Coronary Artery Disease in Women

View online at http://pier.acponline.org/physicians/diseases/d219/d219.html

Module Updated: 2013-01-30
CME Expiration: 2016-01-30

Authors
Jennifer H. Mieres, MD, FACC, FAHA, FASNC
Lawrence M. Phillips, MD, FACP

Table of Contents
1. Prevention ................................................................................................................. 2
2. Screening .................................................................................................................... 8
3. Diagnosis ................................................................................................................... 12
4. Consultation .............................................................................................................. 18
5. Hospitalization ......................................................................................................... 20
6. Therapy ..................................................................................................................... 21
7. Patient Counseling ................................................................................................. 29
8. Follow-up .................................................................................................................. 31
References ................................................................................................................... 33
Glossary ....................................................................................................................... 43
Tables .......................................................................................................................... 45
Figures ......................................................................................................................... 63

Quality Ratings: The preponderance of data supporting guidance statements are derived from:
A level 1 studies, which meet all of the evidence criteria for that study type;
B level 2 studies, which meet at least one of the evidence criteria for that study type; or
C level 3 studies, which meet none of the evidence criteria for that study type or are derived from expert opinion, commentary, or consensus.

Study types and criteria are defined at http://smartmedicine.acponline.org/criteria.html

Disclaimer: The information included herein should never be used as a substitute for clinical judgement and does not represent an official position of the American College of Physicians. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the module updated date on the official web site with any printout to ensure that the information is the most current available.

CME Statement: The American College of Physicians is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing education for physicians. The American College of Physicians designates this enduring material for a maximum of 1 AMA PRA Category 1 Credit™. Physicians should claim only credit commensurate with the extent of their participation in the activity. Purpose: This activity has been developed for internists to facilitate the highest quality professional work in clinical applications, teaching, consultation, or research. Upon completion of the CME activity, participants should be able to demonstrate an increase in the skills and knowledge required to maintain competence, strengthen their habits of critical inquiry and balanced judgement, and to contribute to better patient care. Disclosures: Jennifer H. Mieres, MD, FACC, FAHA, FASNC, current author of this module, has no financial relationships with pharmaceutical companies, biomedical device manufacturers, or health-care related organizations. Lawrence M. Phillips, MD, FACP, current author of this module, has no financial relationships with pharmaceutical companies, biomedical device manufacturers, or health-care related organizations. Deborah Korenstein, MD, FACP, Co-Editor, PIER, has no financial relationships with pharmaceutical companies, biomedical device manufacturers, or health-care related organizations. Richard B. Lynn, MD, FACP, Co-Editor, PIER, has no financial relationships with pharmaceutical companies, biomedical device manufacturers, or health-care related organizations.

PIER is copyrighted ©2014 by the American College of Physicians. 190 N. Independence Mall West, Philadelphia, PA 19106, USA.
1. Prevention

Control modifiable cardiac risk factors with aggressive counseling and treatment to decrease the likelihood of developing CAD.

1.1 Recommend smoking cessation when applicable to decrease risk for CAD.

Recommendations
- Determine the smoking status of all women.
- Counsel smokers regarding smoking cessation.
- Support continued abstinence in those who have quit smoking.
- See module Smoking Cessation.

Evidence
- Smoking is a strong risk factor for CAD in women, and smoking cessation decreases the risk for CAD (1; 2; 3; 4).
- Smoking cessation reduces all-cause mortality by an estimated 36% in patients with CAD (5).
- The risk for MI is three times higher in cigarette smokers. Smoking as little as one to four cigarettes per day has been associated with a relative risk for CAD of 2.4 over nonsmokers in women (6; 7). After smoking cessation, the risk for an initial coronary event decreases to that of nonsmokers within approximately 2 to 3 years (8; 9). Even women who already have had an MI reduce their risks for recurrent MI, mortality, and sudden death with smoking cessation (2; 10; 11).
- Over a lifetime, smoking appears to represent a greater risk to women than to men for the development of CAD (12). A special opportunity for smoking cessation in women occurs during pregnancy. In addition to social pressures to not smoke during pregnancy, women may have special motivation to stop for the health of their child, possibly accounting for the high smoking cessation rate of 40% in pregnancy; however, there is a high rate of relapse for smoking in the postpartum period.
- It is important to determine the smoking status of all women, to counsel smokers in smoking cessation, and to support continued abstinence in those who have quit (13; 14).
- In two randomized, controlled trials, lifestyle changes, including smoking cessation, resulted in angiographic regression of CAD (15; 16).

Rationale
- Smoking is a strong risk factor for CAD in women; risk for CAD is decreased by cessation of smoking.

Comments
- The U.S. Department of Health and Human Services recommends approaches to treating tobacco use and dependence.

1.2 Consider hypertension a common treatable risk factor for CAD in women.

Recommendations
- Screen all women for hypertension by checking blood pressure at all patient visits and treat aggressively with lifestyle modification and medication, if needed.
Coronary Artery Disease in Women

- Be aware that the goal blood pressure in patients with hypertension without diabetes is <140/85 mm Hg, and the goal blood pressure in patients with diabetes is <130/80 mm Hg.
- See the screening section in the module Essential Hypertension.

Evidence
- Hypertension, particularly diastolic hypertension, is associated with a 1.6- to 3-fold increased risk for cardiovascular events in women (17).
- Hypertension is associated with a 10-fold higher increase in death from CAD (18; 19). In elderly women, the presence of hypertension more strongly predicts CAD than in men. More women with CAD have hypertension than do men with CAD (18).
- In the Hypertension and Detection Follow-up Program, which consisted of 10,000 patients (46% women), all races of women who were treated in the stepped-care regimen had lower stroke rates at 5 years. Treated black women had fewer other cardiovascular events, but the benefit of treatment for white women was less clear. (20; 21). When a further analysis was carried out 3.3 years after the end of the original study, all women had a reduction in all causes of mortality (22).
- Hypertension screening and treatment guidelines are available (23; 24; 25; 26; 27; 28).

Rationale
- Hypertension is associated with increased cardiovascular risk in women; however, effective treatment for hypertension lowers the risk for heart failure and stroke in women.

Comments
- The principal reduction of cardiovascular risk by blood pressure reduction is in decreased stroke.

1.3 Control dyslipidemia as a modifiable risk factor for CAD in women, especially those aged 45 years or older.

Recommendations
- Perform a total cholesterol screen and obtain fasting total cholesterol, LDL, HDL, and triglyceride levels if the initial screen is elevated or if there are multiple risks for CAD.
- Base treatment intervention on actual values and presence or absence of additional risk factors, using both lifestyle changes and drug therapy.
- See module Lipid Disorders.

Evidence
- Before age 75, absolute cardiovascular risk is lower for women than men at any age (29). As a result, the number needed to treat to prevent a major cardiovascular event in women aged under 75 years is higher than in men of a corresponding age (30).
- Studies of lipid reduction in the primary and secondary prevention of cardiovascular events have included relatively few women. However, estimates of the relative benefit of lipid-lowering therapy for women have generally corresponded to estimates of benefit for men (30).
- Absolute benefits of lipid-lowering therapy can be calculated from the 10-year Framingham risk estimates according to the recommendations of the National Cholesterol Education Program Adult Treatment Panel III (31).
- Lipid-lowering therapy with statins or other drugs is recommended for all patients with CAD equivalents such as diabetes or established noncoronary vascular disease, as well as for all women and men with dyslipidemia and an estimated 10-year risk for major cardiovascular events of >20%. This therapy should also be considered for all women and men with dyslipidemia and an estimated 10-year risk for major cardiovascular events of 10% to 20% (31).
Lifestyle modification (smoking cessation, regular moderate exercise, and healthful diet) is recommended for all patients (31).

A large study of women with risk factors for or known CAD showed a statistically significant reduction of 24% in major cardiovascular events (32).

Existing data are most compatible with the view that cardiovascular risk exists as a spectrum rather than a binary assessment of the presence or absence of CAD and that the intensity of lipid-lowering therapy should match the level of cardiovascular risk as assessed by the Framingham risk estimates (30; 31).


The U.S. Preventive Services Task Force published recommendations on screening for lipid disorders.

The AHA published guidelines for cardiovascular disease prevention in women (33).

**Rationale**

Dyslipidemia is a modifiable risk factor for CAD and is particularly important for secondary prevention in women.

**Comments**

Low levels of HDL cholesterol (<35 mg/dL) may be particularly predictive of CAD in women. Several studies have suggested that higher levels of HDL cholesterol are protective against CAD risk in women. In a pooled study from the National Heart, Lung, and Blood Institute, HDL cholesterol was inversely related to HDL cholesterol levels in women aged over 65 years (34).

### 1.4 Recommend lifestyle modifications to address weight and exercise as additional potential risk factors for CAD[6]

**Recommendations**

- Determine the BMI in all women.
- Counsel women who have a BMI >30 kg/m² or have a BMI >27 kg/m² plus other cardiac risk factors regarding weight loss.
- Advise all women to participate in moderate-intensity physical activity, such as brisk walking, for 30 to 60 minutes most days of the week.

**Evidence**

- Obesity and physical inactivity are important and prevalent modifiable risk factors for CAD (35).
- Physical activity consisting of moderate (walking) or vigorous exercise is associated with reduced cardiovascular risk in postmenopausal women. Brisk walking or vigorous exercise (≥2.5 hrs/wk) was associated with a 30% reduced risk for cardiovascular events (36).
- Obesity has been associated with an increased risk for MI, death from coronary events, and reinfarction rates (6; 37; Cardiovascular events (36).
- Obesity has been associated with an increased risk for MI, death from coronary events, and reinfarction rates (6; 37; 38; 39; 40). The risk for CAD and death is lower in women who exercise regularly and who are more physically fit (41; 42).
- Particularly high-risk groups of women to target for cardiac risk-factor modification include those of lower socioeconomic and educational status and postmenopausal women. Ethnic minority women have more cardiac risk factors than white women (43).

**Rationale**
• Waist circumference is predictive of heart disease risk in women; BMI between 18 and 24.9 kg/m² and waist circumference less than 35 inches is optimal.

• Obesity and physical inactivity are modifiable risk factors for CAD.

Comments

• Some of the increased cardiac risk associated with obesity may be related to other risk factors associated with obesity, such as hypertension, hyperlipidemia, diabetes mellitus, and physical inactivity.

• Exercise has beneficial effects on many cardiovascular risk factors, including lipid profile, hypertension, diabetes mellitus, and weight control. The benefits of physical activity extend to decreasing mortality from all causes. Women at moderate-to-high risk for CAD may have stress testing before initiating an exercise program.

• Black women have a higher risk for developing heart disease, and aggressive risk-factor modification is needed.

1.5 Recommend a balanced diet that is low in saturated fats and rich in fresh vegetables, fruits, and fiber. BC

Recommendations

• Recommend a well-balanced diet that is rich in fresh vegetables, fruits, and fiber; low in saturated (animal) fats and oils; low in processed starches and simple sugars; and low in trans fatty acids.

• Advise patients that some oils and fats are healthful in moderation, including monounsaturated vegetable oils (olive oil) and omega-3 fatty acids and oils (from fish and certain vegetable oils).

• Do not recommend antioxidant vitamins for the primary or secondary prevention of CAD; instead, recommend abundant fresh vegetables and fruits as a source of micronutrients.

• Discuss the potential risks, benefits, and uncertainties of alcohol intake for cardiovascular health.

Evidence

• Obesity and caloric intake are increasing in the U.S. (44; 45). Increasing obesity is associated with an increase in cardiovascular risk factors: high cholesterol, high blood pressure, and diabetes (44).

• Available epidemiologic studies suggest that diets high in saturated (animal) fat and hydrogenated trans-fatty acids (found in vegetable shortening, stick margarine, and many commercial baked goods) are associated with increased rates of cardiovascular disease (46). The Nurses' Health Study showed this relationship holds true in women as well as men (47).

• Fish intake, a rich source of omega-3 polyunsaturated fatty acids, is associated with a significant reduction in fatal CAD but has less benefit on nonfatal MI (48). Consumption of two or more servings of fish per week was associated with a 30% reduction in cardiovascular risk, particularly fatal cardiac events, in women (49).

• Two randomized, secondary-prevention trials suggest general recommendations for optimal diets for cardiovascular risk reduction. In the Lyon Diet Heart Study, a ‘Mediterranean diet’ was associated with a reduced risk for reinfarction in women and men over 4 years of follow-up (50). Similarly, in patients with CAD, an Indo-Mediterranean diet was associated with a lower risk for cardiovascular events compared with a diet similar to the National Cholesterol Education Program Step 1 diet (51). These diets are low in saturated (animal) fats; rich in whole grains, fresh vegetables, and fruits; and rich in complex micronutrients. Both diets included nuts in moderation. The Mediterranean diet includes fish as a source of omega-3 fatty acids, although omega-3 fatty acids were derived principally from vegetable sources in the Indo-Mediterranean diet.
Although observational studies have suggested a link between intake of antioxidant vitamins and reduced cardiovascular risk, available randomized, controlled studies do not support a benefit (52; 53).

There is a U-shaped relationship between alcohol intake and cardiovascular risk in many epidemiologic studies: no consumption or excessive consumption of alcohol is associated with increased cardiovascular risk compared with moderate consumption. In one representative study, women who consumed one to six drinks per week had a risk for cardiovascular mortality that was approximately 60% lower than women who were abstinent from alcohol or drank several drinks per day (54).

Rationale

- Higher intake of saturated animal fats is associated with an increased cardiovascular risk.
- A balanced diet, rich in whole grains, legumes, fresh vegetables, and fruits, with regular intake of fish, is recommended for optimal cardiovascular health.
- Omega-3 polyunsaturated fatty acids, present in fish and certain vegetable oils, may reduce CAD risk by lowering serum triglyceride levels, preventing cardiac arrhythmia, and improving endothelial function; their principal benefit appears to be reduction of cardiac arrhythmias.
- Although oxidized lipids, particularly LDL cholesterol, are felt to be atherogenic, randomized, controlled trials have not shown any reduction in cardiovascular risk with use of antioxidant vitamins.
- Alcohol, in moderation, may improve vascular endothelial function and reduce platelet reactivity and markers of inflammation.

Comments

- A 2002 structured review summarizes available data on dietary approaches to reducing cardiovascular risk (55).
- Vegetable sources of omega-3 fatty acids (canola oil, flaxseed oil, and mustard-seed oil) may be alternatives to eating fish for prevention of CAD events.
- Alcohol abuse is a significant social concern. There are no randomized, controlled trial data that confirm the healthful effects of moderate alcohol use. Existing epidemiologic studies are subject to important potential confounders. Recommend alcohol for purposes of cardiovascular risk reduction with caution.

1.6 Do not recommend postmenopausal hormone therapy to reduce cardiovascular risk in postmenopausal women.

Recommendations

- Do not prescribe hormone therapy to prevent heart disease in postmenopausal women.

Evidence

- The Women's Health Initiative randomly assigned more than 16,000 previously healthy postmenopausal women to hormone therapy vs. placebo (56). This study showed a small but statistically significant excess of major cardiovascular events (nonfatal MI and coronary death) in women treated with hormone therapy over 5 years of follow-up.
- During the first year of follow-up in the Women's Health Initiative study, women randomly assigned to hormone therapy experienced an increased risk for thromboembolic events (56).
- In a substudy of the Women's Health Initiative, conjugated equine estrogen alone (no progestin) did not protect postmenopausal women who had previously undergone hysterectomy against major cardiovascular events (57).
Coronary Artery Disease in Women

- The AHA evidence-based guidelines for cardiovascular disease prevention in women recommend against hormone therapy for the purpose of cardiovascular risk reduction (33).

Rationale
- Hormone therapy does not reduce cardiovascular risk in postmenopausal women and even increases the short-term risk for thromboembolic complications.

1.7 Do not routinely recommend aspirin and vitamin E for prevention of CAD in women.

Recommendations
- Do not recommend aspirin to prevent CAD in women aged under 65 years.
- Do not recommend vitamin E to prevent CAD in women.

Evidence
- Data from the Women's Health Study did not show a benefit of every-other-day aspirin use (58). However, subgroup analysis of the women aged over 65 in this study did show a benefit.
- A systematic review of the benefits of aspirin for primary prevention of cardiovascular disease found reductions in cardiovascular events (OR, 0.88 [CI, 0.79 to 0.99]) and ischemic stroke (OR, 0.76 [CI, 0.63 to 0.93]) with aspirin use, but no reduction in myocardial infarction or mortality (59).
- Data in the Women's Health Study did not confirm the benefit of vitamin E supplementation on cardiac disease in men and women which was noted in observational studies. (60). In addition, a meta-analysis found increased mortality in vitamin E users at doses over 400 IU daily (61).

Rationale
- Studies have failed to show conclusive benefit of aspirin in preventing CAD in younger women, although aspirin has been shown to prevent stroke in women aged over 65 years.
- Daily doses of vitamin E have not been found to provide prophylaxis for CAD in women and may be harmful.
2. Screening

Do not routinely screen asymptomatic women without cardiovascular risk factors. Consider screening patients with cardiac risk factors and patients in high-risk occupations without cardiovascular risk factors. \(^{BC}\)

2.1 Do not screen for CAD in asymptomatic women without cardiovascular risk factors. \(^{B}\)

**Recommendations**

- **High-value care:** Do not routinely use resting ECG, exercise ECG, or other noninvasive tests to screen for CAD in asymptomatic women.
- See module [Screening for Coronary Artery Disease](#).

**Evidence**

- Only 29% of persons with symptomatic, angiographically proven CAD have normal baseline ECGs \(^{62;63}\).
- A cost-effectiveness analysis noted that most asymptomatic persons with an abnormal exercise ECG do not have clinically significant CAD on angiography (positive predictive value of 20%) \(^{64}\).
- A systematic review for the U.S. Preventive Services Task Force has shown that abnormalities of resting or exercise ECG testing only modestly predict subsequent coronary events, with a pooled hazard ratio of 1.4 to 2.1 after adjustment for other risk factors \(^{65}\).
- A prospective trial found that the risk for sudden death during vigorous exercise has been estimated to be less than 1 death per 1.5 million episodes of vigorous exercise among U.S. male physicians \(^{66}\).

**Rationale**

- Abnormalities of the resting ECG are rare, not specific for CAD, and do not predict subsequent mortality from coronary disease.
- Although exercise testing may identify women with CAD, the utility of exercise testing is limited. Low prevalence of CAD in asymptomatic women results in poor positive predictive value. Exercise testing does not provide evidence that abnormalities accurately predict future events in asymptomatic women.

**Comments**

- Because the positive predictive value of an abnormal exercise test result is low, especially in women, one major consequence of routine exercise testing in asymptomatic persons is the incorrect labeling of otherwise healthy individuals as having CAD.
- In addition, a large number of these persons would have expensive and unnecessary diagnostic procedures.
- Assessment of preoperative cardiac risk in persons without known CAD is addressed in the module [Preoperative Cardiac Risk Assessment](#).

2.2 Consider screening for occult CAD in some asymptomatic women at intermediate or high risk for CAD with ECG, cardiac CT, or ultrasonography for carotid intimal thickness. \(^{B}\)

**Recommendations**
Consider screening women at increased risk for CAD for vascular disease, especially those in whom the results of screening tests will affect management.

Choose from among several tests for CAD or vascular disease, including:
- ECG
- Cardiac CT for coronary artery calcium
- Ultrasonography for carotid intimal thickness
- Ankle-brachial index for peripheral vascular disease, which is a marker for systemic atherosclerosis

See module Screening for Coronary Artery Disease.

Evidence

ACCF/AHA 2010 guidelines for assessment of cardiovascular risk in asymptomatic adults provide useful assessment of each cardiovascular screening test. The guidelines state that several tests are reasonable (class IIa recommendation) to use for risk assessment in asymptomatic adults at high or intermediate risk, including ECG, cardiac CT for coronary artery calcium, ultrasonography for carotid IMT, and ankle-brachial index (67).

A systematic review of cohort studies found that major abnormal findings, such as ST-segment or T-wave changes, conduction blocks, ventricular ectopy, and atrial fibrillation, on screening resting ECG have a sensitivity of 16% to 32% and a specificity of 87% to 96% for predicting future CHD events (68).

A systematic review of cohort studies performed as part of the ACCF/AHA clinical expert consensus document evaluated the predictive information gained from cardiac CT and found that higher coronary artery calcium scores are associated with higher event rates and higher relative-risks for CAD after controlling for measured risk factors and demographic information. A mild-risk CAC score (with scores ranging from 1 to 112) was associated with a near doubling of rates of CHD death or MI risk (RR, 1.9 [CI, 1.3 to 2.8]; P=0.001). For scores ranging from 100 to 400, the summary relative risk was 4.3 (CI, 3.1 to 6.1) when compared with patients with no detectable coronary calcium (P<0.0001). For the high-risk (CAC scores of 400 to 1000) and very-high-risk (>1000) CAC scores, relative-risk ratios were 7.2 (CI, 5.2 to 9.9; P<0.0001) respectively, and 10.8 (CI, 4.2 to 27.7; P<0.0001) respectively, when compared with the low-risk group (CAC score = 0) as reference. Persons with a calcium score of 0 had remarkably low event rates over the next 3 to 5 years (less than 1 event per 1000 person-years follow-up) (69). Impact of testing on clinical outcomes, however, is not clear.

A small number of cohort studies show evidence that carotid ultrasonography (70) and ankle-brachial index (18) provide risk information, but there are questions about whether or not traditional CHD risk factors were adequately controlled. Other studies have demonstrated that carotid intimal thickness (RR, 2.1) is associated with an increased risk for CHD events and mortality (71).

Rationale

Testing for cardiovascular disease can identify patients who would benefit from more aggressive risk-factor management.

Comments

Cardiovascular tests in asymptomatic persons can be used to diagnose unsuspected coronary artery lesions that could be treated with anti-atherosclerotic therapies (i.e., statins, aspirin) to prevent imminent cardiovascular events. This strategy is likely to be most effective in low- to intermediate-risk persons (6% to 20% risk for a cardiovascular disease event in 10 years); providing revascularization to asymptomatic persons has not been shown to improve outcomes and is generally considered inappropriate. Revascularization has only been shown to be helpful in the setting of symptoms of heart disease or an acute coronary syndrome.
The principal tests for detecting asymptomatic CHD include coronary artery calcium testing, resting ECG, and exercise tolerance testing. These tests can provide evidence of atherosclerosis, unrecognized previous MI, silent or inducible myocardial ischemia, or other cardiac abnormalities.

Cardiovascular screening tests could also be used to provide further information about future risk for CHD beyond that of traditional risk-factor assessment and to guide the use of risk-reducing treatments, such as lipid-lowering or aspirin therapies.

The addition of cardiovascular screening tests is likely to be most helpful in patients whose risk for future cardiovascular events is not clear and when better risk stratification would change patient management, such as adding aspirin or initiating or titrating statin therapy for primary prevention. If a patient is considered low risk as determined by such instruments as the Framingham Risk Score calculator, additional screening tests rarely will change that risk. Likewise, if a patient is considered high risk, additional testing is unlikely to change the management plan. The intermediate-risk patient may derive the most benefit from additional tests to better stratify risk. Further studies are needed to determine whether treatment based on cardiovascular screening tests improves outcomes.

2.3 Consider screening for CAD in selected asymptomatic women whose occupations may affect public safety or who engage in high-intensity physical activity.

Recommendations

- Consider exercise testing or baseline ECGs in occupations that require physical fitness or high-intensity physical activity, such as airline pilots, air-traffic controllers, police, and firefighters.
- See module Screening for Coronary Artery Disease.

Evidence

- There is no adequate evidence for or against screening in these occupations (72; 73).

Rationale

- Persons whose occupations involve public safety may be held to a higher standard of physical fitness than the average individual.
- Persons who engage in occupations that involve bursts of high-intensity physical activity, such as police or firefighters, may be at increased risk for cardiovascular events.

Comments

- Policies regarding screening for CAD in certain occupations are frequently codified by local and national regulatory agencies.

2.4 Recognize that exercise tolerance testing, stress echocardiography, and myocardial perfusion testing are generally not useful in screening asymptomatic women. Stress testing may be considered in sedentary women beginning a rigorous exercise program.

Recommendations

- Do not perform stress testing in asymptomatic women, because the rate of finding clinically important CAD is minimal.
- Consider stress testing in women at intermediate risk who are beginning vigorous exercise.
- See module Screening for Coronary Artery Disease.

Evidence
A systematic review of the literature published between 1966 and 2003 identified 13 studies examining the utility of exercise tolerance testing to diagnose asymptomatic coronary artery obstruction. This review concluded that previously unrecognized, clinically important coronary artery obstruction is found in 0.9% to 1.2% of screened persons with at least one risk factor and in 0.06% to 1.6% of screened persons with no risk factors (74).

ACCF/AHA 2010 guidelines recommend that an exercise ECG be considered (class IIb recommendation) for risk assessment in intermediate-risk asymptomatic adults (including sedentary adults considering starting a vigorous exercise program). ACCF/AHA recommend against stress echocardiography and stress myocardial perfusion imaging in asymptomatic persons (class-III recommendation), because testing has not been shown to improve outcomes. A negative test result only shows that patients do not have high-grade obstructive CAD, but patients may be falsely reassured that CAD is not present (67). These guidelines recommend that stress myocardial perfusion imaging should be considered (class IIb recommendation) for risk assessment in asymptomatic adults with diabetes or a strong family history of CHD, or when previous risk assessment testing suggests a high risk for CHD (67).

Rationale
• Stress testing in asymptomatic women is rarely clinically helpful.

Comments
• Data and recommendations specifically for women are lacking.
• Screening of asymptomatic persons with exercise tolerance testing can detect previously unrecognized, clinically important coronary artery obstruction. The diagnostic value of this type of screening is directly related to the cardiovascular risk of the population screened. The ratio of benefits to harms of exercise tolerance test screening for patients with different degrees of risk for CHD is not yet known. The potential risks of exercise tolerance test screening of asymptomatic persons include the concern that exercise tolerance testing will detect only highly obstructive disease, and lesser degrees of disease, such as mild nonobstructive CAD, will be missed. Because myocardial infarction and death can occur from the rupture of nonobstructive lesions, patients may be falsely assured by a negative exercise tolerance test result that CAD is not present.
3. Diagnosis

Perform a thorough history and physical exam including a careful description of symptoms and evaluation for cardiac risk factors to estimate the probability that a woman has CAD.

3.1 Determine the presence of cardiac risk factors to estimate the risk for ischemic heart disease in an individual patient.

Recommendations

- Determine the following in women suspected to have CAD:
  - Smoking status
  - Presence of diabetes mellitus
  - Hypertension
  - Presence of lipoprotein abnormalities
  - Obesity
  - Peripheral vascular disease
  - Sedentary lifestyle
  - Hormonal status (menopausal status)
  - Age
  - Family history of CAD
- Use the Framingham Risk Score to estimate risk for heart disease in women.
- See figure Estimate of 10-Year Risk for Men and Women (Framingham Point Scores).

Evidence

- The presence of cardiac risk factors predicts the presence of CAD (18; 75).
- One study found that the presence and extent of CAD was predicted by cardiac risk factors in 54.5% of women and 39.3% of men (76).
- The Framingham Risk Score is the standard way to estimate likelihood of ischemic heart disease in women (33).
- Diabetes mellitus is a particularly powerful risk factor for CAD in women, as is hormonal status and the presence of peripheral vascular disease (18).
- Cardiac risk factors have a strong predictive value for CAD in women and are particularly strong in young women (18; 76; 77). Risk factors that are especially important in women are hormonal status, diabetes, smoking, and a family history of premature CAD.
- Menopause is associated with a worsened cardiovascular risk profile, including increased levels of LDL cholesterol, decreased levels of HDL cholesterol, decreased insulin sensitivity, increased body mass, decreased fibrinolytic activity, and impaired endothelium-dependent vasodilatation (78). The incidence of morbidity and mortality secondary to CAD increases at menopause. Surgical menopause increases the risk for CAD over that of natural menopause, regardless of whether a woman takes hormonal therapy.

Rationale

- The presence of cardiac risk factors predicts the presence of CAD.

Comments
In the Women's Health Initiative randomized, controlled trial, combination hormone replacement (estrogen and progestin) and estrogen alone increased the risk for cardiovascular events, stroke, and pulmonary embolus compared with placebo (56; 57).

3.2 Estimate the likelihood of CAD by considering elements of the history along with cardiac risk factors.

Recommendations

Several elements of the history can help in estimating the likelihood of CAD.

- 'Typical' chest pain is defined as being substernal, precipitated by exercise, and relieved within 10 minutes by rest or nitroglycerin. Although women present more often than men with atypical symptoms, the presence of typical angina remains helpful in women, with a sensitivity of 89% and a specificity of 63%
- Burning, heavy, or squeezing sensations are considered to be additional features of 'typical' angina pectoris in women
- Ask about other atypical features, such as radiation to the arm, shoulder, or jaw, associated dyspnea, nausea, vomiting, or diaphoresis
- Symptoms occurring with emotional stress, at rest, or during sleep can be suggestive of angina in women

See figure Diagnostic Algorithm for Evaluating Chest Pain in Women Using Diamond Information.

Determine the likelihood of CAD by one of the following means:

- See table Determining Probability of Coronary Artery Disease by Minor, Intermediate, and Major Determinants.
- See table The Probability of Coronary Artery Disease in Women According to Age and Character of Symptoms.
- See figure Determining Probability of Coronary Artery Disease with a Nomogram.

Evidence

A cohort study evaluated the diagnostic accuracy of chest pain characteristics in 2475 consecutive men and women (32%) presenting to the emergency department with acute chest pain. Acute MI was determined by two independent cardiologists with access to all clinical data. Women were more likely to report pressure-like pain (72% vs. 68%, P=0.048) and dyspnea (54% vs. 44%, P<0.001), aggravation by palpation (23% vs. 16%, P<0.001), and radiation to throat (24% vs. 16%, P<0.001) and back (18% vs 11%, P<0.001) The majority of pain characteristics had similar diagnostic performance in men and women, with aggravation by exertion, relief by nitrates, location in the mid-chest or right-chest, radiation to shoulders or arms, and pain area >3 cm increasing the likelihood of MI (79).

Women with CAD are more likely to present with atypical symptoms than men (18; 80; 81; 82; 83).

More women than men present with angina, although rates of angiographically demonstrable CAD are lower in women (84).

The quality of chest pain in women was helpful in determining the likelihood of identifying CAD by angiography in the Coronary Artery Surgery Study (85).

Women are more likely to experience pain with emotional stress and during rest or sleep than are men (80). Women are also more likely than men to experience radiation of pain to the neck and shoulder and to develop associated nausea, vomiting, and shortness of breath with MI (18).

Performance characteristics of diagnostic tests for CAD, including aspects of the history and physical exam, have been determined in a population undergoing coronary angiography (86).

The probability of a woman aged 35 years with 'average risk factors' and atypical chest pain of having CAD is 4.2%, whereas the probability of a woman aged 65 years with typical angina of having CAD is 86% (82).
• Although women may present differently than men, there were no differences in the presentation of 99.6% of women and men with MI in the Myocardial Infarction Triage and Intervention registry (87).

• Women with chest pain may be treated differently than their male counterparts (18). In one study, women presenting the same symptoms to physicians in a businesslike manner were more likely to be investigated than women who presented the same symptoms in a more emotional manner (88).

• Chest pain with all three features of typical angina is considered ‘definite angina’ in the Coronary Artery Surgery Study (85) and ‘typical’ chest pain by Diamond (83). Burning, heavy, or squeezing sensations are considered additional features of ‘typical’ angina pectoris by Douglas and Ginsburg (18).

• Reviews of the evaluation of chest pain in women confirm the clinical usefulness of the classification of chest discomfort and the associated probability of CAD (18; 83).

Rationale
• The pretest probability of CAD is helpful to determine when and what further testing is necessary; due to Bayesian theory, further testing is the most useful in women with an intermediate probability of having CAD (between 10% to 20% and 80% to 90%).

• It is important to consider the diagnosis of CAD in women presenting with symptoms related to anxiety. Even female patients themselves may attribute symptoms to emotional factors and to underestimate their own risk for CAD.

3.3 **Use the physical exam to identify risk factors associated with CAD and evidence of cardiac disease, and to diagnose noncardiac causes of chest pain.**

Recommendations
• Perform a physical exam on patients presenting with possible CAD focusing on:
  • The cardiac, pulmonary, and vascular portions of the exam
  • Signs suggesting noncardiac causes of the patient's symptoms

Evidence
• These recommendations are based on expert opinion from the ACC/AHA guidelines for chronic stable angina (89).

Rationale
• The physical exam provides evidence for the presence of cardiac risk factors, cardiac disease, and clues for alternative causes of symptoms.

3.4 **Obtain an ECG in all women presenting with possible ischemic chest pain.**

Recommendations
• Obtain an ECG in women suspected of having CAD.

• Look for evidence of ischemic heart disease or previous MI on the ECG.

• On an ECG taken during chest pain, look for ischemic changes as important diagnostic information that may preclude the need for further stress testing and support direct cardiac catheterization.

• Be aware that, although a normal ECG does not rule out the presence of CAD, a normal ECG taken when the patient is having chest pain virtually excludes ischemia.

• See table **Laboratory and Other Studies for Coronary Artery Disease in Women**

Evidence
• Baseline ECG abnormal findings, such as ST-segment depression, T-wave flattening, bundle-branch blocks, arrhythmias, left ventricular hypertrophy, and ischemic findings, are associated with increased cardiovascular disease and CAD mortality in women (90).

• A normal ECG result does not rule out the presence of CAD; in the Coronary Artery Surgery Study, 29% of patients with symptomatic, angiographically proven CAD had normal resting ECGs (63).

Rationale

• Abnormal findings on an ECG are associated with increased cardiovascular disease and CAD mortality in women.

3.5 Obtain noninvasive stress testing in women requiring evaluation for CAD, depending on the clinical circumstances, starting with a treadmill exercise tolerance test in women with a normal baseline ECG who are able to exercise.

Recommendations

• Obtain a treadmill exercise tolerance test as the first-line test in women with a normal baseline ECG, and reserve imaging tests for women at higher risk with abnormal baseline ECGs and an inability to achieve >5 metabolic equivalents on the treadmill test.

• Obtain an exercise ECG stress test, radionuclide myocardial perfusion imaging, or stress echocardiography in women suspected to have CAD. Among the stress imaging and nuclear stress tests, stress echocardiography appears to be the most sensitive in women with a sensitivity of 81%.

• Obtain pharmacologic stress imaging or echocardiography in women who are unable to exercise to the appropriate intensity or who have an abnormal baseline resting ECG.

• Recognize that there is a higher false-positive rate of exercise ECG and radionuclide cardiac imaging in women than in men.

• Consider clinical characteristics, local expertise, and availability in determining the optimal testing for a particular patient.

• Note that stress echocardiography is the stress imaging modality of choice in pregnant women.

• See table Laboratory and Other Studies for Coronary Artery Disease in Women.

• See figure Diagnostic Algorithm for the Evaluation for Coronary Artery Disease in Women.

Evidence

• There is a lack of conclusive evidence to suggest that women should undergo different evaluations than men for CAD (89).

• The AHA consensus statement on noninvasive testing of women with suspected CAD describes the accuracy of noninvasive tests (91).

• One study found stress echocardiography to be cost-effective in the initial evaluation of CAD in women when compared with stress ECG (92).

• A prospective study randomized 824 symptomatic women with intermediate pretest likelihood of obstructive CAD to exercise treadmill testing vs. exercise myocardial perfusion imaging. The major adverse cardiac event rate for both groups was similar at 2 years (93).

Rationale

• Exercise ECG, exercise, or pharmacologic stress radionuclide myocardial perfusion imaging and exercise, or pharmacologic stress echocardiography helps identify CAD in women.
• In men and women, stress testing may be helpful in following the success of therapy and for prognosis.

Comments
• There are no reliable noninvasive tests able to identify which patients have left-main or three-vessel CAD.
• Functional capacity, as assessed by exercise stress testing, is linked to prognosis (94).
• Appropriateness criteria have been published for SPECT and echocardiographic stress testing (72; 95).

3.6 Consider cardiac catheterization in patients at very high risk or with significant or unstable angina.‌

Recommendations
• Obtain cardiac catheterization in women with high-risk findings on noninvasive testing who may benefit from revascularization procedures.
• Consider direct cardiac catheterization in women with a high pretest probability for CAD (90%) without previous stress testing or in those for whom a negative result is likely to be false.
• Obtain cardiac catheterization in women with unstable angina or significant angina interfering with lifestyle despite maximal medical therapy.
• Reserve cardiac catheterization for women who are otherwise candidates for revascularization procedures; some women with angina and normal cardiac catheterization have vasospasm and will respond to calcium-channel blockers.
• See table Laboratory and Other Studies for Coronary Artery Disease in Women.

Evidence
• Consensus.

Rationale
• Cardiac catheterization confirms the presence of CAD and delineates the extent of disease in high-risk patients.
• A negative stress test in a woman with a high pretest probability for CAD has a high likelihood of being a false-negative test; in this circumstance, cardiac catheterization is necessary, regardless of the result of stress testing.
• Cardiac catheterization is the ‘gold standard’ for identifying CAD.

3.7 Strongly consider CAD in the broad differential diagnosis for women with potential cardiac symptoms.‌

Recommendations
• Strongly consider CAD in women presenting with suggestive symptoms, but also consider the possibility of other cardiac, pulmonary, gastrointestinal, musculoskeletal, neurologic, and vascular processes.
• See table Differential Diagnosis of Coronary Artery Disease in Women.

Evidence
• Consensus.

Rationale
• CAD is a life-threatening, treatable disease and therefore must be seriously considered in any woman with suggestive symptoms.
Comments

- Although there is an increased incidence of nonischemic causes of chest pain such as mitral-valve prolapse in women over men, there is also an increased incidence of vasospastic, microvascular, and endothelial causes of ischemia in women.
4. Consultation

Consider obtaining consultation for women with suspected CAD if the diagnosis is uncertain, if a specialized procedure is required, or if underlying noncardiac disease is suspected. Consult appropriate specialists for help in managing CAD and underlying contributing comorbid conditions.

4.1 Consider cardiology consultation in women requiring cardiac catheterization or in whom the diagnosis of CAD is uncertain, and other appropriate consultation if noncardiac disease is suspected.

Recommendations

- Consider a cardiology consult in women requiring cardiac catheterization or in whom the diagnosis of CAD is uncertain, despite initial studies.
- Consider a pulmonary consult in women with possible pulmonary causes of chest pain in whom the diagnosis remains unclear or in whom further testing may be indicated.
- Consider a gastroenterology consultation in women with possible gastrointestinal causes of chest pain in whom the diagnosis is unclear or in whom an endoscopic procedure may be indicated.

Evidence

- These recommendations are based on expert opinion from the ACC/AHA guidelines for chronic stable angina (89).

Rationale

- Cardiologists or other specialist consultants often have experience and procedural expertise helpful in making an accurate diagnosis.

4.2 Obtain a cardiology consultation for patients with severe or complex disease and for those who may require revascularization or other procedures.

Recommendations

- Obtain cardiology consultation for help in managing women with unstable CAD or acute MI.
- Obtain a cardiology consultation for women with high-risk CAD who require revascularization procedures.
- Obtain a cardiology consultation for women who have significant coexisting cardiac disease, such as severe valvular heart disease or cardiomyopathy.

Evidence

- Consensus.

Rationale

- Cardiologists have expertise in the diagnosis and management of CAD.
- Revascularization of patients with multivessel disease and/or left ventricular dysfunction may improve mortality.

Comments

- Women with severe ischemic symptoms, symptoms of peripheral vascular disease, or symptoms of left ventricular dysfunction are at increased risk for cardiac death and MI.
4.3 Consider consulting an endocrinologist for help in managing specific cardiac risk factors.

Recommendations
- Consider an endocrinology consultation for management of difficult-to-control hyperlipidemia, diabetes mellitus, or obesity.

Evidence
- Consensus.

Rationale
- Control of weight and lipid levels is essential in decreasing risk, and rigid control of diabetes may require subspecialist expertise.

4.4 Consider consulting behavioral health specialists to help with important lifestyle modifications as well as evaluation and treatment of depression.

Recommendations
- Obtain consultation with a behavioral health specialist for:
  - Difficulty with smoking cessation, weight loss, or stress management
  - Assessment for and treatment of depression

Evidence
- Mainly consensus.
- Depression is commonly seen in patients with CAD, especially after an acute MI (96).

Rationale
- Behavioral health specialists have expertise in the management of smoking cessation, weight loss, and stress management.
- Behavioral health specialists have expertise in the diagnosis and treatment of depression.
5. Hospitalization  

Hospitalize patients with high-risk unstable coronary syndromes in a telemetry or coronary intensive care unit.  

5.1 Immediately hospitalize patients with acute MI or unstable angina in an intensively monitored setting.  

Recommendations  

- Hospitalize women suspected of having acute MI in an intensively monitored setting so that measures to restore coronary perfusion (in appropriate candidates), to treat arrhythmias, and to prevent hemodynamic complications may be instituted as soon as possible.  
- Hospitalize women with unstable angina when there has been an increase in frequency or severity of symptoms, a change in pattern, symptoms at rest, or an inadequate response to medical therapy.  
- See module Acute Coronary Syndromes.  

Evidence  

- Prompt identification and management of arrhythmias and heart failure decrease mortality. Successful early reperfusion decreases infarct size, preserves left ventricular function, and reduces mortality (97).  
- Patients with unstable angina have a 10% to 20% risk for developing MI. Aggressive medical treatment decreases this risk to 5% to 7% (98).  

Rationale  

- Patients with acute MI are at risk for death from arrhythmias and heart failure, which require prompt treatment.  
- The mortality from MI is the greatest within the first 2 hours of symptoms.  
- Women with acute cardiac ischemia are more likely than men to present with atypical symptoms.  
- Women are also more likely to attribute their symptoms to noncardiac causes, which may delay proper diagnosis and treatment, including the ability to use thrombolytics.
6. Therapy

Treat CAD with medications that decrease the incidence of angina symptoms, MI, and death, and focus on aggressive risk-factor modification and coronary revascularization and/or cardiac rehabilitation, as required.

6.1 Use aspirin to decrease the risk for MI and sudden death.

Recommendations
- Instruct patients to take one aspirin (75 to 325 mg) daily if there are no contraindications.
- Do not use the antiplatelet agent dipyridamole in the treatment of CAD.
- Consider the use of clopidogrel if there is an absolute contraindication to aspirin.
- See table Drug Treatment for Coronary Artery Disease in Women.

Evidence
- Aspirin use in patients with angina is associated with approximately a 33% decrease in cardiovascular events (99; 100; 101).
- Aspirin use decreases both the short- and long-term risk for MI in patients with unstable angina (102; 103).
- In asymptomatic men, aspirin use every other day is associated with a decreased incidence of MI (104).
- Dipyridamole can increase exercise-induced ischemia in patients with stable angina (105).
- Ticlodipine has not been shown to decrease adverse cardiovascular events (106; 107).
- Clopidogrel requires further study, but has been shown to decrease the risk for MI, stroke, and death in patients with previous MI, stroke, and peripheral vascular disease (108).

Rationale
- Aspirin use decreases cardiac events.
- Dipyridamole increases exercise-induced ischemia; note that dipyridamole is used for diagnostic testing as a pharmacologic stress to induce ischemia in some patients who cannot exercise adequately for stress testing.

6.2 Use β-blocker therapy as first-line treatment.

Recommendations
- Treat patients with β-blockers if there are no contraindications; titrate to a resting heart rate of 55 to 60 beats/min in women with stable angina.
- In women with stable exertional angina, titrate dose to limit the increase in heart rate during exercise to no greater than 75% of the heart rate associated with ischemia.
- Avoid abrupt discontinuation of β-blockers.
- See table Drug Treatment for Coronary Artery Disease in Women.

Evidence
- In both randomized trials and meta-analyses, β-blockers improve survival in patients with recent MI (89); reduce exertional angina (109; 110; 111; 112); are effective in the treatment of post-MI...
ischemia (113); and are effective in decreasing MI, death, angina, and ventricular arrhythmias in patients with angina (114).

- It appears that all β-blockers are equally effective in the treatment of angina (115; 116; 117; 118; 119).
- In hypertensive patients, β-blockers also improve the survival rate and prevent stroke and CHF (120).
- β-blockers with intrinsic sympathomimetic activity may not decrease heart rate and blood pressure at rest (89).
- β-blockers and calcium-channel antagonists have been reported to be equally effective in controlling stable angina (121; 122; 123; 124). The combination of β-blockers and nitrates appears to be more effective than either alone (89; 125).
- β-blockers are not effective in the treatment of (and may even induce) vasospastic angina and therefore should not be used for this purpose (89). β-blockers may be combined with slow-release dihydropyridines or new-generation, long-acting, dihydropyridine calcium-channel antagonists (123; 126; 127; 128; 129; 130). Bradycardia or atrioventricular block may occur with β-blockers and verapamil or diltiazem.

Rationale
- β-blockers decrease ischemic symptoms (both at rest and with exertion) and have been associated with mortality reduction.

Comments
- β-blockers are effective in decreasing the composite outcomes of MIs, death, angina, and ventricular arrhythmia in patients with angina.

6.3 Use statins in women with CAD and hypercholesterolemia and target a goal LDL <100 mg/dL.

Recommendations
- Use statins in women with CAD and hypercholesterolemia to decrease nonfatal MI and reduce mortality from CAD, with a goal LDL level <100 mg/dL.
- See the Drug Therapy section of the module Lipid Disorders (Dyslipidemia).

Evidence
- A meta-analysis in 2004 of eight lipid-lowering trials of women with cardiovascular disease found no benefit of statin treatment on mortality (RR, 1.00). CAD mortality lowering just met significance (RR, 0.74 [CI, 0.55 to 1.00]), and nonfatal MI was lowered (RR, 0.71 [CI, 0.58 to 0.87]) (30).
- Treatment of hyperlipidemia with a statin drug in patients with CAD was found to decrease mortality and major coronary events by 30% to 35% in the Scandinavian Simvastatin Survival Study (131).
- Treatment of mild-to-moderate hyperlipidemia in men and women with CAD was associated with a 24% reduction in the risk for fatal and nonfatal MI in the Cholesterol and Recurrent Events Trial (CARE) (132).
- Total and cardiovascular mortality were reduced in men and women with CAD who were randomly assigned to simvastatin, 40 mg/d, compared with placebo in the Medical Research Council Heart Protection study (32). Risk was reduced by approximately 25%, regardless of initial LDL cholesterol or total cholesterol levels.

Rationale
Treatment with statins has been shown to reduce CAD events, CAD mortality, and nonfatal MI but not total mortality.

6.4 **Employ aggressive risk-factor modification in the treatment regimen.**

**Recommendations**

- Advise smoking cessation and reinforce continued abstinence in those who have previously quit.
- Advise patients to attain an ideal weight and exercise on a regular basis.
- Treat hypertension with lifestyle changes and medication, if needed.
- Treat diabetes mellitus with lifestyle changes and medication, if needed.
- Treat hyperlipidemia with lifestyle changes and medication, if needed.
- In patients with normal cholesterol levels except for an HDL <35 mg/dL, begin nonpharmacologic therapy to increase HDL (such as exercise); consider medication to raise HDL if there is not an adequate response.
- Recommend stress management.
- Caution patients about activities that may exacerbate angina or cause ischemic symptoms (such as exercising in the cold).
- Refer women with a previous MI to attend a cardiac rehabilitation program.

**Evidence**

- Antianginal agents may be less efficacious in patients who smoke cigarettes (6; 7).
- Smoking is a strong risk factor for CAD in women, and smoking cessation decreases the risk for the development of CAD (1; 2).
- Improvement in exercise tolerance, cardiac symptoms, blood lipid levels and psychological wellbeing occurs in patients attending cardiac rehabilitation (133).
- All women with MI require lipid management for secondary prevention and should begin AHA Step II diet; if LDL lipid remains >125 mg/dL despite dietary therapy, drug therapy should be started with the goal LDL level of <100 mg/dL. Statin therapy should be strongly considered in these patients (134).
- In the Hypertension and Detection Follow-up Program, which consisted of 10,000 patients (46% women), all races of women who were treated in the stepped-care regimen had lower stroke rates at 5 years; treated black women had fewer other cardiovascular events, but the benefit of treatment for white women was less clear (20; 21). When a further analysis was done 3.3 years after the end of the original study, all women had a reduction in all causes of mortality (22).
- The above recommendations are reflected in the latest update of the ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction (98) as well as the ACC/AHA Guideline Update for the Management of Patients with Chronic Stable Angina (89).

**Rationale**

- Coronary events, mortality, as well as delay and even regression of atherosclerotic lesion may occur with risk-factor modification.
- Improvement in exercise tolerance, cardiac symptoms, blood lipid levels, and psychological wellbeing occurs in patients attending cardiac rehabilitation.
- Conditions that increase myocardial oxygen demands may increase ischemia.
- Programs addressing risk-factor modification provide additional opportunity for success in lifestyle changes.
Comments

- Mortality appears reduced among patients who attend cardiac rehabilitation, although this benefit has not yet been fully proven. Women who do not participate in cardiac rehabilitation tend to have less risk-factor modification.
- Fewer women, especially elderly, are referred to cardiac rehabilitation than men (133; 135).
- Some women with identified CAD without MI may benefit from cardiac rehabilitation programs as well (133; 136).

6.5 Consider revascularization procedures for women who are appropriate candidates.

Recommendations

- Obtain cardiac catheterization in women who may benefit from revascularization procedures.
  - Women with unstable angina, significant angina interfering with lifestyle despite maximal medical therapy, and those with high-risk findings on noninvasive testing should undergo coronary catheterization
- Consider coronary artery bypass surgery in patients with:
  - Significant left-main coronary artery stenosis
  - Three-vessel disease and abnormal left ventricular dysfunction
  - Two-vessel disease, including an >75% stenosis in the proximal left anterior descending artery
- Consider PTCA in patients with single- or two-vessel disease who are still symptomatic on optimal medical therapy.
  - The decision to proceed to specific revascularization procedures should carefully consider clinical factors

Evidence

- Patients undergoing coronary artery bypass surgery who have left-main coronary artery stenosis, three-vessel disease, and abnormal left ventricular dysfunction, and those with two-vessel disease including an >75% stenosis in the proximal left anterior descending artery have lowered mortality over medical therapy alone (137; 138; 139; 140; 141).
- Studies in male and elderly patients with single- or two-vessel disease have shown that patients undergoing angioplasty have less angina, better exercise tolerance, and a higher quality-of-life score than those treated with medical therapy; however, CABG rates were higher, and rates of MI and mortality were not affected (142; 143; 144).
- A meta-analysis of six trials of PTCA vs. medical therapy found that PTCA may lead to a greater reduction in angina in patients with CAD than medical treatment, but at the cost of more CABG. Trials have not included enough patients for informative estimates of the effect of angioplasty on MI, death, or subsequent revascularization, although trends so far do not favor angioplasty (145).
- A randomized trial of exercise training vs. percutaneous coronary intervention in male patients with stable CAD found that, compared with percutaneous coronary intervention, a 12-month program of regular physical exercise resulted in superior event-free survival and exercise capacity at lower costs, notably owing to reduced rehospitalizations and repeat revascularizations (146).
- Women who undergo CABG have more cardiac risk factors than men and are also more likely to experience more complications (death, heart failure, bleeding, infarction) (147; 148; 149).
- Women are three times more likely than men to have morbidity and mortality with PTCA. This statistic may in part be explained by the fact that women who undergo PTCA are older and have more cardiac risk factors than men. The success of PTCA is similar for late outcome in men and women, but women are more likely to have increased early mortality and complications than men (147; 150; 151; 152; 153; 154).
Women have higher early mortality in studies of elective and primary percutaneous coronary intervention, as well as higher rates of vascular complications, compared to men. Late outcomes for percutaneous coronary intervention are similar (154).

A randomized trial found that medical therapy is equally effective as percutaneous coronary intervention in the treatment of chronic stable angina (155).

**Rationale**

- Revascularization procedures improve the outcome in selected women.

**Comments**

- These recommendations are reflected in the [guidelines](https://www.ahajournals.org/doi/full/10.1161/01.AHA.0000836770.70480.61) for PTCA from the AHA/ACC Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (156).

- Most trials of revascularization are not detailed enough to evaluate results specifically in women.

- Techniques are continually being improved, such as with the development of stents and glycoprotein IIb/IIIa agents.

### 6.6 Use nitrates to control anginal symptoms.

**Recommendations**

- Instruct patients to use short-acting sublingual nitrates as needed for ischemic symptoms or prophylactically in circumstances known to cause angina.

- Consider the use of long-acting nitrates as an alternative first-line agent to β-blockers in women who have contraindications or unacceptable side effects with β-blocker use.

- Consider long-acting nitrates in addition to β-blockers when a β-blocker alone is insufficient.

- Understand that a nitrate-free period of 8 to 12 hours each day is required to prevent nitrate tolerance; for this reason, many clinicians prefer calcium-channel antagonists to nitrates for maintenance treatment of CAD.

- See table [Drug Treatment for Coronary Artery Disease in Women](https://www.ahajournals.org/doi/full/10.1161/01.HT.0000836770.70480.61).

**Evidence**

- Nitrates improve exercise tolerance and time to onset of angina in stable exertional angina. Nitrates provide a greater antianginal effect when combined with β-blockers or calcium-channel antagonists (89; 157; 158; 159; 160; 161).

- Nitrates have not been shown to reduce mortality in patients with CAD or acute MI (89).

- All long-acting nitrates appear to be equally effective if a nitrate-free period is used (162; 163).

**Rationale**

- Nitrates decrease myocardial oxygen consumption and improve myocardial perfusion.

- Nitrate tolerance develops to the antianginal, antiplatelet, and hemodynamic effects of the drug.

- Both the dihydropyridines and nitrates are vasodilators and may not be optimal treatment when combined because of hypotension.

**Comments**

- Another benefit of nitrates is their relatively low cost.

- Women who use sildenafil or similar phosphodiesterase inhibitors should not use nitrates because of a risk for life-threatening hypotension.

### 6.7 Use ACE inhibitors in women with CAD.

**Recommendations**
- Treat women with MI with ACE inhibitors.
- Treat women with CAD and reduced left ventricular function with an ACE inhibitor.
- Start ACE inhibitor therapy early in selected patients following acute MI.
- See table Drug Treatment for Coronary Artery Disease in Women.
- See module Heart Failure.
- See module Acute Coronary Syndromes.

**Evidence**

- In the HOPE trial, subjects with vascular disease or diabetes and at least one additional cardiovascular risk factor who were treated with ramipril, 10 mg/d, for an average of 4.5 years had a significantly reduced risk for major cardiovascular events (the primary outcome), total mortality, cardiovascular mortality, MI, stroke, heart failure, diabetic complications, revascularization procedures, and cardiac arrest (164). The relative risks for each of these outcomes were consistently in the range of 0.63 to 0.84 and consistent across a range of predefined subgroups, suggesting a robust outcome. The absolute risk reduction of the composite outcome (MI, stroke, or cardiovascular death) was 3.8%, corresponding to an NNT of 26 patients treated for 4.5 years. The absolute risk reduction in total mortality was 2.8%, corresponding to an NNT of 36 patients treated for 4.5 years. The absolute benefit in the subgroup of patients with diabetes was higher than the overall reported benefit (165).

- The EUROPA trial confirmed the results of the HOPE trial. In this randomized, controlled trial, 13,655 patients with stable CAD were randomly assigned to perindopril, 8 mg/d, vs. placebo. Patients treated with perindopril had a 20% relative reduction in the risk for major cardiovascular events (cardiovascular death, MI, or cardiac arrest) over 4.2 years of follow-up (166). The absolute risk reduction of the composite outcome was 2%, corresponding to an NNT of 50 patients treated for 4 years to prevent one major cardiovascular event.

- Several large randomized, controlled trials show that ACE inhibitors confer a significant mortality benefit in patients with reduced left ventricular function (167; 168; 169).

- A systematic review of four trials comprising more than 100,000 patients in the peri-MI period suggests a 7% relative reduction on 30-day mortality if an ACE inhibitor is started within 36 hours of the onset of chest pain (170). The absolute risk reduction in 30-day mortality corresponded to an avoidance of 4.8 deaths per 1000 patients treated (NNT = 208), and 80% of this benefit accrued during the first week after MI (reduced 7-day mortality). The absolute benefit is greatest in persons at highest risk for short-term mortality, e.g., persons with anterior Q-wave MI or clinically evident CHF.

**Rationale**

- The use of ACE inhibitors in patients with CAD reduces major cardiovascular ventricular function.
- The use of ACE inhibitors reduces mortality in patients with reduced left ventricular function.

**Comments**

- Major side effects include hypotension (particularly in the setting of hypovolemia, diuretic use, or acute MI), hyperkalemia (particularly in patients with renal insufficiency and those taking potassium-sparing diuretics or potassium supplementation), and renal insufficiency (particularly in patients with renal artery stenosis, severe CHF, or volume depletion).
- Only 15% of subjects in the EUROPA trial were women, and subgroup analysis showed only a nonsignificant reduction in major cardiovascular events for women. Nonetheless, the magnitude of estimated benefit was similar in women compared with men in the EUROPA trial. Furthermore, the concordance of outcomes between the HOPE and EUROPA trials suggests a benefit independent of gender.
6.8 **Use ACE inhibitors for treatment of hypertension in patients at high risk for CAD.**

**Recommendations**
- Use ACE inhibitors for hypertension in patients at high risk for CAD, including:
  - Patients with diabetic nephropathy
  - Patients with established MI and left ventricular dysfunction
- See Therapy section of the module [Essential Hypertension](#).

**Evidence**
- A case-control study showed decreased cardiovascular mortality in high-risk patients without MI but did not consider women patients separately (98).
- The group in which ACE inhibitors have been shown to have the greatest decrease in mortality is in patients with MI and LV dysfunction (168).

**Rationale**
- The use of ACE inhibitors in high-risk groups without MI may improve overall mortality.
- The use of ACE inhibitors with established MI improves outcome, especially in the presence of left ventricular dysfunction.

**Comments**
- ACE inhibitors are beneficial in patients with diabetic retinopathy or heart failure even in the absence of hypertension.
- ACE inhibitors are contraindicated in pregnancy and thus should be used with caution in women of childbearing age.

6.9 **Consider the addition of slow-release or long-acting calcium-channel antagonists to β-blockers if needed for relief of angina.**

**Recommendations**
- Consider the addition of slow-release or long-acting calcium-channel antagonists to β-blockers when the response to β-blockers is suboptimal.
- Consider the use of slow-release or long-acting calcium-channel antagonists in patients who are unable to take β-blockers.
- Use calcium-channel antagonists in the treatment of women with vasospastic (Prinzmetal's) angina.
- Note that the use of dihydropyridines alone may worsen angina.
- Note that both dihydropyridines and nitrates are vasodilators and may not be optimal treatment when combined; these vasodilators have the same mechanism of action and their combination may result in hypotension.
- Do not use short-acting calcium-channel antagonists.
- See table [Drug Treatment for Coronary Artery Disease in Women](#).

**Evidence**
- Slow-release or long-acting calcium-channel blockers are useful in the treatment of CAD in women (171; 172; 173; 174; 175).
- Slow-release or long-acting calcium-channel antagonists are generally as effective as β-blockers in decreasing angina (89; 169; 176; 177; 178; 179; 180; 181; 182; 183).
Coronary Artery Disease in Women

- Calcium-channel agonists may be useful in the treatment of vasospastic (Printzmetal's) angina based on small studies (184; 185).

- Both dihydropyridine and nondihydropyridine agents are clinically effective in the treatment of CAD. Slow-release or long-acting calcium-channel antagonists should be used over immediate-release or short-acting agents. In retrospective case-control studies, an increased risk for MI of 31%, 63%, and 61% was found in patients with hypertension treated with immediate-acting nifedipine, diltiazem, and verapamil, respectively (186).

- A dose-related increase in mortality associated with immediate-release and short-acting nifedipine was found in a meta-analysis of patients with MI and unstable angina (187).

- The combination of β-blockers and calcium-channel antagonists decreases rest and exertional angina to a greater degree than either alone (126; 127; 128; 129; 130; 188; 189; 190; 191).

Rationale
- Slow-release or long-acting calcium-channel blockers are as effective as β-blockers in reducing angina; short-acting or immediate-release agents may increase post-MI mortality.

6.10 Do not treat women with CAD with hormone therapy.

Recommendations
- Do not treat women with CAD with hormone therapy for the purpose of cardiovascular risk reduction.

- See Therapy section of the module Menopause and Hormone Therapy.

Evidence
- In the Heart and Estrogen/progestin Replacement Study (HERS), postmenopausal women aged under 80 years with established CAD were randomly assigned to hormone therapy vs. placebo (192). After 4 years of follow-up, there was no difference in nonfatal MI or coronary death between women treated with hormone therapy and those who received placebo.

- There was an increase in thromboembolic events during the first year of hormone therapy (192).


Rationale
- Despite observational therapy to the contrary, randomized, controlled trials show that hormone therapy does not protect against cardiovascular events in women with established CAD.
7. Patient Counseling

**Inform women about cardiac risk factors, risk-factor modification, and the signs, symptoms, and management of CAD.**

7.1 Inform women about their personal risk for CAD.

**Recommendations**
- Inform patients that the leading cause of death in women is CAD.
- Discuss cardiac risk factors and the benefits of their modification with patients.

**Evidence**
- Control of modifiable cardiac risk factors with aggressive counseling and treatment will decrease the likelihood of developing CAD (15; 16; 193).
- See sections on Screening and Prevention.

**Rationale**
- Informed women are able to take steps to lower their risk for CAD.

**Comments**
- Many women are under the mistaken impression that their greatest risk is from breast cancer and that CAD is not a woman's disease.

7.2 Instruct women to recognize and respond to the signs and symptoms of CAD.

**Recommendations**
- Instruct patients of the signs and symptoms of CAD.
- Instruct patients to seek medical attention or to call 911 immediately in response to symptoms of ischemia.

**Evidence**
- Women with chest pain may be treated differently than their male counterparts (18). In one study, women presenting symptoms to physicians in a businesslike manner were more likely to be studied than women who presented the same symptoms in a more emotional manner (88).

**Rationale**
- Informed women recognize the presentation of CAD more quickly and will be less likely to attribute their symptoms to nonischemic causes.

**Comments**
- A physician may be influenced by a woman's own perception of the cause of her symptoms.

7.3 Advise patients about their recommended treatment plan.

**Recommendations**
- Explain the goals of treatment, including prognosis.
- Explain the mechanism of action of prescribed medications in an easily understood manner.
- Discuss the risks and benefits of medication with patients and alert them to side effects requiring them to contact a physician.
- Explain any specific instructions about how to administer medication.
• Clarify when routine follow-up should occur and what signs and symptoms should prompt earlier follow-up.
• Reinforce the importance of risk-factor modification.
• Provide educational materials to women about causes and treatment of CAD.

Evidence
• Consensus.

Rationale
• A patient who understands the treatment plan and the use of her medications is more likely to be compliant and benefit from her treatment.

7.4 Advise patients regarding activities that are safe to perform.

Recommendations
• Advise patients about activities, including leisure and vacation planning, that can be performed safely and those that should be avoided.
• Modify activities that consistently reproduce angina.
• Urge patients to avoid excessive fatigue and exhaustion.

Evidence
• Consensus.

Rationale
• Women with cardiac disease should not participate in activities that may induce a cardiac event; however, the woman with CAD should remain as active as is reasonable, because participating in physical activity not only improves the cardiac risk profile, but also improves the perception of wellbeing and quality of life.
8. Follow-up

Plan follow-up in patients to monitor symptoms, adjust treatment, and monitor risk-factor modifications.\[\text{EC}\]

8.1 Assess patients for signs and symptoms suggesting disease progression every 3 to 6 months.\[\text{EC}\]

**Recommendations**

- Ask whether the patient has developed new or worsening chest discomfort, dyspnea, or other anginal equivalent that may require an adjustment to the treatment regimen or possibly further investigation, such as cardiac catheterization.
- Ask how often the patient is using sublingual nitroglycerin and determine whether this frequency is an increase over previous use.
- Examine the patient for findings suggesting advancing atherosclerosis (e.g., newly decreased pulses) or for developing complications, such as heart failure.
- Individualize frequency of follow-up for women with CAD, although a visit every 3 to 6 months is reasonable.

**Evidence**

- Consensus.

**Rationale**

- Women with progressive CAD may benefit from adjustments in treatment regimen.

8.2 Assess adequacy of cardiac risk-factor modification and the development of new risk factors at each visit.\[\text{BC}\]

**Recommendations**

- Assess smoking status on each visit and treat appropriately.
- Assess physical activity and advise regular exercise.
- Measure blood pressure on every visit and treat appropriately.
- Weigh the patient on each visit and treat appropriately.
- Ensure that the patient is up to date on screening for diabetes mellitus, and that those already diagnosed with diabetes are receiving adequate treatment.
- Ensure that the patient is up to date on screening for hyperlipidemia, and that those already diagnosed with hyperlipidemia are receiving adequate treatment. Check lipid levels annually in patients with known CAD and hyperlipidemia.
- Individualize frequency of follow-up for women with CAD.

**Evidence**

- Prevention trials and consensus recommendations (15; 16; 193). See also sections on Prevention and Therapy.

**Rationale**

- Control of modifiable cardiac risk factors with aggressive counseling and treatment will decrease the likelihood of developing CAD.
8.3 Obtain an ECG and stress test in women with known CAD who experience changes in their anginal symptoms.

**Recommendations**
- Obtain an ECG when medication affecting cardiac conduction is begun or changed.
- Obtain an ECG when there is a change in anginal pattern or there is concern about a dysrhythmia.
- Obtain stress testing in patients with new or worsening symptoms.
- Consider periodic stress testing in high-risk patients for risk stratification.
- See module [Coronary Heart Disease](https://www.pier.org).

**Evidence**
- In the absence of clinical change, there is no evidence that routine, periodic ECGs are useful (89).
- Stress testing risk stratifies patients with known or suspected CAD into low-, intermediate-, and high-risk groups (72; 95; 194; 195; 196).

**Rationale**
- ECGs may identify new ischemic changes or MI.
- Stress testing allows risk stratification of patients with CAD.

8.4 Evaluate the medication regimen of patients with CAD at each visit.

**Recommendations**
- Review the patient's medication regimen at each visit:
  - Is the patient taking an aspirin each day?
  - Is or should the patient be on a β-blocker?
  - Is or should the patient be on an ACE inhibitor?
  - Determine whether the patient is taking the prescribed medication in the prescribed dose and manner on each visit.
  - Determine whether the patient is experiencing side effects from her medication on each visit.

**Evidence**
- Consensus.

**Rationale**
- Administration of the appropriate medication for CAD as directed is important; medication errors are common.
References


Coronary Artery Disease in Women


new


Coronary Artery Disease in Women


Coronary Artery Disease in Women


162. Abrams J. Glyceryl trinitrate (nitroglycerin) and the organic nitrates. Choosing the method of administration. Drugs. 1987;34:391-403. (PMID: 3119208)


Coronary Artery Disease in Women

Glossary

ACC
American College of Cardiology

ACCF
American College of Cardiology Foundation

ACE
angiotensin-converting enzyme

ACP
American College of Physicians

AHA
American Heart Association

AV
atrioventricular

bid
twice daily

BMI
body mass index

CABG
coronary artery bypass graft(ing)

CAC
coronary artery calcium

CAD
coronary artery disease

CHD
coronary heart disease

CHF
congestive heart failure

CI
confidence interval

COPD
chronic obstructive pulmonary disease

CT
computed tomography

ECG
Electrocardiography

EUROPA
European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease

GERD
gastroesophageal reflux disease

GI
gastrointestinal

HDL
high-density lipoprotein

HOPE
Heart Outcomes Prevention Evaluation (trial)
Coronary Artery Disease in Women

**HRT**
hormone replacement therapy

**INR**
international normalized ratio

**IU**
international units

**LDL**
low-density lipoprotein

**LV**
left ventricle

**MI**
myocardial infarction

**NNT**
two needed to treat

**OR**
odds ratio

**PTCA**
percutaneous transluminal coronary angiography

**qd**
once daily

**RR**
relative risk

**SPECT**
single-photon emission computed tomography

**tid**
three times daily
# Tables

## Laboratory and Other Studies for Coronary Artery Disease in Women

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Likelihood Ratio Positive</th>
<th>Likelihood Ratio Negative</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting ECG</td>
<td>71%</td>
<td></td>
<td></td>
<td></td>
<td>Often normal in patients with disease, but can show underlying abnormalities and can be helpful during symptoms (63)</td>
</tr>
<tr>
<td>Exercise ECG stress test</td>
<td>61-69</td>
<td>52-70</td>
<td>2.25</td>
<td>0.55</td>
<td>Values derived from (73; 197). Note Q waves, ST and T wave changes, rhythm abnormalities, and chamber enlargement (90)</td>
</tr>
<tr>
<td>Radionuclide myocardial perfusion imaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Exercise ECG is best in patients without baseline ECG abnormalities who can exercise to 85% of maximal predicted heart rate. Patients with high-risk findings include inability to complete stage 2 Bruce protocol, ≥1 mm horizontal or down-sloping depression during stage I of exercise, and failure to increase blood pressure with exercise. ECG stress testing may be done safely in pregnancy.</td>
</tr>
<tr>
<td>Exercise thallium (planar and tomographic)</td>
<td>78</td>
<td>64</td>
<td>2.87</td>
<td>0.36</td>
<td>Values derived from (73)</td>
</tr>
<tr>
<td>Thallium-201 (in women who either underwent treadmill testing or received dipyridamole)</td>
<td>75</td>
<td>62</td>
<td></td>
<td></td>
<td>Values derived from (198)</td>
</tr>
<tr>
<td>Technetium-99m sestamibi perfusion (in women undergoing exercise treadmill or)</td>
<td>72</td>
<td>86</td>
<td></td>
<td></td>
<td>Values derived from (198)</td>
</tr>
</tbody>
</table>
## Coronary Artery Disease in Women

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacologic stress thallium SPECT (dipyridamole or dobutamine)</td>
<td>79</td>
<td>75</td>
<td>Values derived from (199). 99mTc-sestamibi SPECT, especially with gated ECG, has higher specificity than TI-201 SPECT imaging, with similar sensitivities.</td>
</tr>
<tr>
<td>Dobutamine technetium-99m sestamibi SPECT imaging (200)</td>
<td>64</td>
<td>72</td>
<td>High-risk findings include the inability to complete stage 2 Bruce protocol, &gt;1 mm horizontal or down-sloping depression during stage I of exercise, failure to increase blood pressure with exercise, large or multiple reversible lung uptake or LV dilatation on perfusion imaging (200).</td>
</tr>
<tr>
<td>Stress echocardiography</td>
<td>32</td>
<td>86</td>
<td>2.3</td>
</tr>
<tr>
<td>Exercise echocardiography</td>
<td>81</td>
<td>86</td>
<td>Values derived from (91).</td>
</tr>
<tr>
<td>Dobutamine stress echocardiography</td>
<td>50-93</td>
<td>79-92</td>
<td>4.29</td>
</tr>
<tr>
<td>Coronary artery catheterization</td>
<td></td>
<td></td>
<td>The ‘gold standard’ for diagnosis of CAD. May not show abnormalities in women with chest pain caused by vasospasm. Cardiac catheterization is best reserved for patients who may benefit from revascularization procedures.</td>
</tr>
<tr>
<td>Fast CT</td>
<td>For any CAD: 100%; per segment 82%</td>
<td>75</td>
<td>Values derived from (205). There is limited data on accuracy in women and little consensus on the role of CT in the evaluation of CAD in women.</td>
</tr>
</tbody>
</table>

**Notes:**
- CAD = coronary artery disease; CT = computed tomography; ECG = electrocardiography; LV = left ventricle; SPECT = single-photon emission computed tomography.
### Differential Diagnosis of Coronary Artery Disease in Women

<table>
<thead>
<tr>
<th>Disease</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac causes</strong>&lt;br&gt;CAD&lt;br&gt;Syndrome X&lt;br&gt;Aortic dissection&lt;br&gt;Valvular heart disease&lt;br&gt;Hypertrophic cardiomyopathy&lt;br&gt;Pericarditis&lt;br&gt;Myocarditis&lt;br&gt;CHF</td>
<td>Sudden-onset ‘tearing’ or ‘ripping’ pain, especially if in association with hypertension and an aortic murmur, suggests an aortic dissection&lt;br&gt;CellTxtL::Sharp sudden-onset chest pain that improves with sitting forward suggests pericarditis&lt;br&gt;CellTxtL::Women with syndrome X have ischemic chest pain without significant CAD&lt;br&gt;CellTxtL::Hypertension is an important risk factor for aortic dissection. Other risk factors include pregnancy, Marfan’s syndrome, aortic coarctation, congenital bicuspid, or unicommissural aortic valves.</td>
</tr>
<tr>
<td><strong>Vascular causes</strong>&lt;br&gt;Aortic dissection&lt;br&gt;Pulmonary embolism&lt;br&gt;Pulmonary infarction&lt;br&gt;Pulmonary hypertension&lt;br&gt;Right ventricular strain</td>
<td>Sudden-onset pleuritic chest pain associated with shortness of breath suggests pulmonary embolism (or possibly pneumothorax)</td>
</tr>
<tr>
<td><strong>Pulmonary causes</strong>&lt;br&gt;Pleuritis&lt;br&gt;Pneumonia/bronchitis&lt;br&gt;Pneumothorax&lt;br&gt;Pleural effusion&lt;br&gt;Tumor&lt;br&gt;Mediastinitis&lt;br&gt;Mediastinal emphysema&lt;br&gt;Pulmonary hypertension&lt;br&gt;Sarcoidosis</td>
<td>Fever and sputum production suggest pneumonia&lt;br&gt;CellTxtL::Sudden onset pleuritic chest pain and dyspnea suggest pulmonary embolism or spontaneous pneumothorax&lt;br&gt;CellTxtL::Patients with pleuritic chest pain associated with pleural effusion generally have associated pleuritis</td>
</tr>
<tr>
<td><strong>Gastrointestinal causes</strong>&lt;br&gt;Esophageal reflux&lt;br&gt;Esophageal spasm&lt;br&gt;Mallory-Weiss tear&lt;br&gt;Pepitic ulcer disease&lt;br&gt;Biliary disease&lt;br&gt;Pancreatitis&lt;br&gt;Colonic distention</td>
<td>Dyspepsia, regurgitation, and/or acid taste suggests GERD, but CAD should be ruled out definitively before making the diagnosis of GERD&lt;br&gt;CellTxtL::Pain after vomiting suggests esophageal rupture&lt;br&gt;CellTxtL::The response of pain to antacids should not be used to rule out ischemic chest pain&lt;br&gt;CellTxtL::Esophageal pain is easily confused with myocardial ischemia as both organs share similar innervation&lt;br&gt;CellTxtL::Esophageal spasm may improve with treatment with nitroglycerin</td>
</tr>
<tr>
<td><strong>Musculoskeletal causes</strong>&lt;br&gt;Cervical disk disease&lt;br&gt;Arthritis of the shoulders or spine&lt;br&gt;Costochondritis&lt;br&gt;Bursitis&lt;br&gt;Tumors involving chest wall</td>
<td>A history of a strenuous activity involving the arms or upper trunk followed by reproducible pain with arm movement or turning is suggestive of a musculoskeletal source of pain&lt;br&gt;CellTxtL::Tenderness of the upper costal cartilages at the costosternal or costochondral junctions suggests costochondritis&lt;br&gt;CellTxtL::Musculoskeletal chest pain may be more common among women than men&lt;br&gt;CellTxtL::Rheumatic diseases that may be associated with musculoskeletal causes of chest pain include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and fibromyalgia</td>
</tr>
<tr>
<td>Sensory nerves and skin</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td><strong>Psychiatric disorders</strong></td>
<td>Panic disorder</td>
</tr>
<tr>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Hypochondriasis</td>
<td></td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; CHF = congestive heart failure; GERD = gastroesophageal reflux disease.
## Drug Treatment for Coronary Artery Disease in Women

<table>
<thead>
<tr>
<th>Drug or Drug Class</th>
<th>Dosing</th>
<th>Side Effects</th>
<th>Precautions</th>
<th>Clinical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Initial dose of at least 160 mg, then 75-325 mg qd</td>
<td>GI side effects, hypersensitivity reactions, bleeding</td>
<td>Avoid with severe hepatic disease or severe CKD. Caution with: asthma, GI disease</td>
<td>Decrease risk for MI and sudden death</td>
</tr>
<tr>
<td>β-blockers</td>
<td></td>
<td>Bradycardia, hypotension, AV block, bronchospasm (partially if nonselective), CNS side effects, diarrhea, nausea</td>
<td>Caution with: CKD, HF, depression, hyperthyroidism, elderly</td>
<td>Mortality reduction, decreased angina</td>
</tr>
<tr>
<td>Atenolol (Tenormin)</td>
<td>25-100 mg qd</td>
<td></td>
<td>Abrupt withdrawal not advised. Avoid with: pregnancy, breast-feeding. If CrCl&lt;35, decrease dose</td>
<td>β, selective</td>
</tr>
<tr>
<td>Carvedilol (Coreg, Coreg CR)</td>
<td>Regular-release: 6.25 mg bid with food, gradually up to 25 mg bid. Extended-release: 20 mg qd in the AM with food, gradually up to 80 mg qd</td>
<td>Hyperglycemia, weight increase</td>
<td>Avoid abrupt withdrawal. Avoid with hepatic disease. Consider reduced dose in elderly. Substrate of CYP2D6</td>
<td>Nonselective</td>
</tr>
<tr>
<td>Metoprolol (Lopressor)</td>
<td>25-50 mg q6hr for 48 hr, then 50-100 mg bid</td>
<td></td>
<td>Abrupt withdrawal not advised. Consider reduced dose with hepatic disease. Substrate of CYP2D6</td>
<td>β, selective</td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors (Statins)</td>
<td>Generally more effective if given at bedtime</td>
<td>Rhabdomyolysis, myalgia, myopathy, hepatotoxicity, diabetes, rare: hypersensitivity reactions, neuropathy</td>
<td>Avoid with: hepatic disease, pregnancy, cyclosporine, gemfibrozil. Caution with: fenofibrate, niacin. Most have additional CYP450 interactions. Avoid &gt;1 quart daily of grapefruit juice. Elderly may have an increased response</td>
<td>Hyperlipidemia, reduction in cardiac events</td>
</tr>
<tr>
<td>Atorvastatin (Lipitor)</td>
<td>10-80 mg qd</td>
<td></td>
<td>If taking a CYP3A4 inhibitor concomitantly, don't exceed 20 mg qd</td>
<td></td>
</tr>
<tr>
<td>Lovastatin (Mevacor, Altoprev)</td>
<td>Regular-release: 10-80 mg qd with PM meal. Extended-release (Altoprev): 10-60 mg qhs</td>
<td></td>
<td>If CrCl&lt;30, maximum dose 20 mg qd. Avoid CYP3A4 inhibitors</td>
<td></td>
</tr>
<tr>
<td>Simvastatin (Zocor)</td>
<td>40 mg qhs</td>
<td></td>
<td>If CrCl&lt;20, start with 5 mg qhs. Avoid CYP3A4 inhibitors. Caution with &gt;20 mg in Chinese</td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>To avoid tolerance, a 10-12 hr nitrate-free period is required</td>
<td>Headache, flushing, hypotension, bradycardia, tachycardia, tolerance</td>
<td>Avoid with: severe anemia, increased intracranial pressure, closed-angle glaucoma. Caution with hepatic disease. Start low dose in elderly.</td>
<td>Angina</td>
</tr>
<tr>
<td>Nitroglycerin (Nitrostat, NitroMist, Nitrolingual Pumpspray, Minitrans, Nitro-Dur)</td>
<td>Sublingual: 1 tablet (0.3 mg, 0.4 mg, or 0.6 mg) SL. May repeat q5min prn, up to 3 doses. Lingual spray or aerosol: 1-2 sprays (400-800 mcg) SL. May repeat q5min prn, up to 3 doses. Transdermal patch: 1 patch (0.1-0.8 mg/hr) q24hr. Remove patch for 10-12</td>
<td>Dermatologic adverse reactions, methemoglobinemia</td>
<td>Extreme caution with suspected right ventricular infarction. Caution with: constrictive pericarditis, restrictive cardiomyopathy, cardiac tamponade</td>
<td></td>
</tr>
</tbody>
</table>

© 2014 by the American College of Physicians. 190 N. Independence Mall West, Philadelphia, PA 19106, USA.
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Description</th>
<th>Initial Dose</th>
<th>Regimen</th>
<th>Side Effects</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isosorbide dinitrate (Isordil, Dilatrate-SR)</td>
<td>Immediate-release: 5-60 mg bid-tid. Sustained-release: 40-160 mg qd. SL: 2.5-5 mg prior to activity</td>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isosorbide mononitrate</td>
<td>Extended-release: 30-60 mg qd in the AM. May increase to 120 mg qd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiotensin- converting enzyme inhibitors</td>
<td>Hypotension, cough, hyperkalemia, angioedema, anaphylactoid reactions</td>
<td></td>
<td>Pregnancy. Avoid with: history of angioedema, renal artery stenosis</td>
<td>Women with MI or LVD. Also for HTN in women at high risk for CAD</td>
<td></td>
</tr>
<tr>
<td>Captopril (Capoten)</td>
<td>Initially 6.25-12.5 mg tid. Gradually up to 50 mg tid</td>
<td>Not affected by hepatic disease. Decrease dose if CrCl&lt;50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril (Vasotec)</td>
<td>Initially 2.5 mg bid. Gradually up to 20 mg bid</td>
<td>Requires hepatic activation. Decrease dose if CrCl&lt;30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisinopril (Prinivil, Zestril)</td>
<td>Initially 5-10 mg qd. Gradually up to 40 mg qd</td>
<td>Not affected by hepatic disease. Decrease dose if: elderly, CrCl&lt;30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramipril (Altace)</td>
<td>Initially 2.5 mg qd. Gradually up to 10 mg qd</td>
<td>Decrease dose if CrCl&lt;40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-dihydropyridine calcium-channel blockers</td>
<td>Use slow-release or long-acting formulations</td>
<td>Bradycardia, hypotension, AV block, edema, asystole, CNS side effects</td>
<td>Avoid with: WPW syndrome, advanced aortic stenosis. Caution with: HF, hepatic disease, reflex esophagitis. Start low in elderly</td>
<td>Women who cannot take β-blockers or have an inadequate response</td>
<td></td>
</tr>
<tr>
<td>Diltiazem (Cardizem CD, Dilacor XR)</td>
<td>Extended-release: 120-360 mg qd</td>
<td>GI side effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil (Calan SR, Covera-HS, Verelan)</td>
<td>Extended-release: 120 mg qd to 240 mg bid</td>
<td>Constipation, allergic-type reactions</td>
<td>Caution with: CKD, neuromuscular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydropyridine calcium-channel blockers</td>
<td>Use slow-release or long-acting formulations</td>
<td>Headache, edema</td>
<td>Caution with: severe bradycardia, HF, hepatic disease, reflex esophagitis, aortic stenosis</td>
<td>Women who cannot take β-blockers or have an inadequate response</td>
<td></td>
</tr>
<tr>
<td>Amlodipine (Norvasc)</td>
<td>2.5-10 mg qd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felodipine (Plendil)</td>
<td>2.5-10 mg qd</td>
<td>Reflex tachycardia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine (Adalat CC, Procardia XL)</td>
<td>30-120 mg qd</td>
<td>CNS side effects, GI side effects, rare allergic hepatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 = first-line agent; 2 = black box warning; AM = morning; AV = atrioventricular; bid = twice daily; CAD = coronary artery disease; CKD = chronic kidney disease; CNS = central nervous system; CrCl = creatinine clearance; CYP = cytochrome P450 isoenzyme; GI = gastrointestinal; HF = heart failure; HMG-CoA = hydroxymethylglutaryl-coenzyme A; HTN = hypertension; IM = intramuscular; IV = intravenous; LVD = left ventricular dysfunction; MI = myocardial infarction; PM = evening; PO = oral; prn = as needed; q12hr = every 12 hours; q4-6hr = every 4-6 hours; qd = once daily; qhs = every day at bedtime; tid = four times daily; SC = subcutaneous; SCR = serum creatinine; SL = sublingual; SLT = three times daily; WPW = Wolff-Parkinson-White.

PIER provides key prescribing information for practitioners but is not intended to be a source of comprehensive drug information.
## Likelihood of Coronary Artery Disease in Women after an Electrocardiogram Stress Test according to Depression of ST Segment, Age, and Symptoms

<table>
<thead>
<tr>
<th>ST Segment Depression (mm)</th>
<th>Age (y)</th>
<th>Asymptomatic Women</th>
<th>Nonanginal Chest Pain</th>
<th>Atypical Angina</th>
<th>Typical Angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30-39</td>
<td>10.5+9.9</td>
<td>23.9+19.5</td>
<td>63.1+24.5</td>
<td>93.1+6.3</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>28.3+20.8</td>
<td>52.9+25.8</td>
<td>85.7+12.7</td>
<td>98.0+2.1</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>56.3+24.9</td>
<td>78.1+17.3</td>
<td>94.9+4.9</td>
<td>99.3+0.7</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>76.0+18.4</td>
<td>89.9+9.2</td>
<td>97.9+2.1</td>
<td>99.7+0.3</td>
</tr>
<tr>
<td>2.0-2.5</td>
<td>30-39</td>
<td>3.2+2.4</td>
<td>8.2+5.9</td>
<td>32.7+16.7</td>
<td>79.4+12.6</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>10.1+6.5</td>
<td>24.2+13.5</td>
<td>63.0+17.1</td>
<td>93.2+4.7</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>26.8+13.8</td>
<td>50.4+17.7</td>
<td>84.2+9.4</td>
<td>97.7+1.6</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>47.3+17.3</td>
<td>71.7+14.2</td>
<td>93.0+4.5</td>
<td>99.1+0.6</td>
</tr>
<tr>
<td>1.5-2.0</td>
<td>30-39</td>
<td>1.2+1.0</td>
<td>3.3+2.5</td>
<td>15.5+10.1</td>
<td>59.3+18.9</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>4.1+2.8</td>
<td>10.8+7.2</td>
<td>39.1+17.7</td>
<td>83.8+10.2</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>12.2+7.6</td>
<td>27.8+14.4</td>
<td>66.8+15.9</td>
<td>94.2+3.9</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>25.4+13.4</td>
<td>48.9+17.8</td>
<td>83.3+9.8</td>
<td>97.6+1.7</td>
</tr>
<tr>
<td>1.0-1.5</td>
<td>30-39</td>
<td>0.6+0.2</td>
<td>1.7+0.7</td>
<td>8.5+2.8</td>
<td>42.4+9.4</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>2.1+0.5</td>
<td>5.8+1.7</td>
<td>24.5+5.6</td>
<td>72.3+6.2</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>6.5+1.3</td>
<td>16.3+3.1</td>
<td>50.4+5.4</td>
<td>89.1+2.2</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>14.7+2.3</td>
<td>32.6+4.6</td>
<td>71.6+3.9</td>
<td>95.3+0.9</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>30-39</td>
<td>0.3+0.1</td>
<td>0.7+0.4</td>
<td>3.9+1.6</td>
<td>24.2+8.4</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>0.9+0.3</td>
<td>2.6+1.0</td>
<td>12.3+4.3</td>
<td>53.0+10.0</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>2.9+0.9</td>
<td>7.8+2.4</td>
<td>30.5+7.1</td>
<td>77.9+5.3</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>6.9+2.0</td>
<td>17.3+4.7</td>
<td>52.2+7.9</td>
<td>89.8+2.9</td>
</tr>
<tr>
<td>0-0.5</td>
<td>30-39</td>
<td>0.1+0.0</td>
<td>0.2+0.1</td>
<td>1.0+0.4</td>
<td>7.4+2.9</td>
</tr>
<tr>
<td></td>
<td>40-49</td>
<td>0.2+0.1</td>
<td>0.7+0.2</td>
<td>3.4+1.2</td>
<td>22.0+6.2</td>
</tr>
<tr>
<td>Age Group</td>
<td>Heart Rate</td>
<td>Blood Pressure</td>
<td>HDL</td>
<td>LDL</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
<td>----------------</td>
<td>-----</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>0.8±0.2</td>
<td>2.1±0.6</td>
<td>9.9±2.5</td>
<td>46.9±7.2</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>1.8±0.6</td>
<td>5.0±1.3</td>
<td>21.4±4.5</td>
<td>68.8±5.9</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from (82; 83).
### Determining Probability of Coronary Artery Disease by Minor, Intermediate, and Major Determinants

<table>
<thead>
<tr>
<th>Likelihood of CAD</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;20%)</td>
<td>0 major and &lt;1 intermediate or &lt;2 minor determinants</td>
</tr>
<tr>
<td>Moderate (20%-80%)</td>
<td>1 major or multiple intermediate and minor determinants</td>
</tr>
<tr>
<td>High (&gt;80%)</td>
<td>&gt;2 major or 1 major plus &gt;1 intermediate and 1 minor determinants</td>
</tr>
</tbody>
</table>

**Major determinants:**
- Typical angina (substernal; characterized by burning, heavy or squeezing feeling; precipitated by exercise or emotion; promptly relieved by rest or nitroglycerin)
- Postmenopausal status without hormone replacement
- Diabetes mellitus
- Peripheral vascular disease

**Intermediate determinants:**
- Hypertension
- Smoking
- Lipoprotein abnormalities (especially low HDL)

**Minor determinants:**
- Age >65 years
- Obesity (especially central obesity)
- Sedentary lifestyle
- Family history of CAD
- Other risk factors for CAD (such as psychosocial or hemostatic)

CAD = coronary artery disease; HDL = high-density lipoprotein

Adapted from [18].
The Probability of Coronary Artery Disease in Women according to Age and Character of Symptoms

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>Age 30-39 (%)</th>
<th>Age 40-49 (%)</th>
<th>Age 50-59 (%)</th>
<th>Age 60-69 ColHdC::(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>0.3</td>
<td>1.0</td>
<td>3.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Nonanginal chest pain (1 of the 3 following features)</td>
<td>0.8</td>
<td>2.8</td>
<td>8.4</td>
<td>18.6</td>
</tr>
<tr>
<td>Atypical angina (2 of the 3 following features)</td>
<td>4.2</td>
<td>13.3</td>
<td>32.4</td>
<td>54.4</td>
</tr>
<tr>
<td>Typical angina (all 3 of the following features)</td>
<td>25.8</td>
<td>55.2</td>
<td>79.4</td>
<td>90.6</td>
</tr>
</tbody>
</table>

**Features distinguishing typical, atypical, and nonanginal chest pain:**

- Is the discomfort substernal?
- Is the discomfort precipitated by exertion?
- Is the discomfort relieved promptly by rest or by nitroglycerin?

Although there are no data for patients <30 y or >69 y, it is reasonable to assume that the prevalence of coronary artery disease increases with age.

Adapted from (82; 83)
## Probability of Coronary Artery Disease with a Negative Exercise Stress Test Result (Absence of ST Depression with Symptoms)

<table>
<thead>
<tr>
<th>Result</th>
<th>Pretest Clinical Probability Low Nonspecific Chest Pain (%)</th>
<th>Pretest Clinical Probability Intermediate ColHdC::Probable Angina (%)</th>
<th>Pretest Clinical Probability High ColHdC::Definite Angina ColHdC::(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative test result</td>
<td>1-3</td>
<td>7-20</td>
<td>31-57</td>
</tr>
</tbody>
</table>
# Probability of Coronary Artery Disease with a Positive Electrocardiogram Stress Test Result As Defined by Age, Symptoms, and ST Segment Depression

<table>
<thead>
<tr>
<th>Result</th>
<th>Pretest Clinical Probability Low Nonspecific Chest Pain (%)</th>
<th>Pretest Clinical Probability Intermediate Probable Angina (%)</th>
<th>Pretest Clinical Probability High ColHdC::Definite Angina (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive test result</td>
<td>13-21</td>
<td>50-66</td>
<td>85-91</td>
</tr>
</tbody>
</table>
Figures

Diagnostic Algorithm for Evaluating Chest Pain in Women Using Diamond Information

Adapted from 83.

Woman (age >30) with possible CAD

Does the patient have "typical" anginal chest pain?

Yes

Patient is at intermediate to high risk for CAD: see Diagnostic Algorithm for the Evaluation for Coronary Artery Disease in Women

No

Does the patient have "atypical" chest pain?

Yes

Is the patient age 30–59?

Yes

Patient has a very low risk of CAD (<5%)

No

Is the patient age >59?

Yes

Patient is at intermediate to high risk for CAD: see Diagnostic Algorithm for the Evaluation for Coronary Artery Disease in Women

No

Very low risk for CAD: Pretest likelihood of CAD <5%

Low risk for CAD: Pretest likelihood of CAD <10%

Intermediate risk for CAD: Pretest likelihood of CAD >10% and <10%

High risk for CAD: Pretest likelihood of CAD >10%

Does the patient have "nonanginal" chest pain?

Yes

Is the patient age 30–40?

Yes

Patient at very low risk for CAD (pretest likelihood is <5%)

No

Is the patient age 50–59?

Yes

Patient at low risk for CAD (pretest likelihood is 8.4%)

No

Is the patient age >60?

Yes

Patient is at intermediate to high risk for CAD: see Diagnostic Algorithm for Evaluation for Coronary Artery Disease in Women

No

Very low risk for CAD: Pretest likelihood of CAD <5%

Low risk for CAD: Pretest likelihood of CAD <10%

Intermediate risk for CAD: Pretest likelihood of CAD >10% and <10%

High risk for CAD: Pretest likelihood of CAD >10%
## Estimate of 10-Year Risk for Men and Women (Framingham Point Scores)

### Total Cholesterol

<table>
<thead>
<tr>
<th>Age</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>-9</td>
</tr>
<tr>
<td>35-54</td>
<td>-4</td>
</tr>
<tr>
<td>45-64</td>
<td>0</td>
</tr>
<tr>
<td>55-64</td>
<td>3</td>
</tr>
<tr>
<td>65-74</td>
<td>6</td>
</tr>
<tr>
<td>75-79</td>
<td>10</td>
</tr>
<tr>
<td>10-64</td>
<td>11</td>
</tr>
<tr>
<td>70-74</td>
<td>12</td>
</tr>
<tr>
<td>75-79</td>
<td>13</td>
</tr>
</tbody>
</table>

### HDL (mg/dL)

<table>
<thead>
<tr>
<th>HDL (mg/dL)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>1</td>
</tr>
<tr>
<td>50-59</td>
<td>2</td>
</tr>
<tr>
<td>60-69</td>
<td>3</td>
</tr>
<tr>
<td>70-79</td>
<td>4</td>
</tr>
</tbody>
</table>

### Systolic BP (mmHg)

<table>
<thead>
<tr>
<th>BP (mmHg)</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>0</td>
</tr>
<tr>
<td>120-129</td>
<td>1</td>
</tr>
<tr>
<td>130-139</td>
<td>2</td>
</tr>
<tr>
<td>140-159</td>
<td>3</td>
</tr>
<tr>
<td>≥160</td>
<td>4</td>
</tr>
</tbody>
</table>

### Smoking Status

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker</td>
<td>0</td>
</tr>
<tr>
<td>Smoker</td>
<td>1</td>
</tr>
</tbody>
</table>

### Point Total

<table>
<thead>
<tr>
<th>Point Total</th>
<th>10-Year Risk %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>≥17</td>
<td>≥30</td>
</tr>
</tbody>
</table>
Determining Probability of Coronary Artery Disease with a Nomogram

Adapted from 75.

To use:
1. Determine the history-ECG point score

   Angina:
   - Typical—26
   - Atypical—10
   - Non-Anginal—0

   Previous MI:
   - History only—11
   - Electrocardiogram (ECG) Q waves—12
   - Both—30
   - ECG ST-T wave changes—6
   - Diabetes mellitus—7

2. Locate point score on left reading line.
3. Extrapolate to the right reading line the appropriate point from the age scale.
4. Draw a straight line between the left point scale and right reading line. Read the probability of significant CAD from the center scale.
Diagnostic Algorithm for the Evaluation for Coronary Artery Disease in Women

* Absolute contraindications to exercise testing include acute MI, unstable angina not stabilized by medical therapy, uncontrolled cardiac arrhythmias, symptomatic severe aortic stenosis, uncontrolled heart failure, acute pulmonary embolus, acute myocarditis or pericarditis, acute aortic dissection. See other sources for relative risks (206).
† ECG not interpretable for exercise stress testing if following present: preexcitation, electronically paced rhythm, left bundle branch block, or resting ST segment depression >1 mm (206).

CAD = coronary artery disease; ECG = electrocardiogram.