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A Collaborative Ongoing Study by the American College of Cardiology and The Society of Thoracic Surgeons: The ACC-STs Study of 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 two 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 percutaneous coronary intervention (PCI) while others experience more benefit with coronary artery bypass surgery (CABG)^{1, 2}. However, there remains a large population in which the optimal treatment is not well-defined.

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

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multivessel CAD appears to have become more of a reality since the introduction of drug eluting stents, which has shown improved survival in non-randomized trials and reduced repeat revascularization compared to older percutaneous methods. More residual angina and more repeat procedures are the critical shortcomings of PCI³⁻⁵.

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 NHLBI to study the comparative effectiveness of PCI and CABG for the treatment of stable coronary artery disease. This study will compare catheter-based and surgery-based procedures using the existing ACC and STS databases, as well as the Centers for Medicare and Medicaid Services (CMS) 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 impacting the selection of patients clearly described. The findings of this study will help physicians make better decisions and improve healthcare for patients with CAD.

Proposed Methodology

The American College of Cardiology and The Society of Thoracic Surgeons both have large national multi-institutional registries containing detailed clinical information on millions of procedures. Information in these databases generally extends to 1 month following the procedure. Short-term clinical information from the ACC and STS registries will be linked to the administrative data registry from the CMS to provide long-term mortality, rehospitalization, and resource utilization outcomes.

Three to five year outcomes after CABG will be compared to those following contemporary PCI, employing 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 the elderly, 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 score⁴ 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. Cost-effectiveness analysis will be performed, with outcome expressed as the incremental cost per life year saved with CABG. Net benefit methods will be used, which 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 during 2004-2006 at 528 hospitals submitting data to both the STS and ACC databases. After CMS 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 and PCI compared in each subgroup.

Potential significance of the current study

Observational comparisons from registry databases, while subject to treatment selection bias, can supplement randomized controlled trials (RCT) 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 suffer from lack of generalizability to the community, considerable expense, and results that soon become out of date. Observational studies, while suffering from treatment selection bias, can supplement clinical trial data by offering greater generalizability, lower cost, rapid development and large numbers of patients, offering 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 to PCI.

In this study, the focus will be on the patient groups most often seen in clinical practice. Further, the total number of patients studied in all RCTs combined is less than 10,000, but there will be more than 100,000 patients included in this study. Finally the use of the STS and ACC databases provides an unprecedented amount of clinical information. As compared to 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 one trial comparing drug eluting stents to CABG, with 1800 patients, including only 473 from the United States⁶. Previously, only 2221 patients were randomized to PCI vs. CABG in the United States in two trials from the balloon angioplasty era from the late 1980s to the early 1990s¹. More contemporary outcomes collected in broadly applicable patient subsets are needed to assess comparative effectiveness. There have been observational comparisons of PCI to CABG, 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 non-equivalent severity into a single endpoint 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, US dataset could have critical implications for its routine clinical application. Additionally, the economic analysis will generate new information regarding the relative value of the two treatment strategies. Cost effectiveness analysis is a powerful means to guide both individual treatment choices and assess overall healthcare policies⁸.

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, co-morbid 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), use of the two most prominent clinical registries in the country, and the fact that collaboration between STS and ACC covers the entire spectrum of adult cardiovascular disease promises that the results will be of great interest to all physicians. Moreover, the dataset will be large enough to provide sufficient power to examine patient subgroups. This study will be a model for comparative effectiveness using non-randomized data, permitting extensive 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 Society of Thoracic Surgeons, 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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