Treatment strategy for coronary artery disease: a balancing act

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APPROXIMATELY 10 years after the era of coronary artery bypass graft (CABG) surgery began, the advent of percutaneous transluminal coronary angioplasty (PTCA) added a new dimension to the management of patients with coronary artery disease. Technique and equipment refinement, along with improved operator skill and experience, has led to the expansion of angioplasty to include not only patients with single-vessel disease who would have been treated medically or surgically in the recent past, but also patients with multilesion, multivessel, and distal disease; post-coronary artery bypass graft surgery; or acute myocardial infarction. It is estimated that in 1988 in the United States alone, 235,000 coronary angioplasties were performed, similar to the numbers of patients treated surgically.

This rapid increase reflects a typical cycle of reaction by the medical community to an innovative treatment or technique. Initial skepticism is followed by a wave of enthusiasm as the technique's efficacy is proven and the procedure gains acceptance. Skepticism then re-emerges as the expected benefits are not fully and repetitively achieved. This period is characterized by both constructive and negative criticism as the value of alternative and time-established treatments is reaffirmed (reverse enthusiasm).

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The stage is thus set for the final appraisal, which in situations where many variables may affect a final outcome, usually is the result of randomized trials directly comparing the treatments in question. This four-phase process, in which the various periods are frequently an evolving continuum, balances out conflicting views and leads to the crystallization of scientific truth.

Such a cycle was completed for CABG with the large randomized clinical trials of the last decade. These trials compared CABG and medical therapy for the treatment of patients with coronary artery disease. These studies (Veteran's Administration Cooperative Study, European Coronary Surgery Study, and the Coronary Artery Surgery Study) established the superiority of surgical revascularization over medical treatment in prolonging survival and improving quality of life for certain well-defined patient groups.[1-3]

For angioplasty, we are now moving from the phase of enthusiasm and entering the phase of skepticism. Besides panegyrics from its staunchest proponents, the rapidly expanding application of the technique has met constructive criticism and admonition, along with derogatory comments.[4]

With the technological advances of the past decade providing both a less invasive revascularization procedure and significant progress in surgical technique and perioperative care, a more aggressive approach to coronary revascularization has evolved. In this process, angina has been replaced by ischemia in its varied manifestations as the primary target for treatment.[5] During this period, angioplasty has emerged as the treatment of choice for single-vessel disease, combining ease, low morbidity, and a high success rate. Surgery, which is performed rather infrequently in this setting, becomes

competitive as a treatment option in proximal left anterior descending coronary artery disease, where angioplasty is associated with a high restenosis rate (approximately 40%).[6]

However, the role of PTCA in the treatment of multivessel coronary artery disease still needs to be defined. The issues raised by the use of angioplasty in this setting are very complex and include the safety and efficacy of the procedure, restenosis, extent of revascularization, and event-free survival achieved.

Despite the increasingly higher initial success rate of angioplasty in multivessel disease, its relative efficacy in comparison with CABG in relieving ischemia, preventing myocardial infarction, and prolonging life is not yet established. It is reasonable to assume that since 54% of patients in the 1985–86 NHLBI PTCA Registry had multivessel disease, over 100,000 angioplasties were performed in such patients in 1988.[7] This phenomenon constitutes a paradox, as the limitations of the procedure are being tested in an uncontrolled fashion and its use has expanded in the absence of clearly defined indications or information on long-term results.[8] This expansion of angioplasty into more extensive disease focuses on the need for randomized trials to provide a balanced appraisal of the circumstances under which the application of angioplasty is not just technically feasible but, more importantly, provides the longer-term therapeutic goal.[9]

RANDOMIZED TRIALS UNDER WAY

In the complex management of multivessel disease, the goal is to develop a revascularization strategy that optimally uses either or both techniques in a rational way, maximizing the longer-term benefit, and keeping treatment-related complications to a minimum. There are enormous gaps in our knowledge, however, that prevent us from providing such a therapeutic plan. A well-designed, randomized clinical trial comparing the two forms of revascularization is one major approach to obtaining that information.

Several such trials are under way: the Coronary Artery Bypass Revascularization Investigation (CABRI), the Randomized Intervention Trial of Angina (RITA), the German Angioplasty Bypass Investigation (GABI) in Europe, the Emory Angioplasty or Surgery Trial (EAST), and the NHLBI-sponsored Bypass Angioplasty Revascularization Investigation (BARI) in the United States and Canada. All these trials, each from a different perspective, are expected to contribute to our ability to make better therapeutic decisions.

RITA, under the auspices of the British Cardiac Society, presupposes potential for equal revascularization by either treatment for entry into the study. Follow-up at five years is to be noninvasive.

CABRI, coordinated in France, involves 10 major centers in Europe. Patient eligibility is based on consensus between surgeon and interventional cardiologist that either procedure can benefit the patient. So by addressing a more clinically oriented question and not being limited by angiographic exclusion criteria, a larger patient population could be enrolled. Follow-up includes angiography and thallium-201 stress testing. The primary endpoints are subjective improvement in angina, objective ischemia on exercise testing, and quality of life.

GABI involves five medical centers in Germany. Initial randomization efforts were hampered by a series of angiographic exclusion criteria. Four hundred patients will be randomized and followed with thallium-201 stress testing and angiography.

EAST employs less strict angiographic exclusion criteria, compared to the British and German studies, by allowing patients with totally occluded vessels of less than eight weeks' duration to enter the trial; it is expected that 600 patients will be entered. The main endpoint is a composite consisting of activity level and freedom from events such as ischemia, myocardial infarction, and death. Follow-up includes angiography and thallium-201 stress testing at one and three years.

BARI trial

The BARI trial, in which 14 centers in the United States and Canada are participating, commenced in August 1988. Enrollment of 2,400 patients over the next three years is anticipated. The purpose of the study is to evaluate the relative risks and benefits of angioplasty and CABG as initial treatment for selected patients with multivessel disease in whom myocardial revascularization is indicated and either procedure could be applied according to current practice. Multivessel disease is defined as ≥60% stenosis in at least two main coronary arteries or major branches. Although detailed angiographic entry criteria were contemplated in the design stages of the trial, they were ultimately abandoned. A patient is entered into the study if both a BARI surgeon and a BARI angioplaster believe that either procedure could be performed safely and with expectation of good outcome. This method of screening was chosen to ensure that the study patients will truly reflect the ones currently treated with either revascularization procedure and not an ideal subset of low-risk patients. Asympto-

matic patients are not entered in the study, but mildly symptomatic ones will be entered if exercise testing shows objective evidence of severe ischemia.

The patients will be followed for five years. In addition to clinical assessment and exercise testing, a cardiac catheterization will be repeated at five years and, in selected centers, at one year also. The major endpoints of the study are mortality, as well as morbid events, including Q-wave myocardial infarction, angina, ischemia, congestive heart failure, need for subsequent revascularization, and left ventricular function. Cost and quality of life are also being compared between the two groups.

CONCLUSION

One would expect that from these trials, angioplasty will prove effective for revascularization in some patients with multivessel disease and that neither revascularization procedure will emerge as a sole dominant therapy for all forms of multivessel disease. Careful analysis of the data is expected to yield the information necessary to enable us to determine the role of each revascularization procedure for precisely defined patient subgroups. It is likely that the two procedures will emerge as complementary, and it is certain that the number of patients who in the course of their disease benefit from palliation by both treatments will increase in the years ahead.[8]

The road to balance, the measured approach, passes through the randomized trials. Enthusiasm, skepticism, and disapproval bow to the scientific truth that offers a measure of judgment—a reason to do away with preconceived notions and biases. Optimal patient management based on the wealth of information these studies will provide still remains with the physician. This is the ultimate balancing act and, as always, a measure of judgment for the physician.

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