CLINICAL DECISIONS
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Management of Stable Coronary Disease

This interactive feature addresses the diagnosis or management of a clinical case. A case vignette is followed by specific clinical options, none of which can be considered either correct or incorrect. In short essays, experts in the field then argue for each of the options. In the online version of this feature, available at www.nejm.org, readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.

CASE VIGNETTE

A 65-year-old man with hypertension, obesity, and type 2 diabetes mellitus has been under your care for the past 5 years. He has been receiving hydrochlorothiazide (25 mg daily) and metformin (500 mg twice daily); his blood pressure is 130/82 mm Hg, his body-mass index (the weight in kilograms divided by the square of the height in meters) is 32, and his glycated hemoglobin is 7.5%. He comes to your office seeking advice about the management of his recently diagnosed coronary artery disease. Two weeks earlier, he had presented with chest tightness and shortness of breath after walking two blocks. His symptoms resolved within a few minutes at rest. An exercise-tolerance test on a treadmill was performed according to the Bruce protocol, along with myocardial perfusion imaging. The patient exercised for 8 minutes, stopping because of chest pressure and dyspnea; his peak systolic blood pressure was 160 mm Hg, and his peak heart rate was 140 beats per minute. Electrocardiography showed ST-segment depression of 1 mm in the anterolateral leads. The perfusion study revealed a fixed perfusion defect of moderate size in the anterior wall and a reversible defect of moderate size in the anterolateral wall.

The patient underwent cardiac catheterization and was found to have multivessel coronary artery disease, with occlusion of the first diagonal branch of the left anterior descending coronary artery, a long lesion with 70% stenosis in the midportion of the left anterior descending coronary artery, 80% stenosis with a calcified lesion in the proximal left circumflex coronary artery, and 50% stenosis of the posterior descending coronary artery. A left ventriculogram obtained during the procedure showed anterior-wall hypokinesis and a left ventricular ejection fraction of 45%. The patient was advised to discuss management of his coronary artery disease with you before making a decision about how to proceed; you have received the results of his exercise test and his catheterization report.

Which one of the following initial treatment options, any of which could be considered correct, would you find most appropriate for this patient? Base your choice on the published literature, your past experience, recent guidelines, and other sources of information, as appropriate.

1. **Initiate an appropriate medical regimen and follow the patient closely for adherence and efficacy.**
2. **Initiate an appropriate medical regimen and refer the patient for percutaneous coronary intervention (PCI).**
3. **Initiate an appropriate medical regimen and refer the patient for coronary-artery bypass grafting (CABG).**

To aid in your decision making, these approaches to treatment are defended by experts in the management of coronary artery disease in the following short essays. Given your knowledge of the condition and the points made by the experts, which treatment approach would you choose? Make your choice on our Web site (www.nejm.org).

TREATMENT OPTION 1

Appropriate Medical Management and Close Follow-up for Adherence and Efficacy

Salim Yusuf, F.R.S.C., and Ernest Fallen, M.D.

The case vignette describes a 65-year-old man with diabetes, multiple coronary risk factors, previous myocardial infarction, multivessel coronary-artery stenosis, mild left ventricular dysfunction, and new-onset effort-induced angina and dyspnea. He has yet to receive antianginal therapy, and inadequate attention has been given to controlling his risk factors. The initial management needed in this case is clearly medical. Its objectives are to relieve his symptoms, reduce risk factors, prevent left ventricular remodeling, and reduce the likelihood of a major coronary event. There are cogent arguments against rushing in with revascularization procedures such as PCI or CABG.

PCI as initial therapy in this untreated patient poses several problems. First, the patient has multiple lesions, including a long lesion with 70% obstruction in the middle segment of the left anterior descending coronary artery that is technically challenging to treat. Second, the circumflex lesion, arguably the culprit site (according to the nuclear perfusion scan), is less amenable to adequate dilatation, because of its calcified state. Third, it is well known that PCIs of multiple vessels are less likely to result in long-term patency in patients with diabetes than in patients without diabetes.[1] Finally, there is no evidence that PCI in patients with stable angina is more effective than optimal medical management in reducing mortality.

As for CABG, at this early stage, there are a number of operative risks. These include inadequately treated diabetes, obesity, and reduced left ventricular function. The indication for surgery is borderline at best. The patient has two-vessel coronary disease, without involvement of the proximal left anterior descending coronary artery and with potentially reversible ischemia in the circumflex territory. Besides, CABG may be superior to medical therapy for the relief of angina in the long run, but our patient has not yet received medical therapy, and therefore his response to it is not known.

The patient has a glycated hemoglobin level of 7.5%, indicating inadequate glucose control; the recommended therapeutic target for patients with diabetes is less than 6.5%. The simple reduction of calories — especially by means of a low-glycemic-index diet in conjunction with regular physical activity, education about diabetes, and adjustment of the dose of metformin (to up to 2 g per day, if the renal function is not abnormal) — should suffice to achieve both glycemic control and weight loss. Although the patient's lipid profile should be known, there is persuasive evidence in favor of initiating treatment with a statin (with a target low-density lipoprotein cholesterol level of 80 mg per deciliter [2.0 mmol per liter] or less) in any patient with symptomatic coronary artery disease.[2] The combination of symptomatic coronary artery disease, left ventricular dysfunction, and diabetes makes the patient an ideal candidate for an angiotensin-converting–enzyme inhibitor.[3,4] He should also be given aspirin. There are clear indications to initiate a beta-blocker (and, if necessary, a calcium-channel blocker) for control of the angina and hypertension and for secondary prevention of myocardial infarction and death from cardiovascular causes.[5]

This patient's symptoms of angina would benefit from the judicious use of a nitrate preparation. Finally, depending on his preferences, the patient should be encouraged to get involved in his own care by regularly monitoring his own glucose levels, weight, and blood pressure. He should be followed closely over the next 2 to 4 weeks to ensure that the objectives of this initial medical approach are being achieved. It is highly likely that with these measures, both his angina and his prognosis will improve markedly. If, despite optimal medical therapy, his angina worsens and limits his activities, then it would be reasonable to consider revascularization.

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TREATMENT OPTION 2

Appropriate Medical Management and PCI

Robert A. Harrington, M.D.

The decision-making process regarding therapy for this patient with new-onset angina of Canadian Cardiovascular Society class III begins with an assessment of risk. Risk stratification is a dynamic practice whereby the clinician incorporates newly acquired information in a clinical-decision model that also considers the desires and preferences of the patient. In this case, the presence of diabetes carries both an increased risk of death from cardiac causes and an increased likelihood of a benefit from revascularization, as compared with medical therapy.[6]

According to the well-validated Duke treadmill score, this patient's exercise-limiting symptoms, ST-segment depression of 1 mm, and moderate anterior perfusion defect confer on him a risk of death from cardiac causes that is well within the intermediate range, which means that he would preferentially benefit from aggressive therapies.[7] Although coronary angiography revealed three-vessel disease and mildly reduced left ventricular function, the disease of the left anterior descending coronary artery appears to be responsible for his recent symptoms, given the findings on the imaging studies.

The patient's clinical risk factors (especially the presence of diabetes), the abnormal results of the exercise study, and the results of coronary angiography all provide support for coronary revascularization (with a background of aggressive medical therapy) as the best option. The patient does not have disease of the proximal left anterior descending coronary artery, which would have placed him in a high-risk group for which bypass surgery is favored over PCI.[6] Instead, the occlusion of the first diagonal branch of the left anterior descending coronary artery, the long lesion of the middle segment of the left anterior descending coronary artery, and the lesions without inducible ischemia in the circumflex and right coronary arteries indicate that PCI should be the preferred revascularization strategy. Although complete revascularization could be considered, the absence of any functional data suggesting that there is ischemia outside the anterior distribution makes PCI in the left anterior descending coronary artery a very reasonable choice. The 2005 PCI guidelines of the American College of Cardiology, the American Heart Association, and the Society for Cardiovascular Angiography and Interventions give the procedure a class IIa recommendation (with evidence that is conflicting but overall is in support) for patients with angina of Canadian Cardiovascular Society class III, such as our patient.

The results of the recent Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial raise questions about using PCI in patients such as this man. Although the COURAGE study showed no benefit of PCI over optimal medical therapy regarding the composite end point of death or myocardial infarction, angina symptoms were significantly reduced with the use of PCI, a phenomenon that has been shown in multiple clinical trials.[8] The compliance with aggressive medical therapy seen in the COURAGE trial required a Herculean effort, unlike that typically seen in routine clinical practice. Given that the use of PCI was not associated with incremental risk in the COURAGE study, it is reasonable and appropriate to have a discussion with the patient about his hopes and expectations regarding lifestyle improvement and symptom relief from the therapy chosen.

Given recent controversies, it is worth commenting on the selection of either a bare-metal stent or a drug-eluting stent. The patient's long lesion and diabetes increase his risk of restenosis. The risks of restenosis and repeat revascularization can be reduced substantially with the use of a drug-eluting stent. But that choice carries with it obligatory dual antiplatelet therapy (aspirin plus clopidogrel) for at least 1 year and perhaps indefinitely.[9,10] If the patient is thought to be at low risk for a bleeding event and if he is likely to adhere to long-term antiplatelet therapy, then placement of a drug-eluting stent in the lesion of the middle segment of the left anterior descending coronary artery is his best option.

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TREATMENT OPTION 3

Appropriate Medical Management and CABG

Robert A. Guyton, M.D.

Treatment of coronary atherosclerosis has become progressively concordant with our knowledge of coronary pathophysiology. Angina is caused by coronary stenoses that limit flow, whereas myocardial infarction is generally caused by blockage related to unstable plaques, often separate from flow-limiting stenoses. Systemic medical therapy decreases the risks of both infarction and death. PCI treats short vascular segments and is effective in patients with an acute coronary syndrome or angina caused by discrete stenosis. PCI, even with drug-eluting stents, has no demonstrable benefit with regard to infarction or death, since future blockage elsewhere is usually the culprit, not restenosis of the short segment.

CABG bypasses the proximal two thirds of epicardial vessels, thus also bypassing both current stenoses and most future blockages from nascent plaques that are currently hemodynamically insignificant.[11] Accordingly, the addition of CABG to medical therapy in early randomized trials did extend the survival of patients with advanced, multifocal disease, such as three-vessel disease or lesser disease that includes the proximal left anterior descending artery. These trials evaluated the medical therapy that was available at the time and CABG as it was practiced at the time (with higher operative mortality and few arterial conduits). Among patients with multivessel disease, CABG is associated with a survival advantage over PCI that is similar to the survival advantage of CABG over medical therapy. There was minimal survival advantage in patients with early coronary disease when enrollment in randomized, controlled trials was limited to patients in whom PCI was projected to achieve "equivalent revascularization" to CABG (5-year postprocedure risk ratio for death after PCI vs. CABG, 1.13; $P>0.05$; in the Arterial Revascularization Therapies Study [ARTS]).[11] Among patients in trials with less restrictive enrollment, a larger survival advantage has been found for patients with multivessel disease (5-year relative risk of death after PCI vs. CABG, 1.65; $P=0.016$; in the Stent or Surgery Trial [SOS]).[11] Data from "real world" registries provide support for a survival advantage from CABG in patients with any category of multivessel disease, among whom the 3-year risk-adjusted hazard ratio for death after CABG, as compared with death after stenting, is 0.76 to 0.64 ($P<0.05$ for all comparisons).[12]

In this patient with new-onset angina, survival advantage is the only justification for performing early PCI or CABG. Multivessel PCI has no survival advantage in patients with diabetes and, with a 12-month rate of thrombosis of 4.3% when performed with drug-eluting stents,[13] it may be detrimental.

The New York State Registry would categorize this patient as having significant (≥70% stenosis) two-vessel disease with involvement of the nonproximal left anterior descending coronary artery; patients in this group have a 3-year hazard ratio for death after CABG, as compared with PCI with stenting, of 0.76 ($P=0.02$). The patient has diabetes and is obese; among patients in the COURAGE trial, neither of these characteristics was altered by the intensely supervised medical therapy in the study. The patient is a good candidate for CABG, with a predicted risk of death from the procedure of less than 1%, according to the Society of Thoracic Surgeons National Database Risk Calculator, and a 0.8% risk in experienced off-pump centers.[14] He has advanced, multifocal coronary atherosclerosis, with disease in four major epicardial vessels. The patient is on the cusp of being classified as having three-vessel disease, according to the usual definitions used in randomized controlled trials (>50%, or ≥50%, stenosis). His perfusion scan, showing a moderate fixed (perhaps "hibernating") defect plus a moderate reversible defect, adds up to a large area of hypoperfusion. His diminished ventricular function does not increase the relative benefit of CABG when added to medical therapy for multivessel disease, but it does almost double the absolute 5-year potential mortality benefit from the addition of CABG. This patient should receive intense medical therapy and off-pump CABG with at least two arterial conduits.

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The use of drug-eluting stents in multivessel stenting, as discussed in the essays by Drs. Harrington and Guyton, is an off-label use.

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