Editor’s Perspective

Coronary Revascularization for Myocardial Ischemia

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An 80-year-old woman with a history of hypertension and hyperlipidemia presents to her primary care physician for a routine examination and is noted to have a right-sided carotid bruit. Her physician orders a carotid ultrasound that demonstrates an 80% stenosis. She has no symptoms of amaurosis fugax, focal limb weakness, sensory changes, or slurred speech. She is referred for carotid endarterectomy and the surgeon requests a preoperative risk stratification by a cardiologist. On presentation to the cardiologist, she reports no history of chest discomfort with exertion or at rest. She does note some shortness of breath that seems to be limiting her physical activity during the past 6 months. There are no changes on her resting electrocardiogram suggestive of ischemia or infarct. Given symptoms of arthritis that also limit her physical activity, she undergoes a pharmacological nuclear stress test that shows electrocardiographic ST-segment depression of 1.5 mm and a moderate area of ischemia in the inferior wall. Her only medications are hydrochlorothiazide and simvastatin, and aspirin and metoprolol are added to her medication regimen. Her primary care physician refers her for cardiac catheterization.

The approach to this patient raises several important issues given her risk factors, paucity of symptoms, and evidence of what seems to be stable ischemic heart disease with objective evidence of myocardial ischemia. The question of how to approach a patient like this is a highly relevant and important one, as it is unclear whether optimizing medical therapy alone or proceeding to a more definitive diagnostic test and therapy lead to a better outcome.

It is also important to distinguish our patient from others with CAD for whom questions about revascularization and the type of revascularization that might be most suitable have been largely answered. We characterize patients with CAD according to clinical presentation and the location and extent of their coronary disease. For example, we have firm evidence that patients with acute ST-elevation myocardial infarction should be treated with primary percutaneous coronary intervention (PCI) when feasible. Such patients can expect a reduction in subsequent mortality compared with patients treated by medical therapy alone. Similarly, patients with angina and left main CAD have enhanced survival when coronary artery bypass surgery (CABG) is added to medical therapy. Revascularization has also been demonstrated to reduce subsequent myocardial infarction in patients with non–ST-elevation myocardial infarction or unstable angina.

Several studies have investigated the role of revascularization for patients with stable CAD. Many date back to the 1970s, before PCI existed as a therapeutic alternative. Clinical trials, such as the Veterans Administration Cooperative Study, the European Study, and the Coronary Artery Surgery Study, have formed the basis of our current guidelines to revascularize patients with 3-vessel disease, left main disease, and decreased left ventricular ejection fraction. However, medical therapy in that era was much more limited compared with current practice, and aspirin, β-blockers, statins, and angiotensin-converting enzyme inhibitors were not used nearly to the extent or as consistently as they are today. Moreover, although certain subsets of patients seemed to benefit from revascularization, the numbers of patients in these subsets are small, making conclusions difficult to draw. Subsequently, PCI has also developed as a less invasive alternative method for coronary revascularization, necessitating the need for further studies to evaluate the potential benefits of both CABG and PCI.

Trials examining revascularization versus optimal medical therapy in the current age include the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) and Bypass Angioplasty Revascularization Investigation 2D (BARI 2D) trials. In both trials, medical therapy was contemporary and quite aggressive and included antianginal and antiatherosclerotic medications for both groups. COURAGE did not show a reduction in death or myocardial infarction (MI) in patients with stable ischemic heart disease for those treated by PCI in comparison with medical therapy alone. The BARI 2D trial examined patients with diabetes mellitus who received revascularization (PCI or CABG per physician/patient judgment) or optimal medical therapy alone and found no significant difference in all-cause mortality or subsequent MI. When analyzed according to the method of revascularization, there was no difference in mortality for the PCI group, whereas there was a significant difference in the combined end point of death, MI, and stroke for those assigned to CABG.

An important concern for both of these trials was that enrolled patients had a diagnostic cardiac catheterization with coronary angiography before enrollment. In addition, a large proportion of study-eligible patients were not enrolled. One potential explanation for this finding is that in many instances physicians or patients had a bias for certain eligible patients to have revascularization. Such patients did not want to be assigned away from revascularization and subsequently declined to participate in the trial. Similar scenarios occurred in BARI 2D. Thus, patients who participated in COURAGE and BARI 2D likely represented a selected subset of CAD.
patients. Concerns such as these have led physicians to question our ability to generalize the findings of these trials to the broader population of patients seen routinely.8

There have been advances in the manner in which coronary revascularization is now performed for both PCI and CABG that need to be incorporated into decisions on whether revascularization should be recommended for patients and how it should be performed. Physicians are more skilled in PCI and newer drug-eluting stents are more deliverable and associated with higher acute and long-term success rates. The use of fractional flow reserve to determine lesion significance and to guide revascularization for both patients undergoing PCI and CABG allows for a more focused revascularization procedure. Finally, cardiologist and cardiac surgeons have gained knowledge from recently completed clinical trials, such as Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) and Synergy Between PCI with Taxus and Cardiac Surgery (SYNTAX), to permit a better selection of the technique to be used for revascularization.9,10

Currently there are little data to assist the clinician in selecting revascularization or continued medical therapy alone for the patient with stable ischemic heart disease for whom symptoms are not disabling. Such a situation exists for our patient presented earlier. The recently initiated International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial seeks to answer this question in the era of modern revascularization and medical therapy.

ISCHEMIA focuses on the patient with clinical evidence of ischemia and nondisabling symptoms similar to our patient. The purpose of the trial is to test the hypothesis that revascularization will reduce the incidence of cardiovascular death and nonfatal MI for patients with at least moderate ischemia in comparison with medical therapy alone. In this trial, ischemia must be evident by nuclear stress perfusion imaging, echocardiography stress testing, or cardiac MRI. An important secondary end point is whether revascularization will improve angina-related quality of life. Other secondary end points include individual components of the primary end point, hospitalization for unstable angina or heart failure, resource use, and cost.

This trial has an important, unique feature different from any other contemporary study of revascularization. Patients will be enrolled before and not after the performance of a cardiac catheterization. Enrollment will occur after documentation of at least moderate ischemia by means of objective testing. Then study patients will undergo a blinded coronary CT-angiogram to evaluate the patient for possible left main coronary disease. Patients with evidence of significant left main disease or no evidence of any significant coronary disease will be excluded. The remaining patients will be randomized to an early invasive strategy (optimal medical therapy, cath, and optimal revascularization) or a conservative strategy (optimal medical therapy alone, with catheterization reserved for failure of medical therapy). In this regard, ISCHEMIA will evaluate the strategy of not obtaining initial knowledge of the presence or extent of coronary disease by means of cardiac catheterization and also withholding revascularization for patients assigned to the medical group. This approach evaluates a much broader question than prior contemporary trials.

ISCHEMIA is an international trial scheduled to enroll 8000 patients. The average duration of follow-up will be 4 years. Recruitment has started. Investigators believe this trial will have enormous implications and provide guidance for the management of this important subgroup of patients with coronary heart disease.

Disclosures

None.

References


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