Evaluating Medical, Percutaneous Coronary Intervention, and Coronary Artery Bypass Surgery Options for Chronic Angina: An Update of the Revised Guidelines

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Medical therapy is the standard background treatment for all patients with chronic stable angina. Studies show that antianginal therapies such as late sodium channel blockers (ranolazine), β-blockers, calcium channel blockers, and nitrates dispensed alone or in combination can alleviate angina and angina-equivalent symptoms. For risk reduction of ischemic events, modification of coronary risk factors with lifestyle modification and medical therapy is the cornerstone. Effective risk modification strategies include lipid management, smoking cessation, diabetes control, weight management, nutritional enhancements, and physical activity. The pursuit of a more definitive treatment for chronic angina should be guided by the patient's clinical presentation, results of imaging-based risk-stratification evaluations, response to medical therapies, and patient preference. Revascularization by percutaneous coronary intervention or coronary artery bypass surgery may be recommended for patients who have persistent and intolerable symptoms despite optimal medical therapy and for those who are likely to have a survival benefit from revascularization based on the severity and location of the atherosclerotic lesions.

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Current treatments for patients with chronic stable angina can be differentiated between those that relieve symptoms of ischemia and those that offer broad reduction in the risk of major adverse cardiovascular events (hospitalization, disease progression, myocardial infarction [MI], and death) (Table 1). Revascularization is a key approach, but other therapies are also effective,

Table 1
Dual Goals of Management of Coronary Artery Disease

Risk Reduction of Ischemic Events	Treatment of Symptoms
Objective	Objective
Reduce the risk of recurrent cardiovascular events and/or mortality	Reduce symptoms to increase exercise tolerance and functional capacity
Control of Risk Factors to Goal • Smoking (cessation) • Hyperlipidemia (LDL < 70) • Hypertension (blood pressure < 130/85) • Diabetes (hemoglobin A_{1c} < 7)	Revascularization • PCI or CABG
Pharmacologic Therapy • Aspirin • Clopidogrel (post-ACS/stent) • ACE inhibitor/ARB • β-Blocker • Statin	Exercise Training Anti-Ischemic Therapy • β-blockers • Nitrates • Calcium antagonists • Ranolazine

ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; LDL, low-density lipoprotein; PCI, percutaneous coronary intervention.

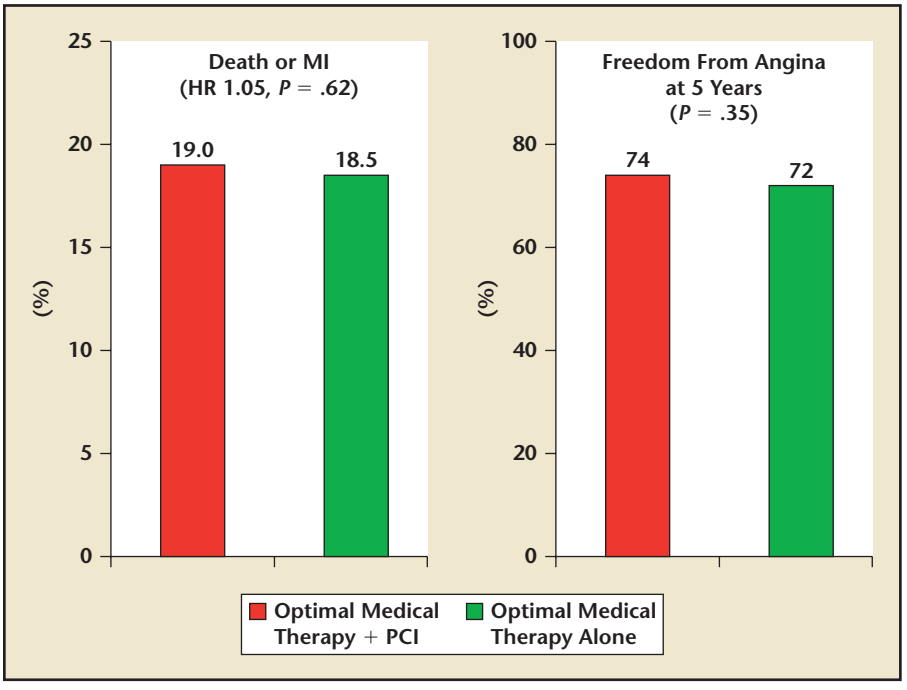
notably exercise training and several of the anti-ischemic therapies, such as β-blockers, nitrates, calcium antagonists, and ranolazine. For risk reduction of ischemic events, risk factor management and medical therapy are the cornerstones. It should be emphasized that medical therapy (summarized in the section below) is the standard background treatment for all patients. Revascularization is applied for relief of symptoms in the vast majority of patients in whom it is used, although in some circumstances, it can also lead to a reduction in mortality—but this is not often the situation. Thus, revascularization has a key place, definitely for symptom relief and sometimes to improve outcomes. This article will examine invasive and conservative approaches to patients with chronic angina.

Invasive Versus Conservative Approach

Recent data from 2 landmark studies have shown that optimal medical therapy is as effective as revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) surgery in reducing the risk of adverse clinical outcomes (death, MI, or other major cardiovascular events). In the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, PCI added to optimal medical therapy did not reduce the incidence of adverse cardiovascular outcomes (death, MI), as compared with optimal medical therapy alone, during follow-up of 2.5 to 7 years (Figure 1).[1] Although the degree of angina relief was significantly higher in the PCI group than in the medical therapy group, there was substantial improvement in the medical therapy group as well. Optimal medical therapy is the first-line treatment for patients with chronic stable angina.

The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial in patients with diabetes, coronary artery disease (CAD), and classic angina compared the effects of prompt revascularization

Figure 1. *In the COURAGE trial,[1] PCI added to optimal medical therapy did not reduce the incidence of adverse cardiovascular outcomes (death, MI), as compared with optimal medical therapy alone, during follow-up of 2.5 to 7 years. COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention. Reprinted with permission from Cardiosource.*



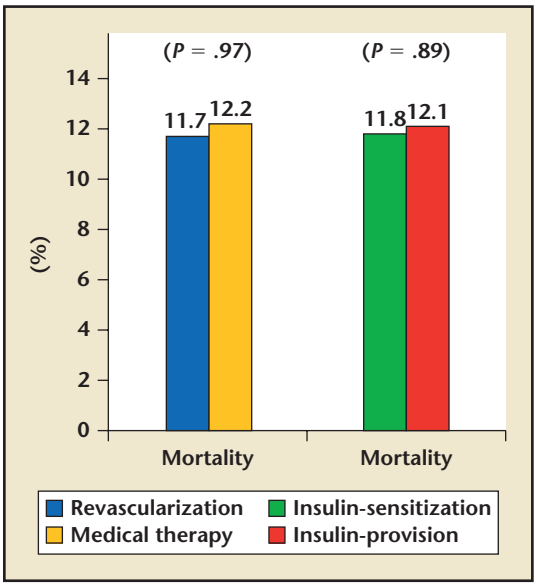


Figure 2. *Data from the BARI 2D trial[2] showed no difference in the primary outcome of all-cause mortality between the revascularization and medical therapy groups. BARI 2D, Bypass Angioplasty Revascularization Investigation 2 Diabetes. Reprinted with permission from Cardiosource.*

by discretionary CABG or PCI with medical therapy alone on clinical outcomes. During the 5-year follow-up, there was no difference in the primary outcome of all-cause mortality between the revascularization and medical therapy groups (Figure 2).[2] Similarly, the rates of freedom from major cardiovascular events also did not differ significantly among the groups: they were 77.2% in the revascularization group and 75.9% in the medical therapy group ($P = .70$). A stratified randomization was carried out based on the type of planned revascularization. In those deemed to need CABG, who were then randomized to CABG or medical therapy, a significant reduction was seen in the composite secondary endpoint among patients randomized to CABG compared with those randomized to medical therapy (22.4% vs 30.5%), and this was predominantly driven by a reduction in MI (7.4% vs 14.6%). In the stratum of patients deemed able to undergo PCI, who were randomized to PCI versus medical therapy, there was no difference in the secondary endpoint among patients treated with PCI or optimal medical therapy. Overall, among patients randomized to optimal medical therapy, 42% crossed over and received revascularization therapy during the follow-up period for worsening symptoms. The results of this trial show that optimal medical therapy is a very reasonable primary approach to diabetic patients with chronic angina and that CAD in diabetic patients represents a disease state that can be rapidly progressive.

Subgroups Who May Benefit From Revascularization

Coronary revascularization is often needed for symptom relief, and in some patient populations, it can be life-saving. The pursuit of revascularization for chronic angina should be guided by the patient's response to medical therapies, results of imaging-based non-invasive risk-stratification, and patient preference. Patients who experience recurrent angina despite optimal medical therapy should be considered for more invasive approaches. The subject of imaging-based risk stratification is very well described in the article by Lepor and Pohost in this issue.

Although the COURAGE trial showed no overall benefit on death or MI of PCI over optimal medical therapy, symptoms of angina were significantly reduced with the use of PCI. Rates of angina were significantly lower in the PCI group than in the medical therapy group during the first 3 years of follow-up, and the rates of subsequent revascularization were likewise lower.

However, one subgroup that emerged from the COURAGE trial where a clinical benefit on events was seen was the group with severe ischemia on nuclear imaging. The COURAGE trial nuclear substudy compared the effectiveness of PCI added to optimal medical therapy for ischemia reduction with the use of myocardial perfusion single-photon emission computed tomography (MPS).[3] Of the 2287 COURAGE patients, 314 were enrolled in this substudy and underwent serial rest/stress MPS performed before treatment and 6 to 18 months after randomization. At follow-up, the reduction in ischemia was greater with PCI plus optimal medical therapy than with optimal medical therapy alone ($P = .0001$). Patients with significant ischemia reduction had a lower unadjusted risk for death or MI, particularly if baseline ischemia was moderate to severe ($P = .001$ [risk-adjusted, $P = .08$]). The results of this substudy concluded that a reduction of ischemic burden, whether by medical or revascularization therapy, is associated with a reduction of adverse cardiac events. When moderate or severe ischemia was present, PCI seemed to provide a greater reduction in ischemic burden compared with optimal medical therapy and in those patients achieved a greater survival benefit compared with optimal medical therapy.

A second subgroup of patients who may benefit from a revascularization

strategy are those with documented silent ischemia. The Asymptomatic Cardiac Ischemia Pilot (ACIP) study published in 1994 of 558 patients with asymptomatic or well-controlled angina but ambulatory electrocardiography (ECG) evidence of ischemia demonstrated a more favorable outcome (absence of cardiac ischemia on the 48-hour ambulatory ECG at the 12-week visit and at 1-year and 2-year follow-up) for those patients randomized to revascularization (percutaneous or surgical) than those patients who continued medical management (atenolol-nifedipine or diltiazem-isosorbide dinitrate).[4] The frequency of MI, unstable angina, stroke, and congestive heart failure was not significantly different. Thus, patients with angina should be continually re-evaluated for progression and subsequent modification of treatment regimens.

Therefore, revascularization by PCI may be recommended for patients who have persistent and intolerable symptoms despite optimal medical therapy and for those who are likely to have a survival benefit from revascularization based on the severity and location of the atherosclerotic lesions. American College of Cardiology/American Heart Association (ACC/AHA) treatment guidelines[5] for chronic stable angina recommend:

- PCI for patients with 2- or 3-vessel disease and significant proximal left-anterior descending artery coronary heart disease who have anatomy suitable for catheter-based therapy and normal left ventricular function and who do not have treated diabetes.
- PCI or CABG for patients who have not been successfully treated by medical therapy and can undergo revascularization with acceptable risk.
- PCI or CABG for patients with 1- or 2-vessel coronary heart disease without significant proximal left-anterior descending artery disease but with a large area of viable myocardium and high-risk criteria on noninvasive testing.
- PCI or CABG for patients with prior PCI to treat recurrent stenosis associated with a large area of viable myocardium or high-risk criteria on noninvasive testing.

Evolution of Percutaneous Coronary Intervention

The earliest form of percutaneous mechanical revascularization therapy, percutaneous transluminal coronary angioplasty (also known as balloon angioplasty), simply dilated focal coronary stenoses. However, recoil of the artery and local restenosis led to the need for repeat intervention in 25% to 40% of patients.[6] Major predictors of restenosis include clinical variables (diabetes, type of acute coronary syndrome, prior restenosis), angiographic data (vessel location, vessel diameter, lesion parameters), and postprocedure results (residual stenosis, minimal luminal diameter).

The advent of stents to maintain patency of stenosed or occluded coronary arteries provided the advantages of improved initial results with angioplasty by reducing elastic recoil and treating dissections and prevention of restenosis of the target lesion. The longer-term clinical benefits are not in reducing clinical events (death, MI), but rather in reducing repeat procedures due to restenosis.[7] In an effort to address the problem of in-stent restenosis, drug-eluting stents were developed. Their coating of immunomodulators (sirolimus, paclitaxel, and everolimus) arrests the cell cycle, thereby limiting local smooth muscle proliferation. This advance has dramatically reduced not only angiographic evidence of in-stent progression of disease, but also target vessel revascularization.[7] However, because these agents are not precisely specific to cell type, they also prolong the protective process of stent endothelialization leading to a small predisposition to very late stent thrombosis and longer duration use of dual antiplatelet therapy.

Coronary Artery Bypass Grafting

CABG is the most invasive method of coronary revascularization, although not usually the first choice. It remains an important treatment for CAD, particularly in those patients with diffuse coronary disease (3-vessel disease), coronary vessels not amenable to stenting (due to size, tortuosity, or characteristics of the lesions), or disease of the left main coronary artery.

The 2002 ACC/AHA guidelines had recommended (class IA) CABG for patients with significant left main coronary stenosis, 3-vessel disease, or 2-vessel disease with significant proximal left anterior descending stenosis, with either left ventricular dysfunction or demonstrable ischemia.[8] Additionally, PCI or CABG was recommended (IB) for patients with 1-vessel or 2-vessel CAD with a large area of viable myocardium and high-risk criteria on noninvasive testing.

PCI Versus CABG Surgery

Although early complications of surgery remain more frequent and more serious than those of PCI, the long-term results of CABG have kept it an attractive procedure. Relative indications for PCI versus CABG are listed in Table 2.

Antianginal Therapies

β-Blockers

β-Blockers are recommended as the first-line therapy for patients with angina, ahead of nitrates—especially

Table 2
Indications for PCI Versus CABG for CAD

Favors PCI	Favors CABG
Discrete lesions of disease	Left main coronary artery disease
Large-caliber vessels with disease	Three-vessel disease
Single- or double-vessel disease	Diffuse disease of small vessels or vessels not amenable to stenting
Patients who are not surgical candidates	Discrete lesions not amenable to stenting
	Patients with concomitant valvular disease

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CAD, coronary artery disease.

in patients with prior or recent history of MI.[9,10] Not only can they alleviate pain by decreasing myocardial demand, but, like nitrates, β-blockers also delay onset of angina, thereby reducing or avoiding ischemia. Unlike nitrates, however, β-blockers have been demonstrated to improve survival in the secondary prevention of MI[11-14] and to aid prevention in patients with known CAD, with or without symptoms, and without history of MI. These effects are thought to be the results of β-blockers' antihypertensive and heart-rate lowering properties.

Although there is a vast amount of available data on the clinical benefit of β-blockers in patients with acute MI, there are few data on the role of β-blockers in patients with stable CAD. Despite that, the ACC/AHA 2007 guidelines update recommended β-blockers as class IA.[5] The Atenolol Silent Ischemia Study (ASIST) primarily studied the effects of a β-blocker (atenolol) versus placebo on clinical outcomes in patients with evidence of asymptomatic CAD (ischemia only during ambulatory ECG monitoring) or mildly asymptomatic CAD (Canadian Cardiovascular Society class I-II).[15] Results have shown that treatment with atenolol resulted in a significant reduction in heart rate, frequency of ischemic episodes, average duration of ischemia, and proportion of patients who experienced ischemia. There was a significantly lower risk ($P = .001$) of the primary composite clinical endpoint (including death, resuscitation from ventricular tachycardia or ventricular fibrillation, nonfatal MI, hospitalization for unstable angina, aggravation of angina requiring known antianginal therapy, or need for myocardial revascularization during the follow-up period of 12 months) in the atenolol group compared with the placebo group. It is important to note that studies have compared the effects of β-blockers with calcium channel blockers in patients with stable angina, but ASIST is the only trial comparing β-blockers with placebo in this patient population.

Some caution should be exercised in prescribing β-blockers to patients with impaired left ventricular function, advanced cardiac conduction abnormalities, obstructive lung disease (eg, asthma, coronary obstructive pulmonary disease), or peripheral arterial disease. However, the ideal approach is to try β-blockers at low doses and continue them if tolerated.

Calcium Channel Blockers

The 2007 guidelines update recommended calcium channel blockers as class IB.[5] In patients in whom β-blockers are contraindicated or insufficient to relieve angina, the use of calcium-channel antagonists is appropriate.[16] Although longer-acting, newer dihydropyridine agents, such as amlodipine, have demonstrated equivalent efficacy at relieving angina,[17] they do not yet have a track record comparable with β-blockers for reducing clinical outcomes. Also, it is important to note that in patients with angina associated with coronary artery vasospasm, calcium channel blockers are particularly effective due to their potent vasodilator effect.

Nitrates

Like the calcium channel blockers, nitrates come after β-blockers for their use in angina, and as per the ACC/AHA 2007 guidelines update, they are a class IB drug.[5] Nitrates, administered in many different ways (sublingual, oral, intravenous, and transdermal), have been the long-standing treatment of choice to relieve anginal pain, but they have never been shown to improve hard clinical endpoints; that is, patients receiving nitrates for relief of pain have not been found to experience fewer major cardiovascular events or deaths than their counterparts who experience angina without nitrates. However, nitrates have been demonstrated to improve time to anginal symptoms, exercise tolerance, and ECG changes on exercise treadmill testing, all important quality of life and prognostic indicators. As a vasodilator, nitrates improve blood flow through the coronary arteries and reduce peripheral afterload, relieving cardiac ischemia and, therefore, angina, by simultaneously increasing supply and decreasing demand. In its sublingual form, nitroglycerin is most often used for immediate relief of angina. Longer-acting preparations

of nitrates can also be used for chronic pain; however, patients can become nitrate-tolerant and experience diminishing returns unless a nitrate-free period is introduced. There are important contraindications to nitrate therapy, including any outflow obstruction (eg, hypertrophic cardiomyopathy, valvular disease) or the use of sildenafil or related compounds because such combinations can induce various degrees of hypotension.

Late Sodium Channel Blockers: Ranolazine

Ranolazine, recently approved for use in patients with chronic angina, is the first new approach to angina in 2 decades. Ranolazine is a selective inhibitor of the late sodium current relative to peak sodium channel current, and via this mechanism, it may decrease sodium-dependent intracellular calcium overload during ischemia and reperfusion.[18] Because ranolazine as compared with other conventional antianginal drugs achieves antianginal effects without affecting hemodynamic parameters (heart rate, blood pressure, preload), it can be safely used in conditions in which other antianginal medications are contraindicated or not safe to use (hypotension, bradycardia, coronary obstructive pulmonary disease, etc.).[19]

Several studies have been conducted evaluating the safety and efficacy of ranolazine and have found it to be effective in reducing symptoms of angina as a stand-alone treatment and in combination therapy. In one, ranolazine was administered at 500 mg to 1500 mg twice daily.[20] It found a significant increase in exercise duration during a follow-up of 12 to 24 months. Another study using ranolazine at 1000 mg twice daily in patients who were still experiencing angina on maximum doses of amlodipine showed that addition of ranolazine significantly reduced the frequency of angina episodes compared with placebo ($P = .017$).[21] Initial concerns regarding the small increase in QT interval with ranolazine have been allayed by the recent publication of the Metabolic Efficiency with Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes–Thrombolysis In Myocardial Infarction 36 (MERLIN-TIMI 36) trial.[22] Clinically significant ventricular arrhythmias on Holter monitoring occurred less frequently in the ranolazine group (73.7% vs 83.1%; $P < .001$). Syncope as an adverse event was reported in 3% of the ranolazine group and 2% of the placebo group ($P = .01$).[22] Of unclear significance is the association between the use of ranolazine and significantly improved hemoglobin A_{1c} in patients with diabetes mellitus; ranolazine reduced the incidence of increased hemoglobin A_{1c} in those without evidence of previous hyperglycemia.[23]

Antiplatelet Therapy: Aspirin

Use of daily aspirin for primary and secondary prevention of CAD events has been the cornerstone of therapy, and remains so. The Antiplatelet Trialists Collaboration meta-analysis[24] and subsequent studies have revealed a robust 30% reduction in CAD morbidity and mortality in patients with stable angina. Few pharmacological therapies available today have such a magnitude of treatment effect. Therefore, ACC/AHA guidelines in 2002[8] and the update in 2007[5] have recommended the use of aspirin as a class IA drug.

As an alternative or adjunct to aspirin, clopidogrel has demonstrated efficacy in secondary prevention of major adverse cardiovascular events, especially after an acute coronary syndrome or PCI, but it does not appear to be beneficial for treatment in the primary prevention setting.[25]

ACE Inhibitors and Angiotensin Receptor Blockers

Angiotensin-converting enzyme (ACE) inhibitors are recommended as a class IA therapy by the ACC/AHA 2007 guidelines update. They are recommended for all patients with left ventricular ejection fraction less than 40% and in those with history of diabetes, hypertension, or chronic kidney disease. These recommendations have come from 2 large, randomized controlled trials: the Heart Outcomes Prevention Evaluation (HOPE) trial[26] and the European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA).[27] These trials have shown that ACE inhibitors significantly lower risk of cardiovascular death, MI, and resuscitated arrest as compared with placebo. The ACC/AHA 2007 guidelines update has recommended angiotensin receptor blockers as a class IA drug in patients who have indications for ACE inhibitors but are unable to tolerate them.

Risk Factor Modification

Lipid Management

Lipid management, including assessment of a fasting lipid profile, is a class IA recommendation in the ACC/AHA guidelines. The recommended low-density lipoprotein cholesterol (LDL-C) goal is less than 100 mg/dL (IA) and, if baseline LDL-C is greater than or equal to 100 mg/dL, further lowering should be initiated to achieve a 30% to 40% reduction (IA). The National Cholesterol Education Program Guidelines also set out a "therapeutic option" of a target LDL-C of less than 70 mg/dL.[28]

As the source of the culprit atherosclerotic plaques in angina, reducing serum LDL-C has been shown to drastically improve clinical outcomes and even regress plaque size by some measures. The placebo-

controlled trials, both for primary and secondary prevention, were summarized in the Cholesterol Treatment Trialists' (CTT) meta-analysis.[29] This collective experience of more than 90,000 patients in 14 randomized trials demonstrated a significant 12% reduction in all-cause mortality for every mmol/L (~38 mg/dL) reduction of LDL-C, significant within the first year of treatment. This was true even for patients who started in the lowest range of LDL-C levels (≤ 3.5 mmol/L ~133 mg/dL), as well as those with higher LDL-C values.

Therapy to increase high-density lipoprotein cholesterol (HDL-C) has also demonstrated efficacy, preventing clinical events in patients with established CAD. The 6% increase in HDL-C and the 31% decrease in triglycerides as a result of gemfibrozil therapy in the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT) produced a significant 24% reduction in death, nonfatal MI, and stroke.[30]

Cigarette Smoking Cessation (IB Recommendation)

In patients who smoke, quitting can be the single most effective prevention strategy available to them, even beyond the effects of daily aspirin prophylaxis. In 2003, Critchley and Capewell[31] reviewed outcomes on more than 12,000 patients in trials of smoking cessation to quantify a 36% relative risk reduction for those patients who quit smoking. Although difficult and usually requiring an average of 3 attempts before long-term success, the dividends are well worth it. Physicians should stress to such patients that there is no other therapy that will prevent them from having an MI more effectively than smoking cessation.

Diabetes Control (IB Recommendation)

Control of diabetes is a mainstay, although the exact degree has recently become a bit uncertain. The UK Prospective Diabetes Study (UKPDS)[32] compared conventional glucose control (fasting glucose < 15 mmol/L) to an intensive strategy (< 6 mmol/L) in more than 4000 patients. Early data from UKPDS demonstrated the relationship between glycated hemoglobin A_{1c} and microvascular events, and only hinted at a relationship with acute myocardial infarction rates. Other trials have also been mixed, with some benefits seen in some trials, but not in others. Thus, in patients with diabetes and angina, keeping the hemoglobin A_{1c} below 7% has been in the guidelines and generally is still accepted.

Weight Management (IB Recommendation)

As the first-line therapy for general cardiovascular risk reduction, dietary modification can reduce both blood pressure and LDL-C,[28,32-34] thereby decreasing the risk of events for patients with and without angina. Dietary therapy should include reduction of saturated fats (to < 7% of total calorie consumption), cholesterol, and trans fats (IB). The ACC/AHA guidelines encourage the use of omega-3 fatty acids in the diet (IIB).[5] The beneficial effects of regimented dietary modification have been proven. The key continues to be long-term adherence to sometimes drastic, undesirable lifestyle modification.

Education

As with all chronic diseases, patient education can have an enormous impact on commitment to therapies, quality of life, and overall well-being. Patients with angina should understand their condition, be aware of the signs of worsening angina or unstable angina, and participate in regular health maintenance.

Main Points

- Optimal medical therapy is the first-line treatment for all patients with chronic stable angina.
- Patients who experience recurrent angina or have signs of severe ischemia despite optimal medical therapy should be considered for more invasive approaches, such as percutaneous coronary intervention or coronary artery bypass grafting.
- β-Blockers have been demonstrated to improve survival in the secondary prevention of myocardial infarction and to aid prevention in patients with known coronary artery disease, with or without symptoms, and without history of myocardial infarction.
- Ranolazine, a late sodium channel blocker, achieves antianginal effects without affecting hemodynamic parameters (heart rate, blood pressure, preload).
- Reduction of serum low-density lipoprotein cholesterol has been shown to drastically improve clinical outcomes and even regress plaque size by some measures.
- Dietary modification can reduce both blood pressure and low-density lipoprotein cholesterol, thereby decreasing the risk of events for patients with and without angina.

Physical Activity
(IB Recommendation)
Studies have demonstrated the benefits of exercise, either as leisure activities or as structured, cardiac rehabilitation. Physical activity of 30 to 60 minutes, 7 days per week (minimum 5 days per week) is recommended by the ACC/AHA.[5] Physical activity has been shown to improve cardiorespiratory fitness and to even halt or regress atherosclerosis in a dose-response fashion.

Conclusion

Treatments for patients with chronic angina include medical therapies, revascularization, and lifestyle modification. Antianginal therapies, including β-blockers, calcium channel blockers, nitrates, and the late sodium channel blocker ranolazine, have been shown to be effective in many studies. Revascularization can improve symptoms in patients who do not benefit from medical therapy and in those with large ischemic burdens. Effective lifestyle modifications include lipid management, smoking cessation, diabetes control, weight management, patient education, and physical activity. New trial data have provided important insights that should influence the selection of therapeutic options for these patients. ■

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