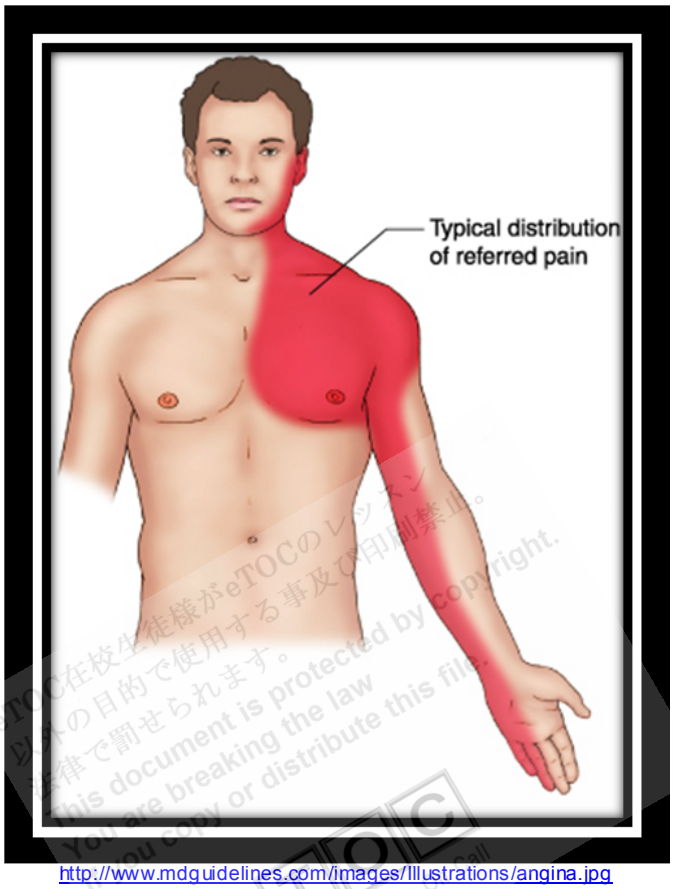
Angina Pectoris



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Angina pectoris *is a clinical syndrome of precordial discomfort or pressure due to* ***transient myocardial ischemia*** *without infarction. It is typically precipitated by* ***exertion*** *or* ***psychologic stress*** *and relieved by rest or* ***sublingual nitroglycerin****. Diagnosis is by symptoms,* ***ECG****, and* ***myocardial imaging****. Treatment may include* ***nitrates****,* ***β-blockers****,* ***Ca channel blockers****, and coronary* ***angioplasty*** *or* ***coronary artery bypass graft surgery****.*

Etiology

Angina pectoris occurs when cardiac workload and resultant **myocardial O_2** demand exceed the ability of coronary arteries to supply an adequate amount of **oxygenated blood**, as can occur when the arteries are narrowed. Narrowing usually results from atherosclerosis but may result from **coronary artery spasm** or, rarely, **coronary artery embolism**. **Acute coronary thrombosis** can cause angina if obstruction is partial or

transient, but it usually causes MI.

Because **myocardial O_2** demand is determined mainly by heart rate, **systolic wall tension**, and **contractility**, narrowing of a **coronary artery** typically results in **angina** that occurs during exertion and is relieved by rest.

In addition to exertion, cardiac workload can be increased by disorders such as **hypertension**, **aortic stenosis**, **aortic regurgitation**, or **hypertrophic cardiomyopathy**. In such cases, angina can result whether **atherosclerosis** is present or not. These disorders can also decrease relative **myocardial perfusion** because **myocardial mass** is increased (causing decreased diastolic flow).

A decreased **O_2** supply, as in severe **anemia** or **hypoxia**, can precipitate or aggravate angina.

Pathophysiology

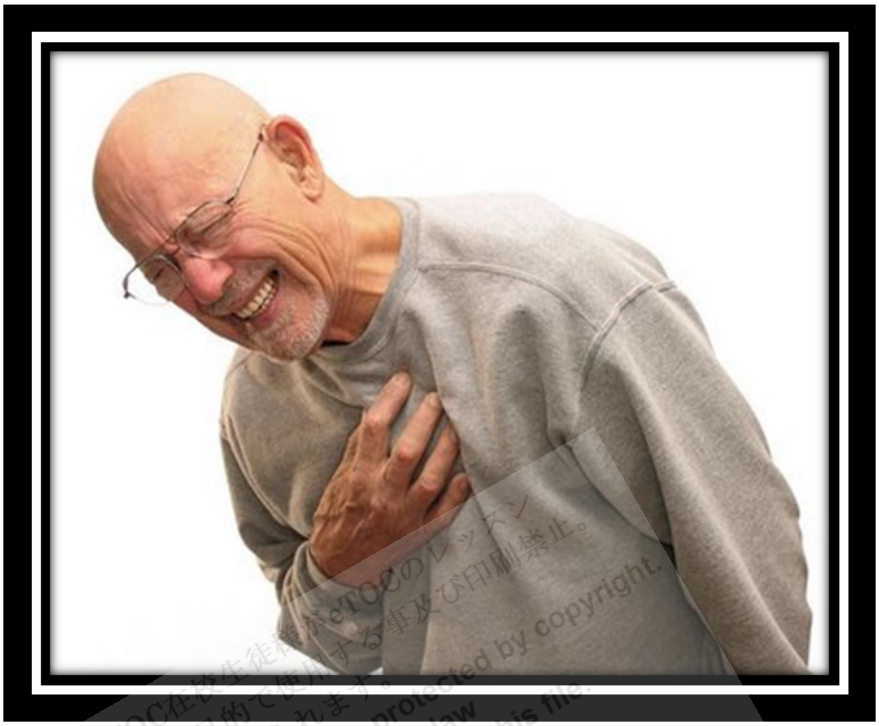
In stable angina, the relationship between workload or demand and **ischemia** is usually relatively predictable. However, **atherosclerotic** arterial narrowing is not entirely fixed; it varies with the normal fluctuations in arterial tone that occur in all people. Thus, more people have angina in the morning, when arterial tone is relatively high. Also, abnormal **endothelial function** may contribute to variations in arterial tone; eg, in **endothelium** damaged by **atheromas**, stress of a **catecholamine** surge causes **vasoconstriction** rather than dilation (normal response).

As the **myocardium** becomes **ischemic**, **coronary sinus blood pH falls**, **cellular K** is lost, **lactate accumulates**, **ECG abnormalities** appear, and **ventricular function** deteriorates. **Left ventricular (LV) diastolic pressure** usually increases during angina, sometimes inducing **pulmonary congestion** and **dyspnea**. The exact mechanism by which **ischemia** causes discomfort is unclear but may involve nerve stimulation by **hypoxic metabolites**.

Symptoms and Signs

Angina may be a vague, barely troublesome ache or may rapidly become a severe, intense precordial crushing sensation. It is rarely described as pain. Discomfort is most commonly felt beneath the **sternum**, although location varies. Discomfort may radiate to the left shoulder and down the inside of the left arm, even to the fingers; straight through to the back; into the throat, jaws, and teeth; and, occasionally, down the inside of the right arm. It may also be felt in the upper abdomen. The discomfort of angina is never

above the ears or below the **umbilicus**.



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Some patients have **atypical angina** (eg, **bloating**, **gas**, **abdominal distress**), often ascribing symptoms to **indigestion**; belching may even seem to relieve the symptoms. Others have dyspnea due to the sharp, reversible increase in LV filling pressure that often accompanies **ischemia**. Frequently, the patient's description is imprecise, and whether the problem is **angina**, **dyspnea**, or both may be difficult to determine. Because **ischemic symptoms** require a minute or more to resolve, brief, fleeting sensations rarely represent angina.

Between and even during attacks of angina, physical findings may be normal. However, during the attack, heart rate may increase modestly, BP is often elevated, heart sounds become more distant, and the apical impulse is more diffuse. The 2nd heart sound may become paradoxical because **LV ejection** is more prolonged during an ischemic attack. A 4th heart sound is common, and a 3rd heart sound may develop. A mid or late **systolic apical murmur shrill**—or blowing but not especially loud—may occur if ischemia causes localized **papillary muscle dysfunction**, causing **mitral regurgitation**.

Angina pectoris is typically triggered by exertion or strong emotion, usually persists no more than a few minutes, and subsides with rest. Response to exertion is usually

predictable, but in some patients, exercise that is tolerated one day may precipitate angina the next because of variations in arterial tone. Symptoms are exaggerated when exertion follows a meal or occurs in cold weather; walking into the wind or first contact with cold air after leaving a warm room may precipitate an attack. Symptom severity is often classified by the degree of exertion resulting in angina.

Table 1

Canadian Cardiovascular Classification System of Angina Pectoris

Class	Activities Triggering Chest Pain
1	Strenuous, rapid, or prolonged exertion
	Not usual physical activities (eg, walking, climbing stairs)
2	Walking rapidly
	Walking uphill
	Climbing stairs rapidly
	Walking or climbing stairs after meals
	Cold
	Wind
	Emotional stress
3	Walking, even 1 or 2 blocks at usual pace and on level ground

	Climbing stairs, even 1 flight
4	Any physical activity
	Sometimes occurring at rest

Adapted from Braunwald E, Antman EM, Beasley JW, et al: ACC/AHA Guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the management of patients with unstable angina). *Journal of American College of Cardiology* 36:970–1062, 2000.

Attacks may vary from several a day to symptom-free intervals of weeks, months, or years. They may increase in frequency (called **crescendo angina**) to a fatal outcome or gradually decrease or disappear if adequate **collateral coronary circulation** develops, if the **ischemic area infarcts**, or if heart failure or **intermittent claudication supervenes** and limits activity.

Nocturnal angina may occur if a dream causes striking changes in respiration, pulse rate, and BP. Nocturnal angina may also be a sign of recurrent LV failure, an equivalent of **nocturnal dyspnea**. The recumbent position increases **venous** return, stretching the myocardium and increasing wall stress, which increases O_2 demand.

Angina may occur spontaneously during rest (called **angina decubitus**). It is usually accompanied by a modestly increased heart rate and a sometimes markedly higher BP, which increase O_2 demand. These increases may be the cause of rest angina or the result of **ischemia** induced by plaque rupture and **thrombus** formation. If angina is not relieved, unmet **myocardial O_2 demand** increases further, making **MI** more likely.

Unstable angina: Because angina characteristics are usually predictable for a given patient, any changes (ie, **rest angina, new-onset angina, increasing angina**) should be considered serious. Such changes are termed unstable angina and require prompt evaluation and treatment.

Unstable angina is classified based on severity and clinical situation. Also considered are whether unstable angina occurs during treatment for chronic stable angina and whether transient changes in ST-T waves occur during angina. If angina has occurred within 48 h and no contributory **extracardiac** condition is present, troponin levels may

be measured to help estimate **prognosis**; **troponin-negative** indicates a better prognosis than **troponin-positive**.

Table 2

Braunwald Classification of Unstable Angina*

Classification	Description	Designation
Severity		
I	New onset of **severe angina** or **increasing † angina** No angina during rest	—
II	Angina during rest within past month but not within preceding 48 h	**Subacute** angina at rest
III‡	Angina during rest within 48 h	**Acute angina** at rest
Clinical situation		
A	Develops secondary to an **extracardiac** condition that worsens **myocardial ischemia**	Secondary UA
B‡	Develops when no contributory **extracardiac** condition is present	Primary UA
C	Develops within 2 wk of **acute MI**	Post-MI UA

*Basic classification consists of Roman numeral and a letter.

†Angina occurs more frequently, is more severe, lasts longer, or is triggered by less exertion.

‡For patients with class **IIIB**, **troponin status** (negative or positive) is determined to estimate prognosis.

UA = unstable angina.

Adapted from Hamm CW, Braunwald E: APACHE II: A classification of unstable angina revisited. *Circulation* 102:118–122, 2000.

Diagnosis

- Typical symptoms
- ECG
- Stress testing with ECG or imaging (**echocardiographic** or **nuclear**)
- **Coronary angiography** for significant symptoms or positive stress test

Diagnosis is suspected if chest discomfort is typical and is precipitated by exertion and relieved by rest. Patients whose chest discomfort lasts > 20 min or occurs during rest or who have syncope or heart failure are evaluated for an acute **coronary syndrome**. Chest discomfort may also be caused by GI disorders (eg, **reflux**, **esophageal spasm**, **indigestion**, **cholelithiasis**), **costochondritis**, anxiety, panic attacks, hyperventilation, and other **cardiac disorders** (eg, **pericarditis**, **mitral valve prolapse**, **supraventricular tachycardia**, **atrial fibrillation**), even when coronary blood flow is not compromised.

ECG: If typical **exertional symptoms** are present, **ECG** is indicated. Because angina resolves quickly with rest, ECG rarely can be done during an attack except during stress testing. If done during an attack, ECG is likely to show reversible ischemic changes: **T wave** discordant to the **QRS vector**, **ST-segment** depression (typically), ST-segment elevation, decreased **R-wave height**, **intraventricular** or bundle branch conduction disturbances, and **arrhythmia** (usually **ventricular extrasystoles**). Between attacks, the ECG (and usually **LV function**) at rest is normal in about 30% of patients with a typical history of **angina pectoris**, even those with extensive **3-vessel disease**. In the remaining 70%, the ECG shows evidence of previous infarction, hypertrophy, or nonspecific ST-segment and T-wave (ST-T) abnormalities. An abnormal resting ECG alone does not establish or refute the diagnosis.

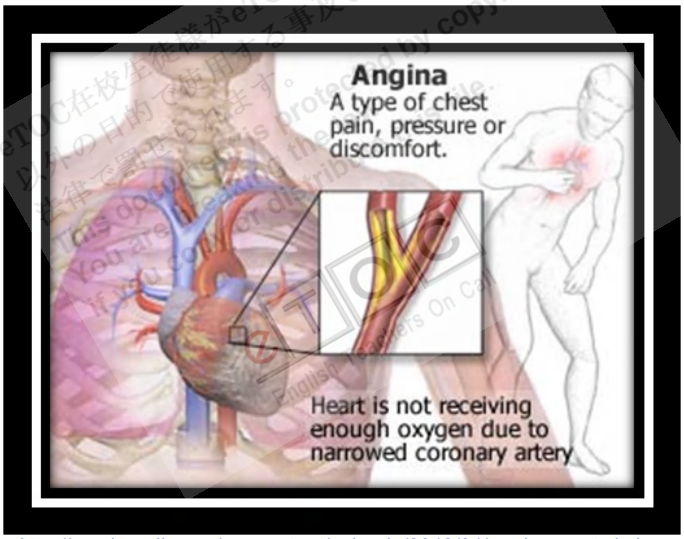
Stress testing: More specific tests include stress testing with ECG or with **myocardial imaging** (eg, **echocardiography**, **radionuclide imaging**) and **coronary angiography**. Further testing is needed to confirm the diagnosis, evaluate disease severity, determine appropriate exercise levels for the patient, and help predict prognosis.

Noninvasive tests are considered first. For **coronary artery disease** (**CAD**), the most accurate are stress **echocardiography** and **myocardial perfusion** imaging with **single-photon emission CT (SPECT) or PET**. However, these tests are more expensive than simple stress testing with ECG.

If a patient has a normal resting ECG and can exercise, exercise stress testing with ECG is done. In men with chest discomfort suggesting angina, stress ECG testing has a specificity of 70%; sensitivity is 90%. Sensitivity is similar in women, but specificity is

lower, particularly in women < 55 (< 70%). However, women are more likely than men to have an abnormal resting ECG when CAD is present (32% vs 23%). Although sensitivity is reasonably high, exercise ECG can miss severe CAD (even left main or 3-vessel disease). In patients with atypical symptoms, a negative stress ECG usually rules out **angina pectoris** and CAD; a positive result may or may not represent coronary ischemia and indicates need for further testing.

When the resting ECG is abnormal, **false-positive ST-segment** shifts are common on the stress ECG, so patients should have stress testing with myocardial imaging. Exercise or **pharmacologic stress** (eg, with **dobutamine or dipyridamole infusion**) may be used. The choice of imaging technique depends on institutional availability and expertise. Imaging tests can help assess LV function and response to stress; identify areas of **ischemia, infarction**, and **viable tissue**; and determine the site and extent of **myocardium** at risk. Stress **echocardiography** can also detect **ischemia-induced mitral regurgitation**.



http://nursingcrib.com/wp-content/uploads/2012/01/angina-pectoris.jpg

Angiography: **Coronary angiography** is the standard for diagnosing CAD but is not always necessary to confirm the diagnosis. It is indicated primarily to locate and assess severity of coronary artery lesions when revascularization **(percutaneous intervention [PCI] or coronary artery bypass grafting [CABG])** is being considered. **Angiography** may also be indicated when knowledge of coronary anatomy is necessary to advise about work or lifestyle needs (eg, discontinuing job or sports activities). Obstruction is assumed to be physiologically significant when the **luminal diameter** is reduced > 70%. This reduction correlates well with the presence of angina pectoris unless spasm or **thrombosis** is superimposed.

Intravascular ultrasonography provides images of **coronary artery structure**. An **ultrasound probe** on the tip of a **catheter** is inserted in the coronary arteries during **angiography**. This test can provide more information about coronary anatomy than other tests; it is indicated when the nature of lesions is unclear or when apparent disease severity does not match symptom severity. Used with **angioplasty**, it can help ensure optimal placement of **stents**.

Imaging: **Electron beam CT** can detect the amount of **Ca** present in coronary artery plaque. The Ca score (from 1 to 100) is roughly proportional to the risk of subsequent coronary events. However, because Ca may be present in the absence of significant stenosis, the score does not correlate well with the need for **angioplasty** or **CABG**. Thus, the **American Heart Association** recommends that screening with electron beam CT should be done only for select groups of patients and is most valuable when combined with historical and clinical data to estimate risk of death or nonfatal MI. These groups may include **asymptomatic patients** with an intermediate **Framingham** 10-yr risk estimate of 10 to 20% and symptomatic patients with equivocal stress test results.

Multidetector row CT (MDRCT) coronary angiography can accurately identify **coronary stenosis** and has a number of advantages. The test is noninvasive, can exclude coronary stenosis with high accuracy, can establish stent or bypass graft patency, can visualize cardiac and coronary venous anatomy, and can assess calcified and **noncalcified plaque burden**. However, radiation exposure is significant, and the test is not suitable for patients with a heart rate of > 65 beats/min, those with irregular heart beats, and pregnant women. Patients must also be able to hold their breath for 15 to 20 sec, 3 to 4 times during the study.

Evolving indications for **MDRCT coronary angiography** include

- Asymptomatic high-risk patients or patients with **atypical** or **typical angina** who have inconclusive exercise stress test results, cannot undergo exercise stress testing, or need to undergo major **noncardiac surgery**
- Patients in whom invasive **coronary angiography** was unable to locate a major coronary artery or graft

Cardiac MRI has become invaluable in evaluating many cardiac and great vessel abnormalities. It may be used to evaluate **CAD** by several techniques, which enable direct visualization of coronary stenosis, assessment of flow in the coronary arteries, evaluation of **myocardial perfusion** and **metabolism**, evaluation of wall motion abnormalities during stress, and assessment of infracted **myocardium** vs **viable myocardium.**

Current indications for cardiac MRI include evaluation of cardiac structure and function, assessment of **myocardial viability**, and possibly diagnosis and risk assessment of patients with either known or suspected CAD.

Prognosis

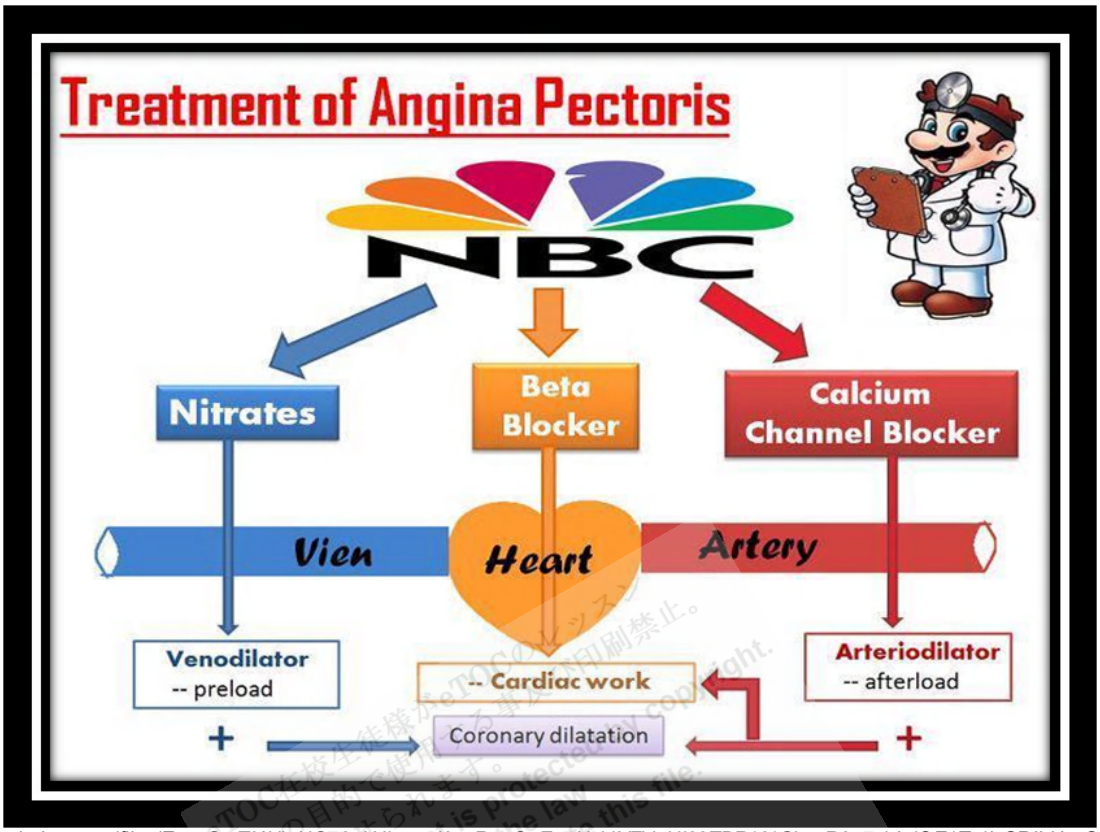
The main adverse outcomes are **unstable angina**, **MI**, and sudden death due to **arrhythmias**. Annual mortality rate is about 1.4% in patients with angina, no history of MI, a normal resting ECG, and normal BP. However, women with CAD tend to have a worse **prognosis**. Mortality rate is about 7.5% when **systolic hypertension** is present, 8.4% when the ECG is abnormal, and 12% when both are present. **Type 2 diabetes** about doubles the mortality rate for each scenario.

Prognosis worsens with increasing age, increasingly severe **anginal symptoms**, presence of **anatomic lesions**, and poor **ventricular function**. Lesions in the **left main coronary artery** or **proximal left anterior descending artery** indicate particularly high risk. Although prognosis correlates with number and severity of coronary arteries affected, prognosis is surprisingly good for patients with stable angina, even those with 3-vessel disease, if ventricular function is normal.

Treatment

- Modification of risk factors (smoking, BP, lipids)
- **Antiplatelet drugs** (aspirin plus clopidogrel)
- **β-Blockers**
- **Nitroglycerin and Ca channel blockers** for symptom control
- **Revascularization** if symptoms persist despite medical therapy
- **ACE inhibitors** and **statins**

Reversible risk factors are modified as much as. Smokers should stop smoking; ≥ 2 yr after stopping smoking, risk of MI is reduced to that of people who never smoked. Hypertension is treated diligently because even mild hypertension increases cardiac workload. Weight loss alone often reduces the severity of angina. Sometimes treatment of mild LV failure markedly lessens angina. Paradoxically, digitalis occasionally intensifies angina, presumably because increased **myocardial contractility** increases O_2 demand, arterial tone is increased, or both. Aggressive reduction of total and LDL cholesterol (via diet plus drugs as necessary) slows the progression of CAD, may cause some lesions to regress, and improves endothelial function and thus arterial response to stress. An exercise program emphasizing walking often improves the sense of well-being, reduces CAD risk, and improves exercise tolerance.



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Drugs: The main goals are to relieve acute symptoms, prevent or reduce **ischemia**, and prevent future ischemic events. For an acute attack, **sublingual nitroglycerin** is the most effective drug.

To prevent ischemia, all patients diagnosed with CAD or at high risk of developing CAD should take an antiplatelet drug daily. **β-Blockers**, unless contraindicated or not tolerated, are given to most patients. For some patients, prevention of symptoms requires Ca channel blockers or long-acting nitrates.

Antiplatelet drugs inhibit platelet aggregation. **Aspirin** binds irreversibly to platelets and inhibits **cyclooxygenase** and platelet aggregation. **Clopidogrel** blocks adenosine **diphosphate**–induced **platelet aggregation**. Either drug can reduce risk of ischemic events (MI, sudden death), but the drugs are most effective when given together. Patients unable to tolerate one should receive the other drug alone.

β-Blockers limit symptoms and prevent infarction and sudden death better than other drugs.β-Blockers block sympathetic stimulation of the heart and reduce **systolic BP**,

heart rate, contractility, and cardiac output, thus decreasing **myocardial O_2 demand** and increasing exercise tolerance. They also increase the threshold for ventricular fibrillation. Most patients tolerate these drugs well. Many β-blockers are available and effective. Dose is titrated upward as needed until limited by bradycardia or adverse effects. Patients who cannot tolerate β-blockers are given a Ca channel blocker with negative **chronotropic effects** (eg, **diltiazem,verapamil**). Those at risk of β-blocker intolerance (eg, those with asthma) may be tried on a **cardioselective β-blocker** (eg, **carvedilol**), perhaps with **pulmonary function testing** before and after drug administration to detect **drug-induced bronchospasm**.

Nitroglycerin is a potent **smooth-muscle relaxant** and **vasodilator**. Its main sites of action are in the peripheral vascular tree, especially in the **venous** or **capacitance system**, and in coronary blood vessels. Even severely **atherosclerotic vessels** may dilate in areas without atheroma. Nitroglycerin lowers systolic BP and dilates systemic veins, thus reducing myocardial wall tension, a major determinant of **myocardial O_2** need. **Sublingualnitroglycerin** is given for an acute attack or for prevention before exertion. Dramatic relief usually occurs within 1.5 to 3 min, is complete by about 5 min, and lasts up to 30 min. The dose may be repeated every 4 to 5 min up to 3 times if relief is incomplete. Patients should always carry **nitroglycerin tablets** or **aerosol spray** to use promptly at the onset of an angina attack. Patients should store tablets in a tightly sealed, light-resistant glass container, so that potency is not lost. Because the drug deteriorates quickly, small amounts should be obtained frequently.

Long-acting nitrates (oral or **transdermal**) are used if symptoms persist after the β-blocker dose is maximized. If angina occurs at predictable times, a nitrate is given to cover those times. Oral nitrates include **isosorbide dinitrate** and **mononitrate** (the active **metabolite** of the **dinitrate**). They are effective within 1 to 2 h; their effect lasts 4 to 6 h. Sustained-release formulations of **isosorbide mononitrate** appear to be effective throughout the day. For transdermal use, cutaneous nitroglycerin patches have largely replaced nitroglycerin ointments primarily because ointments are inconvenient and messy. Patches slowly release the drug for a prolonged effect; exercise capacity improves 4 h after patch application and wanes in 18 to 24 h. Nitrate tolerance may occur, especially when plasma concentrations are kept constant. Because MI risk is highest in early morning, an afternoon or early evening respite period from nitrates is reasonable unless a patient commonly has angina at that time. For nitroglycerin, an 8- to 10-h respite period seems sufficient. **Isosorbide** may require a 12-h respite period. If given once/day, sustained-release **isosorbide mononitrate** does not appear to elicit tolerance.

Ca channel blockers may be used if symptoms persist despite use of nitrates or if nitrates are not tolerated. Ca channel blockers are particularly useful if hypertension or coronary spasm is also present. Different types of Ca channel blockers have different effects. **Dihydropyridines** (eg, **nifedipine**, **amlodipine**, **felodipine**) have no **chronotropic** effects and vary substantially in their negative inotropic effects. Shorter-acting **dihydropyridines** may cause reflex tachycardia and are associated with increased mortality in CAD patients; they should not be used to treat stable angina. Longer-acting formulations of **dihydropyridines** have fewer **tachycardic effects**; they are most commonly used with a β-blocker. In this group,**amlodipine** has the weakest negative **inotropic effects**; it may be used in patients with **LV systolic dysfunction**. **Diltiazem**

and verapamil, other types of Ca channel blockers, have negative chronotropic and inotropic effects. They can be used alone in patients with β-blocker intolerance or asthma and normal LV systolic function but may increase cardiovascular mortality in patients with LV systolic dysfunction.

Table 3

Drugs for Coronary Artery Disease

Drug	Dosage	Use
ACE inhibitors		
Benazepril Captopril Enalapril Fosinopril Lisinopril Moexipril Perindopril Quinapril Ramipril Trandolapril	Variable	All patients with CAD, especially those with large infarctions, heart failure, hypertension, and diabetes Contraindications including hypotension, renal failure, bilateral renal artery stenosis, and known allergy
Angiotensin II receptor blockers		

Candesartan Eprosartan Irbesartan Losartan Telmisartan Valsartan	Variable	An effective alternative for patients who cannot tolerate ACE inhibitors (eg, because of cough); currently, not first-line treatment after MI Contraindications including hypotension, renal failure, bilateral renal artery stenosis, and known allergy
Anticoagulants		
Argatroban	350 µg/kg (bolus) followed by 25 µg/kg/min	Patients with ACS and a known or suspected history ofheparin-induced thrombocytopenia as an alternative to heparin
Bivalirudin	0.75 mg/kg (bolus) followed by 1.75 mg/kg/h	
Fondaparinux	2.5 mg sc q 24 h	
Enoxaparin †	30 mg IV (bolus) followed by 1 mg/kg sc q 12 h (maximum, 100 mg)	Patients with unstable angina or NSTEMI Patients < 75 yr receivingtenecteplase Almost all patients with STEMI as an alternative to unfractionated heparin

		(unless PCI is indicated and can be done in < 90 min); drug continued until **PCI** or **CABG** is done or patient is discharged
Unfractionatedheparin	60–70 units/kg IV (maximum, 5000 units; bolus), followed by 12–15 units/kg/h (maximum, 1000 units/h) for 3 to 4 days or until PCI is complete	Patients with unstable angina or **NSTEMI** as an alternative **toenoxaparin**
	60 units/kg IV (maximum, 4000 units; bolus) given when **alteplase** ,**reteplase** , **ortenecteplase** is started, then followed by 12 units/kg/h (maximum,1000 units/h) for 48 h or until PCI is complete	Patients who have STEMI and undergo urgent angiography and PCI or patients > 75 yr receiving **tenecteplase**
Warfarin	Dose adjusted to	May be useful long-term

	maintain INR of 2.5–3.5	in patients at high risk of systemic emboli (ie, with **large anterior MI**, **known LV thrombus**, or **atrial fibrillation**)
Antiplatelet drugs		
Aspirin	**For stable angina:** 75 or 81 mg po once/day (enteric-coated)	All patients with CAD or at high risk of developing CAD, **unlessaspirin** is not tolerated or is contraindicated; used long-term
	For ACS: 160–325 mg po chewed (not enteric-coated) on arrival at emergency department and once/day thereafter during hospitalization and 81 mg† po once/day long-term after discharge	
Clopidogrel (preferred)	75 mg po once/day	Used with aspirin or, in patients who cannot **tolerateaspirin**, alone
	For patients	For patients undergoing

	undergoing PCI: 300–600 mg po once, then 75 mg po once/day for 1–12 mo	**PCI**,**clopidogrel** loading dose to be administered only in **cardiac catheterization** laboratory after angiography has confirmed that coronary anatomy is amenable to PCI (so as not to delay CABG if indicated) Maintenance therapy required for at least 1 mo for bare-metal stents and for at least 12 mo for drug-eluting stents
Prasugrel	60 mg po once, followed by 10 mg po once/day	Only for patients with ACS undergoing PCI Not used in combination with **fibrinolytic therapy**
Ticlopidine	250 mg po bid	Rarely used routinely because neutropenia is a risk and **WBC count** must be monitored regularly
Glycoprotein IIb/IIIa inhibitors	IV for 24–36 h	Some patients with **ACS**, particularly those who are having PCI with stent placement and high-risk patients with unstable angina or NSTEMI
Abciximab	0.25 μg/kg bolus, then 10μg/min	
Eptifibatide	180 μg/kg bolus, then 2μg/kg/min	Therapy started at least 6 h before PCI and

		continued for 18 to 24 h thereafter
Tirofiban	0.4 μg/kg/min for 30 min, then 0.1 μg/kg/min	
β-Blockers		
Atenolol	50 mg po q 12 h acutely; 50–100 mg po bid long-term	All patients with ACS, unless aβ-blocker is not tolerated or is contraindicated, especially high-risk patients; used long-term
Bisoprolol	2.5–5 mg po once/day, increasing to 10–15 mg once/day depending on heart rate and BP response	
Carvedilol	25 mg po bid (in patients with heart failure or other hemodynamic instability, the starting dose should be as low as 1.625–3.125 mg bid and increased very slowly as tolerated)	
Metoprolol	1–3 boluses of 5	

	mg given 2–5 min apart as tolerated (up to 15 mg); then 25–50 mg po q 6 h, beginning 15 min after last IV dose and continued for 48 h; then 100 mg bid or 200 mg once/day given long term	
Calcium channel blockers		
Amlodipine	5–10 mg po once/day	Patients with stable angina, if symptoms persist despite nitrates use or if nitrates are not tolerated
Diltiazem (extended-release)	180–360 po once/day	
Felodipine	2.5–20 mg po once/day	
Nifedipine (extended-release)	30–90 mg po once/day	
Verapamil (extended-release)	120–360 mg po once/day	
HMG-CoA reductase inhibitors (statins)		
Atorvastatin **Fluvastatin** **Lovastatin** **Pravastatin**	Variable	Patients with CAD to achieve a target LDL of 70 mg/dL (1.81 mmol/L)

Rosuvastatin **Simvastatin**		
Nitrates: Short acting		
Sublingualnitroglycerin (tablet or spray)	0.3–0.6 mg q 4–5 min up to 3 doses	All patients for immediate relief of chest pain; used as needed
Nitroglycerin as continuous **IV drip**	Started at 5 μg/min and increased 2.5–5.0 μg every few minutes until required response occurs	Selected patients with ACS: During the first 24 to 48 h, those with heart failure (unless hypotension is present), large anterior MI, persistent angina, or hypertension (BP is reduced by 10–20 mm Hg but not to <80–90 mm Hg systolic) For longer use, those with recurrent angina or persistent **pulmonary congestion**
Nitrates: Long acting		
Isosorbide dinitrate	10–20 mg po tid; can be increased to 40 mg tid	Patients who have unstable angina or persisternt severe angina and continue to have anginal symptoms after theβ-blocker dose is maximized A nitrate-free period of 8–10 h (typically at night) recommended to
Isosorbide dinitrate (sustained-release)	40–80 mg po bid (typically given at 8 AM and 2 PM)	

Isosorbide mononitrate	20 mg po bid, with 7 h between 1st and 2nd doses	avoid tolerance
Isosorbide mononitrate (sustained-release)	30 or 60 mg once/day, increased to 120 mg or, rarely, 240 mg	
Nitroglycerin patches	0.2–0.8 mg/h applied between 6:00 and 9:00 AM and removed 12 to 14 h later to avoid tolerance	
Nitroglycerin ointment 2% preparation (15 mg/2.5 cm)	1.25 cm spread evenly over upper torso or arms q 6 to 8 h and covered with plastic, increased to 7.5 cm as tolerated, and removed for 8–12 h each day to avoid tolerance	
Opioids		
Morphine	2–4 mg IV, repeated as needed	All patients with chest pain due to ACS to relieve pain (but **ischemia** may persist) Best used after drug

	therapy has been started or the decision to perform **revascularization** has been made

*Of low **molecular weight heparins** (**LMWHs**), **enoxaparin** is preferred.

†Higher doses of aspirin do not provide greater protection and increase risk of adverse effects.

ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; CAD = coronary artery disease; LV = left ventricular; NSTEMI = non–ST-segment elevation MI; PCI =percutaneous intervention; STEMI = ST-segment elevation MI.

Revascularization: **Revascularization**, either with PCI (eg, **angioplasty**, **stenting**) or **CABG** should be considered if angina persists despite drug therapy and worsens quality of life or if anatomic lesions (noted during angiography) put a patient at high risk of mortality. The choice between **PCI** and CABG depends on extent and location of anatomic lesions, the experience of the surgeon and medical center, and, to some extent, patient preference.

PCI is usually preferred for 1- or 2-vessel disease with suitable **anatomic lesions**. Lesions that are long or near bifurcation points are often not amenable to PCI. However, as stent technology improves, PCI is being used for more complicated cases.

CABG is very effective in selected patients with angina. The ideal candidate has severe angina pectoris and localized disease, or **diabetes mellitus**. About 85% of patients have complete or dramatic symptom relief. Exercise stress testing shows positive correlation between graft patency and improved exercise tolerance, but exercise tolerance sometimes remains improved despite graft closure.

CABG improves survival for patients with left main disease, those with 3-vessel disease and poor LV function, and some patients with 2-vessel disease. However, for patients with mild or moderate angina (class I or II) or 3-vessel disease and good ventricular function, CABG appears to only marginally improve survival. For patients with 1-vessel disease, outcomes with drug therapy, PCI, and CABG are similar; exceptions are left main disease and proximal left anterior descending disease, for which **revascularization** appears advantageous.

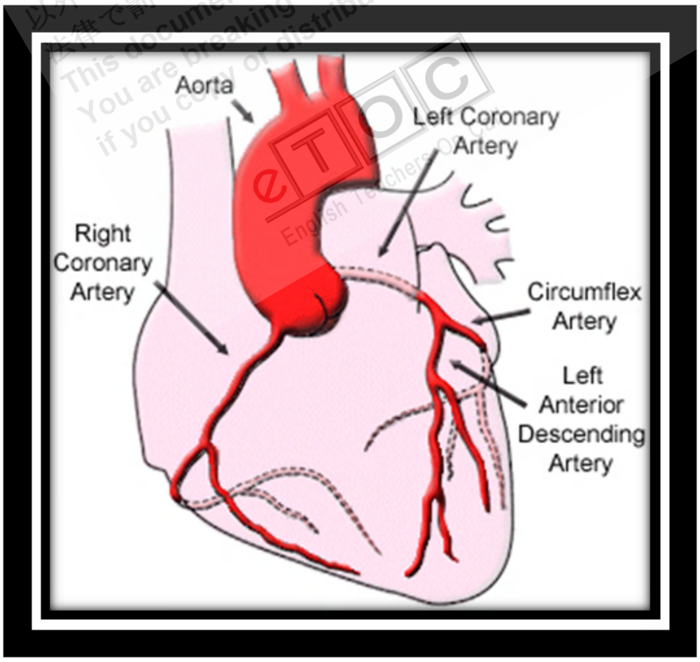
VARIANT ANGINA

Variant angina *is* ***angina pectoris*** *secondary to* ***epicardial coronary artery spasm*** *(****Prinzmetal's angina****).*

Most patients with variant angina have significant fixed proximal obstruction of at least one major coronary artery. Spasm usually occurs within 1 cm of the obstruction (often accompanied by ventricular arrhythmia).

Symptoms are **anginal discomfort** occurring mainly during rest, often at night, and only rarely and inconsistently during exertion (unless significant coronary artery obstruction is also present). Attacks tend to occur regularly at certain times of day.

Diagnosis is suspected if ST-segment elevation occurs during the attack. Between **anginal attacks**, the ECG may be normal or show a stable abnormal pattern. Confirmation is by provocative testing with **ergonovine** or **acetylcholine**, which may precipitate coronary artery spasm, identified by significant **ST-segment** elevation or by observation of a reversible spasm during cardiac catheterization. Testing is done most commonly in a cardiac catheterization laboratory and occasionally in a coronary care unit.



http://www.texasheartinstitute.org/HIC/images/coronill_1.gif

Average survival at 5 yr is 89 to 97%, but mortality risk is greater for patients with both variant angina and **atherosclerotic coronary artery obstruction**. Usually, **sublingual nitroglycerin** promptly relieves variant angina. Ca channel blockers may

effectively prevent symptoms. Theoretically, β-blockers may exacerbate spasm by allowing unopposed α-adrenergic vasoconstriction, but this effect has not been proved clinically. Oral drugs most commonly used are sustained-release **diltiazem** 120 to 540 mg once/day, **sustained-releaseverapamil** 120 to 480 mg once/day (dose must be reduced in patients with renal or hepatic dysfunction), or amlodipine 15 to 20 mg once/day (dose must be reduced in elderly patients and patients with hepatic dysfunction). In refractory cases, **amiodarone** may be useful. Although these drugs relieve symptoms, they do not appear to alter prognosis.

SYNDROME X

*Syndrome X is **cardiac microvascular dysfunction** or constriction causing angina (**microvascular angina**).*

Some patients with typical angina that is relieved by rest or nitroglycerin have normal coronary arteriograms (eg, no atherosclerosis, embolism, or inducible arterial spasm). Some of these patients have ischemia detected during stress testing; others do not. In some patients, the cause of ischemia seems to be reflex **intramyocardial coronary constriction** and reduced coronary flow reserve. Other patients have **microvascular** dysfunction within the myocardium: The abnormal vessels do not dilate in response to exercise or other cardiovascular stressors; sensitivity to cardiac pain may also be increased. Prognosis is good, although symptoms of ischemia may recur for years. In many patients, β-blockers relieve symptoms. This disorder should not be confused with variant angina due to **epicardial coronary spasm** or with another disorder called syndrome X, which refers to the metabolic syndrome.

SILENT ISCHEMIA

Patients with CAD (particularly diabetics) may have ischemia without symptoms. Ischemia is evidenced by **transient asymptomatic ST-T abnormalities** seen during 24-h Holter monitoring. Radionuclide studies can sometimes document asymptomatic myocardial ischemia during physical or mental stress (eg, **mental arithmetic**). Silent ischemia and angina pectoris may coexist, occurring at different times. Prognosis depends on severity of CAD.

Reference: http://www.merckmanuals.com