Coronary Revascularization: New Evidence, New Challenges

Between 1970 and 2000, life expectancy in the United States increased by 6.0 years (1). Nearly two thirds of this increase (3.9 years) is credited to reductions in mortality from cardiovascular disease and stroke, and approximately 7% of the cardiovascular survival benefit has been attributed to coronary revascularization (2). After the introduction of coronary artery bypass grafting (CABG) in the 1970s, trials of revascularization from the United States and Europe demonstrated improved survival with this technique in selected subgroups of high-risk patients (such as those with left main coronary artery disease) compared with medical therapy of that era (3, 4). However, the morbidity and mortality associated with CABG encouraged development of percutaneous coronary intervention (PCI) in the 1980s. Techniques of PCI have evolved to include coronary artery stenting with bare-metal stents and, more recently, drug-eluting stents. The use of PCI to treat multivessel CAD rather than only single-vessel disease led to several randomized, controlled trials (RCTs) comparing PCI and CABG (5–8).

In this issue, Bravata and colleagues (9) present a sophisticated meta-analysis of 23 RCTs that compare health outcomes after PCI and CABG. They also compare their findings with data from selected large observational studies.

The major results of this rigorous review are that early procedural mortality rates (1.15% vs. 1.8%) and 5-year survival rates (89.7% vs. 90.7%) are similar after PCI and CABG. In addition, 5-year survival was similar after PCI and CABG in patients with and without diabetes in the 7 RCTs that reported on this subgroup. Compared with PCI, CABG provided more complete relief of angina in 5% to 10% of patients over 5 years, and repeated revascularization was less common. However, these 2 advantages of CABG are offset by more procedural strokes (1.2% vs. 0.6%). Data from large observational registries show that patients with single-vessel disease are much more likely to undergo PCI, whereas patients with triple-vessel disease are much more likely to undergo CABG. The registries indicate a lower mortality rate with CABG across the spectrum of disease, but mortality rates are similar with PCI or CABG in patients whose extent of disease is similar to that of patients in the randomized trials.

The equivalence in procedural mortality may surprise some patients and clinicians, who often assume that the reduced morbidity and recovery time with PCI also translate into a lower mortality rate. The observation that late outcomes were no worse in patients with diabetes than in those without diabetes contrasts with the widely publicized advantage of CABG in the BARI (Bypass Angioplasty Revascularization Investigation) trial (5). Bravata and colleagues acknowledge the limitations of their review, which merely reflect limitations in the entry criteria, sample size, outcome assessment, and reporting of available trials. For example, they could not analyze procedural myocardial infarction because of variable diagnostic criteria. Current techniques and devices, including drug-eluting stents, were not evaluated, and few patients older than 75 years or with poor left ventricular function, clinical instability, or previous revascularization were enrolled. These shortcomings limit the generalizability of the findings and emphasize the need for additional trials.

What are the most immediate implications of this review for the practicing internist? Clinicians must recognize that these results may be relevant only to patients like those who were enrolled in the randomized trials. In practice, patients with single-vessel coronary artery disease and normal left ventricular function usually undergo PCI, and those with triple-vessel disease and abnormal left ventricular function more often undergo CABG. Because RCTs have generally included few patients at opposite ends of the disease spectrum, Bravata and colleagues’ findings cannot be generalized to such patients. Rather, they are more applicable to patients with an intermediate disease severity, who constituted the majority of participants. The short-term and long-term mortality rates associated with PCI and CABG are similar in these patients. In discussing revascularization options with their patients, physicians should make this equivalence clear, because patients often have preconceived notions that one procedure or the other is superior. The advantages of CABG are better relief of angina and a lower likelihood of subsequent revascularization; however, the magnitude of the latter benefit may decrease in future randomized trials that include drug-eluting stents. The increase in stroke with CABG offsets these advantages. Physicians must ensure that their patients understand these differences.

For many patients, however, the larger question is whether neither PCI nor CABG is warranted. Until recently, recommendations for PCI or CABG in patients other than those in the highest risk group were based on observational data and consensus opinion. For example, clinical practice guidelines strongly recommended PCI or CABG for symptomatic or asymptomatic patients with “1- or 2-vessel CAD . . . with high-risk criteria in noninvasive testing” until 2002 (10, 11). More recent guidelines are more cautious but still suggest that either PCI or CABG is reasonable in such patients, because revascularization “may reduce their risk of serious or fatal cardiac events” (12). The wide variation in rates of PCI across the United States suggests great variation in compliance with these guidelines.

Newer studies have challenged the widely held assumptions that revascularization consistently reduces cardiac events and prolongs survival (13, 14). The OAT (Occluded Artery Trial) enrolled 2166 patients who had an occluded infarct-related coronary artery early after myocar-
dial infarction and another high-risk criterion, such as proximal stenosis in a different coronary artery (13). In OAT, PCI did not confer an advantage over medical therapy for the combined end point of death, reinfarction, or New York Heart Association class IV heart failure. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial, the largest reported RCT in chronic coronary artery disease, enrolled 2287 patients with significant coronary artery disease and inducible ischemia; 70% had multivessel disease, and more than one third had stenoses in the proximal left anterior descending artery (14). The trial compared optimal medical therapy with and without PCI. Unlike medical therapy in earlier trials that focused on antianginal medication, all patients in the COURAGE trial received intensive, goal-directed risk factor reduction therapy that resulted in very high rates of adherence to guideline recommendations for blood pressure, lipid levels, exercise, diet, and smoking cessation. When added to such intensive medical therapy, PCI had no advantage in terms of the primary end point of death or myocardial infarction and only a modest advantage in relief of angina that decreased over time (possibly because more late PCIs were done in the group that initially received only medical therapy). These results suggest that revascularization can safely be deferred for many patients if the standards for medical therapy in the COURAGE trial are scrupulously followed.

From a broad societal perspective, Bravata and colleagues’ review raises several concerns. The 23 RCTs included 9963 patients and span 4 decades; however, in 2005 alone, more than 900 000 revascularization procedures were performed in the United States (15). How many of these procedures were performed on patients like those in the trials is unknown, but the modest number of patients in RCTs is disturbing. In comparison, approximately 1200 000 myocardial infarctions occur in the United States annually (16). The RCTs of fibrinolytic therapy versus placebo for myocardial infarction included 58 600 patients (17), whereas the RCTs on acute PCI versus fibrinolytic therapy included another 7739 patients (18). More worrisome still is that only 3 of the RCTs were performed in the United States. Although many U.S. political leaders have supported expanding studies of comparatives, these initiatives require much greater funding to conduct the necessary RCTs, as well as a greater commitment from U.S. patients and physicians to increase enrollment in future RCTs. Far greater effort is needed to generate the scientific evidence that is absolutely essential to effective and efficient care of patients with ischemic heart disease.

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Potential Financial Conflicts of Interest: Consultancies: R.J. Gibbons (King Pharmaceuticals). Grants received: R.J. Gibbons (King Pharmaceuticals).

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