Choosing Between Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting for Patients With Multivessel Disease

What Can We Learn From the Arterial Revascularization Therapy Study (ARTS)?

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The ARTS trial was one of 11 randomized trials comparing an initial strategy of percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) in the treatment of patients with multivessel coronary artery disease.1–11 Six of these trials used balloon angioplasty in the PCI arm,1–6 whereas the 5 most recent trials (of which ARTS was the largest, with 1205 patients) used stents in the PCI arm.7–11 The results of these 11 trials were concordant in that the frequency of death and myocardial infarction in both arms was similar, although freedom from repeat procedures and angina was superior in the surgical arms. Few trials included stroke as an end point (the exclusion of stroke would generally favor the CABG arm); in the ARTS trial, however, the combined end point of survival free of myocardial infarction or stroke was similar in the 2 groups at 3 years (87.2% for PCI versus 88.4% for CABG, P=NS), whereas the composite end point, which included repeat revascularization, markedly favored CABG.

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Balloon Angioplasty Versus Stent Placement

The results of the trials using balloon angioplasty and stents differed in 2 important ways. In the balloon angioplasty trials, the frequency with which urgent or emergency CABG was required in the PCI arm during the index hospitalization ranged from 5% to 10%, whereas in the stent trials, fewer than 1% of PCI patients required urgent or emergency CABG. The second difference relates to the frequency of restenosis in the PCI arms of the trials. Those trials in which stents were used had less than half the frequency of restenosis and target vessel revascularization of the earlier balloon angioplasty trials. This difference was only partly due to the large reduction in restenosis seen with bare (non–drug-eluting) stents; it was also due in part to less follow-up angiography and exercise testing. Such protocol-mandated procedures increase the frequency of repeat revascularization procedures, and they do so more in the PCI than the CABG arms of trials.12

The ARTS Trial

In the present issue of Circulation, Legrand et al13 extend the results of the ARTS trial out to 3 years. The results are similar to the previously published results after 1 year of follow-up, except that the need for repeat revascularization continued to increase more in the stent than the CABG arm. As a result, the incremental cost difference for surgery versus PCI for each event-free patient, which had been €19 257 at 1 year, decreased to €10 492 at 3 years.

This most recent analysis of the ARTS study raises 2 important questions. What relevance, if any, do the results of ARTS and the other 10 randomized trials have in the drug-eluting stent era? And what role should economic considerations play when comparing therapies?

Drug-Eluting Stents

Drug-eluting stents do not reduce the frequency of death or myocardial infarction below the frequency seen with bare stents, nor do they influence the frequency of stroke.14,15 However, pivotal randomized trials of patients undergoing PCI of a single coronary artery with drug-eluting stents have demonstrated a reduction in restenosis and repeat revascularization procedures of as much as 70%.14,15 On the basis of these results, it seems likely that drug-eluting stents will result in similar reductions after multivessel PCI. If this belief is borne out, the difference in repeat revascularization between CABG and stents may disappear. Given the approximate 7% frequency of in-hospital vein graft occlusion, drug-eluting stents may in fact be a more durable means of coronary revascularization than CABG using vein grafts.14–17 The relatively high early occlusion rate of vein grafts is not true of mammary grafts, for which both short- and long-term patency rates are excellent.16,17

Unresolved Clinical Issues

Important clinical concerns are raised when one considers replacing CABG with multivessel PCI using drug-eluting...
stents. First, we must remember that the number of patients undergoing PCI who were screened for the 11 randomized trials of PCI versus CABG vastly exceeded the number of patients enrolled in the trials. Therefore, we must be very careful when applying the results of these trials to patients in the general population, only a small minority of whom would have fit the enrollment criteria of these trials. The results may not apply to patients dissimilar to those enrolled in the trials.

Second, several of the trials suggested an increased mortality rate in patients with diabetes mellitus undergoing PCI rather than CABG3,4,6,10 (although one suggested the opposite,1 and most did not indicate a difference). The reason for the increased mortality among diabetics, if true, is probably related to that fact that an occlusion anywhere in the left anterior descending artery proximal to the anastomosis of a mammary artery graft may result in only a small infarction or be entirely subclinical, whereas a stent can be expected to reduce the frequency of infarction (when reendothelialized) only in that portion of the coronary artery covered by the stent (and may actually increase the risk of infarction until it is reendothelialized). To further evaluate this issue, the Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease (FREEDOM) trial will evaluate treatment with a drug-eluting stent versus bypass surgery in patients with diabetes mellitus and multivessel coronary disease.

Other patient groups characterized by severe atherosclerosis and a prothrombotic state, such as those with chronic kidney disease, may also be better treated with CABG using arterial grafts. Such patients have a markedly increased frequency of death and infarction, not only during a PCI procedure, but also in the years after a successful PCI.18 Despite an exponential increase in chronic kidney disease in the United States and abroad, these patients have been excluded from all of the randomized trials comparing PCI and CABG and most other trials evaluating therapies for coronary disease. The effectiveness of multivessel PCI in patients with diabetes mellitus and chronic kidney disease relative to CABG, particularly when drug-eluting stents are used, remains unclear.

**Economic Impact of Drug-Eluting Stents**

The economic impact of a strategy of multivessel stenting with drug-eluting stents could be profound. In the United States, the only commercially available drug-eluting stent, the sirolimus-eluting CYPHER stent, costs approximately $3000, compared with approximately $500 to $1000 for a bare metal stent. Reimbursement by governmental and private payers has been increased for PCI procedures using a drug-eluting stent, although in most parts of the country, the reimbursement is exceeded by subsequent additional costs of the procedure. Hospitals lose money if more than ~1.5 drug-eluting stents are placed during a single PCI procedure. The loss of income to hospitals and of the margin coronary revascularization procedures generate could be even greater if the number of CABG cases drops significantly, owing to the large fixed cost of maintaining surgical facilities and personnel. Therefore, it would be overly simplistic to assume that greatly reducing the frequency of repeat revascularization procedures by replacing bare with drug-eluting stents would favorably influence the relative costs of PCI versus CABG.

The economic impact of such a change on hospitals and society could be profound, and the impact on the health and well-being of patients is incompletely understood. The dynamics will change again with the imminent availability of a second drug-eluting stent. The choice of revascularization procedure has an easily measurable impact on the incomes of cardiologists, cardiac surgeons, and anesthesiologists.19,20 (An upcoming Bethesda Conference will address the issue of self-referral as a major concern in modern cardiology.) Given that professionalism, by definition, places the patient’s needs over those of the provider, physicians must strive to ensure that patients receive a balanced picture of the relative advantages of PCI and CABG.

**What Role Should Economic Analyses Play?**

In an era of large governmental deficits, in which many poor and elderly patients go without much-needed therapies, no one can deny that the economics of healthcare delivery are critically important. However, what role, if any, should economic analyses play when a physician must recommend a therapy to an individual patient? It is our belief that such considerations are valid and important, even critical, when comparing treatments that are similar in safety and efficacy. But what if the 2 treatments being considered differ substantially in important ways, as do PCI and CABG? We believe that the primary consideration of a physician should be the welfare of the patient. The argument that the doctor should be concerned only about the individual patient is, however, no longer tenable. Indeed, quality health care recently has been defined by the Institute of Medicine as including 6 attributes (effective, safe, timely, efficient, patient centered, and equitable); meeting these criteria requires placing the primary patient/physician relationship in a broader context.21 Many hospitals and health systems depend on margins from cardiovascular services to pay for other services, such as psychiatric and emergency services. Given the large impact of these margins on the ability of hospitals to deliver care to populations whose care is not well reimbursed, choices among revascularization techniques could have very broad implications. Accordingly, it is incumbent on every cardiovascular practitioner to stay current with this rapidly evolving evidence base, including methods of optimizing efficiency. Every effort should be made to include the patient in the choice of procedure. Some patients and physicians may prefer the advantages of PCI over CABG when the anatomy is suitable for either procedure, and others will prefer CABG over PCI. But the relative merits of the procedure for an individual patient, informed without self-interest, ought to govern the decision-making for the physician providing care. Within the context of multiple individual decisions and evolving technology and outcomes, we must strive to deliver the technology in the most efficient and effective manner.

**Summary**

What then, are physicians to learn from the 3-year follow-up of the ARTS trial? This report confirms and builds on the results of earlier analyses from ARTS and the other trials of
PCI versus CABG in patients with multivessel coronary artery disease. The frequency of death and infarction are approximately equivalent when one compares an initial strategy of PCI versus CABG. The frequency of repeat revascularization procedures is lower with stents than was previously reported with balloon angioplasty; it is still greater than CABG in the first 3 years after placement of a bare stent but will be lower when drug-eluting stents are used. The need for more frequent repeat revascularization procedures associated with bare stents versus CABG at 3 years reduces the cost savings initially associated with PCI with bare stents versus CABG. Understanding the clinical and economic impact of using drug-eluting stents to treat patients with multivessel disease, and in particular those high-risk patients with diabetes mellitus and chronic kidney disease, awaits further trials.

References


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