Care after Coronary-Artery Bypass Surgery

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A 71-year-old woman who had a myocardial infarction five years previously and underwent coronary-artery bypass surgery six months ago visits a primary care physician. She had no complications after surgery, but intraoperative transesophageal echocardiography revealed a grade V atheroma in the descending aorta. She has no cardiac or neurologic symptoms but notes that she feels depressed and has difficulty concentrating. She had not been depressed before. Her blood pressure is 110/80 mm Hg, and her pulse is 76 and regular. The physical examination is notable only for a weight of 160 lb (72 kg) at a height of 5 ft 4 in. (1.6 m). The fasting plasma glucose level is 109 mg per deciliter (6.1 mmol per liter), the low-density lipoprotein cholesterol level is 128 mg per deciliter (3.3 mmol per liter), the high-density lipoprotein cholesterol level is 40 mg per deciliter (1.0 mmol per liter), and the triglyceride level is 200 mg per deciliter (2.3 mmol per liter). What would you advise to improve her long-term outcome?

Despite the fact that an increasingly older population with a higher rate of coexisting conditions is undergoing coronary-artery bypass grafting (CABG), outcomes have been improving steadily. Over the long term, patients with successful CABG may be at risk for angina, myocardial infarction, or stroke, as well as for cognitive deterioration and depression. In this article we focus on CABG with cardiopulmonary bypass, since the long-term outcomes of “off-pump” surgery remain to be defined.

After CABG, the majority of patients report a clinically significant improvement in physical function and energy level.† Despite the risk for angina, myocardial infarction, or stroke, and cognitive deterioration or depression, patients who want to work are doing so by one year after surgery. By five years after CABG, anginal symptoms recur in 15 percent of patients, and 10 percent have ischemic events.† Patients who have had a postoperative myocardial infarction have a risk of angina and ischemic events that is two to three times as high as that in patients who have not had such an infarction.† By 10 years after surgery, patients who have received internal-thoracic-artery grafts have a mortality rate that is 10 percent lower than that among patients who have had saphenous-vein grafts.

Stroke is a less common long-term problem. The single most important cause of stroke is aortic atheromatous disease, which is detected with high reproducibility by intraoperative transesophageal echocardiography or epiaortic scanning.‡,§ Patients with large (>5 mm) or mobile aortic atheromas have an increase in the rate of perioperative stroke by a factor of 5 to 10 and are likely to have a significantly increased long-term risk of stroke.

Up to 27 percent of patients report some forgetfulness after CABG, but most of these patients have no measurable impairment on neuropsychological testing.∥ Comparing a given patient’s preoperative and postoperative scores on neuropsychological tests is the only certain method of evaluating the cognitive effects of cardiac surgery, but such
testing is rarely performed before surgery. The reported rates of cognitive deterioration six months after CABG vary widely, from 5 percent to over 33 percent. This large variation reflects differences in study methods, including the specific tests used, the criteria for deterioration on each test, and the ways of combining the results of different tests to determine whether or not the patients had cognitive deterioration.

Patients who are depressed after CABG surgery may not have obvious affective features; they tend to have more cognitive and functional impairment than other surgical patients and are more likely to perceive themselves as having had cognitive deterioration after surgery. Thus, patients who report having impaired memory or cognition should be evaluated for depression. Between 25 and 50 percent of patients who undergo CABG have symptoms of depression before surgery; such patients typically have greater emotional stress and less social support than other patients before surgery. About half of those who are depressed before surgery have resolution of depressive symptoms by six months after CABG.

Patients who have had rapid progression of cardiac symptoms before surgery are at particular risk of worsening depressive symptoms after surgery. About 18 percent of patients who are not depressed before surgery have a significant increase in depressive symptoms after surgery. These newly depressed patients are at higher risk than nondepressed patients for long-term cardiovascular events and death from cardiovascular causes. These findings are consistent with data showing that patients with coronary heart disease who have more symptoms of depression also have an increased risk of cardiovascular events. Progressive atherosclerosis may be responsible for both depression and subsequent cardiovascular events.

### Strategies and Evidence

#### Changes in Lifestyle

Changes in lifestyle to reduce cardiovascular risk are especially important after CABG. In patients enrolled in the Bypass Angioplasty Revascularization Investigation (BARI), health behavior was significantly improved one year after CABG. The proportion of patients who smoked decreased from 24 percent to 12 percent; the proportion participating in regular exercise increased from 16 percent to 47 percent; and the percentage of patients who reported that they followed a low-fat diet increased from 34 percent to 72 percent (although lipid levels were unchanged). Nonetheless, many patients do not adopt such changes in lifestyle after CABG, and the best strategies for motivating patients to initiate and maintain such changes have not been clearly identified.

#### Smoking Cessation

Patients who quit smoking after CABG have a survival benefit of 3 to 5 percent at 5 years and a benefit of 15 percent at 10 to 20 years, as compared with those who continue to smoke. Patients who quit smoking are also less likely to require repeated CABG and have half the rate of subsequent myocardial infarction. The risk associated with nicotine-replacement therapy is no greater than that associated with smoking, and such an approach to helping patients quit smoking should be considered. Bupropion should be used with caution in patients who have recently had a myocardial infarction.

#### Cardiac Rehabilitation

Cardiac rehabilitation programs, which focus on monitored aerobic exercise as well as the reduction of risk factors (smoking cessation, control of hypertension and hyperlipidemia, and psychosocial interventions), are important for improving the quality of life after CABG. Only one small study with matched controls has suggested that rehabilitation reduces the risk of cardiac events in patients who have undergone CABG. However, exercise training improves exercise tolerance, reduces the severity of anginal symptoms, and improves both physical and psychological functioning.

#### Psychosocial Management

Overall emotional functioning or mental health generally improves 6 to 12 months after CABG. Many patients have dramatic improvements in their ability to perform daily activities after CABG. By one year, 80 percent of patients have no limitations on their social life, sex life, or hobbies, as compared with 60 percent before surgery. Patients who perceive themselves as having more social support report fewer depressive symptoms and less functional impairment at six months. Patients who adopt approaches to stress management have significantly reduced rates of cardiac events and improved quality of life. These approaches may include relaxation, meditation, individual counseling, and obtaining social support.
PHARMACOLOGIC INTERVENTIONS

Antiplatelet Drugs
Therapy with antiplatelet agents such as aspirin, started within 24 hours after CABG, reduces the risk of early occlusion of a saphenous-vein graft and remains effective in reducing the risk of occlusion for one year. Antiplatelet agents do not afford additional protection against occlusion of a vein graft between one and three years after surgery.31 However, almost half the patients who undergo CABG have had a previous infarction,32-34 and the benefit of aspirin in secondary prevention after a myocardial infarction has been well established. In one study, aspirin therapy begun after a myocardial infarction led to a 12 percent reduction in the rate of death, a 31 percent reduction in the rate of reinfarction, and a 42 percent reduction in the rate of stroke.35 Therefore, aspirin is a standard intervention for patients who have undergone CABG.

There are no conclusive data indicating that patients who are allergic to aspirin would benefit from clopidogrel therapy. However, some patients may benefit from the use of this agent after CABG. In particular, patients with a grade V aortic atheroma, among whom the risk of subsequent stroke is high, generally start to receive clopidogrel or warfarin postoperatively, although definitive evidence of benefit is lacking. Clopidogrel should probably not be used preoperatively, especially in combination with aspirin, since patients who received clopidogrel before CABG had more perioperative bleeding and required more reoperations for bleeding.36

Beta-Blockers and Angiotensin-Converting–Enzyme Inhibitors
In a large cohort of patients who underwent CABG after myocardial infarction, beta-blockers reduced one-year mortality from 12 percent to 4 percent.33 On the other hand, in a trial involving patients randomly assigned to receive metoprolol after CABG, only half of whom had had a previous myocardial infarction, there was no decrease in the rates of a composite end point including death, cardiovascular events, or the need for revascularization; however, 40 percent of patients were withdrawn from the trial because they required a beta-blocker.37 Many patients who have undergone CABG but have not had a myocardial infarction are given cardioselective beta-blockers such as metoprolol or atenolol postoperatively, primarily because of the strong evidence of the efficacy of beta-blockers after myocardial infarction.

Angiotensin-converting–enzyme (ACE) inhibitors decrease rates of myocardial infarction, stroke, and death in patients with coronary disease, although there are limited data to support their use specifically in patients who have undergone CABG. In the Heart Outcomes Prevention Evaluation (HOPE) trial, use of the ACE inhibitor ramipril decreased the rates of myocardial infarction, stroke, and death among patients with diabetes or known vascular disease but without left ventricular dysfunction36; about 25 percent of the participants had previously undergone CABG.38 The ACE inhibitor quinapril has been shown in a blinded, randomized, controlled trial to reduce the risk of ischemic events among patients who have undergone CABG but who do not have heart failure, valvular disease, or atrial fibrillation.39 In this single small trial, the rate of the combined outcome of death, myocardial infarction, recurrent angina, stroke, transient ischemic attack, or the need for reoperation decreased from 15 percent to 4 percent at one year of follow-up, with most of the decrease attributable to a lower rate of recurrent angina.39 At present, ACE inhibitors should be used as indicated for patients with coronary disease.

Lipid-Lowering Agents
There are abundant data to support the use of lipid-lowering agents in patients with ischemic disease,32,35,40 including several studies of patients who have undergone CABG. In a study involving 1351 patients who had undergone CABG with saphenous-vein grafts, aggressive lipid-lowering therapy with lovastatin, with a target low-density lipoprotein (LDL) cholesterol level of 60 to 85 mg per deciliter (1.6 to 2.2 mmol per liter), was compared with a moderate lipid-lowering strategy, with a target LDL cholesterol level of 120 to 140 mg per deciliter (3.1 to 3.6 mmol per liter).34 Although there were no differences in mortality from cardiovascular causes or the rate of myocardial infarction, there was a lower rate of revascularization in the aggressive-treatment group.34 The aggressive strategy delayed the progression of atherosclerosis regardless of age, sex, the presence or absence of hypertension, and the presence or absence of diabetes.41

Control of Blood Pressure and Diabetes
Blood-pressure control reduces the extent of progression of atherosclerosis in patients who have undergone CABG with saphenous-vein grafts and, as is well recognized,42 reduces the risk of stroke and
recurrent myocardial infarction in the general population. Although the BARI trial established that among patients with diabetes, CAGB leads to a greater improvement in survival than does angioplasty, whether control of the blood glucose level after CAGB reduces the long-term risk of cardiovascular events has not been evaluated. It is clear that patients with diabetes who undergo CAGB are at high risk for subsequent cardiovascular events, and aggressive lipid-lowering therapy may be especially important in this group.

Treatment of Depression
Several strategies, including the use of selective serotonin-reuptake inhibitors and cognitive–behavioral therapy, have been useful in treating depression in the general population. However, there are limited data about the effectiveness of interventions targeted at patients with depression after CAGB. Patients with cardiac disease who are depressed may have relief of depressive symptoms and improved quality of life with cardiac rehabilitation. In the Enhancing Recovery in Coronary Heart Disease (ENRICHD) trial, which enrolled patients who had had a myocardial infarction and were depressed or lacked social support, cognitive–behavioral and social-support interventions did not reduce the risk of reinfection or death, but the interventions reduced depressive symptoms and increased social ties. In the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART), the treatment of major depression in patients who had acute myocardial infarction or unstable angina with sertraline, a selective serotonin-reuptake inhibitor, was associated with slight but not significant reductions in the rates of cardiovascular events.

Areas of Uncertainty
Although cognitive changes were previously believed to be relatively specific sequelae of cardiac surgery, recent studies suggest that cognitive decline may also occur after noncardiac surgery. In the BARI trial, the level of cognitive function after five years was identical in patients who had undergone CAGB and those who had undergone angioplasty (although no preoperative evaluations were performed). There is a strong association between homocysteine levels and cardiovascular risk, and homocysteine levels are inversely related to the levels of folic acid, vitamin B, and vitamin B. However, it remains unknown whether there is benefit to taking folic acid or vitamin B after CAGB.

Whether patients who undergo CAGB should receive anticoagulant therapy also remains uncertain. The Post-CABG trial showed a reduced rate of progression of atherosclerosis with lipid-lowering therapy, but warfarin therapy had no effect on this risk. The case for long-term anticoagulation is more compelling with regard to patients with a grade IV or V aortic atheroma.

There have been no randomized trials of exercise testing in asymptomatic patients who have undergone CAGB. However, since exercise testing without imaging studies has been shown to have limited prognostic value in patients who have undergone CAGB, stress testing in symptomatic patients should include imaging studies.

Guidelines
The American College of Cardiology, with the American Heart Association, has published recommendations for the care of patients undergoing CAGB and for the management of risk factors after revascularization (http://www.acc.org/clinical/guidelines/bypass/dirIndex.htm). The major recommendations are listed in Table 1; blood-pressure and diabetes control are also stressed. The Agency for Healthcare Research and Quality has also published recommendations for cardiac rehabilitation that include exercise training, education, counseling, and behavioral interventions for all patients who undergo CAGB.

Conclusions and Recommendations
After CAGB, all patients should begin taking aspirin, and patients with a history of myocardial infarction (such as the patient described in the vignette) should also be given a beta-blocker, unless it is contraindicated. ACE inhibitors should be used in high-risk patients, as described in Table 1. All patients should be encouraged to change their diet and pursue a rehabilitation program involving exercise and stress management. Cessation of smoking is especially important. Weight reduction may also be helpful. Statins should be used to achieve targets for LDL cholesterol (preferably a level of 60 to 85 mg per deciliter, but certainly less than 100 mg per deciliter).

In addition, patients should be screened for
Table 1. Recommendations for Pharmacologic and Lifestyle Interventions in Patients Who Have Undergone CABG.*

<table>
<thead>
<tr>
<th>Medications</th>
<th>Patients with Indications</th>
<th>Contraindications</th>
<th>Dose or Recommended Approaches</th>
<th>Benefits or Goals</th>
<th>Monitoring</th>
<th>Interactions</th>
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</thead>
<tbody>
<tr>
<td>Antiplatelet agents</td>
<td>All patients</td>
<td>Active bleeding or coagulation disorders</td>
<td>Reduces risk of closure of saphenous-vein graft</td>
<td></td>
<td></td>
<td>May alter metabolism of ACE inhibitors</td>
</tr>
<tr>
<td>Aspirin</td>
<td>All patients without allergy to aspirin</td>
<td>Active bleeding or coagulation disorders; should not be used preoperatively</td>
<td>325 mg per day†</td>
<td></td>
<td></td>
<td>May increase levels of angiotensin II–receptor blockers, fluvastatin, and other CYP2C9 substrates</td>
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<tr>
<td>Clopidogrel (as a postoperative alternative to aspirin)</td>
<td>Patients with allergy to aspirin</td>
<td>Active bleeding or coagulation disorders; should not be used preoperatively</td>
<td>50–100 mg per day</td>
<td>Monitor for bleeding</td>
<td></td>
<td>Additive effects when given with calcium-channel blockers, antiarrhythmic agents, and blood-pressure–lowering drugs; NSAIDs and ampicillin reduce effect</td>
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<tr>
<td>Cardioselective beta-blockers‡</td>
<td>All patients</td>
<td>Bradycardia, heart block, low blood pressure; use with caution in patients with diabetes, bronchospasm, myasthenia</td>
<td>Start with lower dose in elderly patients</td>
<td>Reduces risk of cardiac events</td>
<td></td>
<td>Antacids may reduce bioavailability</td>
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<td>Metoprolol</td>
<td></td>
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<td>25–50 mg twice a day initially; titrate up to a total of 300–400 mg per day</td>
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<td>Fluoxetine may inhibit metabolism</td>
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<td>Atenolol</td>
<td></td>
<td></td>
<td>50–100 mg per day</td>
<td></td>
<td></td>
<td>Niacin may increase risk of myopathy</td>
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<tr>
<td>HMG-CoA reductase inhibitors‡</td>
<td>All patients with LDL cholesterol &gt;100 mg/dl (2.6 mmol/liter)</td>
<td>Active liver disease, persistent elevation of amino-transferases, myositis</td>
<td>Slows progression of atherosclerosis; reduces LDL cholesterol level; reduces likelihood of need for revascularization</td>
<td>Measure ALT, AST at base line, at 3 mo, then every 12 mo; assess CK and muscle symptoms at base line; assess muscle symptoms at 6–12 wk and CK if there are muscle symptoms</td>
<td></td>
<td>Antacids may reduce bioavailability</td>
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<td>Lovastatin</td>
<td>Pregnancy</td>
<td></td>
<td>20 mg per day initially (titrate to 80 mg per day)</td>
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<td></td>
<td>Avoid CYP3A3 and CYP3A4 inhibitors; effect of warfarin may be increased; avoid grapefruit juice</td>
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<tr>
<td>Medications</td>
<td>Patients with Indications</td>
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<tr>
<td>Pravastatin</td>
<td>Patients with CAD, stroke, peripheral vascular disease, or diabetes, plus one other risk factor — hypertension, smoking, increased cholesterol, or microalbuminuria</td>
<td>Pregnancy</td>
<td>10 mg per day initially (titrate to 40 mg per day)</td>
<td>Reduces risk of MI, stroke, and death from cardiovascular causes</td>
<td>Blood-pressure monitoring with first dose; follow potassium and creatinine; in patients with renal impairment, baseline white-cell count, differential blood count, and serum creatinine; may cause cough</td>
<td>Potassium, potassium-sparing diuretics, or trimethoprim may increase risk of hyperkalemia</td>
</tr>
</tbody>
</table>

| ACE inhibitors | 10 mg per day; increase to 20–40 mg per day; lower doses in elderly patients | Lower dose in patients with renal or hepatic impairment | Reduces risk of MI, stroke, and death from cardiovascular causes | Blood-pressure monitoring with first dose; follow potassium and creatinine; in patients with renal impairment, baseline white-cell count, differential blood count, and serum creatinine; may cause cough | Potassium, potassium-sparing diuretics, or trimethoprim may increase risk of hyperkalemia |

| Quinapril§ | 10 mg per day; increase to 20–40 mg per day; lower doses in elderly patients | Lower dose in patients with renal or hepatic impairment | Reduces risk of MI, stroke, and death from cardiovascular causes | Blood-pressure monitoring with first dose; follow potassium and creatinine; in patients with renal impairment, baseline white-cell count, differential blood count, and serum creatinine; may cause cough | Potassium, potassium-sparing diuretics, or trimethoprim may increase risk of hyperkalemia |

| Ramipril¶ | 10 mg per day; increase to 20–40 mg per day; lower doses in elderly patients | Lower dose in patients with renal or hepatic impairment | Reduces risk of MI, stroke, and death from cardiovascular causes | Blood-pressure monitoring with first dose; follow potassium and creatinine; in patients with renal impairment, baseline white-cell count, differential blood count, and serum creatinine; may cause cough | Potassium, potassium-sparing diuretics, or trimethoprim may increase risk of hyperkalemia |

| Lifestyle | Current smokers | None | Counseling, nicotine-replacement therapy, bupropion | Reduces risk of mortality and morbidity | Nicotine causes sympathetic activation; bupropion may cause hypertension |

| Smoking cessation | Current smokers | None | Counseling, nicotine-replacement therapy, bupropion | Reduces risk of mortality and morbidity | Nicotine causes sympathetic activation; bupropion may cause hypertension |

| Exercise | All patients with stable CAD | Unstable angina, severe valvular disease, class IV congestive heart failure | Cardiac rehabilitation program for 8–12 wk; then 3–5 times per wk | Improved exercise tolerance and function; less depression | All initial exercise after surgery should be done in a monitored cardiac program |

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* CABG denotes coronary-artery bypass grafting, ACE angiotensin-converting enzyme, NSAIDs nonsteroidal anti-inflammatory drugs, HMG-CoA hydroxymethylglutaryl coenzyme A, LDL low-density lipoprotein, ALT alanine aminotransferase, AST aspartate aminotransferase, CK creatine kinase, CAD coronary artery disease, and MI myocardial infarction.

† A dose of 325 mg daily should be given for the first year to prevent graft occlusion.

§ Quinapril is the only ACE inhibitor that has been specifically evaluated in patients who have undergone CABG.

¶ About 25 percent of patients in the Heart Outcomes Prevention Evaluation trial had undergone CABG.
depression, since it is common and treatable. Depressed patients should be informed that treatment of depression is likely to improve their ability to concentrate. Aerobic exercise, as part of a rehabilitation program, may also help to alleviate depressive symptoms.

Because the patient described in the vignette has a grade V atheroma and an associated high risk of stroke, therapy with warfarin should be strongly considered in addition to aspirin, although the risk of bleeding may be increased. The patient will need to be followed closely, and therapy will have to be adjusted periodically. Follow-up strategies are shown in Table 1.

### REFERENCES


46. Berkman LF, Jaffe AS. The effects of treating depression and low social support on clinical events after a myocardial infarction. Circulation 2001;104(25):1B.


