**Management of stable ischemic heart disease**

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**Abstract:**

Patients with stable ischemic heart disease (SIHD) require appropriate diagnosis, risk assessment, guideline-directed medical therapy, treatment, and follow up. The 2012 American College of Cardiology Foundation/American Heart Association guideline for the diagnosis and management of patients with SIHD assists nurse practitioners in the care of these patients. Knowledge of the treatments and the evidence supporting their use is essential to reduce morbidity and mortality in patients with SIHD.

**Keywords:** clinical guideline | heart disease | medical therapy

**Article:**

Ischemic heart disease (IHD), also called coronary heart disease or coronary artery disease, makes up more than half of all cardiovascular events in men and women younger than 75. The lifetime risk of developing IHD after age 40 is about 1 in 2 for men and 1 in 3 for women. The incidence of IHD in women lags behind men by 10 years for total disease and by 20 years for serious clinical events (eg, myocardial infarction [MI] and sudden cardiac death). Since 1968, deaths from IHD have declined as a result of medical and surgical treatments along with reduction in modifiable risk factors.

In 2012, the American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Task Force on Practice Guidelines, along with several other partnering associations, published a guideline for the diagnosis and management of adult patients with stable IHD (SIHD). The aim of this brief article is to review the 2012 guideline, placing emphasis on how nurse practitioners (NPs) can use these recommendations to manage patients with SIHD. Information from related research and guideline statements will also be included, as appropriate.
**Definition of IHD**

IHD is defined as the presence of atherosclerotic plaques in 1 or more of the major coronary arteries that supply blood to the heart muscle. Ischemia refers to an imbalance between myocardial oxygen supply and demand that is most commonly caused by plaques that impede blood flow to tissue distal to the stenosis. Angina pectoris, or angina for short, is the most common symptom of ischemia that occurs when oxygen demand exceeds oxygen supply. Stable angina, a manifestation of SIHD, is frequently described as retrosternal or substernal chest pressure that is typically precipitated by physical or emotional stress, is relieved by rest or sublingual nitroglycerin, and has a predictable pattern.

However, NPs need to be aware that, although resolution of symptoms with sublingual nitroglycerin (tablets or spray) heightens the clinician's suspicion for angina, esophageal spasm is described similarly by some patients and is also relieved by nitroglycerin. Furthermore, some patients experience atypical symptoms, such as dyspnea, fatigue, jaw or neck pain, nausea, or recurrent belching with exertion rather than chest discomfort. These symptoms are referred to as the patient's anginal equivalent (also known as ischemic equivalent).

**Application of the Guidelines**

The 2012 guideline applies to patients with stable known or suspected IHD, including those with new-onset chest pain that are deemed to have low-risk unstable angina (UA). The classification of low-risk UA applies to individuals who are younger than 70, with symptoms of pain or discomfort during exertion lasting less than 20 minutes that does not rapidly accelerate, with a normal (or unchanged) 12-lead electrocardiogram (ECG), and no elevation of cardiac enzymes. Thus, recommendations for treatment from the 2012 guideline on SIHD do not apply to those with intermediate or high-risk UA or to those with an evolving MI, collectively known as acute coronary syndromes (ACS).

**Diagnosis**

Patients who present with chest pain or other symptoms suggestive of ischemia but are not known to have IHD should undergo a thorough history and physical examination to determine the probability of heart disease. As part of this assessment, NPs need to distinguish if the patient's symptoms are consistent with stable angina or low-risk UA, as opposed to intermediate or high-risk UA or an evolving MI (as discussed above). Assessment for the presence of risk factors for atherosclerosis should be performed at the initial presentation. Refer to Table 1 for a list of risk factors.

According to the guideline, a resting 12-lead ECG is recommended for all adults with nontraumatic chest pain or other symptoms suggesting ischemia. However, most patients will require further testing to confirm the diagnosis of IHD. If, during the evaluation, the patient has active symptoms or symptoms consistent with an ACS event, more immediate aggressive treatment is required (ie, aspirin and sublingual nitroglycerin administration, unless contraindicated, 12-lead ECG, and transportation to the nearest hospital).
Table 1. Major Risk Factors for Ischemic Heart Disease

- Family history defined as cardiovascular disease in a male first-degree relative younger than 55 or female first-degree relative younger than 65
- Cigarette smoking
- Diabetes mellitus
- Dyslipidemia: elevated total or low-density lipoprotein cholesterol; high-density lipoprotein cholesterol
- Hypertension
- Physical inactivity
- Obesity (body mass index ≥ 30 kg/m²)
- Low fruit and vegetable consumption
- Alcohol overconsumption
- Men older than 45 and women older than 55

*Data from Chobanian et al.*

Noninvasive Versus Invasive Diagnostic Testing

The 2012 guideline recommends that patients with suspected ischemia (who are considered at low-risk) undergo noninvasive testing via stress testing. Factors that determine the initial choice for stress testing include the interpretability of the resting ECG, the patient's physical functioning, the pretest probability of IHD, and the availability of appropriate technology in the facility.

According to the guideline, a standard exercise stress test (exercise treadmill) is the first choice to diagnose IHD in patients who have an interpretable ECG (a normal baseline ECG) and are able to exercise at least 4 metabolic equivalents (equivalent to engaging in moderate activities such as climbing stairs, vacuuming, walking 3-3.5 mph, or heavy gardening). In patients who can exercise but have an abnormal resting ECG (eg, left ventricular [LV] hypertrophy, digitalis effect, or other reasons for ST-segment deviation at baseline), an exercise stress test with nuclear myocardial perfusion imaging or echocardiography is recommended to improve detectability of IHD.

If patients are unable to exercise, a pharmacologic stress is recommended. Coronary angiography, the gold standard for diagnosing IHD, is recommended for patients whose noninvasive testing indicates a high likelihood of severe IHD and when the benefits exceed risk. Those patients need a diagnostic angiography, unless third party payers require noninvasive testing first.

The guideline also recommends Doppler echocardiography to assess resting left ventricular (systolic and diastolic function) and evaluation for abnormalities of myocardium, heart valves, or pericardium in patients with known or suspected IHD, a prior MI, pathological Q waves, symptoms or signs suggestive of heart failure (HF), complex ventricular arrhythmias, or an undiagnosed heart murmur. In addition, coronary angiography is also a reasonable option to assess risk in patients with depressed left ventricular function (ejection fraction [EF] < 50%) to evaluate the etiology of the HF.
SIHD Management

Management of SIHD includes medical relief of symptoms and for secondary prevention of MI or death, patient education, risk factor modification, and revascularization, when indicated. Goals for treating SIHD include symptomatic relief (decrease the severity and frequency of angina symptoms), an increase in functional capacity and longevity, and a reduction in the incidence of ACS.

Pharmacotherapy for Symptom Relief

Therapies to treat angina symptoms are directed toward improving the imbalance of oxygen supply and demand. Traditionally, anti-ischemic medications, such as beta-blockers, calcium channel blockers, and nitrates, have been directed at improving symptoms. Beta-blockers are the cornerstone of therapy for angina and are prescribed as first-line therapy for symptom relief in patients with SIHD, especially those with a history of MI.

Beta-blockers antagonize catecholamine-mediated stimulation of $\beta_1$ and $\beta_2$ receptors, lowering heart rate, decreasing contractility, and decreasing myocardial oxygen demand. By lowering heart rate, beta-blockers lengthen diastole, consequently increasing coronary blood flow. In addition, beta-blockers are effective for the treatment of hypertension, arrhythmias, post-MI angina, and anxiety-induced anginal symptoms and have been shown to reduce mortality in patients with HF. However, it should be noted that only certain beta-blockers are approved by the Food and Drug Administration to treat chronic HF, including bisoprolol, carvedilol, and metoprolol.

Major adverse effects of beta-blockers include hypotension, bradycardia, heart block, bronchospasm, and worsening HF. Other potential adverse effects include fatigue, depression, and sexual dysfunction. However, NPs need to keep in mind that beta-blockers, like other medications that are known to improve symptoms and survival, should not be withheld because of concerns of sexual side effects by the patient or the provider. In fact, only about 3-5 patients per 1,000 have sexual side effects from beta-blockers. If, however, beta-blocker therapy causes erectile dysfunction, the patient may be converted to nebivolol, unless the patient has HF (a contraindication).

Finally, NPs should be mindful that abrupt withdrawal of beta-blockers may increase the frequency and severity of angina; thus, if discontinued, the drug should be tapered over several days to weeks.

Calcium channel blockers (CCBs) are reasonable options for symptom relief if a beta-blockers are contraindicated, poorly tolerated, or as an add-on agent if symptoms persist. CCBs inhibit calcium ion movement into vascular smooth muscle and cardiac cells, resulting in blocking the calcium-dependent process leading to contraction. They reduce oxygen demand by causing systemic vasodilation and decreasing afterload. CCBs can also increase myocardial oxygen supply by dilating the coronary arteries.
Nondihydropyridine CCBs (eg, verapamil and diltiazem) have the additional ability to slow sinoatrial (SA) and atrioventricular (AV) node conduction, decreasing heart rate. Thus, they should be used cautiously when given in combination with other agents with negative chronotropic properties (eg, beta-blockers, digoxin). Dihydropyridine CCBs (eg, amlodipine, felodipine) do not inhibit SA and AV node conduction, so the antianginal mechanism of action is primarily from vasodilation. All CCBs, however, should be used cautiously in patients with severe ventricular dysfunction because of possible negative inotropic effects.

Organic nitrates have a well-established role in pharmacotherapy for angina. The major mechanism of action is to relax vascular smooth muscle, which reduces preload, afterload, and decreasing oxygen demand. Sublingual nitroglycerin is commonly used to treat acute angina symptoms and can be taken prophylactically during exertion known to produce angina. Long-acting nitrates can be used for long-term prophylaxis in combination with beta-blockers or CCBs. Long-acting nitrates are available in both oral and transdermal formulations for chronic use.

A major limitation of nitrate therapy is the development of tolerance with continuous use, regardless of route. Tolerance may occur within 24 hours of continuous exposure to the nitrate. To avoid tolerance and maintain antianginal properties of nitrates, it is recommended that a daily nitrate-free interval (NFI) of a minimum 8 hours and perhaps 12 hours be provided. The NFI is most commonly scheduled during the night when angina is unlikely to occur. Monotherapy with nitrates is not recommended because of reflex sympathetic stimulation from venodilation, and patients are not protected during the NFI.

Ranolazine, a relatively new medication, is indicated as an add-on agent to beta-blockers and CCBs for stable angina. It may also be considered for patients who are on CCB but unable to tolerate beta-blockers, yet still have angina. Ranolazine has a unique mechanism of action that is not completely understood. It is thought to inhibit the late inward sodium current during systole, which leads to reductions in intracellular calcium accumulation, left ventricular wall tension, and oxygen consumption. It has a neutral effect to oxygen supply and demand; antianginal properties do not affect heart rate, blood pressure, contractility, or coronary blood flow.

However, ranolazine may cause QT prolongation and is contraindicated with concurrent QT-prolonging drugs or pre-existing prolonged QT. The medication also has several drug interactions and should be avoided with concurrent use of strong CYP3A4 inhibitors (ketoconazole, itraconazole, clarithromycin, ritonavir, indinavir, saquinavir, nefazodone) because of the potential for QT prolongation. In addition, the dose of ranolazine should be reduced if given in combination with moderate CYP3A4 inhibitors (diltiazem, verapamil, erythromycin, fluconazole), P-gp inhibitors (cyclosporine), P-gp or metabolized by CYP2DE agents (digoxin). See the packet insert for further details.

Pharmacotherapy for Secondary Prevention

Optimal medical management in patients with SIHD requires more than therapy for angina symptoms. Specific medical therapy aimed at secondary prevention includes the use of aspirin 75
to 162 mg daily, in the absence of contraindications.\textsuperscript{2,8} According to the 2012 guideline, clopidogrel is a reasonable option when aspirin is contraindicated.\textsuperscript{2}

Beta-blocker therapy should be started and continued for 3 years in all patients with normal LV function after an MI or ACS.\textsuperscript{2} Beta-blockers should also be used in those with LV systolic dysfunction (EF \(\leq 40\%\)), unless contraindicated.\textsuperscript{2}

Currently, the optimal duration of beta-blocker therapy after MI is unknown. In the past it was thought that beta-blocker therapy should be continued indefinitely. However, the 2011 AHA Secondary Prevention Guideline was one of the first AHA guidelines to specify a time period for beta-blocker therapy (3 years).\textsuperscript{8} Beyond 3 years is optional if the patient is symptom free and has not had a subsequent MI or ACS event. In fact, a recent observational study of 5,000 patients with ST-segment elevation MI treated with primary percutaneous coronary intervention (PCI) found that adjusted mortality rates did not differ based on whether the patients were on beta-blocker therapy or not.\textsuperscript{9} In subgroup analyses, the high-risk patients (those with HF associated with their MI) had a mortality benefit if beta-blockers were administered.\textsuperscript{9}

Angiotensin-converting enzyme (ACE) inhibitors should also be prescribed in all patients with SIHD who have hypertension, diabetes, LVEF \(\leq 40\%\), or chronic kidney disease, unless contraindicated.\textsuperscript{2} Angiotensin-receptor blockers are recommended for patients intolerant of ACE inhibitors.\textsuperscript{2} An annual influenza vaccine is also recommended for patients with SIHD.\textsuperscript{2} In addition, according to the Centers for Disease Control and Prevention, all adults older than 65 with chronic heart disease should receive a pneumococcal polysaccharide (PPSV23) vaccine.\textsuperscript{10}

Pharmacotherapies to Avoid

Several pharmacotherapies are \textit{not} recommended for the intent of reducing the risk of an MI or death. For example, hormone therapy has failed to demonstrate a reduction in the risk for IHD in postmenopausal women, thus should not be used.\textsuperscript{2,8,11} In addition, antioxidants (vitamin C, vitamin E, beta carotene), treatment for elevated homocysteine (folate, vitamin B6, and vitamin B12), chelation therapy, and certain dietary supplements (garlic, coenzyme Q10, selenium, chromium) are not recommended to reduce cardiovascular risk or improve clinical outcome and thus should not be used as primary or secondary prevention of IHD.\textsuperscript{2,8}

Patient Education

Patients with SIHD should be provided individualized education that teaches them about heart-healthy living, self-monitoring skills, and what action to take if symptoms worsen.\textsuperscript{2} Self-monitoring skills include knowing how to pace their activities and set goals based on the impact of stress, anxiety, or depression on symptoms. Patients should know the common symptoms of stress and depression and how to manage those in an effort to minimize angina caused by emotional stress.\textsuperscript{2}

Patients should also be assisted in developing an action plan for what to do if they experience recurrent angina symptoms. The plan should include advising them to stop their activity any time symptoms occur, take a sublingual nitroglycerin as prescribed (unless contraindicated), and, if
symptoms continue, call emergency medical services (EMS). However, there is variation for when to call EMS. For example, some patients are instructed to call EMS if symptoms persist 5 minutes after the first nitroglycerin; others are instructed to take up to 3 nitroglycerin doses, 5 minutes apart, before calling EMS. This decision is individualized, based on past anginal episodes and the patient’s response to nitroglycerin use.

In addition to individualized teaching by the NP, there are many ways to offer patient (and family) education. One of the most effective ways is to make referrals to community resources (eg, cardiac rehabilitation programs, support groups, or other educational programs). To be highly effective in helping patients recover physically from a cardiac event, cardiac rehabilitation programs also provide a venue for safe exercise along with a comprehensive patient education program for patients with SIHD. However, despite proven benefits, many patients with SIHD are not routinely referred for structured cardiac rehabilitation programs or secondary prevention programs.12

Patient education may be provided in varied formats (eg, written materials, Web-based, face-to-face) and should consider culture and literacy levels. For example, innovative strategies such as mobile phone interventions or telemonitoring may be used with appropriate patients. A recent systematic analysis concluded that the use of smartphone applications and text messaging interventions, combined with education or additional interventions to promote weight reduction and physical activity, have found a beneficial impact to outcomes and cost.13

Combined with patient education, it is also important for NPs to maintain regular communication with their patients to provide a feedback loop. NPs should work closely with patients to set treatment goals, discuss potential barriers to lifestyle measures or other medical therapy, and solicit ideas from patients for overcoming nonadherence. NPs are ideally positioned to develop relationships, assess readiness for lifestyle change, and empower patients to find ways to improve outcomes. For example, motivational interviewing can be used to help patients increase their confidence in making behavior changes, especially if they are ambivalent.14

Risk Factor Modification

The 2012 guideline recommends guideline-directed medical therapy for modifiable risk factors aimed at preventing cardiovascular events. NPs should address risk factor modification at each patient encounter. Lifestyle modifications coexist within the same realm as pharmacotherapy for secondary prevention and may help lower doses of certain medications. Furthermore, some medications that patients take for comorbid conditions may negatively influence risk factors (eg, progestins, corticosteroids).

According to the guideline, risk-factor modification includes management of lipids, blood pressure, and diabetes; addressing physical activity and weight management; counseling on smoking cessation, alcohol use, and avoidance of pollution; and the management of psychological factors (eg, depression).2 Refer to Table 2.

NPs should ask patients about smoking status and advise each tobacco user to quit at each visit. For those considering cessation, developing a plan that includes pharmacotherapy or referral to a
formal program has been shown to be more effective in long-term cessation. Some patients and providers may be concerned about using nicotine replacement therapy in patients with SIHD, fearing these agents may trigger ischemia. However, a randomized, controlled trial of 10 Veterans Affairs medical centers, including 584 patients with at least 1 cardiovascular diagnosis, found no difference in the primary endpoints (death, MI, cardiac arrest, and hospital admission for cardiovascular disease) at 14 weeks between the nicotine and placebo groups. Overall, the risks of nicotine replacement are lower than those of smoking and the benefits outweigh the risk of continuing to smoke.15

Table 2. Guideline-directed Medical Therapy for Stable Ischemic Heart Disease

<table>
<thead>
<tr>
<th>Guideline-directed Medical Therapy for SIHD</th>
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<tbody>
<tr>
<td>• Dietary modifications: reduce saturated fat (&lt; 7% of total calories), trans fatty acids (&lt; 1% of total calories), and cholesterol intake (&lt; 200 mg/day); reduce sodium intake; increase fruits, vegetables, low-fat dairy. All incorporating cultural and ethnic preferences</td>
</tr>
<tr>
<td>• Physical activity: 30-60 minutes of moderate aerobic activity on 5-7 days per week supplemented by an increase in daily activities; medically supervised programs for at-risk patients with a first-time diagnosis</td>
</tr>
<tr>
<td>• Moderate to high dose statin, unless contraindicated</td>
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<tr>
<td>• Body mass index between 18.5 and 24.9 kg/m² and waist circumference &lt; 102 cm (40 inches) in men and &lt; 88 cm (35) inches in women</td>
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<tr>
<td>• Blood pressure goal &lt; 140/90 mmHg</td>
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<tr>
<td>• Hemoglobin A1c &lt; 7% for most individuals with diabetes</td>
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<tr>
<td>• Smoking cessation; avoid environmental tobacco exposure (secondhand smoke and air pollution)</td>
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<tr>
<td>• Screening for depression and increased stress</td>
</tr>
<tr>
<td>• Alcohol intake: no more than 1 serving/day for nonpregnant women or low weight men; no more than 1-2 servings/day for men. 1 serving = 4 oz of wine, 12 oz of beer, 1 oz spirits</td>
</tr>
</tbody>
</table>

Data from Fihn et al.2

All patients with SIHD should have a goal of attaining 30-60 minutes of moderate-intensity aerobic activity at least 5 days/week.2 Brisk walking supplemented with walking breaks at work, gardening, household work, and taking the stairs when possible should be encouraged. Patients should be reminded that the activity does not need to occur at 1 sitting; it may be cumulative.

Weight management is one of the toughest risk factors to address in caring for those with SIHD. Per the guideline, the waist circumference should be measured during each visit on the patient's side horizontally at the iliac crest and should be ≤ 35 inches (89 cm) for women and ≤ 40 inches (102 cm) for men.2,16 If a patient is overweight or obese, the initial goal for weight loss should be to decrease weight by 5%-10%, followed by further weight loss over 6-12 months until they meet and maintain a body mass index goal between 18.5-24.9 kg/m².2,16

NPs should counsel patients about appropriate recommendations for alcohol use. No patient should be encouraged to ingest alcohol to improve cardiovascular health. However, if a patient with SIHD elects to use alcohol, women should have no more than 1 serving per day; men no more than 2 servings per day. The guideline provides a more stringent recommendation for serving size for wine or liquor as compared to other guidelines (ie, JNC-7).5 One serving is considered 4 ounces of wine, 12 ounces of beer, or 1 ounce of spirits. Contraindications for alcohol include pregnancy, history of alcohol abuse or dependence, or liver impairment/disease.2
Revascularization

When optimal medical therapy fails or if extensive atherosclerosis is present, PCI with stenting (bare metal or drug eluding) or coronary artery bypass grafting (CABG) surgery may be performed to relieve symptoms and restore blood flow to the coronary arteries. The choice between these options is based on disease complexity, culprit lesion locations, LV function, and ischemia associated arrhythmias. However, results from the COURAGE trial suggest that there is no reduction in major adverse cardiac events or mortality with PCI compared to optimal medical therapy alone in patients with SIHD.

Patient Follow-Up

Patients with SIHD should receive follow up on at least an annual basis to assess for the following: presence of symptoms and functional ability, surveillance for complications such as HF or arrhythmias, monitoring of risk factors, and adherence to recommended lifestyle changes and medical therapy. Patients who present with new or worsening symptoms of HF or evidence of an MI (by history or ECG) should undergo assessment of LV function by echocardiography or radionuclide imaging. Although, in the absence of symptoms or a chance in clinical status, assessment of LV function is not recommended. However, a resting 12-lead ECG is reasonable in patients with stable symptoms. It is also reasonable to screen periodically for comorbidities, such as diabetes mellitus, depression, and kidney disease.

Similar to initial noninvasive testing, exercise testing is recommended in patients with known IHD with new, recurrent, or worsening symptoms not consistent with ACS, UA, or MI. Similar factors determine the mode of testing recommended in known IHD, including exercise ability and ECG interpretability.

Special Circumstances

NPs should also educate patients with SIHD about recommendations for sexual activity. According to the AHA 2012 Scientific Statement on Sexual Activity and Cardiovascular Disease, sexual activity is reasonable for patients with SIHD who are at low risk for cardiovascular complications and are experiencing no more than mild angina. A good rule of thumb for NPs to use when considering if sexual activity is reasonable for a patient is to ask if the patient can exercise > 3-5 metabolic equivalents without angina, excessive dyspnea, ischemic ST-segment changes, or arrhythmias. However, patients with unstable, decompensated, or severe symptomatic IHD should defer sexual activity until they are stabilized. Likewise, if the patient experiences symptoms that are precipitated by sexual activity, they should refrain from intercourse until optimally managed.

For patients recovering from an uncomplicated MI, PCI, or bypass surgery and having no recurrent symptoms during mild-moderate physical activity, a period of 1 or more weeks should pass before they engage in sexual activity. For patients of unknown risk, exercise stress testing is reasonable to determine exercise capacity and development of symptoms, ischemia, or arrhythmias. For additional information related to sexual side effects from medications and how
to treat them, NPs may refer to the 2012 Statement on Sexual Activity and Cardiovascular Disease.7

Conclusion

With the use of national guidelines to treat patients with SIHD, NPs are ideally positioned to evaluate symptoms, conduct risk assessment, promote required lifestyle modifications, prescribe guideline-directed medical therapy, and partner with patients to address barriers to adherence. In addition to referring patients to a structured cardiac rehabilitation programs, NPs can personally educate patients about ways to adopt a heart-healthy lifestyle, be engaged in self-monitoring of symptoms and other comorbid conditions, and live a life at their fullest functional capacity.

References


**Vitae**

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