# Chapter 11: Ischemic Heart Disease

## INTRODUCTION

- *Ischemic heart disease* (IHD) is defined as lack of oxygen and decreased or no blood flow to the myocardium resulting from coronary artery narrowing or obstruction. It may present as acute coronary syndrome (ACS), which includes unstable angina and non–ST-segment elevation (NSTE) or ST-segment elevation (STE) myocardial infarction (MI), chronic stable exertional angina, ischemia without symptoms, microvascular angina, or ischemia due to coronary artery vasospasm (variant or Prinzmetal angina). The focus of this chapter is stable IHD.

## PATHOPHYSIOLOGY

- Angina pectoris usually results from increased myocardial oxygen demand ($MVo_2$) in the setting of a fixed decrease in myocardial oxygen supply because of atherosclerotic plaque.
- Major determinants of $MVo_2$ are heart rate (HR), myocardial contractility, and intramyocardial wall tension during systole. A doubling in any of these individual parameters requires a 50% increase in coronary flow to maintain myocardial supply.
- Coronary atherosclerotic plaques typically develop in larger epicardial ($R_1$ or conductance) vessels, which normally offer little resistance to myocardial flow. As plaques grow and narrow the lumen, the affected vessel begins to provide considerable resistance to blood flow. Smaller endocardial ($R_2$ or resistance) vessels provide most resistance to flow in normal coronary arteries and can contract and dilate to maintain blood flow based on metabolic demands of the myocardium (referred to as autoregulation). As a result, coronary plaques that occupy less than 50%–70% of the vessel luminal diameter rarely produce ischemia or angina. However, smaller plaques have a lipid-rich core and thin fibrous cap and are more prone to rupture and cause acute thrombosis. When the luminal diameter of epicardial vessels is reduced by 70% or more, endocardial vessels are maximally dilated, much of the coronary flow reserve has been used, and minimal physical exertion may result in a flow deficit with myocardial ischemia and often angina. When epicardial stenosis exceeds 90%, endocardial flow reserve is exhausted (referred to as critical stenosis).
- When coronary stenosis exceeds 70%, ischemic episodes lead to production of vascular endothelial growth factor and basic fibroblast growth factor which, combined with endogenous vasodilators (eg, nitrous oxide, prostacyclin), cause native collateral vessels to increase in diameter (arteriogenesis) to maintain perfusion. New collateral vessels can also develop (angiogenesis).
- Inflammation also plays a role in IHD; macrophages and T-lymphocytes produce cytokines, chemokines, and growth factors that activate endothelial cells, increase vasoreactivity, and cause proliferation of vascular smooth muscle cells. C-reactive protein may be elevated and correlates with adverse cardiovascular events.
- Some patients have plaque that causes a fixed decrease in supply but also have reduced myocardial oxygen supply transiently due to vasospasm at the site of the plaque. Vasospasm is typically caused by endothelial damage induced by the plaque. Patient symptoms depend on the extent of the fixed obstruction and the degree of dynamic change in coronary arterial tone. The pattern of ischemic symptoms can change due to a variable amount of vasospasm under certain conditions (referred to as *variable threshold angina*). Ischemic episodes may be more common in the morning hours (due to circadian release of vasoconstrictors) and be precipitated by cold exposure and emotional or mental stress.
- Patients with *variant (Prinzmetal) angina* usually do not have a coronary flow-obstructing plaque but instead have significant reduction in myocardial oxygen supply due to vasospasm in epicardial vessels.

## CLINICAL PRESENTATION

- Patients typically complain of chest pain precipitated by exertion or activities of daily living that is described as squeezing, crushing, heaviness, or chest tightness. It can also be more vague and described as a numbness or burning in the chest. The location is often substernal and may radiate to the right or left shoulder or arm (left more commonly), neck, back, or abdomen. Ischemic symptoms may be associated with diaphoresis, nausea, vomiting, and dyspnea. Chest pain generally lasts from 5 to 20 minutes and is usually relieved by rest or sublingual nitroglycerin (SL NTG).
- Some patients (especially women and older individuals) present with atypical chest pain, characterized by midepigastric discomfort, effort intolerance, dyspnea, and excessive fatigue. Patients with diabetes mellitus may have decreased pain sensation due to neuropathy.
- Patients with variant (Prinzmetal) angina are typically younger and may present with chest pain at rest, often early in the morning, and may have transient ST-segment elevation on the ECG.

## DIAGNOSIS

- Obtain the medical history to identify the quality and severity of chest pain, precipitating factors, location, duration, pain radiation, and response to nitroglycerin or rest. Ischemic chest pain may resemble pain from noncardiac sources, and diagnosis of anginal pain may be difficult based on history alone.
- Assess nonmodifiable risk factors for coronary artery disease (CAD): age, sex, and family history of premature atherosclerotic disease in first-degree relatives (male onset before age 55 or female before age 65). Identify the presence of modifiable CAD risk factors: hypertension, diabetes mellitus, dyslipidemia, and cigarette smoking.
- Physical exam findings are usually nonspecific, but patients having an ischemic episode may present with tachycardia, diaphoresis, shortness of breath, nausea, vomiting, and lightheadedness. Other findings related to CAD risk factors may include increased blood pressure (BP) and a fourth heart sound reflecting longstanding hypertension. Other positive findings may include pulmonary crackles, displaced point of maximal impulse, and a third heart sound in patients with heart failure with reduced ejection fraction (HFrEF).
- Markers of inflammation, such as high-sensitivity C-reactive protein (hs-CRP), may be elevated.
- Cardiac troponin concentrations are not typically elevated in stable IHD.
- Resting ECG is normal in at least half of patients with angina who are not experiencing acute ischemia. About 50% of patients develop ischemic ST-T wave changes during an episode of angina, which can be observed on the ECG during an exercise stress test. Patients who cannot endure stress testing can have the myocardium stressed pharmacologically with adenosine, regadenoson, dipyridamole, or dobutamine.
- Coronary angiography is the most accurate test for confirming CAD but is invasive and requires arterial access. Myocardial perfusion imaging, cardiac magnetic resonance, coronary artery calcium scoring, and CT angiography can also be used to detect CAD.

## TREATMENT

- Goals of Treatment: A primary goal of therapy is complete (or nearly complete) elimination of anginal chest pain and return to normal activities. Long-term goals are to slow progression of atherosclerosis and prevent complications such as MI, heart failure, stroke, and death.

### Nonpharmacologic Therapy

- Risk factor modification is the primary nondrug approach for primary and secondary prevention of CAD events. Lifestyle modifications include daily physical activity, weight management, dietary therapy (reduced intake of saturated fats, trans-fatty acids, and cholesterol), smoking cessation, psychological interventions (eg, screening and treatment for depression if appropriate), limitation of alcohol intake, and avoiding exposure to air pollution.
- Surgical revascularization options for select patients include coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) with or without stent placement.

## Pharmacologic Therapy

- Guideline-directed medical therapy (GDMT) reduces the rates of death and MI similar to revascularization therapy. See **Figure 11-1** for a treatment algorithm based on the American College of Cardiology/American Heart Association (ACC/AHA) guidelines.
- Approaches to risk factor modification include the following recommendations:

  ✔ Dyslipidemia: Use moderate- or high-dose statin therapy in the absence of contraindications or adverse effects, in addition to lifestyle changes. Addition of ezetimibe (first) or a PCSK9 inhibitor (second) is reasonable for patients who do not tolerate statins or do not attain a 50% decrease in LDL cholesterol (or LDL remains above 70–100 mg/dL).

  ✔ Blood pressure: If BP is ≥130/80 mm Hg, institute drug therapy in addition to or after a trial of lifestyle modifications.

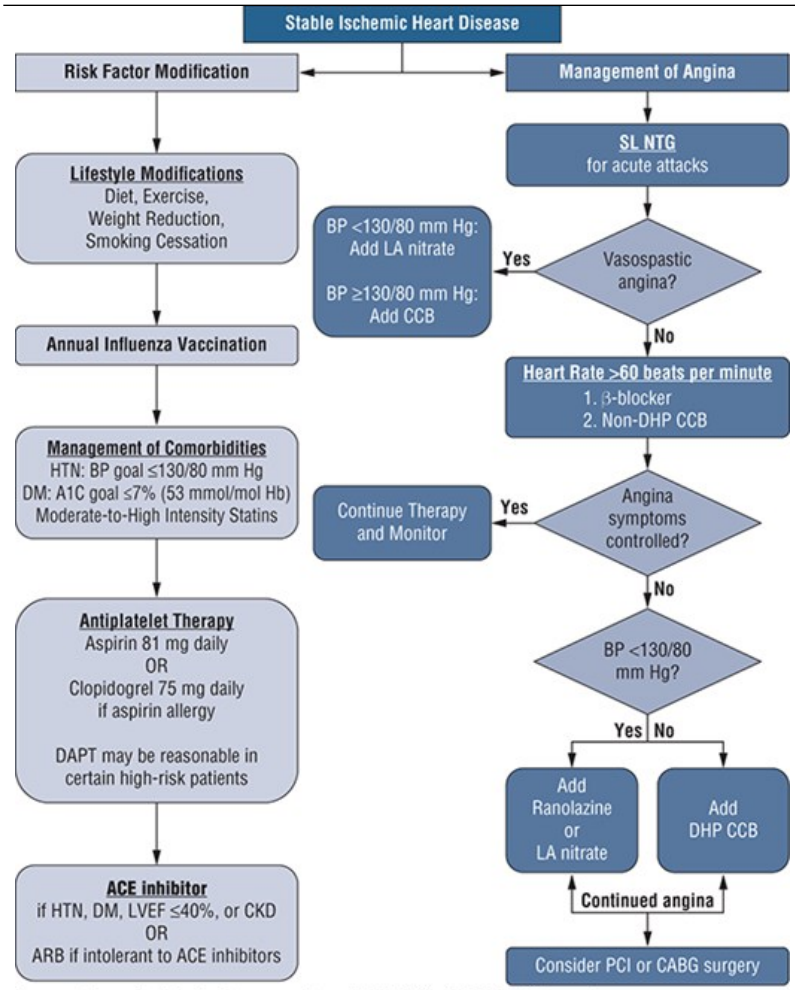
  ✔ Diabetes mellitus: Pharmacotherapy to achieve a target A1C of ≤7% (53 mmol/mol Hb) is reasonable for select patients (eg, short duration of diabetes and long life expectancy). An A1C goal of <8% is reasonable for other patients, such as those with micro- or macrovascular complications or coexisting medical conditions.

  ✔ Annual influenza vaccinations are recommended.

**FIGURE 11-1**

**Algorithm for treatment of stable ischemic heart disease (guideline-directed medical therapy).**

(ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass graft; CCB, calcium channel blocker; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; DHP, dihydropyridine; DM, diabetes mellitus; Hb, hemoglobin; HTN, hypertension; LA, long-acting; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SL NTG, sublingual nitroglycerin.)




Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*


### Antiplatelet Therapy

- Aspirin irreversibly blocks cyclooxygenase-1 (COX-1) activity and subsequent thromboxane $A_2$ production, leading to reduced platelet activation and aggregation. A small percentage of patients are nonresponsive to aspirin's antiplatelet effects. Anti-inflammatory drugs (NSAIDs) may interfere with aspirin's antiplatelet effect when coadministered by competing for the site of action in the COX-1 enzyme. The ACC/AHA guidelines contain the following recommendations for stable IHD:

  ✔ **Aspirin:** 75–162 mg daily should be continued indefinitely in the absence of contraindications.

  ✔ **Clopidogrel:** 75 mg daily is an appropriate alternative when aspirin is contraindicated. Patient responsiveness to clopidogrel is highly variable, with estimates of nonresponsiveness ranging from 5% to 44% of patients. The most common cause of nonresponsiveness is nonadherence, but genetic polymorphisms to CYP2C19 may contribute in some patients. Some studies have suggested that patients receiving a proton pump inhibitor (most often omeprazole) together with clopidogrel have reduced antiplatelet activity and more ischemic events due to inhibition of cytochrome P450 enzymes involved in converting clopidogrel to its active metabolite. However, the only prospective randomized clinical trial conducted to date found no increased rate of clinical events in patients given clopidogrel plus omeprazole.

  ✔ **Dual antiplatelet therapy (DAPT)** with aspirin plus a $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, ticagrelor) is beneficial after PCI with coronary stent placement and after treatment for ACS. Its benefits in other situations are less clear. The combination of aspirin (75–162 mg daily) and clopidogrel 75 mg daily may be reasonable in certain high-risk patients.

### Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs)

- In the setting of IHD, ACE inhibitors stabilize coronary plaque, restore or improve endothelial function, inhibit vascular smooth muscle cell growth, decrease macrophage migration, and possibly prevent oxidative stress. However, ACE inhibitors have not been shown to improve symptomatic ischemia or reduce chest pain episodes. Clinical trials of the role of ACE inhibitors or ARBs in reducing cardiovascular events (eg, cardiovascular death, MI, stroke) in high-risk patients have produced conflicting results. The ACC/AHA guidelines for stable IHD recommend the following strategies:

  ✔ Use ACE inhibitors in patients who also have hypertension, diabetes, HFrEF, or chronic kidney disease, unless contraindicated.

  ✔ ARBs are recommended for the same populations if patients are intolerant to ACE inhibitors.

  ✔ Combination ACE inhibitor/ARB therapy should be avoided due to the lack of additional benefit and a higher risk of adverse events (eg, hypotension, syncope, renal dysfunction).

  ✔ **Table 11-1** provides the usual dosage ranges for ACE inhibitors and ARBs in stable IHD.

TABLE 11-1

**Drugs and Regimens for Stable Ischemic Heart Disease**

| Drug Class and Generic Names | Usual Dosage Range[a] |
|---|---|
| **Angiotensin-Converting Enzyme Inhibitors** | |
| Captopril | 6.25–50 mg 3 times daily |
| Enalapril | 2.5–40 mg daily in 1–2 divided doses |
| Fosinopril | 10–80 mg daily in 1–2 divided doses |
| Lisinopril | 2.5–40 mg once daily |
| Perindopril | 4–8 mg once daily |
| Quinapril | 5–20 mg twice daily |
| Ramipril | 2.5–10 mg daily in 1–2 divided doses |
| Trandolapril | 1–4 mg once daily |
| **Angiotensin Receptor Blockers** | |
| Candesartan | 4–32 mg once daily |
| Valsartan | 80–320 mg daily in 1–2 divided doses |
| Telmisartan | 20–80 mg once daily |
| **β-Adrenergic Blockers** | |
| Atenolol[b] | 25–200 mg once daily |

| | |
|---|---|
| Betaxolol[b] | 5–20 mg once daily |
| Bisoprolol[b] | 2.5–10 mg once daily |
| Carvedilol[c] | 3.125–25 mg twice daily |
| Carvedilol phosphate[c] | 10-80 mg once daily |
| Labetalol[c] | 100–400 mg twice daily |
| Metoprolol[b] | 50–200 mg twice daily (once daily for extended release) |
| Nadolol[d] | 40–120 mg once daily |
| Nebivolol | 5–10 mg once daily |
| Propranolol[d] | 20–120 mg twice daily (60–240 mg once daily for long-acting formulation) |
| Timolol[d] | 10–20 mg twice daily |
| **Calcium Channel Blockers: Nondihydropyridine Type** | |
| Diltiazem, extended release | 120–360 mg once daily |
| Verapamil, extended release | 180–480 mg once daily |
| **Calcium Channel Blockers: Dihydropyridine Type** | |
| Amlodipine | 5–10 mg once daily |
| Felodipine | 5–10 mg once daily |
| Nifedipine, extended release | 30–90 mg once daily |
| Nicardipine | 20–40 mg three times daily |
| **Nitrates** | |
| Nitroglycerin extended-release capsules | 2.5 mg three times daily initially, with up-titration according to symptoms and tolerance; allow a 10- to 12-hour nitrate-free interval |
| Isosorbide dinitrate tablets | 5–20 mg two to three times daily, with a daily nitrate-free interval of at least 14 hours (eg, dose at 7 AM, noon, and 5 PM) |
| Isosorbide dinitrate slow-release capsules | 40 mg one to two times daily, with a daily nitrate-free interval of at least 18 hours (eg, dose at 8 AM and 2 PM) |
| Isosorbide mononitrate tablets | 5–20 mg two times daily initially, with up-titration according to symptoms and tolerance; doses should be taken 7 hours apart (eg, 8 AM and 3 PM) |

| | |
|---|---|
| Isosorbide mononitrate extended-release tablets | 30–120 mg once daily |
| Nitroglycerin transdermal extended-release film | 0.2–0.8 mg/hr, on for 12–14 hours, off for 10–12 hours |

[a]Consult official prescribing information. In patients with renal and hepatic dysfunction, adjust initial and maintenance doses for all agents as appropriate based on FDA-approved labeling.

[b]Relatively $\beta_1$-selective (selectively is lost at higher doses).

[c]Blocks $\alpha_1$, $\beta_1$, and $\beta_2$ receptors.

[d]Nonselective (blocks both $\beta_1$ and $\beta_2$ receptors).

*Data from Landup D, DiDomenico RJ. Stable ischemic heart disease. In: Chisholm-Burns MA, et al., eds. Pharmacotherapy Principles & Practice. 5th ed. New York: McGraw-Hill Education; 2019.*

### β-Adrenergic Blockers

- β-Blockers competitively inhibit the effects of neuronally released and circulating catecholamines on β-adrenoceptors. Blockade of $\beta_1$-receptors in the heart and kidney reduces HR, contractility, and BP, thereby decreasing $MVo_2$.
- β-Blockers are recommended over calcium channel blockers (CCBs) for initial control of angina episodes in patients with stable IHD. The target is to lower the resting HR to 50–60 beats/min and the exercise HR to <100 beats/min. For patients (eg, elderly) who cannot tolerate these ranges, the target HR should be as low as can be tolerated above 50 beats/min. β-Blockers may be combined with CCBs or long-acting nitrates when initial treatment with β-blockers alone is unsuccessful.
- Only the β-blockers **carvedilol**, **metoprolol succinate**, and **bisoprolol** should be used in patients with HFrEF, starting with low doses and titrating upward slowly.
- Selection of a particular agent depends on the presence of comorbid states, preferred dosing frequency, and cost. $\beta_1$-Selective agents are preferred in patients with chronic obstructive pulmonary disease, peripheral arterial disease (PAD), diabetes, dyslipidemia, and sexual dysfunction. Drugs with combined $\alpha_1$- and β-blockade are effective for IHD, but agents with intrinsic sympathomimetic activity provide little to no reduction in resting HR and are not preferred except perhaps in patients with PAD or dyslipidemia.
- Common adverse effects include bradycardia, hypotension, heart block, impaired glucose metabolism, altered serum lipids (transiently increased triglycerides, decreased HDL-C, and no change in LDL-C), fatigue, depression, insomnia, and malaise. β-Blockers are contraindicated in patients with preexisting bradycardia, hypotension, 2nd- or 3rd-degree atrioventricular (AV) block, uncontrolled asthma, severe PAD, hypotension, HFrEF with unstable fluid status, and diabetes associated with frequent episodes of hypoglycemia.
- If β-blocker therapy must be discontinued, doses should be tapered over 2–3 weeks to prevent abrupt withdrawal, which can significantly increase in $MVo_2$ and induce ischemia and even MI because of up-regulation of β-receptors in the myocardium.
- See **Table 11-1** for the usual dosage ranges of β-blockers in stable IHD.

### Calcium Channel Blockers

- CCBs modulate calcium entry into the myocardium, vascular smooth muscle, and other tissues, which reduces the cytosolic concentration of calcium responsible for activation of the actin–myosin complex and contraction of vascular smooth muscle and myocardium. All CCBs reduce

$MVO_2$ by reducing wall tension via lowering arterial BP and (to a minor extent) depressing contractility. CCBs also provide some increase in supply by inducing coronary vasodilation and preventing vasospasm.

- CCBs or long-acting nitrates should be prescribed for relief of symptoms when β-blockers are contraindicated or cause unacceptable side effects.
- Dihydropyridine CCBs (eg, **nifedipine**, **amlodipine**, **isradipine**, and **felodipine**) primarily affect vascular smooth muscle with little effect on the myocardium. These drugs produce minimal reduction in contractility and either no change or increased HR due to reflex tachycardia from direct arterial dilation. Nifedipine produces more impairment of LV function than amlodipine and felodipine. Short-acting agents should not be used because of their greater propensity to cause reflex tachycardia. Other side effects of these CCBs include hypotension, headache, gingival hyperplasia, and peripheral edema. Although most CCBs are contraindicated in patients with HFrEF, amlodipine and felodipine are considered safe options in these patients.
- Nondihydropyridine CCBs (**verapamil** and **diltiazem**) mostly affect the myocardium with minimal effects on vascular smooth muscle; they reduce HR, contractility, and $MVO_2$. Initial therapy for relief of symptoms with a long-acting nondihydropyridine CCB instead of a β-blocker is a reasonable approach. Common side effects of these CCBs include bradycardia, hypotension, AV block, and symptoms of LV depression. These agents should be avoided in patients with concomitant HFrEF due to negative inotropic effects. Verapamil may cause constipation in ~8% of patients. Verapamil and diltiazem inhibit clearance of drugs that utilize the cytochrome P450 3A4 isoenzyme such as carbamazepine, cyclosporine, lovastatin, simvastatin, and benzodiazepines. Verapamil, and to a lesser extent diltiazem, also inhibit P-glycoprotein–mediated drug transport, which can increase concentrations of digoxin and cyclosporine. Verapamil also decreases digoxin clearance. Agents that induce the 3A4 isoenzyme can reduce the effectiveness of all CCBs.
- See **Table 11-1** for the usual dosage ranges of CCBs in stable IHD.

### Nitrates

- Nitrates increase concentrations of cyclic guanosine monophosphate in vascular endothelium, leading to reduced cytoplasmic calcium and vasodilation. Most vasodilation occurs on the venous side, leading to reduced preload, myocardial wall tension, and $MVO_2$. Arterial vasodilation increases as doses are escalated, which can produce reflex tachycardia that can negate some of the antianginal benefits. This effect can be mitigated with concomitant β-blocker therapy. Nitrates also produce vasodilation of stenotic epicardial vessels and intracoronary collateral vessels, increasing oxygen supply to the ischemic myocardium.
- All patients should have access to sublingual (SL) NTG 0.3 or 0.4 mg tablets or spray to treat acute angina episodes. Relief typically occurs within 5 minutes of administration.
- SL nitrates can also be used to prevent acute episodes if given 2–5 minutes before activities known to produce angina; protection can last for up to 30 minutes with SL NTG and up to 1 hour with SL isosorbide dinitrate (ISDN).
- Long-acting nitrates (or CCBs) should be prescribed for relief of symptoms when β-blockers are contraindicated or cause unacceptable side effects. Various nitrate formulations are available for acute and chronic use (**Table 11-1**).
- Transdermal patches and isosorbide mononitrate (ISMN) are most commonly prescribed for long-term prevention of angina episodes. ISDN is also effective, but the three times daily regimen requires dosing every 4–5 hours during the day to provide a nitrate-free interval. Chronic nitrate use should incorporate a 10- to 14-hour nitrate-free interval each day to reduce nitrate tolerance. Because this approach places the patient at risk for angina episodes, the nitrate-free interval is usually provided during the nighttime hours when the patient has a reduced $MVO_2$ while sleeping. The extended-release ISMN products that are dosed twice daily should be given 7 hours apart (eg, 7:00 AM and 2:00 PM). An extended-release, once-daily ISMN product is available that provides 12 hours of nitrate exposure followed by a 12-hour nitrate-free interval. Transdermal NTG patches are typically prescribed as "on in the AM and off in the PM" but patients should be given specific application and removal times (eg, apply at 8:00 AM and remove at 8:00 PM).
- Nitrates should not be used routinely as monotherapy for stable IHD because of the lack of angina coverage during the nitrate-free interval, lack of protection against circadian rhythm (nocturnal) ischemic events, and potential for reflex tachycardia. Concomitant β-blocker or diltiazem therapy

can prevent rebound ischemia during the nitrate-free interval.

- Common nitrate side effects include headache, flushing, nausea, postural hypotension, and syncope. Headache can be treated with acetaminophen and usually resolves after about 2 weeks of continued therapy. Transdermal NTG may cause skin erythema and inflammation. Initiating therapy with smaller doses and/or rotating the application site can minimize transdermal nitroglycerin side effects.

### Ranolazine

- Ranolazine reduces ischemic episodes by selective inhibition of late sodium current ($I_{Na}$), which reduces intracellular sodium concentration and improves myocardial function and perfusion. It does not impact HR, BP, the inotropic state, or increase coronary blood flow.
- Ranolazine is effective as monotherapy for relief of angina symptoms but should only be used if patients cannot tolerate traditional agents due to hemodynamic or other adverse effects. Because it does not substantially affect HR and BP, it is recommended as add-on therapy to traditional antianginal agents for patients who achieve goal HR and BP and still have exertional angina symptoms, patients who cannot achieve these hemodynamic goals due to adverse effects, and patients who reach maximum doses of traditional agents but still have angina symptoms.
- The initial ranolazine dose is 500 mg twice daily, increased to 1000 mg twice daily within the next 1–2 weeks if tolerated. It can be combined with a β-blocker when initial treatment with β-blockers alone is unsuccessful.
- Adverse effects include constipation, nausea, dizziness, and headache. Ranolazine can prolong the QTc interval and should be used with caution in patients receiving concomitant QTc-prolonging agents.
- Potent inhibitors of CYP3A4 and P-glycoprotein (ketoconazole, itraconazole, protease inhibitors, clarithromycin, and nefazodone) or potent inducers of CYP3A4 and P-glycoprotein (phenytoin, phenobarbital, carbamazepine, rifampin, rifabutin, rifapentine, St. John's wort) are contraindicated with ranolazine due to significant increases and decreases in ranolazine drug concentrations, respectively. Moderate CYP3A4 inhibitors (eg, diltiazem, verapamil, erythromycin, and fluconazole) can be used with ranolazine, but the maximum dose should not exceed 500 mg twice daily.

### Treatment of Variable Threshold Angina and Prinzmetal Angina

- Patients with variable threshold angina require pharmacotherapy for vasospasm. Most patients respond well to SL NTG for acute attacks.
- Both CCBs and nitrates are effective for chronic therapy. CCBs may be preferred because they are dosed less frequently. Nifedipine, verapamil, and diltiazem are equally effective as single agents for initial management of coronary vasospasm; dose titration is important to maximize the response. Patients unresponsive to CCBs alone may have nitrates added.
- β-Blockers are not useful for vasospasm because they may induce coronary vasoconstriction and prolong ischemia.

## EVALUATION OF THERAPEUTIC OUTCOMES

- Assess for symptom improvement by number of angina episodes, weekly SL NTG use, and increased exercise capacity or duration of exertion needed to induce angina.
- Use statins for dyslipidemia, strive to achieve BP and A1C goals, and implement the lifestyle modifications of dietary modification, smoking cessation, weight loss, and regular exercise.
- Once patients have been optimized on medical therapy, symptoms should improve over 2–4 weeks and remain stable until the disease progresses. Patients may require evaluation every 1–2 months until target endpoints are achieved; follow-up every 6–12 months thereafter is appropriate.
- The Seattle Angina Questionnaire, Specific Activity Scale, and Canadian Cardiovascular Society classification system can be used to improve reproducibility of symptom assessment.

- If the patient is doing well, no other assessment may be necessary. Although follow-up exercise tolerance testing with or without cardiac imaging can be performed to objectively assess control of ischemic episodes, this is rarely done if patients are doing well because of the expense involved.
- Monitor for adverse drug effects such as headache and dizziness with nitrates; fatigue and lassitude with β-blockers; and peripheral edema, constipation, and dizziness with CCBs.

*See Chapter 32, Stable Ischemic Heart Disease, authored by Paul P. Dobesh, Robert J. DiDomenico, and Kelly C. Rogers, for a more detailed discussion of this topic.*