

## ACC INTERVENTIONAL SCIENTIFIC COUNCIL: NEWS AND VIEWS

# ASCERT: The American College of Cardiology Foundation–The Society of Thoracic Surgeons Collaboration on the Comparative Effectiveness of Revascularization Strategies

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Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide. Despite intensive appraisal, there remain questions regarding the comparative effectiveness of the 2 forms of coronary revascularization therapy: percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery. Clinical experience and randomized clinical trials have shown that some patients are better served with PCI, whereas others experience more benefit with CABG surgery (1,2). However, there remains a large population in which the optimal treatment is not well defined. For example, there has been significant controversy lately concerning unprotected left main stenting; although CABG has long been considered the optimal treatment choice, many interventionalists believe that recent evidence may indicate that there may now be equipoise between the 2 modalities.

All the existing randomized trials over the past 15 years comparing PCI with CABG surgery in multivessel CAD have concluded that, overall, CABG surgery is associated with fewer long-term major clinical events. However, the observed im-

provement in survival is limited to patients with diabetes, and the benefit of fewer repeat procedures is most prominent in those with very extensive CAD. The major advantages of CABG surgery are its ability to achieve complete revascularization, particularly in the setting of chronic total occlusion, and the superior durability of its results, with less residual angina. Its drawbacks include a relatively long recuperation period and a significant incidence of morbidity, including more cerebrovascular events. In contrast, the major advantages of contemporary PCI are its noninvasive nature, the speed of achieving normal or near-normal perfusion in acute coronary syndromes, and relatively minimal morbidity. Additionally, PCI is also effective in diminishing anginal symptoms, particularly in high-risk patients. The opportunity for a less invasive approach in multivessel CAD seems to have become more of a reality since the introduction of drug-eluting stents, which have shown improved survival in nonrandomized trials and reduced repeat revascularization compared with older percutaneous methods. More residual angina and more repeat procedures are the critical shortcomings of PCI (3–5).

The National Cardiovascular Disease Registry working groups of the American College of Cardiology (ACC) in collaboration with the ACC Interventional Scientific Council and the Society of Thoracic Surgery (STS) effectively collaborated in developing a unique grant proposal that was recently awarded a Grand Opportunity grant by the National Heart, Lung, and Blood Institute to study the comparative effectiveness of PCI and CABG surgery for the treatment of stable CAD.

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This study will compare catheter- and surgery-based procedures using the existing ACC and STS databases, as well as the Centers for Medicare and Medicaid Services 100% denominator file data. This study will attempt to bring clarity to the therapeutic decisions required for patients with multivessel CAD. The specific patient characteristics that favor one mode of treatment over the other will be sought and details affecting the selection of patients clearly described. The findings of this study will help physicians make better decisions and improve health care for patients with CAD.

### **Proposed Methodology**

The ACC and the STS both have large national multi-institutional registries containing detailed clinical information on millions of procedures. Information in these databases generally extends to 1 month after the procedure. Short-term clinical information from the ACC and STS registries will be linked to the administrative data registry from the Centers for Medicare and Medicaid Services to provide long-term mortality, rehospitalization, and resource utilization outcomes.

The 3- to 5-year outcomes after CABG surgery will be compared with those after contemporary PCI, using primarily drug-eluting coronary stents. In addition to survival, the need for additional procedures and hospitalizations, new cardiac disease conditions, and the medications being taken at various points in time after the coronary artery procedure will be assessed. The relative incidences and predisposing factors to renal failure, stroke, and repeat revascularization will be appraised. Special considerations in the selection of revascularization procedures in important subgroups will be characterized in detail, such as patients with other severe diseases, women, and elderly patients, and addressed. A comparative analysis in specific anatomic and clinical subsets will be undertaken to assess which therapeutic modality, if either, would be more favored in a particular population.

In an angiographic substudy, the potential value of the application of the SYNTAX score (4) will be studied. A subset of 2,000 patients will be evaluated with regard to SYNTAX score at an angiographic core laboratory. In addition, cost analyses as a function of severity of illness and length of time from the procedure will be conducted. A cost-effectiveness analysis will be performed, with the outcome expressed as the incremental cost per life-year saved with CABG surgery. Net benefit methods will be used that will incorporate the propensity for one therapy over another.

### **Patient Population**

Approximately 101,000 isolated CABG operations and 186,000 PCI procedures were performed on patients meeting eligibility criteria from 2004 to 2006 at 528 hospitals

submitting data to both the STS and ACC databases. After Centers for Medicare and Medicaid Services data for 2007 are included, we anticipate approximately an additional 32,000 isolated CABG patients and 70,000 PCI patients being available for this study. Various patient subsets can be created using a series of clinical and angiographic criteria and results of CABG surgery and PCI compared in each subgroup.

### **Potential Significance of the Current Study**

Observational comparisons from registry databases, although subject to treatment selection bias, can supplement randomized controlled trials (RCTs) with larger numbers, more “real-world” type patients, and more contemporary data, which can be regularly updated. RCT data have been the cornerstone for comparing therapy for decades. The RCT offers the most satisfactory approach for eliminating treatment selection bias. However, RCTs have a lack of generalizability to the community, considerable expense, and results that soon become out of date. Observational studies, although having treatment selection bias, can supplement clinical trial data by having greater generalizability, lower cost, rapid development, large numbers of patients, and the opportunity to consider subgroups. RCTs offer a powerful study design advantage, but they also have significant drawbacks. The study population of an RCT can be very selective, so much so that the study population does not closely approximate the “average” patient. This is one of the criticisms of previous RCTs comparing CABG surgery with PCI.

In this study, the focus will be on the patient groups most often seen in clinical practice. Furthermore, the total number of patients studied in all RCTs combined is <10,000, but there will be >100,000 patients included in this study. Finally, the use of the STS and ACC databases provides an unprecedented amount of clinical information. Compared with RCTs, there is considerably more clinical information gathered in these patients prospectively and from a much broader range of centers across the country.

Furthermore, many of these trials date from the period of balloon angioplasty; there has only been 1 trial comparing drug-eluting stents with CABG surgery, with 1,800 patients, including only 473 from the U.S. (6). Previously, only 2,221 patients were randomized to PCI or CABG surgery in the U.S. in 2 trials from the balloon angioplasty era from the late 1980s to the early 1990s (1). More contemporary outcomes collected in broadly applicable patient subsets are needed to assess comparative effectiveness. There have been observational comparisons of PCI with CABG surgery, specifically from New York State (1), but with smaller numbers than will be available from the STS and ACC registries.

The most significant aspect of the study will be the generation of large populations of specific anatomic and

clinical subsets, with the power to discern the relative advantages and disadvantages of each treatment method. Rather than grouping all adverse events of nonequivalent severity into a single end point category, each type of adverse event will be analyzed separately. This approach will allow patients and physicians to make their own value judgments as to risk and benefit.

Important subsidiary analyses will also have vital connotations for the practice of cardiology in the future. The SYNTAX score has been reported to be highly predictive of which therapeutic revascularization procedure should be favored, based on disease extent, complexity, and severity (6,7). Confirmation in an independent, U.S. dataset could have critical implications for its routine clinical application. Additionally, the economic analysis will generate new information regarding the relative value of the 2 treatment strategies. Cost-effectiveness analysis is a powerful means to guide both individual treatment choices and assess overall health care policies (8).

The STS and ACC registries have been at the forefront of quality improvement activities in cardiovascular medicine for a number of years. Combined, STS and ACC registries cover virtually the entire spectrum of coronary revascularization. These registries contain detailed information collected prospectively, including demographics, cardiovascular history, patient risk factors, comorbid illnesses present on admission, interventions, care processes, and risk-adjusted outcomes surrounding specific clinical events.

In conclusion, this study has the potential to provide significant new information that may confirm or change current clinical practice. The focus of the research (PCI vs. CABG surgery), the use of the 2 most prominent clinical registries in the country, and the fact that collaboration between STS and ACC covers the entire spectrum of adult cardiovascular disease promise that the results will be of great interest to all physicians. Moreover, the data set will be large enough to provide sufficient power to examine patient subgroups. This study will be a model for comparative effectiveness using nonrandomized data, permitting exten-

sive assessment of long-term clinical and economic outcomes after coronary revascularization from the largest clinical databases concerning revascularization in the world.

Members of the Interventional Scientific Council of the ACC, the STS, and the Cardiothoracic Surgeons Council of the ACC will be encouraged to generate further hypotheses for substudies as this project develops.

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