

Diagnosis and Management of Stable Angina

A Review

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IMPORTANCE Nearly 10 million US adults experience stable angina, which occurs when myocardial oxygen supply does not meet demand, resulting in myocardial ischemia. Stable angina is associated with an average annual risk of 3% to 4% for myocardial infarction or death. Diagnostic tests and medical therapies for stable angina have evolved over the last decade with a better understanding of the optimal use of coronary revascularization.

OBSERVATIONS Coronary computed tomographic angiography is a first-line diagnostic test in the evaluation of patients with stable angina due to higher sensitivity and comparable specificity compared with imaging-based stress testing. Moreover, coronary computed tomographic angiography allows detection of nonobstructive atherosclerosis that would not be identified with other noninvasive imaging modalities, improving risk assessment and potentially triggering more appropriate allocation of preventive therapies. Novel therapies treating lipids (proprotein convertase subtilisin/kexin type 9 inhibitors, ezetimibe, and icosapent ethyl) and type 2 diabetes (sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 receptor agonists) have improved cardiovascular outcomes in patients with stable ischemic heart disease when added to usual care. Randomized clinical trials showed no improvement in the rates of mortality or myocardial infarction with revascularization (largely by percutaneous coronary intervention) compared with optimal medical therapy alone, even in the setting of moderate to severe ischemia. In contrast, revascularization provides a meaningful benefit on angina and quality of life compared with antianginal therapies. Measures of the effect of angina on a patient's quality of life should be integrated into the clinic encounter to assist with the decision to proceed with revascularization.

CONCLUSIONS AND RELEVANCE For patients with stable angina, emphasis should be placed on optimizing lifestyle factors and preventive medications such as lipid-lowering and antiplatelet agents to reduce the risk for cardiovascular events and death. Antianginal medications, such as β -blockers, nitrates, or calcium channel blockers, should be initiated to improve angina symptoms. Revascularization with percutaneous coronary intervention should be reserved for patients in whom angina symptoms negatively influence quality of life, generally after a trial of antianginal medical therapy. Shared decision-making with an informed patient is important for effective treatment of stable angina.

JAMA. 2021;325(17):1765-1778. doi:10.1001/jama.2021.1527

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Section Editor: Mary McGrae McDermott, MD, Deputy Editor.

Nearly 10 million US adults have stable angina, which occurs when myocardial oxygen supply does not meet demand, resulting in myocardial ischemia. Angina is typically defined as chest discomfort precipitated by physical exertion or emotional distress.^{1,2} Patients with acute coronary syndromes require rapid evaluation and management. In contrast, those with stable angina can be managed with a judicious outpatient approach to diagnosis and treatment aimed at reducing the risk of ischemic complications and improving angina symptoms and quality of life.

In the past decade, new evidence has led to significant changes in the diagnosis and management of stable angina, compared with the most recent US guidelines on stable ischemic heart disease pub-

lished in 2012.^{3,4} Recommended diagnostic approaches for stable angina now include coronary computed tomographic angiography (CCTA), an increasingly used anatomic imaging modality capable of detecting nonobstructive coronary plaque that may be missed with stress testing.^{2,5} Multiple new medications, largely targeting lipid pathways, have been demonstrated to improve outcomes in patients with established coronary artery disease (CAD). Furthermore, accumulating evidence has shown that the benefits of coronary revascularization are limited to improvements in quality of life rather than reductions in cardiovascular events for most patients with stable angina. Accordingly, the rates of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery have declined.⁶

This review highlights recent updates to diagnostic approaches and treatment strategies for stable angina. The review also discusses shared decision-making between patients and their clinicians.

Methods

We performed a literature search in PubMed through January 22, 2021, to identify high-quality observational studies, randomized clinical trials (RCTs), meta-analyses, and clinical practice guidelines for stable ischemic heart disease as well as chest pain evaluation and management. We also examined bibliographies for relevant references and prioritized large, randomized trials and meta-analyses of diagnostic and treatment approaches for stable angina in this review.

Observations

Pathophysiology

Stable angina occurs when the myocardial oxygen supply cannot meet the demand, leading to myocardial ischemia. Ischemia primarily occurs when oxygen demand increases (from exercise or psychosocial stress) in the setting of reduced coronary blood flow because of a fixed atherosclerotic coronary obstruction, but may also occur when perfusion is reduced due to abnormalities in the coronary microcirculation.^{7,8} Atherosclerosis is the result of a complex interaction between lipoprotein deposition in the subintimal space of the arterial wall and a subsequent counterproductive immune or inflammatory response.^{9,10} Some coronary atheroma progress over years to more advanced stages with the development of concentric arterial remodeling, calcifications, and eventually focal luminal stenosis, a process that may be accelerated through a series of healed plaque rupture or erosion events.¹⁰

In contrast to the quiescent plaque in patients with stable CAD, an acute coronary syndrome results when an acute plaque rupture or erosion event stimulates local luminal platelet-rich thrombus formation that either obstructs coronary blood flow or embolizes to the coronary microcirculation.¹¹ Treatment of the acute atherothrombosis requires intensive antiplatelet and anticoagulant therapies and urgent coronary revascularization in high-risk patients and those with ST elevation.^{12,13} Higher-risk morphological features for plaque rupture include plaques with thinner fibrous caps and larger necrotic lipid cores.¹⁴ Importantly, both angiographic and postmortem data suggest that many acute coronary syndrome and sudden death events occur from plaque rupture at the sites of moderate coronary stenosis that were unlikely to result in ischemia prior to the event (ie, <70% luminal stenosis).¹⁵⁻¹⁷

The pathophysiology of atherosclerosis has implications for patient management. In patients with stable CAD, the diffuse nature of atherosclerosis and the knowledge that acute coronary syndrome events commonly arise from nonobstructive plaques requires systemic treatment (ie, preventive medical therapies) to reduce risk. On the other hand, the role of focal treatment (ie, PCI) for obstructions causing ischemia can reasonably be expected to improve ischemic symptoms if present.

Epidemiology, Prognosis, and Risk Assessment

The prevalence of angina increases with age, ranging from 4% to 7% in adults aged 40 to 79 years to greater than 10% in those older than 80 years.¹ More frequent or severe angina is associated with risk for coronary events.^{18,19} Moreover, angina is potentially more common among women and among younger age groups (<75 years) and is associated with higher coronary standardized mortality ratios (SMRs) for women compared with men.¹⁹⁻²¹ A large study from Finland showed higher coronary SMRs among women vs men aged 55 to 64 years (4.69 vs 2.40, respectively; $P < .001$ for interaction) and aged 65 to 74 years (2.50 vs 1.87; $P < .001$ for interaction) with comparable SMRs in other age groups.¹⁹ Angina results in significant health care costs and reductions in quality of life.^{22,23}

The average annual risk for death or myocardial infarction (MI) among patients with stable CAD receiving medical therapy is approximately 3% to 4% per year, with generally consistent findings from registries and RCTs, including those performed recently.^{18,24-27} Among patients with stable ischemic heart disease, the presence of either angina or ischemia portends a higher risk for cardiovascular events. Among 26 000 patients with established CAD in the Reduction of Atherothrombosis for Continued Health registry,¹⁸ slightly more than half had angina at baseline. Over a 4-year follow-up, patients with stable angina had higher rates of cardiovascular death, MI, or stroke than those without angina (16.3% vs 14.2%, respectively; hazard ratio [HR], 1.19 [95% CI, 1.11-1.27]).¹⁸ In addition, a larger burden of ischemia detected on stress imaging studies, reflected by multiple or large perfusion defects or wall motion abnormalities, is associated with higher risk for cardiovascular events.²⁸ Important factors associated with adverse clinical outcomes in stable ischemic heart disease are poor exercise capacity or functional status and left ventricular dysfunction.^{29,30} The presence of left ventricular dysfunction carries greater prognostic importance than the severity of CAD or ischemia.²⁹

Clinical Presentation

Angina has been described as a recurrent discomfort in the retrosternal chest that is predictably provoked by exertion, anxiety, or stress, crescendos over a period of minutes, and dissipates with rest or nitroglycerin treatment within minutes.³¹ This discomfort is typically described as a squeezing or tightening, is typically hard to localize, and may radiate up to the neck or jaw, down either arm (more commonly the left arm), or to the epigastric area. Other symptoms from ischemia that may be considered anginal equivalents in some patients include dyspnea and indigestion. Sex differences in the relationship of angina symptoms to the burden of obstructive epicardial CAD have been noted and may be attributable in part to higher rates of microvascular disease in women than in men.^{8,21,32-34} Angina may progress, improve, or remain stable for many years. Progression of symptoms merits attention, particularly when angina occurs more frequently, is unprovoked, is more severe, or lasts longer. This may reflect progression of underlying coronary or microvascular disease; if severe rest symptoms are noted, acute coronary syndrome should be suspected and evaluated immediately (Box 1).

Clinicians often underestimate the effects of stable angina on quality of life.³⁵ Several grading systems have been proposed to assess the severity of angina in terms of frequency and limitations

on daily activities. The 4-level grading system from the Canadian Cardiovascular Society has been used for decades with higher grades reflecting significantly more limitations due to angina.³⁶ The 19-question Seattle Angina Questionnaire has been used in research studies as a validated tool for capturing patient-reported angina-related quality-of-life measures.³⁷ However, the abbreviated 7-question Seattle Angina Questionnaire may represent a more practical clinical tool to assess quality of life.^{22,38} Understanding the effect of angina on quality of life (through either open-ended subjective patient-physician communication or an objective tool) is an essential prerequisite for shared decision-making.

Assessment and Diagnosis

The patient history should clarify the angina diagnosis and delineate the effects of symptoms on the patient's quality of life, including angina frequency and severity, the degree of functional limitation, and indication of any desired activities the patient is unable to perform. A focused examination is necessary to evaluate for physical findings suggestive of nonatherosclerotic causes of angina such as aortic stenosis, hypertrophic cardiomyopathy, or pulmonary hypertension. A crescendo-decrescendo systolic murmur is present in both aortic stenosis and hypertrophic cardiomyopathy, but these can be distinguished with maneuvers such as Valsalva, squatting, and hand grip. Clues to pulmonary hypertension include a loud and widely dispersed P₂ component of the second heart sound or a right ventricular heave.

Electrocardiography should be performed to screen for prior infarction or left ventricular hypertrophy. Routine blood work can identify important comorbidities including kidney impairment, diabetes, dyslipidemia, and may identify anemia, which can lower the anginal threshold. Selective measurement of biomarkers of neurohormonal activation (B-type natriuretic peptide or NT-terminal pro-brain natriuretic peptide) or chronic myocardial injury (high-sensitivity cardiac troponin) can provide additional risk information. Individuals with chronic CAD and low-level elevations in NT-terminal pro-brain natriuretic peptide and high-sensitivity cardiac troponin are at substantially higher risk of death and heart failure than those with normal biomarker levels.^{39,40} Moreover, increases in these biomarkers over time identify individuals at higher risk compared with those with stable levels.⁴¹ Echocardiography may be considered, particularly among individuals with an abnormal electrocardiogram or elevated levels of natriuretic peptides or cardiac troponin to exclude left ventricular systolic dysfunction or concomitant abnormalities such as valvular heart disease, which can significantly influence diagnostic and therapeutic decision-making. Clinical models, including the Diamond-Forrester algorithm and the more comprehensive and accurate European consortium CAD score, incorporate symptoms and risk factors to estimate the pretest probability of CAD.^{31,42,43} Although these models overestimate the probability of obstructive CAD, they may still help to guide whether to pursue further diagnostic testing.^{44,45}

Stress testing with or without adjunctive imaging traditionally has been the mainstay for evaluating patients with angina. The sensitivity and specificity of each noninvasive test modality varies according to local expertise and characteristics of the underlying population (Figure 1).^{3,46-48} Exercise is the preferred method of stress testing because it provides functional and prognostic information.^{49,50} Assessment of a patient's cardiopulmonary fit-

Box 1. Commonly Asked Questions About Stable Angina

What Are Typical Symptoms of Stable Angina?

Stable angina is the clinical manifestation of myocardial ischemia, which is the result of inadequate oxygen supply to meet demand of the myocardium. Frequently this occurs due to obstructive atherosclerotic coronary artery disease. It typically presents as substernal chest discomfort that crescendos and resolves over minutes and is provoked by exertion or anxiety in a reproducible fashion.

Which Tests Are Commonly Used to Diagnose Stable Angina?

Functional stress testing to provoke ischemia with exercise or pharmacological agents is typically combined with electrocardiographic monitoring as the primary diagnostic tool for stable angina. Noninvasive anatomical assessment for coronary artery disease by coronary computed tomographic angiography has emerged as a first-line test based on recent evidence. The choice of whether to pursue testing and with which test is based on a combination of pretest probability, availability, local expertise, and the presence or absence of contraindications.

What Are the Common Treatments for Stable Angina?

The focus of treatment for stable angina is to reduce the risk of death, myocardial infarction, and stroke while improving quality of life through a reduction in the burden of angina. Effective lifestyle changes include smoking cessation, exercise, weight loss, and certain dietary patterns. Optimal medical therapy includes high-intensity statin therapy, aspirin, or another antiplatelet medication and blood pressure control with a systolic/diastolic target of less than 130/80 mm Hg. Options for more intensive lipid lowering in selected patients who do not reach goal with statin therapy include ezetimibe and proprotein convertase subtilisin/kexin type 9 inhibitors. Sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists are now the preferred medications for cardiovascular risk reduction in patients with type 2 diabetes and coronary artery disease. Anti-anginal therapies including β -blockers, calcium channel blockers, and nitrates can improve angina symptoms.

When Should Revascularization Be Considered for Stable Angina?

In the absence of high-risk features such as left ventricular dysfunction or surgical-grade multivessel disease, revascularization with percutaneous coronary intervention (coronary stent placement) does not affect risk for myocardial infarction or death but can provide significant relief of angina. It should be considered for patients with angina that moderately or severely affects quality of life, generally after a trial of antianginal medical therapies.

ness may uncover significant functional limitations not evident by history alone, identify an accentuated blood pressure response to exercise, and help in tailoring an exercise prescription. When exercise stress testing cannot be performed due to physical limitations or when specific circumstances are present (ie, left bundle-branch block or a pacemaker), pharmacological stress testing can be performed with either vasodilators (such as adenosine derivatives) or dobutamine, which is sympathomimetic.

Coronary computed tomographic angiography has emerged as a useful diagnostic and prognostic test for patients at low to intermediate risk when presenting with symptoms consistent with angina but without a known history of CAD.⁵¹⁻⁵³ Compared with

Figure 1. Common Diagnostic Tests for Stable Angina

Test	Stress electrocardiography	Stress echocardiography	Stress myocardial perfusion imaging	Coronary computed tomographic angiography	Invasive coronary angiography
Requirements and considerations	Exercise stress on a treadmill Requires interpretable electrocardiogram (eg, no left bundle-branch block or major ST- and T-wave changes) at baseline	Exercise or pharmacological stress (dobutamine [with atropine if necessary to achieve target heart rate] or adenosine derivatives) For patients with poor-quality echocardiographic images, contrast may improve the interpretability of the test	Exercise or pharmacological stress (vasodilator) Higher radiation exposure than other noninvasive tests	β -Blocker to lower heart rate and nitroglycerin for vasodilation Use with caution for patients with kidney impairment	Invasive procedure with bleeding risks (lower with radial vs femoral approach) Use with caution for patients with kidney impairment
Sensitivity	0.58 (95% CI, 0.46-0.69)	0.85 (95% CI, 0.80-0.89)	0.87 (95% CI, 0.83-0.90)	0.97 (95% CI, 0.93-0.99)	NA
Specificity	0.62 (95% CI, 0.54-0.69)	0.82 (95% CI, 0.72-0.89)	0.70 (95% CI, 0.63-0.76)	0.78 (95% CI, 0.67-0.86)	NA
Findings indicating high risk	>2-mm ST-segment depressions at low workload ST-segment elevations or ventricular tachycardia or ventricular fibrillation	Decrease in left ventricular ejection fraction (LVEF) >10% or left ventricular (LV) dilation Wall motion abnormalities in multiple coronary territories Baseline LV dysfunction	Decrease in LVEF >10% or LV dilation Perfusion defect in >10% of myocardium Baseline LV dysfunction	Multiple coronary arteries with $\geq 70\%$ stenosis Left main stenosis $\geq 50\%$	Multiple coronary arteries with $\geq 70\%$ stenosis Left main stenosis $\geq 50\%$

The sensitivity and specificity were reported in meta-analyses using anatomically significant coronary artery disease determined by coronary angiography as the outcome.⁴⁶ Not shown are less commonly available cardiac magnetic resonance imaging and positron emission tomography myocardial

perfusion stress tests that demonstrate higher sensitivity and are comparable with slightly higher specificity vs stress myocardial perfusion imaging.⁴⁷ NA indicates data not applicable.

a reference standard of obstructive CAD by invasive coronary angiography ($\geq 50\%$ stenosis), CCTA has high sensitivity (Figure 1) and negative predictive value, but only moderate specificity and positive predictive value (range, 64%-91%).⁵⁴⁻⁵⁷ Two large RCTs assessed the use of CCTA in the evaluation of patients with stable angina.^{58,59}

The Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial⁵⁸ randomized 10 003 ambulatory outpatients with potential coronary ischemic symptoms to either CCTA or functional testing. In the functional testing group, 67% underwent nuclear stress imaging, 22% underwent stress echocardiography, and 10% underwent exercise electrocardiographic testing.⁵⁸ There was no difference in the primary composite outcome of death, MI, unstable angina hospitalization, or procedural complications between the CCTA and functional testing groups at 2.2 years (3.3% vs 3.0%, respectively; HR, 1.04 [95% CI, 0.83-1.29]). In the CCTA group, there was more use of invasive angiography but fewer of the coronary angiograms were considered normal.

In the Scottish Computed Tomography of the Heart (SCOT-HEART) trial,⁵⁹ 4146 patients with suspected stable angina were randomized to CCTA plus usual care vs usual care alone in which the majority underwent exercise stress testing without imaging. Although no significant difference in fatal or nonfatal MI was seen between the CCTA and usual care group at 2-year follow-up (1.3% vs 2.0%, respectively; HR, 0.62 [95% CI, 0.38-1.01]), the rate of fatal or nonfatal MI at 5 years was lower in the CCTA group compared with the usual care group (2.3% vs 3.9%; HR, 0.59 [95% CI, 0.41-0.84]) due to fewer nonfatal MIs.^{59,60} A meta-analysis of nearly 15 000 participants of studies evaluating stable chest pain using CCTA suggested that the use of CCTA was associated with significant reductions in MI compared with usual care, which consisted primarily of exercise stress testing with or without imaging (risk ratio [RR], 0.69 [95% CI, 0.49-0.98]).⁶¹

The SCOT-HEART investigators have shown increased allocation of preventive therapies among those randomized to CCTA compared with the usual care group.^{60,62} Coronary computed tomographic angiography can identify patients with nonobstructive atherosclerosis who would likely benefit from aggressive preventive therapies but would have had normal stress test results. More than half of the events in the CCTA group in the PROMISE trial occurred among patients with nonobstructive CAD (<70% luminal stenosis).⁶³ On the other hand, patients with obstructive CAD on CCTA ($\geq 70\%$ stenosis) had similar event rates as those with abnormal stress test results. Importantly, CCTA was shown to be safe in the PROMISE trial with lower radiation exposure than nuclear stress imaging.⁶⁴

In aggregate, these data support CCTA as a first-line examination for patients with symptomatic angina when the patient and clinician determine that testing is indicated (Figure 1). The 2019 European Society of Cardiology guidelines now provide a similar class 1 recommendation for the use of either CCTA or exercise stress testing with imaging (typically echocardiography or nuclear perfusion) as an initial diagnostic test.² Several factors should be considered when choosing a test including availability, local expertise, patient characteristics, and contraindications.

High-quality CCTA images are less common in patients with inadequate heart rate control, irregular rhythm or ectopy, extensive coronary artery calcification, or large body habitus and in those with prior CABG surgery or placement of intracoronary stents. CCTA may overestimate the severity of intermediate stenoses, particularly in those lesions that are heavily calcified.^{2,61} However, recent technological advances may help to improve the specificity of CCTA. Non-invasive estimation of the fractional flow reserve (a measure of the hemodynamic significance of a coronary stenosis) from the existing CCTA scan is now possible, although image processing is complex and is not available at the point of care.^{65,66} Recent

studies have suggested that adding computed tomography-derived fractional flow reserve analysis to CCTA is feasible, may help to improve patient selection for invasive angiography, and may be more cost-effective than stress testing, though this approach requires validation from large ongoing RCTs.⁶⁷⁻⁷⁰

Treatment

The primary goals of treatment for stable angina are to reduce the risk of cardiovascular events including death, MI, and stroke and to improve quality of life by reducing angina symptoms. This can be achieved through routine lifestyle modification and optimal medical therapy (OMT) with selective use of coronary revascularization. Optimal medical therapy includes both preventive medications designed to favorably influence the natural history of CAD (Table 1) and antianginal medications such as β -blockers, calcium channel blockers, nitrates, and ranolazine (Table 2), which reduce angina frequency and improve quality of life.

Adherence to lifestyle modifications including smoking cessation, intentional weight loss, healthy diet pattern, and exercise can have important effects on cardiovascular risk (Table 1).^{71-74,87,88} Maintaining a physically active lifestyle may be particularly important. An observational study of 3300 participants with CAD suggested that physical activity was associated with lower mortality over 30 years of follow-up in a graded fashion with the lowest risk among those achieving high levels of activity (HR, 0.64 [95% CI, 0.50-0.83] vs inactive participants).⁸⁹ A meta-analysis distinguishing intentional from unintentional weight loss showed a cardiovascular risk reduction of 26% with presumed intentional weight loss (Table 1).⁷³

Statin therapy is the primary cholesterol level-based treatment for cardiovascular risk reduction and it should be administered at the highest intensity tolerated among those with stable CAD.^{75,90,91} If more intensive reduction of low-density lipoprotein cholesterol is desired, ezetimibe and proprotein convertase subtilisin/kexin type 9 inhibitors have shown modest incremental risk reduction when added to statin therapy.^{76,77,91-95} Icosapent ethyl, an omega-3 fatty acid consisting of purified eicosapentaenoic acid, reduced cardiovascular risk compared with placebo among participants with established CAD and elevated levels of triglycerides when added to statin therapy.⁷⁸ However, uncertainty remains regarding the role of omega-3 fatty acids for cardiovascular risk reduction. A trial of combination eicosapentaenoic and docosahexaenoic acid was stopped early due to futility and further validated concerns for an increased risk of incident atrial fibrillation with these drugs.⁹⁶ Differences in the formulations of the omega-3 fatty acids tested and in the lipid-modifying effects of the control therapies have been suggested as potential explanations for these conflicting results.^{97,98}

Antiplatelet therapy is another important therapy for reducing cardiovascular risk in patients with stable CAD, typically with low-dose aspirin (<100 mg/d) or adenosine diphosphate receptor (P_2Y_{12}) inhibitors when aspirin is contraindicated.^{79,99} Dual antiplatelet therapy with aspirin and a P_2Y_{12} inhibitor is recommended for at least 6 months after PCI for stable CAD.¹⁰⁰ Low-dose rivaroxaban (2.5 mg twice daily) in combination with aspirin was shown to reduce death and ischemic events compared with aspirin monotherapy among 16 574 participants with stable CAD enrolled in the Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease trial, but the drug increased major bleeding.⁸⁰ A target systolic/diastolic blood pressure level of

less than 130/80 mm Hg is recommended for stable CAD, with recommendations to preferentially prescribe angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to lower risk for cardiovascular events and β -blockers to treat angina.^{81,82,101} Diabetes management for stable CAD may include sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide 1 receptor agonists for cardiovascular risk reduction.^{83,84,102,103} Anti-inflammatory therapies including colchicine have shown promise for cardiovascular risk reduction, though more data are needed to determine the effect of these agents on mortality.⁸⁵ Influenza vaccination has been associated with significantly lower cardiovascular risk.⁸⁶ Emerging targets for further cardiovascular risk reduction include lipoprotein(a), triglyceride-modifying apolipoproteins, inflammation, and thrombosis.¹⁰⁴⁻¹⁰⁷

In addition to lifestyle modification, antianginal medications play an important role in reducing the symptoms of stable angina (Table 2). The efficacy of individual antianginal medications is typically modest and generally similar between different classes. Selection of drugs is therefore guided by comorbid conditions and adverse effect profiles. β -Blockers, particularly for patients with left ventricular dysfunction or prior MI, and calcium channel blockers are first-line therapies for angina treatment.^{108,109} If angina is not sufficiently suppressed after 2 to 4 weeks, titration to higher dosages or initiation of long-acting nitrates or ranolazine may be considered.²⁵ Short-acting sublingual nitrates are used as needed for breakthrough angina, but also can be administered just prior to exercise for those with predictable exertional angina.² Emerging targets for treating refractory angina are focused on improving perfusion or addressing the sensory pathways and require further investigation to determine their effects on quality of life.¹¹⁰

Revascularization has been used to treat stable angina since data from RCTs published in the 1970s and 1980s suggested CABG surgery in patients with stable CAD improved mortality out to 10 years compared with medical therapy, particularly among those with left main or triple vessel disease.¹¹¹ Since then, there have been significant advances in both OMT and revascularization options. With the introduction of balloon angioplasty and especially intracoronary stenting, PCI became a mainstay of treatment for stable angina from focal stenoses, although there were no RCTs testing the effects on cardiovascular events. A series of 4 larger studies evaluated a strategy of PCI plus OMT vs OMT alone for cardiovascular events and angina beginning with the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial and culminating with the recent International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial (Table 3).^{24-27,112}

The COURAGE trial was the first adequately powered RCT to compare PCI plus OMT vs OMT alone for clinical event reduction and followed up 2287 patients for a median of almost 5 years.²⁴ All participants had at least 1 severe stenosis ($\geq 70\%$) in a proximal epicardial coronary artery. No difference in the primary composite outcome of death and MI was seen with PCI vs OMT (19.0% vs 18.5%; HR, 1.05 [95% CI, 0.87 to 1.27]), and a post hoc substudy confirmed no benefit with PCI even in those with a larger ischemic burden.^{24,113} Although important, there were concerns that the COURAGE trial did not reflect a contemporary practice of PCI with modern drug-eluting stents, and that patients with more severe ischemia may have been excluded. Shortly after the COURAGE trial,

Table 1. Medical Therapies for Cardiovascular Risk Reduction in Patients With Established or at High Risk of Stable Ischemic Heart Disease

		Observed efficacy or effectiveness ^a		
Therapy	Study details	Relative risk reduction	Risk ratio (95% CI) ^b	Absolute rate, %
Lifestyle modifications				
Smoking cessation ⁷¹	Random-effects meta-analysis of 6 high-quality cohort studies comparing smoking cessation vs ongoing smoking in participants with CAD and >2 y of follow-up (n = 8408)	29% for all-cause mortality ^c	0.71 (0.65-0.77)	
Mediterranean diet ⁷²	Umbrella meta-analysis of RCTs comparing Mediterranean dietary pattern vs usual diet (n = 12 894; not limited to CAD)	38% for MACE plus ≥1 other event ^d	0.62 (0.45-0.86)	
Intentional weight loss ⁷³	Random-effects meta-analysis of 4 studies comparing presumed intentional weight loss vs no weight loss in participants with CAD (n = 10 866) over 3-6 y of follow-up	33% for MACE plus ≥1 other event ^{c,d}	0.67 (0.56-0.80)	3.3 vs 5.1
Physical activity ⁷⁴	Meta-analysis of 27 RCTs comparing exercise vs no exercise among patients with CAD (n = 7469) over 6->36 mo of follow-up	26% for cardiovascular mortality	0.74 (0.64-0.86)	7.6 vs 10.4
Medications				
Aid in lowering lipid levels				
Statins ⁷⁵	Meta-analysis of 26 RCTs of participants with CAD (n = 169 138) over a median follow-up of 5 y	22% annually for MACE plus ≥1 other event ^d per 39-mg/dL (1-mmol/L) reduction in LDL cholesterol level	0.78 (0.76-0.80)	3.2 vs 4.0 per year
		10% annually for all-cause mortality per 39-mg/dL (1-mmol/L) reduction in LDL cholesterol level	0.90 (0.87-0.93)	2.1 vs 2.3 per year
Ezetimibe ⁷⁶	Meta-analysis of 7 RCTs comparing ezetimibe vs control (n = 31 048; approximately 80% also were treated with a statin; not limited to patients with CAD) over a mean follow-up of 3 y	13% for myocardial infarction	0.87 (0.80-0.93)	7.3 vs 8.4
		16% for stroke	0.84 (0.74-0.95)	3.0 vs 3.6
		No difference for all-cause mortality	1.00 (0.95-1.05)	15.8 vs 15.9
PCSK9 inhibitors ⁷⁷	Random-effects meta-analysis of 23 RCTs comparing PCSK9 inhibitors vs control in participants with CAD or hyperlipidemia (n = 88 041; approximately 85% also were treated with a statin) over a weighted mean follow-up of 18 mo	18% lower odds for MACE	OR, 0.82 (0.78-0.87)	5.0 vs 6.5
		No difference for all-cause mortality	OR, 0.91 (0.78-1.05)	2.0 vs 2.3
Icosapent ethyl for triglycerides level >150 mg/dL (>1.69 mmol/L) ⁷⁸	RCT comparing icosapent ethyl vs placebo in participants at high risk for or with established CAD (n = 8179) over a median follow-up of 4.9 y	25% for MACE plus ≥1 other event ^d	HR, 0.75 (0.68-0.83)	17.2 vs 22.0
		20% for cardiovascular mortality	HR, 0.80 (0.66-0.98)	4.3 vs 5.2
		No difference for all-cause mortality	HR, 0.87 (0.74-1.02)	
		Increased risk for atrial fibrillation		5.3 vs 3.9; P = .003
Antiplatelet				
Aspirin or P ₂ Y ₁₂ inhibitor if contraindication ⁷⁹	Meta-analysis of 16 RCTs comparing aspirin vs control in participants with prior stroke, transient ischemic attack, or myocardial infarction (n = 17 000)	19% annually for MACE	0.81 (0.75-0.87)	6.7 vs 8.2 per year
		No significant difference in vascular death	0.91 (0.82-1.00)	3.7 vs 4.1
Anticoagulation				
Low-dose rivaroxaban ⁸⁰	RCT comparing 2.5 mg of rivaroxaban twice/d plus aspirin vs aspirin alone in participants with stable CAD (n = 16 574) over a mean follow-up of 2 y	26% for MACE	HR, 0.74 (0.65-0.86)	4 vs 6
		23% for all-cause mortality	HR, 0.77 (0.65-0.90)	3 vs 4
		66% increased risk of major bleeding	HR, 1.66 (1.37-2.03)	3.0 vs 2.0
Hypertension management				
Aggressive target for systolic/diastolic blood pressure level of <130/80 mm Hg ^{81,82}	Meta-analysis of 18 RCTs comparing blood pressure lowering vs control in participants with established atherosclerotic cardiovascular disease (n = 83 125)	23% for MACE plus ≥1 other event ^d per 10-mm Hg reduction in systolic blood pressure	0.77 (0.71-0.81)	12.8 vs 14.3
		10% for all-cause mortality per 10-mm Hg reduction in systolic blood pressure	0.90 (0.83-0.98)	8.3 vs 8.8

(continued)

Table 1. Medical Therapies for Cardiovascular Risk Reduction in Patients With Established or at High Risk of Stable Ischemic Heart Disease (continued)

		Observed efficacy or effectiveness ^a		
Therapy	Study details	Relative risk reduction	Risk ratio (95% CI) ^b	Absolute rate, %
Diabetes management				
SGLT2 inhibitors ⁸³	Meta-analysis of 3 RCTs comparing SGLT2 inhibitors vs placebo in participants with type 2 diabetes and atherosclerotic cardiovascular disease (n = 20 650) over a median follow-up of 3 y	14% for MACE	HR, 0.86 (0.80-0.93)	
		29% for heart failure hospitalization	HR, 0.71 (0.62-0.82)	
		17% for all-cause mortality	HR, 0.83 (0.75-0.92)	
GLP1 receptor agonists ⁸⁴	Meta-analysis of 7 RCTs comparing GLP1 receptor agonists vs placebo in participants with type 2 diabetes and atherosclerotic cardiovascular disease (n = 42 455) over a median follow-up of 3.2 y	14% for MACE	HR, 0.86 (0.79-0.94)	11.4 vs 13.0
		12% for all-cause mortality ^e	HR, 0.88 (0.83-0.95)	7 vs 8
Anti-inflammatory				
Colchicine ⁸⁵	RCT comparing 0.5 mg/d of colchicine vs placebo in participants with chronic CAD (n = 5522) over a median follow-up of 2.4 y	31% for MACE plus ≥1 other event ^d	0.69 (0.57-0.83)	6.8 vs 9.6
		Potential increase in all-cause mortality	HR, 1.51 (0.99-2.31)	
Vaccination				
Influenza ⁸⁶	Meta-analysis of RCTs comparing influenza vaccine vs placebo in participants at high risk of atherosclerotic cardiovascular disease (n = 6735) over a mean follow-up of 8 mo	36% for MACE plus ≥1 other event ^d	0.64 (0.48-0.86)	2.9 vs 4.7
		No difference for cardiovascular mortality	0.81 (0.36-1.83)	1.3 vs 1.7

Abbreviations: CAD, coronary artery disease; GLP1, glucagon-like peptide 1; LDL, low-density lipoprotein; MACE, major adverse cardiovascular events of cardiovascular death, myocardial infarction, or stroke; P₂Y₁₂, adenosine diphosphate receptor; PCSK9, proprotein convertase subtilisin/kexin type 9; RCT, randomized clinical trial; SGLT2, sodium-glucose cotransporter 2.

^a Effect estimates are from meta-analyses of RCTs unless otherwise indicated. Some event rates are not provided because they were not available.

^b Some of the data are expressed as a hazard ratio (HR) or an odds ratio (OR) instead of a risk ratio as indicated.

^c Indicates an association from nonrandomized observational studies.

^d Unstable angina, revascularization, or hospitalization for heart failure.

^e Estimate based on entire population and includes those without baseline atherosclerotic cardiovascular disease.

Table 2. Common Antianginal Therapies Used in the US

Therapy	Indication	Relative or absolute contraindication	Adverse effect
β-Blockers	- First-line therapy unless contraindication or intolerance - Prior myocardial infarction or left ventricular systolic dysfunction - History of tachyarrhythmia - Hypertension	- Severe bradycardia or advanced heart block without a pacemaker^a - Severe reactive airway disease (asthma, chronic obstructive pulmonary disease) - Severe depression - Vasospastic angina - Diabetes with hypoglycemic episodes	- Bradycardia or atrioventricular block - Bronchoconstriction - Fatigue or lethargy - Depression - Sexual dysfunction - Masked hypoglycemia - Vasoconstriction - Raynaud phenomenon (occurs with nonselective β-blockers)
Calcium channel blockers	Dihydropyridines (amlodipine, nifedipine, nicardipine)	- Hypotension - Severe aortic stenosis or heart failure (nifedipine) - Do not use short-acting nifedipine^a	- Leg edema (dihydropyridines) - Hypotension - Constipation - Headache or dizziness - Flushing or palpitations - Bradycardia or atrioventricular block (occurs with nondihydropyridines) - Gingival hyperplasia (occurs with verapamil)
	Nondihydropyridines (diltiazem, verapamil)	- Severe bradycardia or advanced heart block without a pacemaker^a - Caution if combined with a β-blocker - Left ventricular systolic dysfunction	
Nitrates	- Short-acting nitrates are commonly used for anginal attacks or administered prior to exercise to prevent exercise-induced angina - Long-acting nitrates are a second-line therapy often used in conjunction with β-blockers or calcium channel blockers	- Severe aortic stenosis - Hypertrophic cardiomyopathy (with obstruction) - Concomitant use of phosphodiesterase 5 inhibitors^a	- Headache - Flushing - Hypotension - Nitrate tolerance
Ranolazine	- Second-line therapy in refractory angina - Useful for patients in whom low heart rate or blood pressure limits titration of other agents - Type 2 diabetes (small benefit on hemoglobin A_{1c} level)	- Severe hepatic or kidney disease - Prolonged QT interval - Some antiarrhythmic medications	- Nausea or constipation - Dizziness - QT prolongation

^a Indicates an absolute contraindication.

Table 3. Key Randomized Clinical Trials of Revascularization in Patients With Stable Angina

Trial	Participant criteria	Primary outcome	Cardiovascular and mortality outcomes	Additional information
COURAGE ²⁴ (n = 2287); conducted from 1999-2006	Stable CAD with • Stenosis $\geq 70\%$ plus abnormal stress test result or • Stenosis $\geq 80\%$ plus angina	No difference in death or MI over a median of 4.6 y	Death or MI • PCI (19%) vs OMT (18.5%) • HR, 1.05 (95% CI, 0.87 to 1.27)	• Excluded markedly abnormal stress test results • Excluded patients with indications for CABG surgery • Outdated stent technology • 32.6% of OMT group underwent revascularization over a median of 4.6 y
BARI 2D ²⁵ (n = 2368); conducted from 2001-2008	Stable CAD in patients with type 2 diabetes and • Stenosis $\geq 50\%$ plus abnormal stress test result or • Stenosis $\geq 70\%$ plus angina	No difference in death or composite outcome of death, MI, or stroke at 5 y	Death, MI, or stroke • Revascularization (22.8%) vs OMT (24.1%) • Between-group difference, 1.3% (95% CI, -2.2% to 4.9%)	• Included patients with indications for CABG surgery • Benefit on composite outcome was seen in CABG surgery stratum vs OMT • No difference between PCI and OMT • 42% of OMT group underwent revascularization over 5 y
FAME 2 ^{26,112} (n = 888); conducted from 2010-2012 with 5-y follow-up in 2018	Stable CAD and angiogram shows lesion suitable for PCI with a fractional flow reserve ≤ 0.80	Lower rate of death, MI, or urgent revascularization at both 7 mo and 5 y in PCI group driven by benefit from urgent revascularization	Death or MI • At 7 mo: PCI (3.4%) vs OMT (3.9%); HR, 0.61 (95% CI, 0.28 to 1.35) • At 5 y: PCI (11.9%) vs OMT (16.1%); HR, 0.72 (95% CI, 0.50 to 1.03)	• Excluded patients with indications for CABG surgery • Trial stopped early due to benefit from urgent revascularizations in PCI group • 51% of OMT group underwent revascularization over 5 y
ISCHEMIA ²⁷ (n = 5179); conducted from 2012-2019	Stable CAD with moderate to severe reversible ischemia on imaging stress test or severe ischemia on exercise stress test	No difference in death, MI, hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest over a median of 3.2 y	Cardiovascular death or MI • At 6 mo: invasive (4.8%) vs conservative (2.9%); between-group difference, 1.9% (95% CI, 0.9% to 3.0%) • At 5 y: invasive (14.2%) vs conservative (16.5%); between-group difference, -2.3% (95% CI, -5.0% to 0.4%)	• 73% of participants underwent blinded coronary computed tomographic angiography to verify obstructive CAD and exclude left ventricular main stenosis $>50\%$ • Approximately 25% underwent CABG surgery in invasive group • 21% of conservative group underwent revascularization over a median of 3.2 y • Procedural MI may have masked modest benefit for risk of spontaneous nonfatal MI

Abbreviations: BARI 2D, Bypass Angioplasty Revascularization Investigation 2 Diabetes; CABG, coronary artery bypass graft; CAD, coronary artery disease; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; FAME 2, Fractional Flow Reserve vs Angiography for Multivessel

Evaluation 2; HR, hazard ratio; ISCHEMIA, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches; MI, myocardial infarction; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

the Bypass Angioplasty Revascularization Investigation 2 Diabetes trial of 2368 patients with stable CAD and type 2 diabetes also showed no benefit of revascularization with PCI vs OMT on major cardiovascular events at 5 years (between-group difference, 1.3% [95% CI, -2.2% to 4.9%]).²⁵ The Fractional Flow Reserve vs Angiography for Multivessel Evaluation 2 trial randomized 888 patients with stable CAD and an abnormal fractional flow reserve to PCI plus OMT vs OMT alone. The trial was stopped early after 7 months due to significant benefit from PCI plus OMT on the primary end point of death, MI, or urgent revascularization (4.3% vs 12.7% for OMT alone; HR, 0.32 [95% CI, 0.19 to 0.53]).²⁶ However, the benefit from PCI plus OMT was only seen for urgent revascularization and there was no significant difference in the composite of death or MI when patients were followed up for 5 years (11.9% vs 16.1% for OMT alone; HR, 0.72 [95% CI, 0.50 to 1.03]).¹¹² These 3 trials were limited by knowledge of coronary anatomy prior to randomization, likely leading to a selection bias whereby individuals at higher risk were excluded while those with mild ischemia were preferentially randomized.

These studies provided background for the ISCHEMIA trial,²⁷ which tested an initial strategy of invasive vs conservative management among 5179 patients with stable CAD and moderate to severe ischemia on stress testing and who were followed up for a median of 3.2 years. All patients without contraindications under-

went blinded CCTA to identify those with obstructive CAD and exclude those with left main stenosis greater than 50% in whom CABG surgery would be appropriate. In the invasive group, 96% underwent coronary angiography and 79% received revascularization (74% with PCI and 26% with CABG surgery). In the conservative group, only 21% underwent a revascularization procedure during follow-up. There was no difference in the primary composite outcome of cardiovascular death, MI, resuscitated cardiac arrest, or hospitalization for unstable angina or heart failure at 5 years between the invasive (16.4%) and conservative (18.2%) groups (between-group difference, -1.8% [95% CI, -4.7% to 1.0%]). There was also no difference in the key secondary outcome of cardiovascular death or nonfatal MI at 5 years between revascularization (14.2%) and conservative (16.5%) management (between-group difference, -2.3% [95% CI, -5.0% to 0.4%]). With regard to the individual components, no difference was seen in death but procedure-related MI may have masked a possible modest benefit for risk of longer-term spontaneous MI in the PCI group; extended follow-up is planned to further address this question. In contrast to the lack of benefit on definite cardiovascular events, the invasive strategy led to modest improvements in angina burden as measured by Seattle Angina Questionnaire summary scores (range, 0 to 100) over the short term (4.1-point improvement with PCI

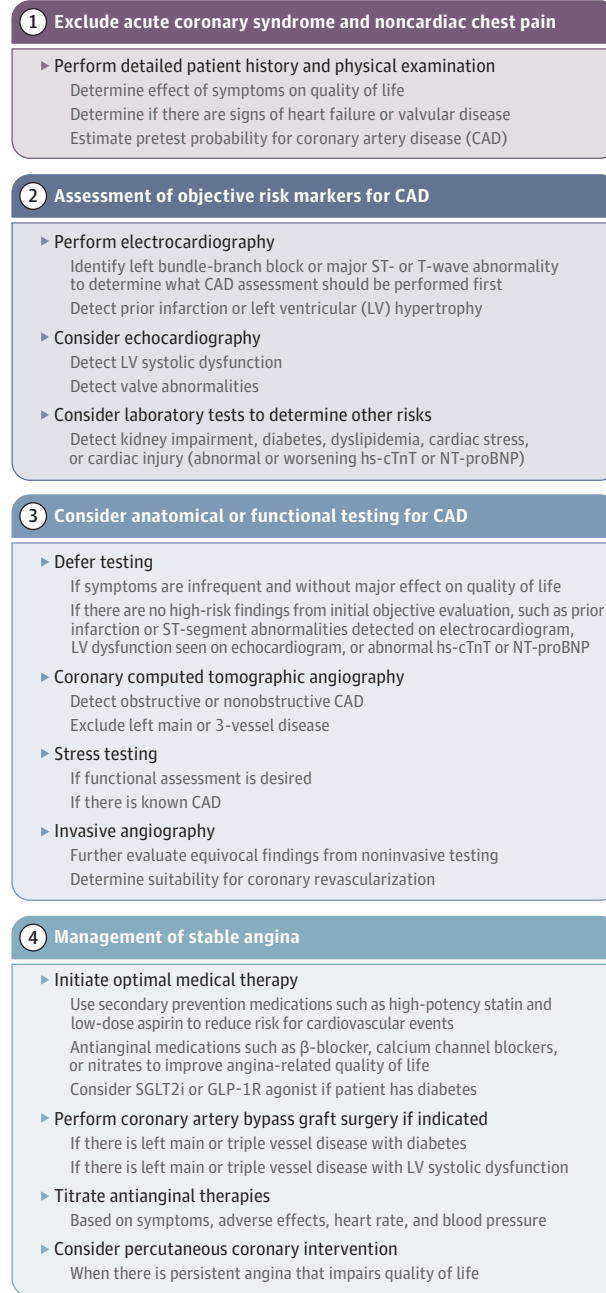
over 3 months [95% CI, 3.2 to 5.0 points]) and long term (2.9-point improvement with PCI over 36 months [95% CI, 2.2 to 3.7 points]).²² Participants reporting worse angina at baseline (based on lower Seattle Angina Questionnaire summary scores) derived greater symptom improvement from the invasive approach than those with milder angina. A meta-analysis of 14 RCTs including nearly 15 000 participants with stable angina showed no significant association of revascularization with mortality compared with medical therapy (RR, 0.99 [95% CI, 0.90 to 1.09]) and for MI overall (RR, 0.93 [95% CI, 0.83 to 1.03]) but found a significant association with lower rates of unstable angina (RR, 0.64 [95% CI, 0.45 to 0.92]) and an association with fewer angina symptoms (RR, 1.10 [95% CI, 1.05 to 1.15]).¹¹⁴

Although the trials completed to date present a consistent message regarding the role of PCI to improve angina rather than reduce the risk for cardiovascular events in stable CAD, it is more difficult to reach a clear conclusion regarding CABG surgery in the contemporary era, given improvements in medical therapies and accumulating expertise with complex PCI. Three of 4 trials excluded patients with left main CAD based on the previously established benefit of CABG surgery in this group. The exception is the Bypass Angioplasty Revascularization Investigation 2 Diabetes study that found a benefit from revascularization with CABG surgery but not with PCI ($P = .002$ for interaction) compared with OMT alone among patients with type 2 diabetes ($n = 763$; major cardiovascular event rate of 22.4% with CABG surgery vs 30.5% with OMT at 5 years; $P = .01$).²⁵ These data suggest that there are subgroups of patients with stable but severe CAD in whom CABG surgery likely has benefit vs OMT alone, including those who have left main or 3-vessel CAD involving the proximal left anterior descending artery, with the benefit of CABG surgery augmented among patients with diabetes or left ventricular dysfunction.¹¹⁵

Percutaneous coronary intervention continues to have an important role among selected patients with severe CAD, particularly when risk for operative mortality or complications with CABG surgery is high. Moreover, PCI has emerged as a reasonable alternative to CABG surgery for patients with isolated left main CAD. A meta-analysis of more than 4500 participants with left main CAD from 5 RCTs comparing contemporary PCI with CABG surgery who were followed up for more than 5 years suggested no association of PCI, compared with CABG surgery, with lower mortality (RR, 1.03 [95% CI, 0.81-1.32]) but was associated with higher rates of unplanned revascularization after PCI (RR, 1.73 [95% CI, 1.49-2.02]).¹¹⁶ The merits of CABG surgery, PCI, and medical therapy for patients with left main or complex multivessel CAD should be discussed among a team of heart specialists that involves medical and interventional cardiologists and cardiothoracic surgeons and should include shared decision-making with the patient.

Although there is strong evidence of benefit from PCI to reduce angina and improve quality of life, there is some debate over the size of benefit due to a lack of a sham control group in PCI trials. The Objective Randomized Blinded Investigation with Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA) trial was the first blinded placebo-controlled RCT of PCI for stable angina.¹¹⁷ Over the short follow-up of 6 weeks in this small trial ($n = 200$), neither the primary outcome of change in exercise time (increase of 16.6 seconds with PCI [95% CI, -8.9 to 42.0 seconds]),

Figure 2. Approach to Diagnosis and Management of Stable Angina



Patient preference should inform each decision. This algorithm has not been validated in a randomized clinical trial. hs-cTnT indicates high-sensitivity cardiac troponin T; NT-proBNP, NT-terminal pro-brain natriuretic peptide.

nor the secondary outcomes of angina scores from the Seattle Angina Questionnaire and the Canadian Cardiovascular Society grading system differed between the PCI and placebo groups. These findings raised the possibility of a placebo effect of PCI on angina; however, subsequent ORBITA analyses suggested that the baseline burden of ischemia played a role. Among participants with greater baseline ischemia, freedom from angina was improved with PCI compared with a placebo control and angina frequency was improved more with PCI.^{118,119}

Collectively, RCTs of invasive management supported the important role that PCI plays in the relief of angina, even when compared with a placebo control, particularly when there is significant baseline ischemia and a high burden of angina.^{22,114} The ISCHEMIA trial was consistent with this finding and there were clinically meaningful improvements in Seattle Angina Questionnaire scores among participants with daily or weekly angina (mean difference, 5.3 points at 36 months [95% CI, 3.4-7.5 points]).²² Patient preference, taking into account routine clinical assessments of the severity of angina and the effects on quality of life, is a critical component in the shared decision of whether to proceed with PCI. Although generally PCI should be reserved for patients with persistent symptoms after a trial of antianginal therapy, in our opinion it is reasonable to offer PCI as a first-line treatment for angina relief in the context of shared decision-making. The patient must understand the procedural risks of PCI, such as bleeding and contrast-induced kidney injury, their options for alternative medical treatments for angina relief, and that PCI would not be expected to improve longevity or MI risk.

Summary Approach

Informed and shared decision-making is essential to the contemporary evaluation and management of stable angina (Figure 2). Clinicians must assess the effects of angina on the patient's quality of life to inform the decision-making process and should routinely assess adherence to medical therapies and lifestyle modifications. It is important to establish whether functional or anatomical information is needed and how each will affect subsequent decisions prior to proceeding with testing. For many patients with known CAD, testing can be deferred unless high-risk features are present (eg, worsening exercise tolerance, suspected left ventricular dysfunction) or new findings from a laboratory evaluation prompt concern (eg, abnormal or worsening concentrations of troponin T or NT-terminal pro-brain natriuretic peptide).

For individuals without a prior CAD diagnosis, anatomical information can be obtained noninvasively by CCTA to exclude surgical disease but still guide medical therapy. Detection of even nonobstructive CAD by CCTA should lead to intensive lifestyle modifications and consideration of preventive medical therapies. The patient should be educated about the benefit of preventive medical therapies on their overall risk for cardiovascular events. CABG surgery improves angina and also improves clinical outcomes in patients with advanced CAD, particularly in the presence of diabetes or left ventricular dysfunction. Although PCI did not improve longevity or reduce the risk for MI in patients with stable angina, it has improved quality of life when angina was frequent or burdensome and PCI remains an important complement to antianginal medical therapies (Box 2).

Box 2. Bottom Line

- Diagnostic testing for stable angina has expanded to include coronary computed tomographic angiography as a first-line option.
- Risk for myocardial infarction and cardiovascular death can be reduced by adopting favorable lifestyle factors and prescribing medications, such as high-potency statins and low-dose aspirin, for secondary prevention.
- Percutaneous coronary intervention does not improve longevity or risk for myocardial infarction in patients with stable angina and should be reserved for patients in whom angina symptoms negatively affect quality of life, generally after a trial of antianginal medical therapy.
- Shared decision-making between patient and clinician should guide choices between medical therapy and revascularization and should be informed by objective assessment of the effect of angina on quality of life.

Limitations

This review has several limitations. First, the focus of the review is on stable angina, which is one predominant form of stable ischemic heart disease. The management of patients with chronic CAD who are asymptomatic (such as survivors of MI or those with prior revascularization procedures) was not addressed. These individuals also would benefit from many of the lifestyle modifications and pharmacological treatment recommendations in this review. Second, cardiac magnetic resonance imaging and cardiac positron emission tomography were not addressed as potential stress imaging modalities because they continue to be less commonly available. Third, this was not a systematic review. Fourth, the literature search may have missed some relevant studies.

Conclusions

For patients with stable angina, emphasis should be placed on optimizing lifestyle factors and preventive medications such as lipid-lowering and antiplatelet agents to reduce the risk for cardiovascular events and death. Antianginal medications, such as β -blockers, nitrates, or calcium channel blockers, should be initiated to improve angina symptoms. Revascularization with percutaneous coronary intervention should be reserved for patients in whom angina symptoms negatively influence quality of life, generally after a trial of antianginal medical therapy. Shared decision-making with an informed patient is important for effective treatment of stable angina.

ARTICLE INFORMATION

Accepted for Publication: February 1, 2021.

Author Contributions: Drs Joshi and de Lemos had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Both authors.

Drafting of the manuscript: Joshi.

Critical revision of the manuscript for important intellectual content: Both authors.

Administrative, technical, or material support: Joshi.

Supervision: de Lemos.

Conflict of Interest Disclosures: Dr Joshi reported receiving grant support from the American Heart Association, NASA, Novartis, Novo Nordisk, Sanofi, GlaxoSmithKline, AstraZeneca, and Pfizer; receiving personal fees from Bayer and Regeneron; and having an equity interest in G3 Therapeutics. Dr de Lemos reported receiving grant support from the National Institutes of Health, the American Heart Association, the National Space Biomedical Research Institute, Roche Diagnostics, and Abbott

Diagnostics; receiving personal income from Novo Nordisk, Amgen, Regeneron, Eli Lilly, Abbott Diagnostics, Siemens Healthcare Diagnostics and Ortho Clinical Diagnostics for serving on data monitoring committees, steering committees, or end point committees; and receiving consulting income from Janssen and Quidel Inc.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

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