Treatment for Chronic Stable Angina: A Guidelines-Based Approach

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Quality care in clinical cardiology, as in all of medicine, relies on the incorporation of evidence from clinical trials to help inform and drive management of patients. Stable ischemic heart disease (SIHD) presenting with stable angina is a common clinical scenario seen by internists and clinical cardiologists in multiple settings. The management of patients with chronic stable angina requires consideration of risk factors, comorbidities, symptoms, coronary anatomy, and ischemic burden. The physician has a variety of tools at his or her disposal, ranging from lifestyle modification and pharmacotherapy, to percutaneous and surgical procedures. The past two decades have witnessed an explosion in the amount of evidence that is currently available to inform the clinical care of these patients, which has led to the development and dissemination of clinical guidelines that have systematically assessed the different lifestyle, pharmacologic, and revascularization strategies in patients with SIHD. Patients with SIHD demonstrate higher rates of cardiovascular morbidity and mortality and, therefore, their management includes two distinct goals: to mitigate major cardiovascular mortality and morbidity and to reduce symptom burden. This article reviews the intersection of two of these guidelines: the recently published 2012 SIHD guidelines and the Appropriate Use Criteria for Revascularization, first published in 2009 and recently revised in 2012. The overlap between the two guidelines is discussed, as well as the gaps within them, particularly as they relate to the role of pharmacologic therapies, in an effort to build a case for evidence-based management of patients with SIHD.

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KEY WORDS

Stable ischemic heart disease • Guidelines-based management • Revascularization • Appropriate use criteria

Quality care in the practice of clinical cardiology relies on the incorporation of evidence from clinical trials, and management of chronic stable angina is no exception. The culmination of the present evidence-based approach to management of clinical conditions is the development and dissemination of clinical guidelines that have systematically assessed the amount and quality of data of the different lifestyle, pharmacologic, and revascularization strategies in patients with stable ischemic heart disease (SIHD).[1-3] In these guidelines, the management of patients with SIHD includes two distinct goals: to mitigate the major cardiovascular mortality and morbidity associated with it and to reduce symptom burden. This article reviews these guidelines as they pertain, in particular, to the second goal of symptom relief. It discusses the strength of the evidence supporting the guideline recommendations, and reviews more recently developed and investigational strategies, of which more evidence is needed before being incorporated into the guidelines. Unfortunately, there are multiple guidelines that are relevant to patients with SIHD, providing, at times, inconsistent guidance.

Risk-factor Modification and Secondary Prevention Therapies

Risk-factor modification is essential in preventing adverse events in patients with coronary artery disease (CAD), and all risk-factor modifications are recommended as Class I therapies. Smoking and smoking cessation should be discussed at every visit, and consideration should be given to pharmacotherapy and referral to a smoking cessation program. Lipid and blood pressure goals are based on recommendations from the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), and Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, respectively.[4,5] Depending on an individual's lipid profile, the prescription of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, fibrates, niacin, and ezetimibe may be appropriate to achieve lipid targets.

Antiplatelet agents such as aspirin, prasugrel, and ticagrelor play a central role both in medical management and revascularization strategies for ischemic heart disease. Angiotensin-converting enzyme (ACE) inhibitors should be given to patients with CAD and left ventricular ejection fraction (LVEF) $\leq$ 40%, type 2 diabetes mellitus, hypertension, or chronic kidney disease.[3] Angiotensin receptor blockers (ARBs) are appropriate for patients unable to tolerate ACE inhibitors. The β-adrenergic blockers carvedilol, metoprolol, and bisoprolol have reduced mortality in patients with LV systolic dysfunction and history of myocardial infarction (MI), and both β-blockers and ACE inhibitors are recommended as first-line agents for the treatment of hypertension in patients with CAD. The main secondary prevention and risk-reduction recommendations from the American Heart Association (AHA)/American College of Cardiology Foundation (ACCF) guidelines for patients with coronary heart disease are summarized in Table 1.[3]

Relief of Angina

Many patients with ischemic heart disease seek attention following the development of angina pectoris or its equivalent. Whereas lifestyle modification and secondary prevention therapies may address their long-term risks related to ischemic heart disease, the effective relief of angina is not only desired but also enhances compliance with secondary prevention therapies.

Currently available classes of antianginal therapies in the United States include β-blockers, nitrates, calcium channel blockers (CCBs), and ranolazine. The use of these antianginal agents is recommended in the current guidelines and often forms an important measure for classifying appropriateness of revascularization. A brief consideration of the following classes of antianginal therapies is followed by a more detailed evaluation of the interplay among these therapies and revascularization appropriateness according to current guidelines.

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β-*Blockers*

Specific β-blockers that have been shown to reduce mortality in patients with a history of heart failure or prior MI and LVEF $\leq$ 40% include metoprolol succinate, carvedilol, and bisoprolol.[6-8] They are also recommended to be given for at least 3 years to patients with preserved LVEF and a history of acute coronary syndrome (ACS) or MI, and may be considered in patients with reduced LVEF and no history of clinical heart failure or MI.[3]

β-Blockers have not been shown to reduce cardiovascular events in patients with stable angina and

TABLE 1

Main Recommendations From the American Heart Association/American College of Cardiology Foundation for Secondary Prevention and Risk Reduction Guidelines in Patients With Coronary Heart Disease

Recommendation	Class	Level of Evidence
Blood pressure < 140/90 mm Hg	I	A
LDL-C < 100 mg/dL	I	C
LDL-C < 70 mg/dL in very high-risk patients	IIa	C
Non–HDL-C < 130 mg/dL if triglycerides > 200 mg/dL	I	B
Non–HDL-C < 100 mg/dL if triglycerides > 200 mg/dL in very high-risk patients	IIa	B
Smoking cessation	I	A
Physical activity 30-60 min 5-7 d/wk	I	B
BMI goal 18.5-24.9 kg/m^2	I	B
Waist circumference goal < 35 in for women or 50 in for men	I	B
Aspirin 75-162 mg/d in all patients with CAD unless contraindicated	I	A
$P2Y_{12}$ receptor antagonist with aspirin after PCI or ACS with stent placement	I	A
ACE inhibitors in patients with EF ≤ 40% or DM, HTN, or chronic kidney disease unless contraindicated, or ARBs if ACE inhibitor intolerant	I	A
ACE inhibitors in all other patients with CAD, or ARBs if ACE inhibitor intolerant	IIa	B
Aldosterone blockade in patients post-MI without renal dysfunction or hyperkalemia, LVEF ≤ 40%, and DM or heart failure	I	A
Carvedilol, metoprolol succinate, or bisoprolol in patients with LVEF ≤ 40% and heart failure or prior MI unless contraindicated	I	A
β-blockers for 3 y in patients with normal LVEF and MI or ACS	I	B
β-blockers beyond 3 y in patients with normal LVEF and MI or ACS	IIa	B
β-blockers in patients with LVEF ≤ 40% without heart failure or prior MI	IIa	C
β-blockers in all other patients with coronary or vascular disease	IIb	C

ACE, angiotensin-receptor blocker; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; DM, type 2 diabetes mellitus; EF, ejection fraction; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MI; myocardial infarction; PCI, percutaneous coronary intervention.
Reprinted with permission from Smith SC Jr et al.[3]

no history of MI or heart failure. They have proven, however, to be very useful in reducing ischemia and anginal symptoms, especially in combination with other agents. Furthermore, they can be safely combined with long-acting CCBs.[9,10] There also have been studies showing efficacy in combination with ranolazine.[11]

In the recently published longitudinal observational analysis of β-blocker use in nearly 35,000 patients both with and without CAD in the Reduction of Atherothrombosis for Continued Health (REACH) registry,[12] there was no lowering of cardiovascular event risk in patients with known CAD and prior MI, those without prior MI, or those with CAD risk factors only. This does not support previous guideline recommendations placing β-blockers as a first-line agent (Figure 1). Caution should be taken in patients with vasospastic angina because symptoms may be worsened with nonselective β-blockers.[13] Adherence to β-blocker therapy can be influenced by the occurrence of adverse effects such as fatigue, lethargy, sexual dysfunction, or sleep disturbances. Randomized clinical trials are needed in this area of improved medical and device therapies to determine who is best suited to receive β-blocker therapy and which β-blockers should be used, and to identify the optimal duration of therapy. Despite the lack of randomized trial data on the efficacy of the different β-blockers in most patients with chronic stable angina, they receive a Class I recommendation from the ACCF/AHA 2012 stable ischemic heart disease guidelines for prescription as initial therapy for symptomatic relief (Level of Evidence: B).[1]

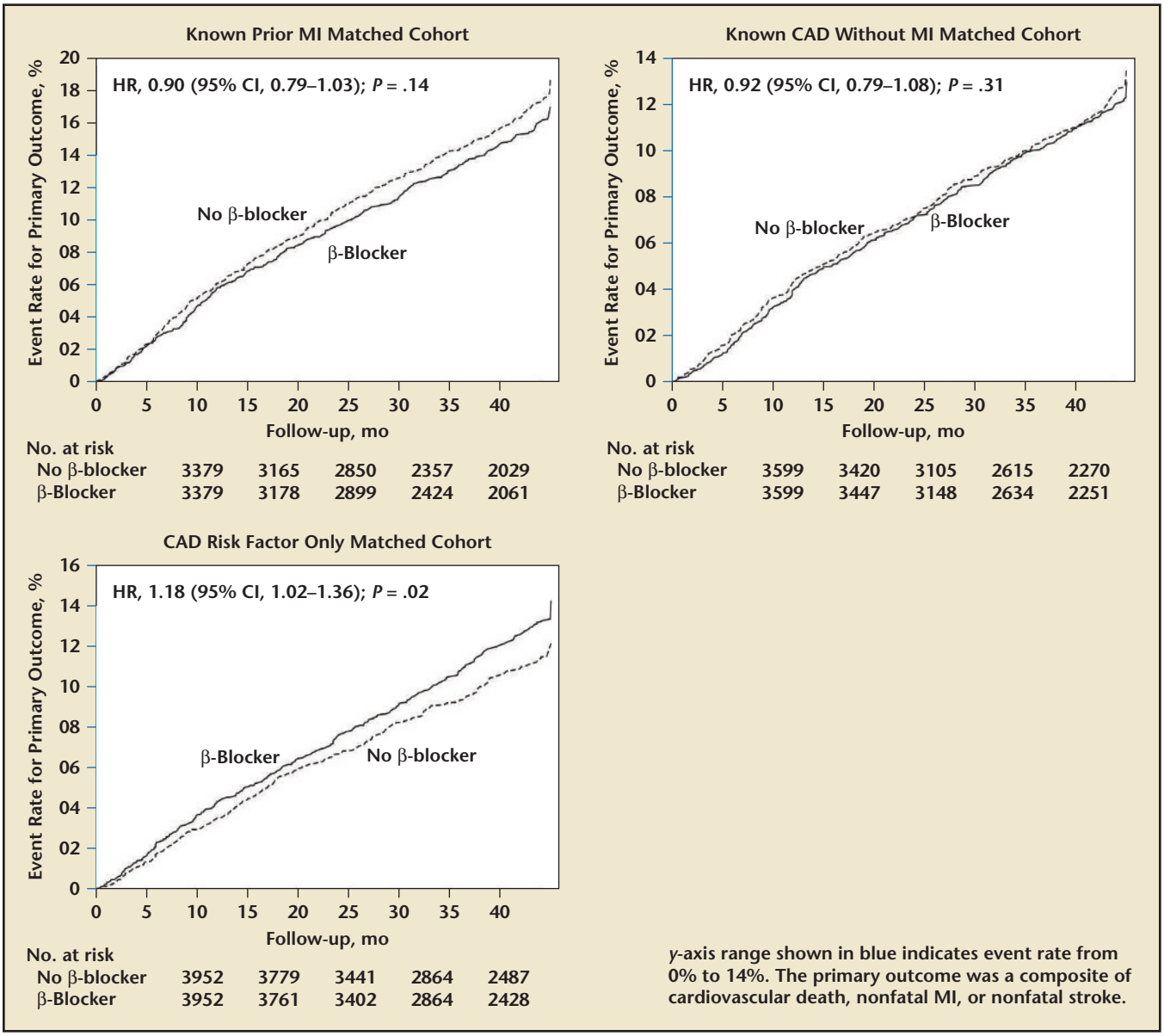

Figure 1. Cumulative index curve for the risk of primary outcome by β-blocker use. Y axis range (shown in *blue*) indicates event rate from 0% to 14%. The primary outcome was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction. Reprinted with permission from Bangalore S et al.[12]

Nitrates

Sublingual nitroglycerin or nitroglycerin spray is highly effective in providing immediate relief of angina. Long-acting nitrates reduce the frequency and severity of anginal attacks and may increase exercise tolerance, but do not improve prognosis. Nitrates receive a Class I recommendation to be considered as initial therapy for the treatment of angina when β-blockers are contraindicated or result in adverse effects, or when used in combination with β-blockers when symptoms persist. Patients should have a daily nitrate-free period of at least 10 to 14 hours to preserve efficacy.[1]

Calcium Channel Antagonists

Similar to long-acting nitrates, calcium channel antagonists receive a Class I recommendation to be given as second-line therapy after β-blockers for the relief of angina, or as initial therapy if β-blocker use is problematic.[1] However, cardiovascular events were not reduced by long-acting dihydropyridines in the A Coronary Disease Trial Investigating Outcome with Nifedipine Gastrointestinal Therapeutic System (ACTION) and Comparison of Amlodipine Versus Enalapril to Limit Occurrences of Thrombosis (CAMELOT) trials,[14,15] and short-acting dihydropyridines should be avoided due to an increased risk of MI. Long-acting nondihydropyridines can be used as initial therapy for

angina instead of β-blockers, but should not be given to patients with LV systolic dysfunction. Treatment with a long-acting nondihydropyridine CCB (verapamil or diltiazem) instead of a β-blocker as initial therapy for relief of symptoms is reasonable in patients with SIHD and receives a Class IIa recommendation.[1] According to the ACCF/AHA 2012 stable ischemic heart disease guidelines, dihydropyridines are preferred over other CCBs in patients with cardiac conduction defects such as sick sinus syndrome, sinus bradycardia, or significant atrioventricular conduction disturbances. In patients with severe aortic valve stenosis, dihydropyridines should be used with caution.[1] Many drug interactions are associated with CCBs due to high first-pass metabolism by the cytochrome P450 system (CYP450). These drugs should be used with caution when combined with cyclosporine, carbamazepine, lithium carbonate, amiodarone, or digoxin (50% to 70% increases in digoxin concentrations are seen in the first week of therapy). Combining verapamil or diltiazem with β-blockers should be avoided because of potentially profound adverse effects on atrioventricular nodal conduction, heart rate, or cardiac contractility.[1]

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Ranolazine

Ranolazine inhibits late sodium channels in myocytes, which prevents intracellular calcium overload, which is believed to play a role in ischemia. It has been approved by the US Food and Drug Administration for the treatment of chronic stable angina. Several randomized studies have demonstrated the efficacy of ranolazine in reducing the burden of angina.[11,16,17] In the Monotherapy Assessment of Ranolazine In Stable Angina (MARISA) trial[16] there was a dose-dependent increase in total exercise time, time to 1-mm ST depression, and time to angina during exercise compared with placebo. In the Combination Assessment of Ranolazine In Stable Angina (CARISA) trial,[11] patients who received ranolazine over baseline antianginal therapy had improved symptoms during exercise, as well as decreased incidence of angina and use of nitroglycerin. In the Combination Assessment of Ranolazine In Stable Angina (ERICA) trial,[17] patients with at least three episodes of angina per week who were taking amlodipine and possibly nitrates (but not β-blockers) were assigned to ranolazine, 1000 mg, twice daily versus placebo. Ranolazine significantly reduced the number of angina attacks and use of sublingual nitroglycerin. Ranolazine is currently indicated for the treatment of chronic angina and may be used in combination with β-blockers, nitrates, dihydropyridine CCBs, ACE inhibitors, ARBs, as well as antiplatelet and lipid-lowering therapies. The lack of an effect on blood pressure and heart rate makes ranolazine an attractive alternative in patients with bradycardia or low blood pressure.[1] The Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes-Thrombolysis In Myocardial Infarction (MERLIN-TIMI) 36 trial[18] did not show a reduction in adverse cardiac events in patients with ACS treated with ranolazine, but did show a reduction in recurrent ischemia in the postinfarction period; however, there was also no increase in safety outcomes, including symptomatic documented arrhythmias or total mortality.[18] A reduction in ventricular arrhythmias and hemoglobin A_{1c} was also observed in the MERLIN-TIMI 36 trial.[19] Based on the existing data of efficacy and safety, ranolazine received a Class IIa recommendation when prescribed as a substitute for β-blockers for relief of symptoms in patients with SIHD if initial treatment with β-blockers leads to unacceptable side effects or is ineffective, or if initial treatment with β-blockers is contraindicated. It also received a Class IIa recommendation, in combination with β-blockers, when prescribed for relief of symptoms when initial treatment with β-blockers is not successful in patients with SIHD.[1]

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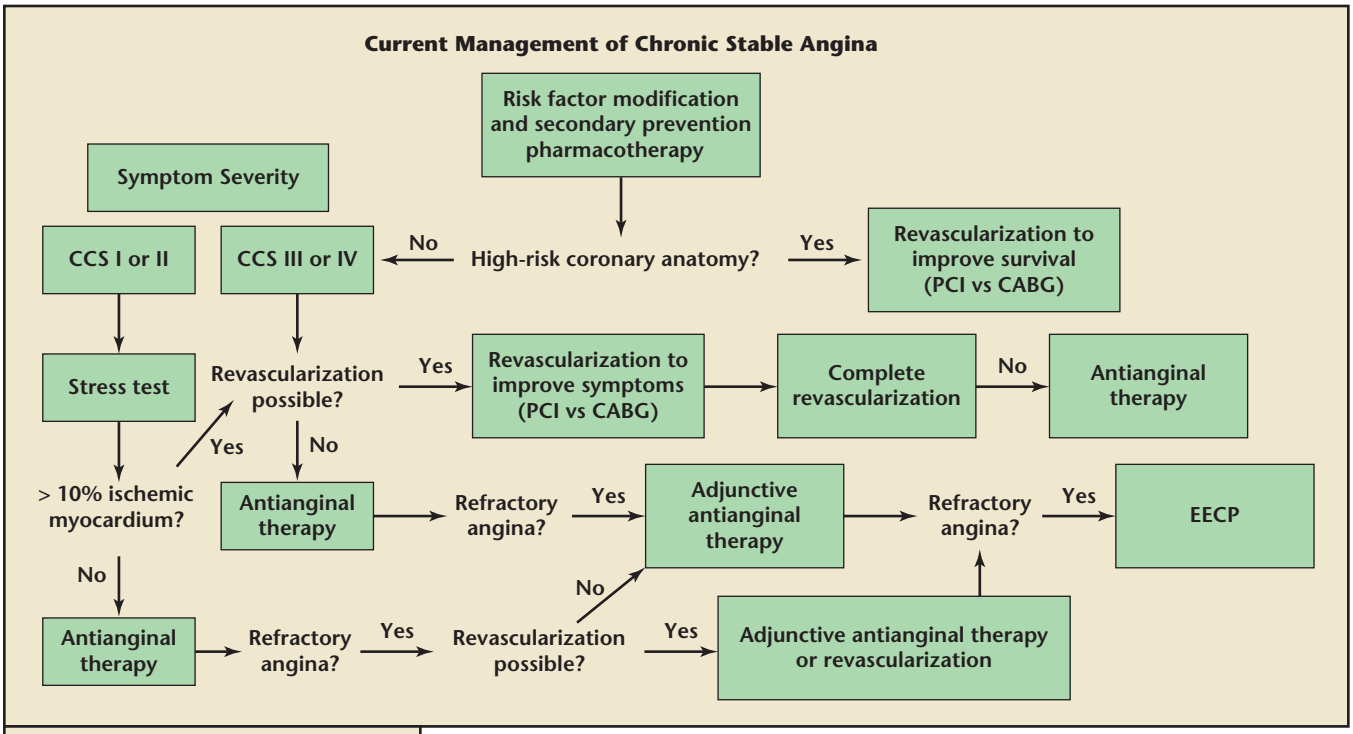
Revascularization

Any consideration of the relief of stable angina pectoris symptoms must contend with the need for and choice of revascularization. Although both percutaneous and surgical revascularization are effective modalities to ameliorate angina, due to their invasive nature, these decisions are not only the most scrutinized, but also have been the subject of extraordinary investigation, thus providing ample opportunity to practice evidence-based medicine. Along these lines, the



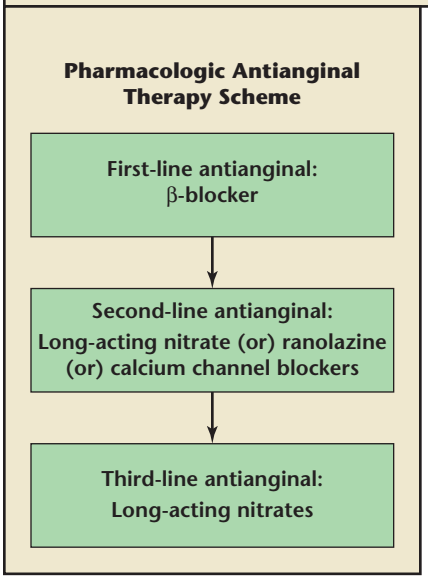


Figure 2. Strategy for medical management of chronic stable angina. CCS, Canadian Cardiovascular Society; CABG, coronary artery bypass graft; EECP, enhanced external counterpulsation; PCI, percutaneous coronary intervention.

most recent guidelines for revascularization for stable angina include the 2011 ACCF/AHA/Society for Cardiovascular Angiography and Interventions guidelines on percutaneous coronary intervention (PCI)[20] and the revised Appropriate Use Criteria (AUC) for coronary revascularization, published in 2012.[21] A key feature of the indications for revascularization in these two documents is the requirement that, in general, patients referred for coronary revascularization should be on maximal medical therapy. As a result, the decision to refer for revascularization should be based on the following criteria:

1. Results of noninvasive testing (high-risk stress tests, large areas of ischemia)
2. Extent of coronary disease (left main disease, severity of CAD burden)
3. Extent of symptoms (Canadian Cardiovascular Society [CCS] angina score)
4. The ability to maximize medical therapy

If one were to implement a guideline-based revascularization strategy, it would appear much like the one presented in Figure 2. A careful review of the current guidelines for revascularization and the appropriateness criteria, therefore, offers several insights:

1. The current guidelines support revascularization when it has been shown to improve survival, although the support for such an approach is based on earlier studies from the 1970s and 1980s that showed improved survival following surgical revascularization of left main disease over medical therapy.[22,23] In general, coronary artery bypass grafting (CABG) is the recommended means of revascularization for left main disease, except in cases of low PCI procedural risk (Synergy Between PCI With TAXUS and Cardiac Surgery [SYNTAX] score < 22, ostial or trunk left main) and high surgical risk. Other scenarios that receive a Class I recommendation to improve survival is CABG for three-vessel disease, CABG for disease in the proximal left anterior descending (LAD) artery plus one other vessel, and revascularization (PCI or CABG) for

survivors of sudden cardiac death with presumed ischemia-mediated ventricular tachycardia.[1]

2. Revascularization is supported when large areas of ischemia are identified on stress test. Patients with high-risk stress test results and large areas of ischemia have better survival with revascularization compared with those treated medically.[24] Therefore, in the recent AUC, almost all scenarios of patients with high-risk findings on noninvasive testing received a rating of appropriate. The exceptions were patients with chronic total occlusions who were asymptomatic or had minimal symptoms and patients with single- and two-vessel disease not involving the proximal LAD who were asymptomatic.
3. Revascularization is supported for severe, disabling angina. Patients with severe symptoms (CCS Class III or IV) have improved survival with revascularization with CABG over medical therapy.[25] This, too, is reflected in the AUC, as most patients with Class III or IV symptoms are deemed appropriate for revascularization.[21]
4. For a majority of scenarios that do not meet the above criteria, revascularization is only supported for failure of medical therapy. In patients with more mild disease (CCS Class I or II symptoms), mild to intermediate areas of ischemia on stress test, the decision to revascularize is based on the intensity of medical therapy, noninvasive risk assessment, extent of CAD, and ventricular function status.[20]

In most scenarios, the guidelines and AUC do not differentiate between the methods of revascularization. The method is often based on location and extent of anatomy, and on the level of experience at individual institutions. However, in certain situations, one method is preferred over the other. Like CABG, PCI is appropriate in two-vessel CAD with proximal LAD stenosis or three-vessel CAD with low CAD burden.[21] However, in patients with multivessel disease with high CAD burden, it is reasonable to choose CABG over PCI. This is, in large part, based on the one large, randomized trial evaluating CABG versus drug-eluting stents, the SYNTAX trial.[26] In post hoc analysis of that trial, patients with a low SYNTAX score (≤ 22) had similar major adverse cardiac events (MACE; a composite of death, stroke, MI, or repeat revascularization during the 3 years after randomization) between CABG and PCI, but patients with intermediate or high SYNTAX scores (≥ 23) had more MACE in the PCI group. In addition, it is also appropriate to pursue PCI in patients with prior CABG with multiple failed grafts and the left internal mammary artery has already been used and is no longer functional.[20]

Heart Team Approach

An important recommendation of the current guidelines is the concept of shared decision making, using a Heart Team approach. Thus, the decision to proceed with revascularization (and the type of revascularization) or to treat with goal-directed optimal medical therapy should be a collaborative approach of the heart team. The Heart Team should consist of an interventional cardiologist, a cardiac surgeon, and the patient's general cardiologist. A careful assessment of the current guidelines and the AUC demonstrates that this stepwise approach to revascularization is recommended, not as a means to limit patient access to revascularization, but to identify areas in which existing evidence would clearly support the revascularization decision and the type of revascularization.[20,21]

Gaps in Guidelines and AUC

No one single approach, however extensive, can claim to account for all the differences and nuances in clinical presentation in SIHD. Nonetheless, it can provide a framework for making decisions in these patients.

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To fill the gap in terms of the complexity of applying guidelines and AUC into practice, the specialty societies have developed education and quality improvement initiatives that not only educate physicians, but also provide easily accessible tools to help in real-time management of patients. One such tool is the Society for Cardiovascular Angiography and Interventions Quality Improvement Toolkit (SCAI-QIT) Catheterization Laboratory AUC & Guidelines App that is available on the SCAI Web site (http://www.scai-qit.org), and is meant to be used as a desktop application applied in real time to help guide revascularization decisions.

Even when applied appropriately, limitations of current guidelines must be acknowledged. The benefit of revascularization on survival is based on data collected

when medical therapy (both secondary prevention and symptom relief) was limited. For instance, the stated benefit of CABG over medical therapy in patients with left main and significant coronary disease is based on studies from the 1970s and 1980s. In those studies, the main medical therapy was β-blockers and nitrates. Since then, medical therapy has significantly improved. Now, with the addition of medications such as ACE inhibitors and HMG-CoA reductase inhibitors, this benefit might be minimized. The more contemporary Medicine, Angioplasty, or Surgery Study (MASS) II[27] trial showed no mortality benefit, but reduced MACE with CABG over PCI and optimal medical therapy in patients with multivessel disease. However, even in MASS II, the rate of medical therapy was low, with rates of ACE inhibitor use in the 20% to 30% range and rates of β-blocker, aspirin, and statin use in the 40% to 80% range.[28]

Although the guidelines support revascularization in the presence of ischemia, the evidence for such an approach is not based on large-scale randomized clinical trials. The International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial will begin soon and it is hoped that it will clarify this (http://www.clinicaltrials.gov/ct2/show/NCT01471522).

Even in patients with left main CAD, the evidence demonstrating a benefit of CABG over PCI for revascularization of left main disease was based on older studies. Recently, there have been multiple randomized studies comparing CABG with PCI using drug-eluting stents. In a recent meta-analysis of CABG versus PCI for left main disease, PCI was associated with nonsignificantly different 1-year rates of MACE and cerebrovascular events, MI, and death, and lower rate of stroke but a higher rate of target vessel revascularization.[29] Perhaps with further use of newer-generation drug eluting stents, these differences might even be erased.

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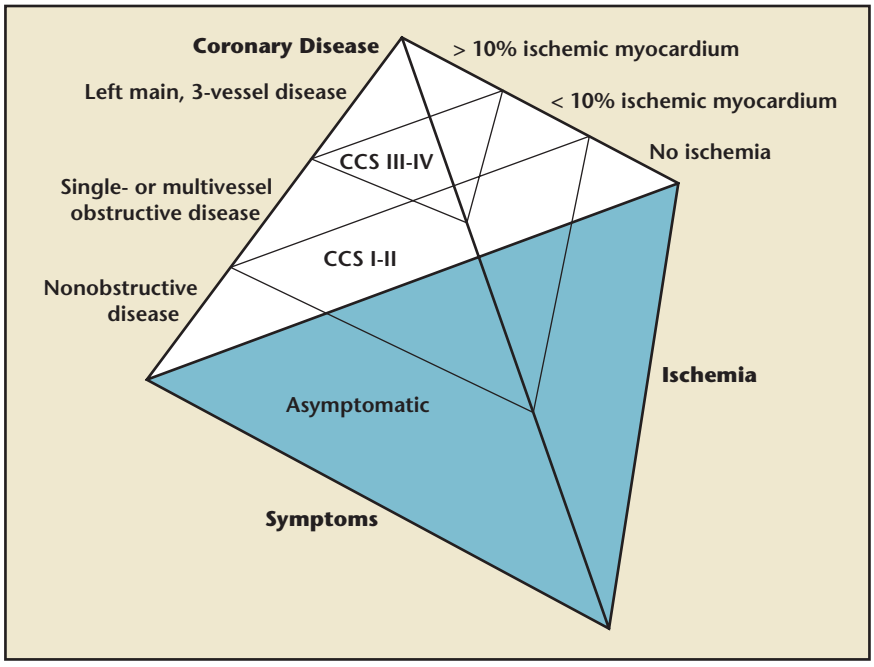
Despite these limitations, perhaps, the biggest strength of the current guidelines and the AUC for revascularization procedures rests on its focus on optimization of medical therapy as a primary treatment strategy for a large number of patients. We know that patients presenting with SIHD all fall on a spectrum of severity, from patients without symptoms and less severe degrees of CAD and ischemia, to those with severe symptoms, extensive CAD, and severe or extensive ischemia. Conceptually, this schema might be represented as a pyramid with the larger number of patients with lesser degrees of coronary disease and ischemia forming the base and a correspondingly smaller proportion of patients with more extensive disease and more severe symptoms reaching the apex (Figure 3). In this framework, the AUC support revascularization in those patients higher on the pyramid, whereas for those at the base of the pyramid (which comprises the majority of patients with ischemic heart disease), initial medical therapy including both secondary prevention strategies and antiischemic agents is recommended, and revascularization is reserved for those who fail medical therapy. In particular, the definition of optimization of antianginal therapies requiring the use of at least two classes of agents represents a

Figure 3. Strategy for revascularization for chronic stable angina refractory to medical therapy. CCS, Canadian Cardiovascular Society.



significant advance in laying the groundwork for uniformity of definition of failure of medical therapy. In addition, the guidelines and AUC do not recommend a single strategy for optimal medical therapy, in part because the use of a specific antianginal agent should be driven by a consideration of the underlying clinical condition and allow the practitioner to tailor the regimen according to the patient's tolerance of the various antianginal medications.

Alternative Therapies

Despite advances in medical therapy, surgical techniques, and stent development, there are still a significant number of patients who are unable to achieve relief from angina. Several novel pharmacologic and mechanical therapies have been investigated. Although they were not considered to have sufficient evidence to warrant specific recommendations at the time of the most recent guidelines update, they do warrant further discussion. Although these agents are unavailable in the United States, they are available in several markets in Europe, Asia, and South America.

There are limited data suggesting that allopurinol, which decreases myocardial oxygen demand in heart failure patients, reduces angina-free exercise duration.[30] Some agents, such as trimetazidine, perhexiline, and nicorandil, are not available in the United States. Others, such as endothelin receptor blockers and testosterone, which are approved for other conditions, will require significantly more clinical trial data before they should be considered.

Nonpharmacologic Therapies

The benefits of enhanced external counterpulsation (EECP) were demonstrated in the Multicenter Study of Enhanced External Counterpulsation (MUST-EECP) trial,[31] which randomized patients to 35 hours of active or inactive counterpulsation. The group that underwent active EECP had fewer episodes of angina and increased exercise time to ischemia. Furthermore, it was well tolerated. Observational studies have also demonstrated safety and efficacy out to 2 years following EECP.[32] Transmyocardial laser revascularization (TMLR) has been shown in some studies to improve symptoms in refractory angina. However, the only blinded study of TMLR failed to show benefit.[33] Data on the use of spinal cord stimulation at the T1 to T2 level is another technique that requires more data.

Thoracic sympathectomy was first performed in the 1920s and can now be performed thoracoscopically. It can be considered as a last line of therapy for refractory nonrevascularizable angina, though there have been no recent studies comparing it with other modern therapies. EECP, spinal cord stimulation, and TMLR receive a Class IIb recommendation as alternative therapies for relief of symptoms in patients with refractory angina.[1]

Conclusions

A treatment protocol for patients with chronic CAD needs to meet two goals: reducing future cardiovascular events and eliminating anginal symptoms. Cardiovascular event rate reduction is achieved with the use of multiple medications, including antiplatelet agents, HMG-CoA reductase inhibitors, ACE inhibitors, and ARBs, in addition to lifestyle modifications. Elimination of anginal symptoms has been enhanced with the addition of ranolazine, along with the older agents, including β-blockers, nitrates, and CCBs, and improvements in revascularization strategies, particularly percutaneous coronary approaches. The management of patients with SIHD requires consideration of risk factors, comorbidities, symptoms, coronary anatomy, and ischemic burden. The medical team has a variety of tools at its disposal, ranging from lifestyle modification and pharmacotherapy to percutaneous and surgical procedures. When deciding on a therapeutic strategy it is important to make a distinction between the goals of secondary prevention and symptom relief, especially when revascularization is being considered. Medical treatment of angina often requires multiple drugs, and may include newer agents and procedures as adjunctive or alternative therapy. American and European cardiology societies will need to consider current and future research when updating their guidelines in order to help clinicians make optimal use of all available treatments. ■

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MAIN POINTS

- Currently available classes of antianginal therapies in the United States include β-blockers, nitrates, calcium channel blockers, and ranolazine. The use of these antianginal agents is recommended in the current guidelines and often forms an important measure for classifying appropriateness of revascularization.
- The decision to refer for revascularization should be based on the following criteria: (1) results of noninvasive testing (high-risk stress tests, large areas of ischemia), (2) extent of coronary disease (left main disease, severity of coronary artery disease burden), (3) extent of symptoms (Canadian Cardiovascular Society angina score), and (4) the ability to maximize medical therapy.
- In most scenarios, guidelines and appropriate use criteria (AUC) do not differentiate between the methods of revascularization.
- To bridge the gap in terms of the complexity of applying guidelines and AUC into practice, specialty societies have developed education and quality improvement initiatives that both educate the physicians and provide easily accessible tools to help in real-time management of patients. One such tool is the Society for Cardiovascular Angiography and Interventions Quality Improvement Toolkit.
- The stated benefit of coronary artery bypass grafting over medical therapy in patients with left main and significant coronary disease is based on studies from the 1970s and 1980s. In those studies, the main medical therapy was β-blockers and nitrates. Since then, medical therapy has significantly improved. American and European cardiology societies will need to consider current and future research when updating their guidelines in order to help clinicians make optimal use of all available treatments.

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