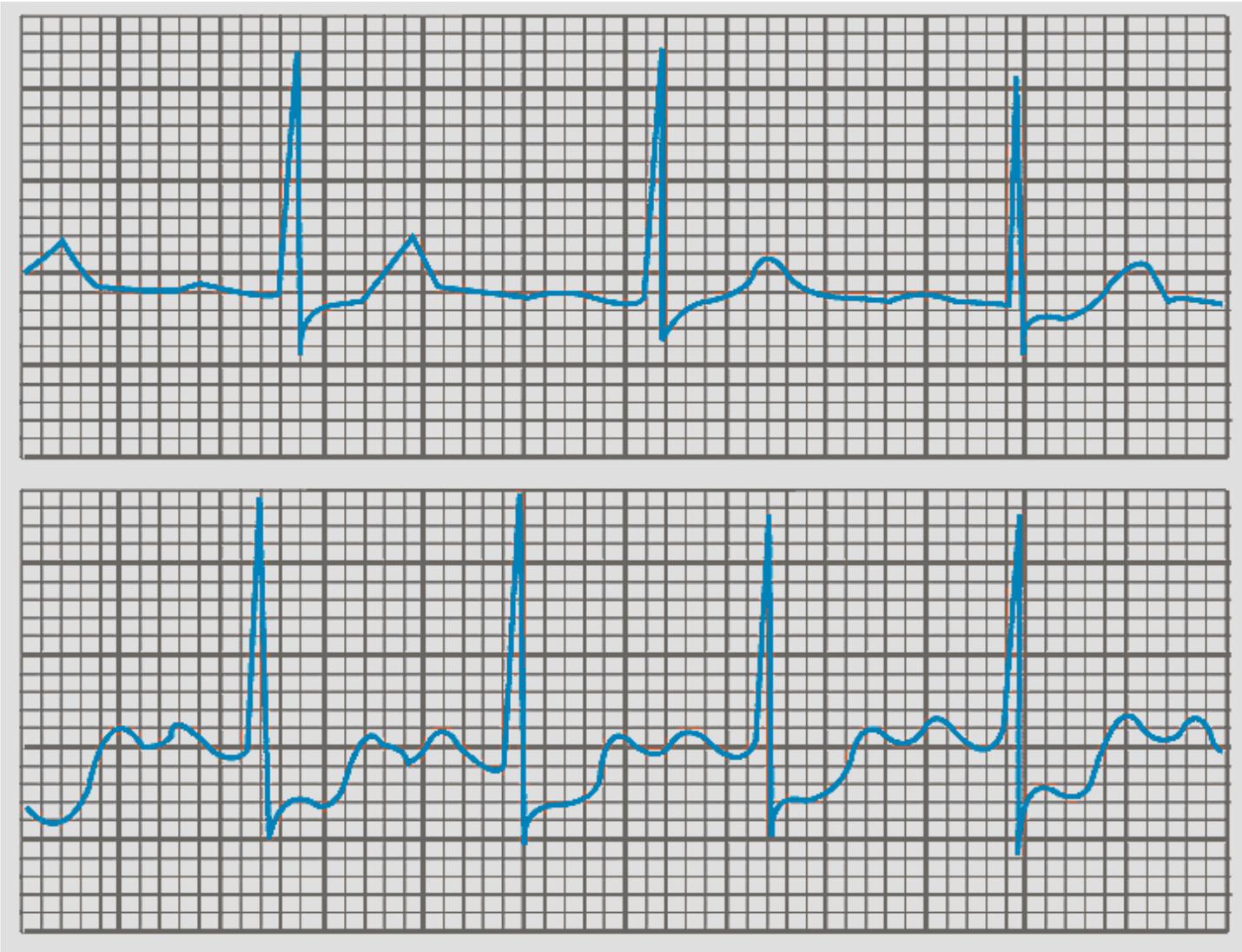


Illustration of exercise electrocardiographic patterns at rest and at peak exertion. The patterns represent a gradient of worsening ECG response to myocardial ischemia.

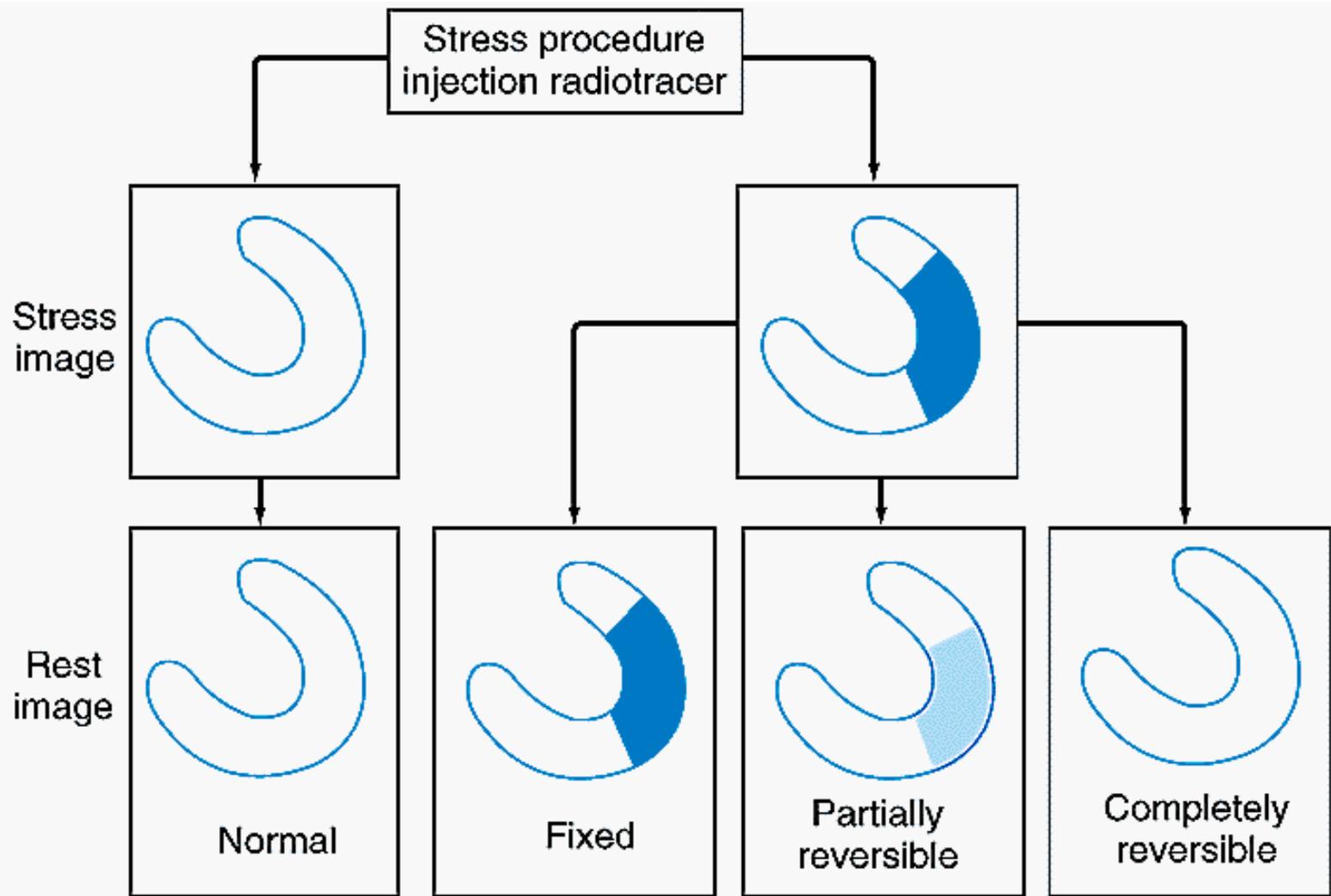


Lead V₄ at rest (*top*) and after 4¹/₂ min of exercise (*bottom*). There is 3 mm (0.3 mV) of horizontal ST-segment depression, indicating a positive test for ischemia.

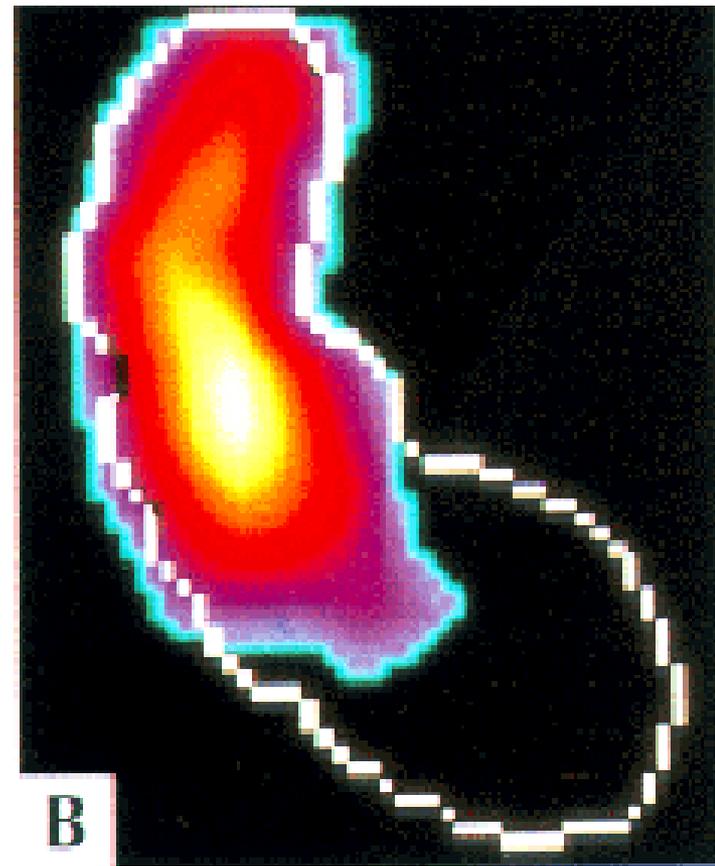
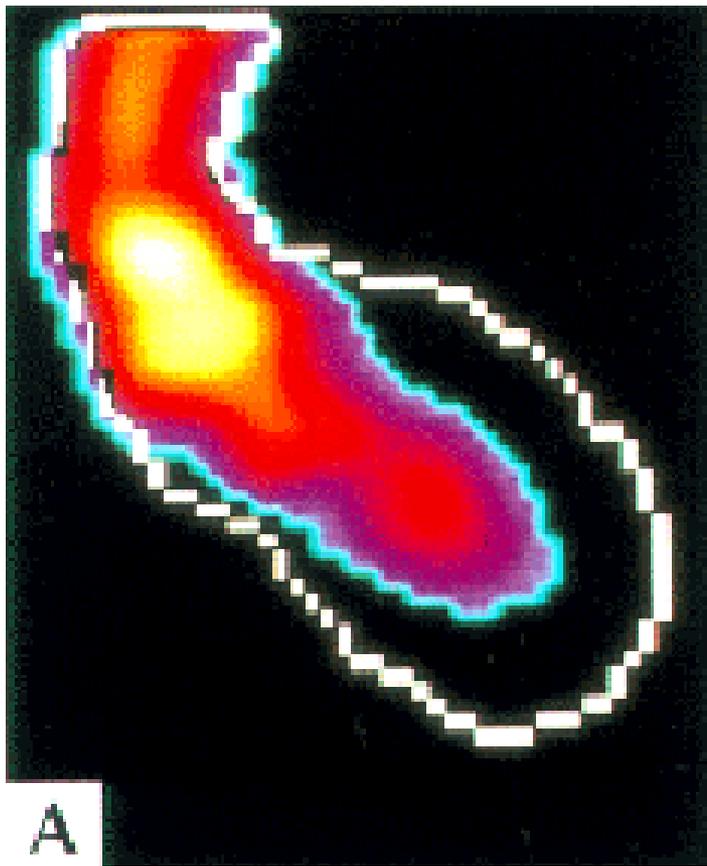
The information gained from *an exercise test* can be enhanced by *stress myocardial perfusion imaging* after the intravenous administration of a radioisotope such as *thallium 201* or *technetium 99m* sestamibi during exercise (or a pharmacologic stress); the imaging is carried out both immediately after cessation of exercise and 4 h later.

Technetium 99m can also be used to label the blood pool for gated radioisotope angiography, which provides a measure of ventricular volume and ejection fraction at rest and during exercise. A reduction in ejection fraction during exercise is an important, albeit nonspecific, finding, and when present in CAD suggests the presence of severe ischemia and/or multivessel coronary disease.

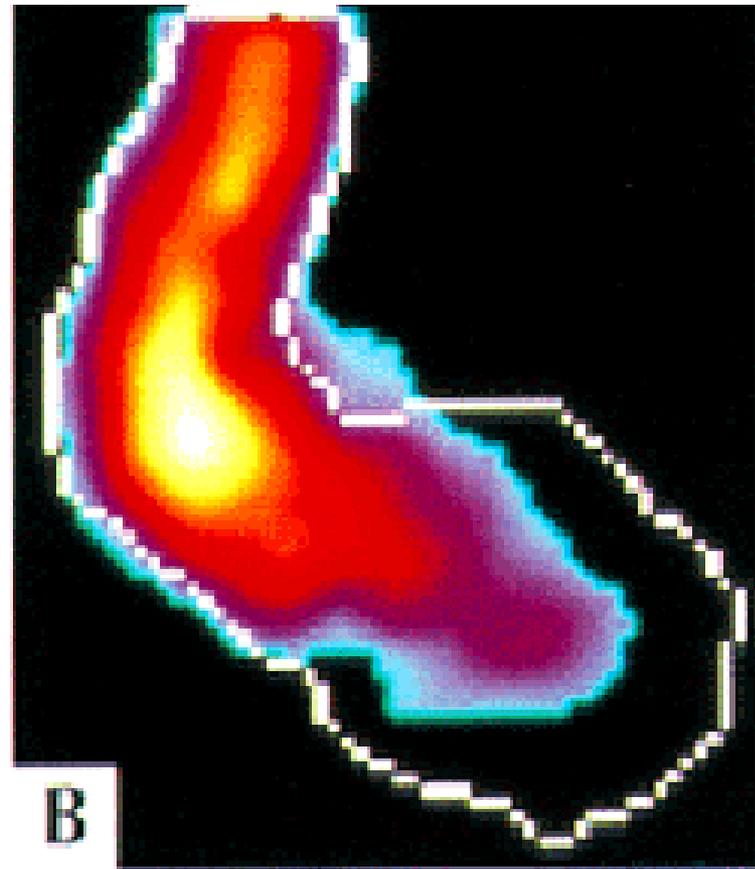
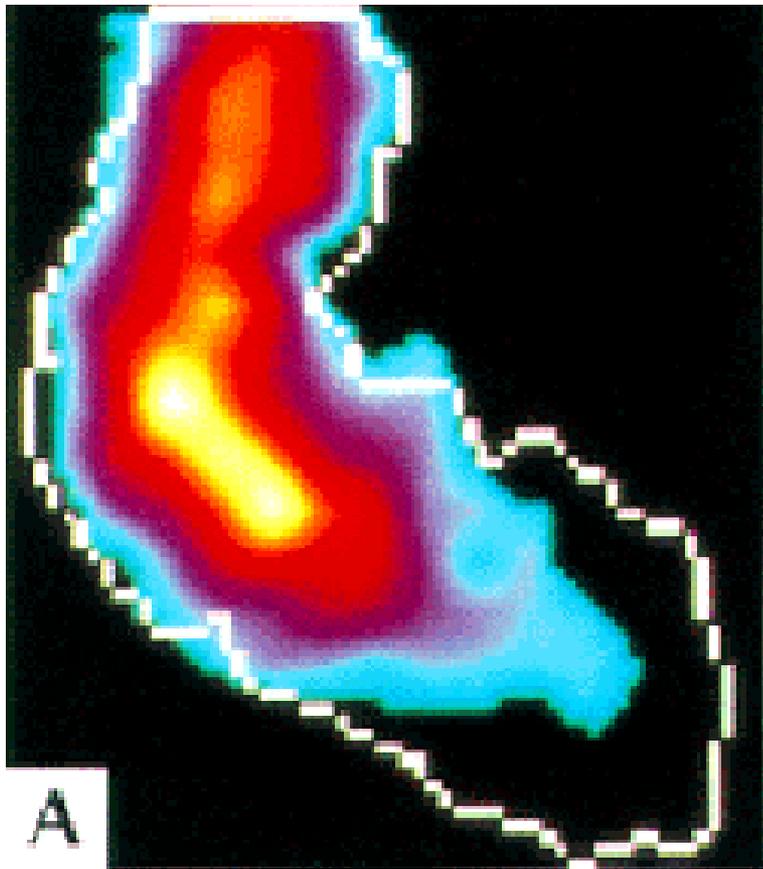
Ambulatory monitoring of the EGG can assess myocardial ischemia as episodes of ST-segment depression.



Interpretation of stress (exercise) and rest myocardial perfusion images. A normal image will show homogeneous accumulation of radiotracer on the exercise and rest (or delayed) image. An area with decreased uptake of the radiotracer (which appears as a darker area on a perfusion image) is referred to as a *defect*. A patient with a fixed perfusion defect will have an abnormal exercise image and an identical rest or delayed redistribution image (scarring). A partially reversible perfusion defect appears as an abnormal exercise image and an improved but still abnormal rest image (ischemia and scarring). A reversible perfusion defect appears as an abnormal exercise image and a normal rest or delayed image (ischemia).



Normal first-pass radionuclide angiography at rest and during exercise. The left ventricular end-diastolic (ED) outline (white) in the anterior position is superimposed on the end-systolic (ES) image. This display allows assessment of regional wall motion from a static image. Maximum count activity is yellow and the lowest activity is green. Resting left ventricular ejection fraction (LVEF) in this patient is 60 percent (A), and peak exercise LVEF is 80 percent (B). Regional wall motion shows uniformly increased contraction. (LVEF = $\frac{ED \text{ volume} - ES \text{ volume}}{ED \text{ volume}}$). A normal LVEF response is defined as an increase in LVEF of 5 percent or greater compared with baseline LVEF and a uniform increase of regional wall motion.



Abnormal first-pass radionuclide angiograms at rest and during exercise. In this patient, resting left ventricular ejection fraction (LVEF) is 60% (A), and peak exercise LVEF is 45% (B), with uniformly decreased regional wall motion. An abnormal response is defined as either a decrease greater than 5%, or no change in LVEF compared with baseline.

Two-dimensional echocardiography of the left ventricle can assess both global and regional wall motion abnormalities due to myocardial infarction or persistent ischemia.

Stress (exercise or dobutamine) echo may cause the emergence in regions of akinesis or dyskinesis not present at rest.

Exercise echo, in which imaging is performed at rest and immediately after exercise, is useful in evaluation of patients with chronic CAD because it can assess global and regional LV function in the absence and presence of ischemia, and it can detect LV hypertrophy and associated valve disorders.

In ***dobutamine stress echo*** constant echo imaging is performed during the infusion of dobutamine, beginning at 5-10 mcg/kg/min with graded increases to a maximum of 40-45 mcg/kg/min. Dobutamine increases both heart rate and contractility and produces diagnostic changes in regional wall motion and systolic wall thickening as ischemia develops.

Coronary Arteriography is indicated in

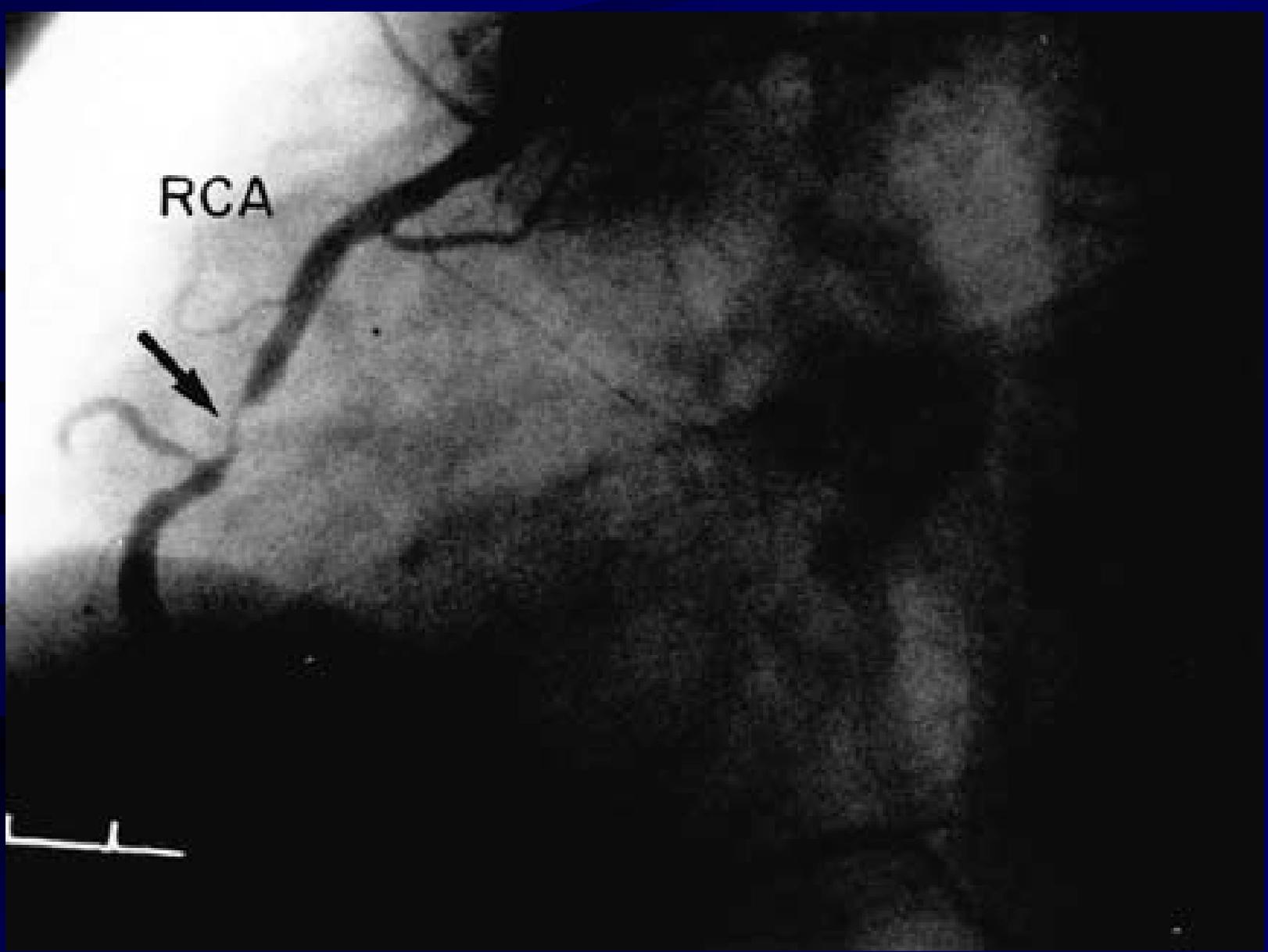
(1) patients with chronic stable or unstable angina pectoris who are severely symptomatic despite medical therapy and who are being considered for revascularization, i.e., percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft surgery;

(2) patients with troublesome symptoms that present diagnostic difficulties in whom there is need to confirm or rule out the diagnosis of CAD:

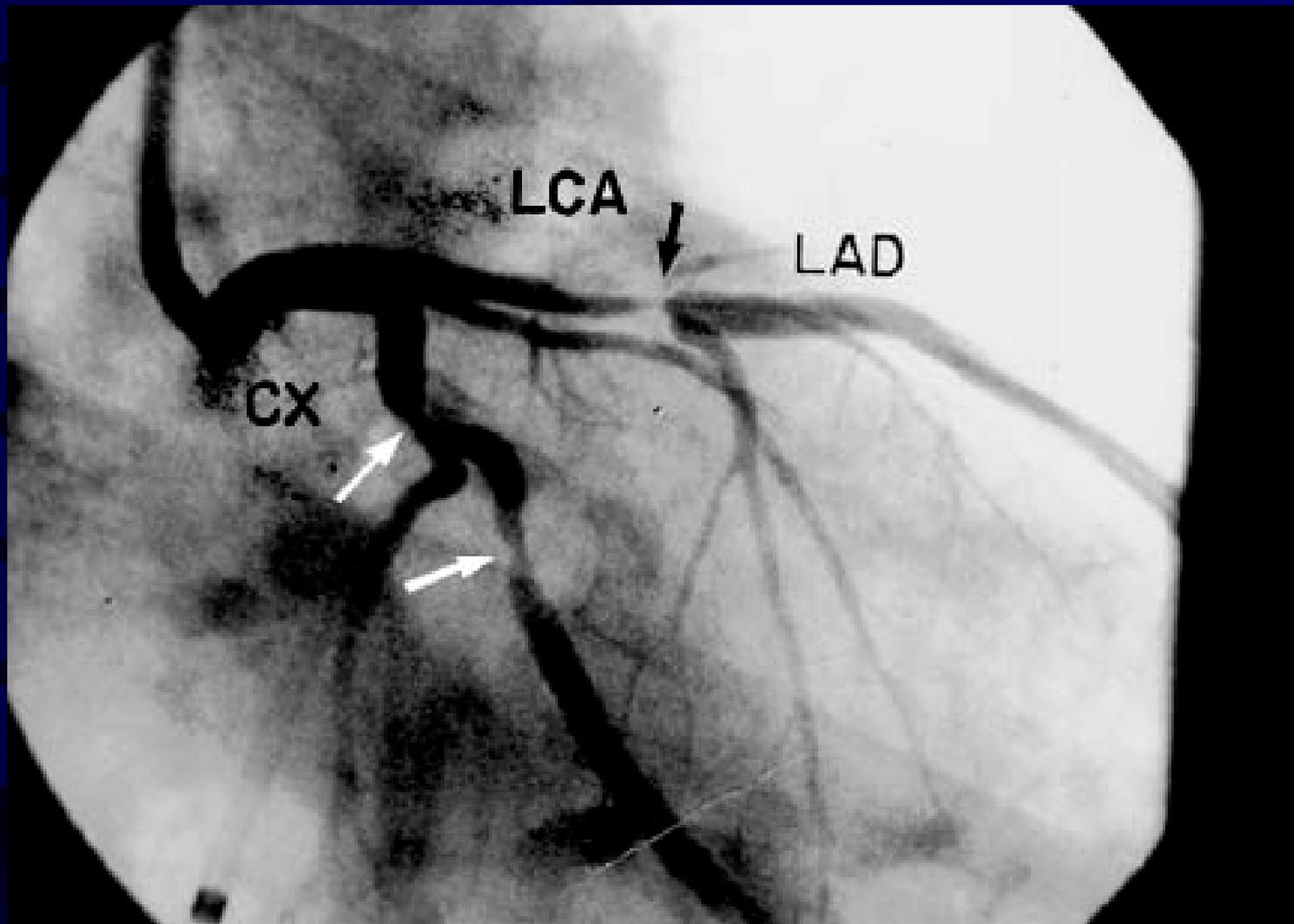
(3) patients judged to be at high risk of sustaining coronary events based on signs of severe ischemia on noninvasive testing, regardless of the presence or severity of symptoms.

Examples of other possible clinical situations include:

1. Patients with chest discomfort suggestive of angina pectoris but a negative exercise test.
2. Patients who have been admitted repeatedly to the hospital for suspected acute myocardial Infarction but in whom this diagnosis has not been established and in whom the presence or absence of CAD should be determined.
3. Patients with careers that involve the safety of others (e.g., airline pilots) who have questionable symptoms, suspicious or positive noninvasive tests.
4. Patients with aortic stenosis or hypertrophic cardiomyopathy and angina in whom the pain could be due to CAD.
5. Male patients aged 45 and females aged 55 years of age or older who will undergo valve replacement and who may or may not have clinical evidence of myocardial ischemia.
6. Patients who are at high risk after myocardial infarction because of the recurrence of angina, heart failure, frequent ventricular premature contractions, or signs of ischemia in the stress test.
7. Patients with angina pectons, regardless of severity, in whom noninvasive testing reveals signs of severe ischemia.



Coronary angiogram showing a right coronary artery (RCA) with a severe (95 percent) stenosis at its midpoint (arrow).



Coronary angiogram of a left coronary artery (LCA) with a tight stenosis in the proximal left anterior descending (LAD) artery (black arrow) immediately prior to the origin of a large septal branch. The circumflex artery(CX) has two moderately severe stenoses (white arrows).

PROGNOSIS

Angina pectoris of recent onset, unstable angina, angina that is unresponsive or poorly responsive to medical therapy or is accompanied by symptoms of congestive heart failure all indicate an increased risk for adverse coronary events.

The same is true for the physical signs of heart failure, episodes of pulmonary edema, or for echocardiographic (or roentgenographic) evidence of cardiac enlargement.

An abnormal resting ECG or positive evidence of myocardial ischemia during a stress test indicate increased risk. Most importantly, the following signs during noninvasive testing indicate a high risk for coronary events: a strongly positive exercise test showing onset of myocardial ischemia at low workloads [≥ 0.1 mV ST-segment depression in the exercise test; ≥ 0.2 mV ST depression in any stage; ST depression for >5 min following the cessation of exercise; a decline in systolic pressure >10 mmHg during exercise; the development of ventricular tachyarrhythmias during exercise]; the development of large or multiple perfusion defects or increased lung uptake during stress radioisotope perfusion imaging; and a decrease in left ventricular ejection fraction during exercise on radionuclide ventriculography.

TREATMENT

Adaptation Of Activity Therapy of angina consists of eliminating the discrepancy between the demand of the heart muscle for oxygen and the ability of the coronary circulation to meet this demand (reducing the speed to avoid physical stress). In some patients, anger and frustration may be the most important factors precipitating myocardial ischemia.

Risk-factor modification Obesity: when the patient is more than 30 percent above ideal body weight it increases the risk of adverse coronary events. Cigarette smoking accelerates coronary atherosclerosis in both sexes and at all ages and increases the risk of myocardial infarction and death.

Medical therapy for risk factor reduction

Treatment of hypertension with ACE inhibitors and beta-blockers to satisfactory endpoints of systolic blood pressure of less than 130 mm Hg and diastolic blood pressure of less than 85 mm Hg is strongly recommended.

The lowering of lipid levels is a critical aspect of the management of established CAD. Patients with LDL cholesterol concentrations exceeding 3.2 mmol/L (125 mg/dL) should have these levels reduced. The statins, such as atorvastatin (Lipitor), simvastatin (Zocor), pravastatin (Pravachol), lovastatin (Mevacor, Altocor), and fluvastatin (Lescol) are the first-line agents in the treatment of hyperlipidemias. Their use has led to rapid and significant improvement in endothelium-dependent dilation of coronary and peripheral arteries in patients with hyperlipidemia.

Numerous studies have demonstrated that statins are effective in both secondary and primary prevention of MI and cardiac death, even in individuals with only minimally elevated LDL cholesterol (>100 mg/dL).

Risk reduction in women with CAD The incidence of clinical CAD in premenopausal women is very low. However, following the menopause, the atherogenic risk factors increase (e.g., increased LDL, reduced HDL) and the rate of clinical coronary events accelerates to the levels observed in men. The postmenopausal use of hormone replacement therapy (estrogen with or without a progestin) reduces adverse coronary outcomes but should not be given to patients at higher than usual risk of breast cancer.

Pharmacologic treatment of CAD can be divided into agents that prolong **survival** (eg, aspirin, statin drugs, ACE inhibitors, beta-blockers) and those that treat **symptoms** (eg, calcium channel blockers, nitrates).

Drugs Used for Angina Pectoris

| Drug | Usual Dose | Side Effects | Contraindications |
|---|---|--|--|
| NITRATES | | | |
| NTG (Nitrostat, Deponit, Nitro-Bid, Nitrol) | Injection: Continuous 10-20 mcg/min IV inf. Spray: 0.4 mg; dose may be repeated q3-5min as hemodynamics permit, not to exceed 1.2 mg Sublingual: 0.2-0.6 mg; not to exceed 3 doses in 15 min. | Flushing, headache | Intolerance of side effects |
| Isosorbide dinitrate SR | 80-120 mg | Flushing, headache, tolerance after 24 h | As above, worsening ischemia on withdrawal |
| Isosorbide-5-monitrate | Oral 20-30 mg bid Oral SR 60-240 mg once daily | As above | As above |

Drugs Used for Angina Pectoris

BETA-ADRENOCEPTOR BLOCKING DRUGS

| Drug | Usual Dose | Side Effects | Contraindications |
|--------------------------|-------------------------|--|--|
| Propranolol (Inderal) | 20-80 mg qid | Depression, constipation, impotence, bronchospasm, heart failure, bradycardia | Asthma, AV conduction block, heart failure |
| Metoprolol (Spesicor) | 25-200 mg bid | As above | As above |
| Atenolol | 50-150 mg once daily | As above | As above |

Drugs Used for Angina Pectoris

CALCIUM CHANNEL BLOCKING DRUGS

| Drug | Usual Dose | Side Effects | Contraindications |
|--|--------------------------|---|---|
| Nifedipine XL (Adalat XL) | 30-90 mg once daily | Hypotension, flushing, edema, worsening angina | Hypotension, intolerance of side effects |
| Diltiazem SR | 60-120 mg bid | Constipation, AV conduction block, worsening heart failure | AV conduction block, impaired LV function, bradycardia |
| Verapamil SR (Galan, Procardia) | 180-240 mg once daily | Constipation, AV conduction block, worsening heart failure | AV conduction delay, impaired LV function, bradycardia |
| Felodipine (Plendil) | 2.5-5 mg PO bid | lower extremity edema; allergic hepatitis (rare) | Hypotension |
| Amlodipine (Narvasc) | 5-10 mg once daily | Edema | Intolerance of side effects |

Since beta blockers have been shown to improve life expectancy following myocardial infarction, they may be preferable in patients with chronic CAD.

Calcium antagonists are indicated in patients with the following:

- (1) angina and a history of asthma or chronic obstructive pulmonary disease;
- (2) sick-sinus syndrome or significant arteriovenous conduction disturbances;
- (3) Prinzmetal's angina;
- (4) symptomatic peripheral vascular disease; and
- (5) adverse reactions to beta blockers—depression, sexual disturbances, fatigue.

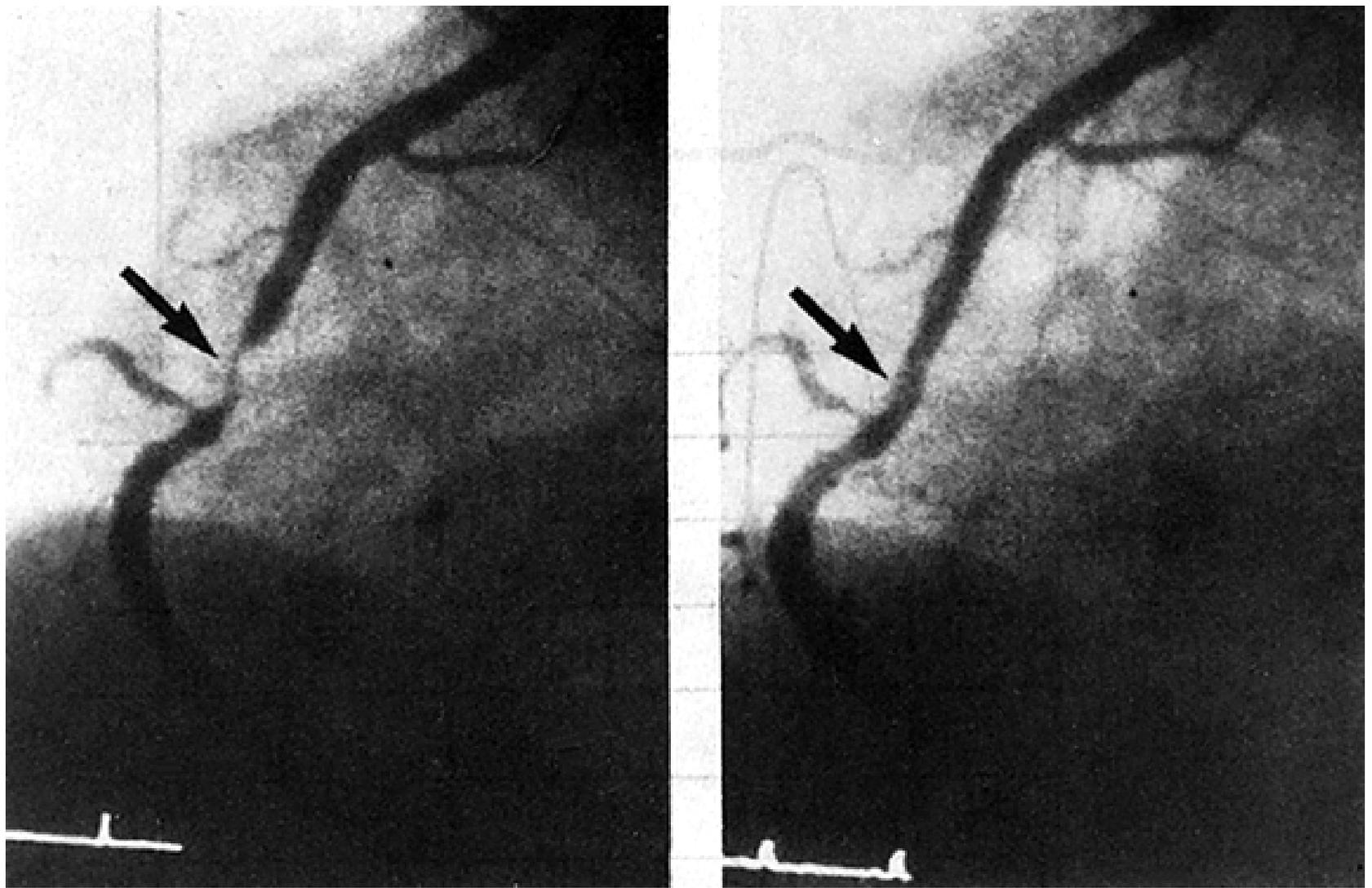
Many patients with angina do well with a combination of a beta blocker and dihydropyridine calcium antagonist.

Antiplatelet therapy, with aspirin, clopidogrel (Plavix), ticlopidine (Ticlid), or dipyridamole (Persantine), is useful in both prevention and treatment of acute coronary syndromes from ruptured coronary plaques and subsequent thrombus formation. Of these, aspirin is most effective in reducing risk for MI, stroke, and cardiac death, while combinations of aspirin and clopidogrel are useful after coronary stenting.

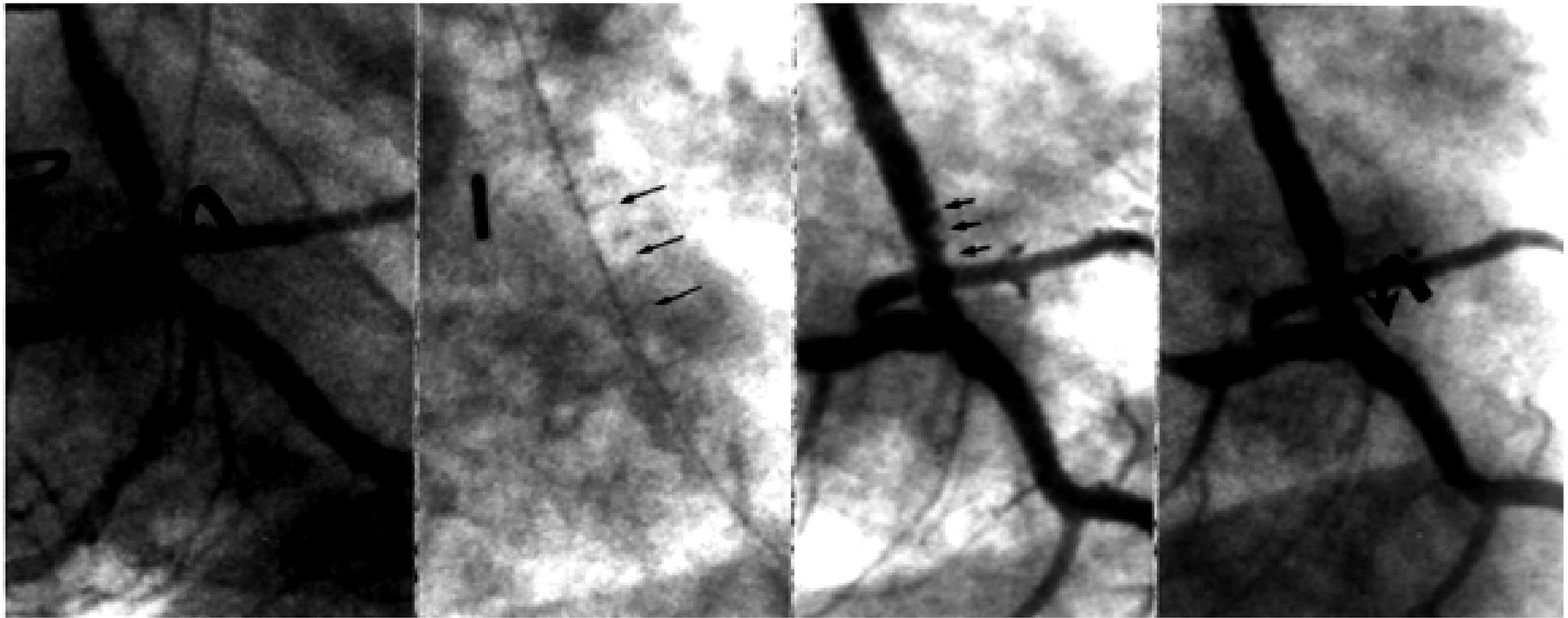
Percutaneous Transluminal Coronary Angioplasty and Related Catheter-based Techniques

The clinical indication for PTCA is angina pectoris, stable or unstable, accompanied by evidence of ischemia in an exercise test. PTCA can be used to dilate stenoses in native coronary arteries as well as in bypass grafts in patients who have recurrent angina following coronary artery surgery. Angioplasty has also been carried out in patients with recent total occlusion (within 3 months) of a coronary artery and severe angina; in this group the primary success rate is decreased to approximately 50 percent.

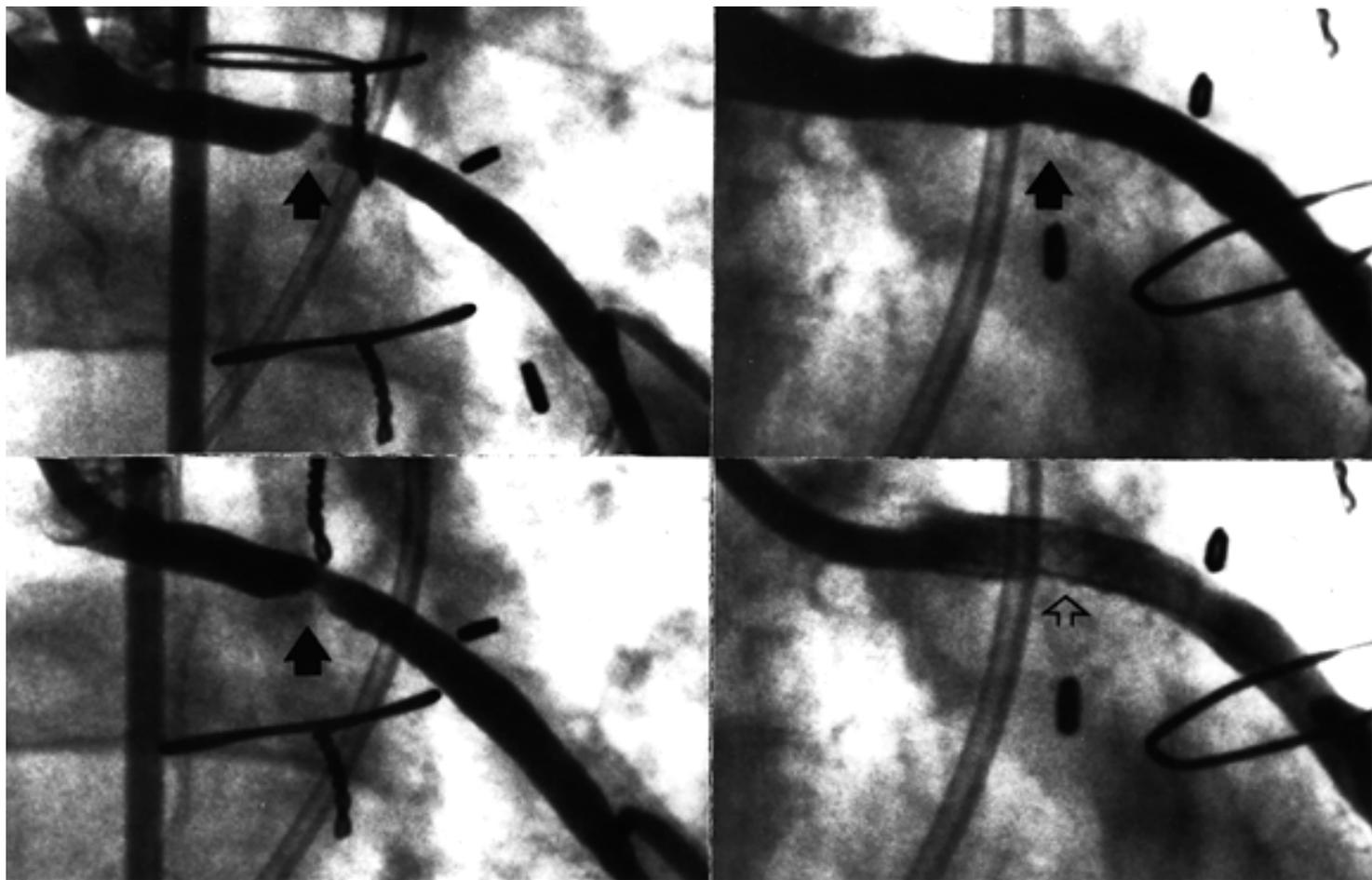
The major complications are due to dissection or thrombosis with vessel occlusion, uncontrolled ischemia, and ventricular failure. In experienced hands, the overall mortality rate should be less than 1 percent, the need for emergency coronary surgery less than 3 percent, and the occurrence of clinical myocardial infarction less than 5 percent of cases.



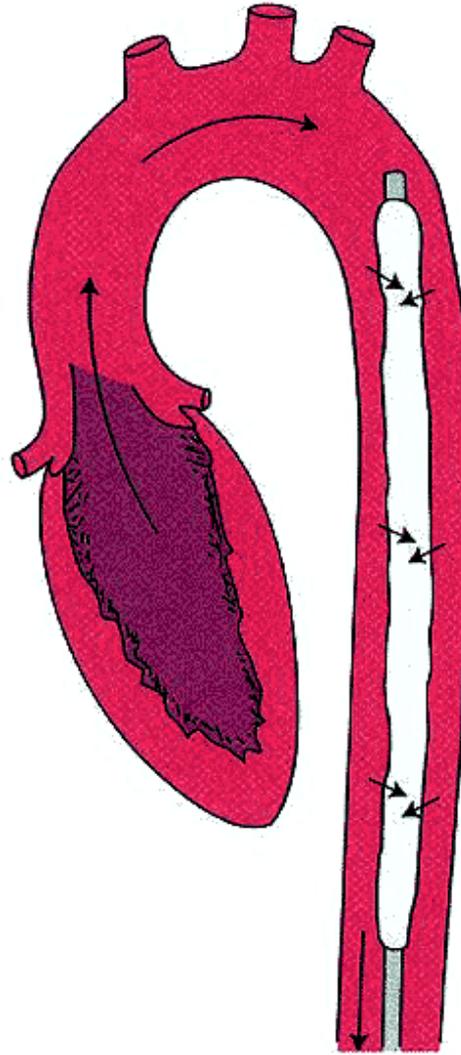
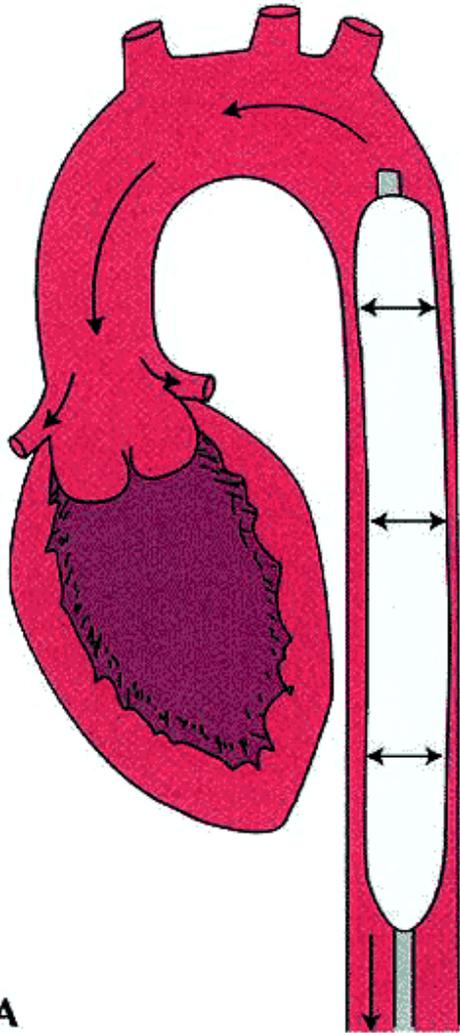
Right coronary angioplasty in a patient with unstable angina. The lesion is shown before (*left panel*) and after (*right panel*) inflation of the PTCA balloon catheter.



Placement of coronary stent for dissection after angioplasty. *Left-hand panel:* A prominent filling defect (*curved arrow*) is visible at the site of attempted PTCA in the distal anastomosis of a saphenous vein graft to the circumflex. *Left center panel:* The coils of a Gianturco-Roubin stent are faintly visible (*arrows*). *Right center panel:* Angiogram following stent placement shows small filling defects (*arrows*) representing prolapse of dissected plaque between stent coils. *Right panel:* Following high-pressure postdilation, luminal appearance is near normal (*curved arrow*). The availability of coronary stents to manage actual and threatened abrupt closure has dramatically reduced the need for emergency bypass surgery in current angioplasty practice.



Stenting of a diseased saphenous vein graft. Upper left: Severe eccentric stenosis in an 8-year-old saphenous vein graft to the left anterior descending coronary artery. Lower left: Following balloon dilatation, significant stenosis persists owing to elastic recoil of the graft atherosclerotic plaque. Upper right: Further lumen enlargement following placement of a slotted-tube stent (arrow). Lower right: Diamond pattern is visible (open arrow) as contrast clears from the graft.



A

The major mode of action of the intra-aortic balloon pump (IABP) in unstable angina is improvement of diastolic coronary blood flow. During diastole (left panel), the balloon is inflated, which increases volume in the aorta, raises diastolic pressure, and increases perfusion of coronary arteries. Just before and during systole (right panel), the balloon is deflated, which decreases the volume in the aorta, decreases aortic pressure (afterload), and facilitates ejection by the left ventricle.

Indications for Coronary Artery Bypass Grafting

1. The operation is relatively safe, with mortality rates less than 1 percent when the procedure is performed in patients without serious comorbid disease and normal left ventricular function.
2. Intraoperative and postoperative mortality increases with the degree of ventricular dysfunction, comorbidities, age above 80 years, and surgical inexperience.
3. *Occlusion of vein grafts* is observed in 10 to 20 percent during the first postoperative year and in approximately 2 percent per year during 5- to 7-year follow-up and 4 percent per year thereafter.
4. Angina is abolished or greatly reduced in approximately 90 percent of patients following complete revascularization. Within 3 years, angina recurs in about one-fourth of patients but is rarely severe.
6. Mortality is reduced by operation in patients with stenosis of the left main coronary artery as well as in patients with three-vessel CAD and impaired left ventricular function.

Comparison of Revascularization Procedures in Multivessel Disease

| Procedure | Advantages | Disadvantages |
|--|---|--|
| Percutaneous transluminal coronary angioplasty | <ul style="list-style-type: none"> Less invasive Shorter hospital stay Lower initial cost Easily repeated Effective in relieving symptoms | <ul style="list-style-type: none"> Restenosis High incidence of incomplete revascularization Relative inefficiency in patients with severe left ventricular dysfunction Uncertain long-term outcome (>10 years) Limited to specific anatomic subsets Poor outcome in diabetics with 2 plus coronary disease |
| Coronary artery bypass grafting | <ul style="list-style-type: none"> Effective in relieving symptoms Improved survival in certain subsets Ability to achieve complete revascularization Wider applicability | <ul style="list-style-type: none"> Cost Increased risk of a repeat procedure due to late graft closure Morbidity |

Unstable angina is meant to signify the intermediate state between myocardial infarction (MI) and the more chronic state of stable angina.

An interplay between disrupted atherosclerotic plaque and overlaid thrombi is present in cases of unstable angina, with consequent hemodynamic deficit or microembolization.

Pathophysiologic factors of unstable angina:

- supply-demand mismatch,
- plaque disruption,
- thrombosis,
- vasoconstriction,
- cyclical flow.

Unstable Angina Pectoris (Acute Coronary Insufficiency)

- (1) Patients with ***new onset*** (<2 months) ***angina*** that is severe and/or frequent (>3 episodes per day) (***angina de novo***);
- (2) Patients with ***accelerating angina***, i.e., those with chronic stable angina who develop angina that is distinctly more frequent, severe, prolonged, or precipitated by less exertion than previously (***crescendo angina***);
- (3) Those with ***severe angina at rest***;
- (4) Patients with prolonged and **severe ischemic chest pain without ECG or enzyme evidence** of significant myocardial infarction. It may present as a new phenomenon or against a background of chronic stable angina (non-Q-wave MI).
- (5) Patients with angina developed shortly after myocardial infarction (***angina reccurens***).
- (6) ***Prinzmetal's variant angina***.
- (7) ***Early postrevascularization angina***.

Braunwald Classification of Unstable Angina

| Characteristic | Class/Category | Details |
|-------------------------------|----------------|---|
| Severity | I | Symptoms with exertion |
| | II | Subacute symptoms at rest (2-30 d prior, >48 h since last pain) |
| | III | Acute symptoms at rest (within prior 48 h) |
| Clinical precipitating factor | A | Secondary (anemia, fever, hypoxia) |
| | B | Primary |
| | C | Postinfarction (<2 wk after infarction) |
| Therapy during symptoms | 1 | No treatment |
| | 2 | Usual angina therapy |
| | 3 | Maximal therapy |

The current standard of care includes drawing blood for total creatine kinase (CK) and its MB isoenzyme (CK-MB) every 6-8 hours during the first 24 hours.

Determine cardiac-specific troponin (T or I) levels at least twice, 6-8 hours apart, because these may be initially negative, especially within 2-4 hours of chest pain.

Absolute elevations of CK-MB or troponin levels are specific evidence of myocardial cell death. This finding is indicative of an unstable coronary plaque that has produced coronary occlusion or distal arterial microemboli.

Troponin I levels of 0.4 ng/mL or higher or troponin T levels of 0.1 ng/mL or higher are considered positive and have been associated with higher short-term and midterm mortality.

The Treatment of Unstable Angina Pectoris

- Patient should be admitted promptly to the hospital;
- ECG monitoring; bed rest; nasal O₂;
- Patients should receive reassurance and sedation;
- **Nitroglycerin** should be given by the sublingual route. Intravenous nitroglycerin is begun at a dosage of 10 µg/min and is raised in 5-µg/min increments to a level at which chest pain is abolished but systolic arterial pressure is maintained or reduced only slightly and other side effects are avoided.

Antithrombotic agents

- Heparin 80 U/kg IV bolus, followed by infusion of 18 U/kg/h; titrate to maintain aPTT 1.5-2.5 times control (1000 Units/hour); decrease initial bolus dose to 50 U/kg IV when used in conjunction with GP IIb/IIIa antagonist.

Low-molecular-weight heparin

- Enoxaparin: 1 mg/kg SC q12h or 1.5 mg/kg SC qd
Prophylaxis against DVT: 30 mg SC q12h.
- Dalteparin: 120 IU/kg q12h SC; not to exceed 10,000 IU for at least 5 d or until revascularization is performed.

Subcutaneous administration of a preparation for 3 to 5 days to maintain the partial thromboplastin time at 2 to 2.5 times control.

Antiplatelet agents

- Aspirin at a dose of 160 - 324 mg/d.
- Clopidogrel (Plavix) 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.

HMG-CoA reductase inhibitors

- Atorvastatin (Lipitor) 10 mg PO qd in the evening; titrate to a maximum 80 mg/d prn.

Glycoprotein IIb/IIIa receptor antagonists

- Tirofiban (Aggrastat) 0.4 mcg/kg/min IV for 30 min, followed by 0.1 mcg/kg/min for up to 72 h.
- Eptifibatide (Integrilin) - 180 mcg/kg IV bolus, followed by continuous infusion of 2 mcg/kg/min for up to 72 h.

Platelet aggregation inhibitors

- Abciximab (ReoPro) 0.25 mg/kg IV bolus, followed by 10 mcg/min IV for 12 h after PCI.

Beta-adrenergic blocking agents

- metoprolol 5 mg IV slow infusion q5min up to 3 times until resolution of angina or titrate to reduce heart rate to 50-70 bpm 50-100 mg 12-hourly).

Calcium channel blockers

- Verapamil or diltiazem are therefore preferable if a beta-adrenoceptor antagonist is contraindicated.

If angina and/or ECG evidence of ischemia do not diminish within 24 to 48 h of the comprehensive treatment described above in patients with no obvious contraindications for revascularization, then cardiac catheterization and coronary arteriography should be performed. In patients who have persistent ischemia and hemodynamic instability intra-aortic balloon counterpulsation may be useful before, during, and immediately after coronary arteriography and revascularization. If the anatomy is suitable, PTCA can be performed with surgical standby. PTCA in this condition, particularly in the presence of thrombus, is attended by a slightly increased risk of acute closure and ischemia. If angioplasty cannot be done, coronary artery bypass grafting should be considered to relieve symptoms and myocardial ischemia and as a means of preventing myocardial damage. The factors that influence the choice between catheter-based and surgical revascularization are similar to that in chronic stable angina.

Prinzmetal's Variant Angina

This relatively uncommon form of unstable angina is characterized by recurrent, prolonged attacks of severe ischemia, caused by episodic focal spasm of an epicardial coronary artery. Ischemic pain usually occurs at rest or awakens the patient from sleep and is characterized by multilead ST-segment elevation. The diagnosis may be confirmed by detecting transient spasm occurring spontaneously or following a provocative stimulus (intravenous ergonovine, intracoronary acetylcholine, hyperventilation) on coronary arteriography.

Treatment

Management of the acute attack consists of multiple doses of sublingual nitroglycerin and short-acting nifedipine (10 to 30 mg); hypotension should be avoided. In chronic management, long-acting nitrates and calcium antagonists are useful. Beta-adrenergic blockers are of little value, while prazosin, a selective alpha-adrenoceptor blocker, may be useful. Occasionally, mechanical revascularization is helpful in patients with accompanying severe discrete obstructive lesions.

Silent myocardial ischemia

Silent myocardial ischemia Includes individuals who truly have no symptoms whatsoever and those with evidence of CHD manifested as decreased endurance or energy.

Silent myocardial ischemia is indicated by lack of symptoms in the presence of documented ECG or nuclear imaging evidence of myocardial ischemia. It occurs frequently in patients with CAD, particularly frequently in diabetic patients and in patients who have undergone cardiac transplantation.

Stratification patients with silent ischemia Cohn

Type I silent ischemia. It occurs asymptomatic patients with obstructive CAD (which may be severe), and these patients do not experience angina at any time.

Type II silent ischemia is the form that occurs in patients with documented previous MI.

Type III silent ischemia. It occurs in patients with the usual forms of chronic stable angina, UA, and variant angina. When monitored, patients with this form of silent ischemia exhibit some episodes of ischemia that are associated with chest discomfort and other episodes that are not, ie, episodes of silent (asymptomatic) ischemia.