Highlights from the 57th Annual Scientific Session of the American College of Cardiology

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The Annual Scientific Session of the American College of Cardiology, held in Chicago from March 29 to April 1, 2008, provided a forum for discussion of many current topics of interest to cardiothoracic surgeons. This review provides a brief overview of some of the most innovative and important developments from the scientific session.

Coronary Stents

Evidence of Drug-eluting Stent Safety

A variety of conflicting reports regarding the long-term safety of drug-eluting stents (DES) have been released during the past 24 months. The data presented at the American College of Cardiology Scientific Session, however, supported the overall safety of DES compared with bare metal stents (BMS) on the basis of several randomized trials and large observational registries. Of particular interest was the analysis of the Massachusetts angioplasty registry exploring the use and outcomes of patients treated with coronary stents for acute myocardial infarction between 2003 and 2004. The researchers found that in 5258 matched patients, those treated with DES had lower rates of 2-year mortality, reinfarction, and repeat revascularization compared with patients treated initially with BMS.¹

Role of Drug-eluting Stents in Treatment of Multivessel and Left Main Coronary Artery Disease

Optimizing revascularization strategies for patients with complex multivessel coronary artery disease continues to be an area of intense research interest for the cardiovascular community. The experience of Emory University's novel program of hybrid revascularization for patients with complex multivessel coronary artery disease using endoscopic atraumatic off-pump coronary artery bypass combined with DES treatment of non-left anterior descending artery disease was reviewed. A total of 91 patients were treated under the hybrid protocol with impressive 12-month clinical outcomes including only 1 mortality (1.1%) and 5 patients (5.5%) requiring a repeat percutaneous coronary intervention. The investigators concluded that this technique may offer optimal revascularization outcomes with minimal postoperative recovery time, but a larger experience is required.²

The role of stents for the treatment of left main coronary artery disease was reviewed with the presentation of the 3-year outcomes of the MAIN-COMPARE registry of coronary DES treatment versus coronary bypass surgery in Korea. This large registry included more than 1100 patients with complex left main bifurcation lesions, in whom there were no significant differences in death, myocardial infarction, or stroke between the patients treated with DES and the patients who underwent coronary artery bypass

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
 LDL = low-density lipoprotein

grafting (CABG). However, there was a significantly lower rate of repeat revascularization at 3 years in the patients who underwent surgery.³ The role of percutaneous intervention versus surgery in the treatment of 3-vessel and left main coronary disease is the subject of the 2 large international randomized trials, the SYNTAX trial SYNTAX Study: Synergy Between PCI With TAXUS and Cardiac Surgery, and the FREEDOM trial FREEDOM - Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), both of which are expected to have preliminary results available in the next 24 months.

Catheter-based Treatment for Valvular Heart Disease Preliminary Safety and Efficacy Results for Catheter-based Aortic Valve Replacement Technologies

The treatment of calcific aortic stenosis using catheter-based aortic valve stented prostheses was an area of great interest at the meeting, and the results of the first 216 patients who were treated with the Edwards Sapien pericardial valve (Edwards Lifesciences, Irvine, Calif) via the transfemoral route were reported as an interim update. These high-risk patients had a mean age of 83.2 years and an aortic valve area of 0.60 cm². Procedural success was achieved in 88% of patients (successful implant), with a 12-month survival of 74%. The mean aortic gradient was reduced from 48 mm Hg to less than 15 mm Hg, with minimal residual aortic insufficiency. These hemodynamic results were durable to 12 months. However, 14.8% of the patients had a vascular complication because of the relatively large delivery catheter (21F). The Edwards system is currently undergoing a randomized trial in the United States, the PARTNER study THE PARTNER TRIAL: Placement of aortic transcatheter Valve Trial Edwards SAPIEN Transcatheter Heart Valve, which includes a high-risk surgical cohort, with subjects randomized to receive the device or surgical aortic valve replacement, as well as a nonoperative cohort. Included in the PARTNER study is a transapical catheter approach to be used in those patients in whom femoral access is not feasible.

A second device for catheter-based aortic valve replacement therapy, the CoreValve (CoreValve Inc, Irvine, Calif), a self-expanding stented pericardial valve system, has been deployed in more than 540 patients worldwide. This 18F diameter system led to a 1% rate of major vascular complications and similar improvement in hemodynamics compared with the Edwards system, but was associated with permanent pacemaker implantation in 13% to 24% of patients. The 30-day mortality for the CoreValve system was 17% in these very high-risk

patients (average EuroScore of 24), with a cardiac mortality of 9% at 30 days. This system has received Conformité Européenne Mark approval and is currently only available outside of the United States.⁴ Although the 12-month results are promising for both transcatheter aortic valve replacement technologies, these first-generation devices have unknown valve durability. The results of the pivotal randomized trial of the Edwards valve will be critical to determine the role of this technology in future clinical practice.

Preliminary Results of Percutaneous Edge-to-Edge Clip Repair for Functional Mitral Regurgitation

Another area of interest was the varied approaches to catheter-based treatment of mitral regurgitation. Early testing of percutaneous annular reduction technologies was reviewed, including strategies using the coronary sinus approach or direct ventricular or atrial suturing methods. The interim results of the EVEREST trial EVEREST - A Study of the Evalve Cardiovascular Valve Repair System Endovascular Valve Edge-to-Edge REpair Study (EVEREST II) for the evaluation of the edge-to-edge mitral repair procedure using the MitraClip technology (eValve Incorporated, Irvine, CA) mimicking the Alfieri repair, were reviewed for patients with functional mitral regurgitation. The procedure, which involves a transseptal approach to the position and deployment of the nitinol clip without associated annuloplasty, has been performed in more than 300 patients with 3 to 4+ mitral regurgitation with associated A2-P2 malcoaptation, as part of the EVEREST trials. Of these patients, 23 had pure functional mitral regurgitation, 19 of whom underwent successful clip implantation. In these patients, there was a significant reduction in mitral regurgitation to less than grade 2 in 74% of patients, and reduction in ventricular dimensions associated with significant improvement in functional class at 12 months follow-up. There were no clip embolizations, and 83% of patients remained free of mitral surgery after 12 months.⁵ However, the small sample size and lack of physiologic preservation of the mitral valve architecture remain areas of concern for this technique. The results of the randomized EVEREST II study, expected in the next 18 months, will clarify the role of this technology relative to surgical mitral valve repair.

Outside of the data available for transcatheter aortic and mitral valve therapies, preliminary results were reviewed in other areas of transcatheter structural heart disease approaches. Among these were ongoing trials for stents and stent-grafts for the primary transcatheter treatment of aortic coarctation (COAST trial COAST - Coarctation Of the Aorta Stent Trial), continuing enrollment updates in the prevention of stroke with transcatheter closure of patent foramen ovale (CLOSURE CLOSURE II Trial - A Prospective, Multicenter, Randomized Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex® Septal Closure System Versus Best Medical Therapy in Patients With a Stroke and/or

Transient Ischemic Attack Due to Presumed Paradoxical Embolism Through a Patent Foramen Ovale and RESPECT Trial - Patent Foramen Ovale Closure With the AMPLATZER PFO OCCLUDER in Patients With Recurrent Cryptogenic Stroke Due to Presumed Paradoxical Embolism Through a Patent Foramen Ovale), and transcatheter occlusion of the left atrial appendage in the nonpharmacologic management of atrial fibrillation (WATCHMAN trial - WATCHMAN Left Atrial Appendage System for Embolic protection in Patients With Atrial Fibrillation). The results of these important trials will become available during the next 12 to 36 months.

Coronary Artery Disease Pharmacology

Lack of benefit of Ezetimibe in the Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression Trial

Most controlled trials of lipid-lowering therapy have shown significant reductions in cardiovascular events that correlate tightly with the degree of achieved low-density lipoprotein (LDL) reduction.⁷ Ezetimibe, a novel cholesterol-lowering compound, selectively inhibits dietary cholesterol absorption and, in combination with statins, provides significant incremental reductions in LDL cholesterol levels. The Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression trial⁶ sought to determine whether the combination of ezetimibe and simvastatin could reduce progression of atherosclerosis in patients with familial hypercholesterolemia relative to high-dose simvastatin alone. During 2 years of observation in 720 patients in this study, despite an incremental 16.5% reduction in LDL among ezetimibe-treated patients, there was no difference in the primary outcome of change in carotid artery intimal mean thickness between the 2 treatment groups. Because the rate of intimal mean thickness progression is historically a good correlate of cardiovascular events, this study raises concern that the lowering of LDL cholesterol with ezetimibe may not be clinically beneficial. Although definitive data regarding the clinical efficacy of ezetimibe await the results of ongoing trials, such as IMPROVE-IT (expected in 2011 IMPROVE-IT - (IMproved Reduction of Outcomes: Vytorin Efficacy International Trial), the Ezetimibe and Simvastatin in Hypercholesterolemia Enhances Atherosclerosis Regression trial results caution physicians treating patients with cardiovascular disease to first optimize the dosing of statins to meet guideline-based LDL targets and then to add drugs with proven clinical benefits (nicotinic acid, fibrates, and bile-acid sequestrants) for those who fail to achieve target with statins alone.

Benefits of Intensive Antiplatelet Therapy in Acute Coronary Syndromes

A secondary analysis of patients undergoing intracoronary stenting during an acute coronary syndrome after randomization in the TRITON TIMI-38 trial TRITON-TIMI-38 - A

Comparison of Prasugrel and Clopidogrel in Acute Coronary Syndrome Subjects Who Are to Undergo Percutaneous Coronary Intervention of Prasugrel (a potent thienopyridine) versus Clopidogrel was presented. This analysis revealed that treatment with prasugrel was associated with a significant reduction in the rate of stent thrombosis (prasugrel 0.88% vs clopidogrel 2.03%, hazard ratio 0.42, $P < .0001$) independently of the type of stent used (BMS vs DES).⁸ The clinical implication from this analysis is the likelihood that if prasugrel is approved for use in the United States, it will likely become a front-line agent in the prevention of stent-associated thrombosis for patients with acute coronary syndrome.

Lack of Benefit of MC-1 in Ischemia-Reperfusion Injury

The results of the MEND-CABG I trial MEND-CABG I-A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging, Multi-Center Study to Evaluate the Cardiovascular and Cerebrovascular Effects of MC-1 in Patients Undergoing High-Risk Coronary Artery Bypass Graft (CABG) Surgery suggested potential benefit of MC-1 (pyridoxal-5'-phosphate, a purinergic P2-receptor antagonist that reduces intracellular calcium influx) in reducing perioperative myocardial infarction among patients undergoing CABG. However, the MEND-CABG II,⁹ a pivotal, phase-3, placebo-controlled trial of MC-1 (250 mg/d, administered immediately before and 30 days after surgery) among 1519 patients undergoing CABG, revealed no difference in the primary end point of cardiovascular death or nonfatal myocardial infarction at 30 days. MC-1 therefore joins the list of agents that fail to affect reperfusion injury after CABG.

New Treatment for Acute Heart Failure

The HORIZON-HF trial HORIZON HF - A Phase II Study to Assess the Hemodynamic Effects of Istaroxime, a Novel Lusitotropic Agent, in Patients Hospitalized With Worsening Heart Failure and a Reduced Left Ventricular Systolic Function¹⁰ randomized 120 patients with a left ventricular ejection fraction $\leq 35\%$ and acute decompensated heart failure stabilized with conventional medical therapy to a 6-hour infusion of istaroxime or placebo. In this dose-ranging study, istaroxime administration was associated with a rapid, sustained decrease in pulmonary capillary wedge pressure and improvement in some measures of systolic and diastolic function. In contrast with many currently available inotropic agents, the observed improvements in cardiac function seen with istaroxime were associated with an *increase* in systolic blood pressure and a *decrease* in heart rate. Whether these differential hemodynamic effects will be replicated in patients with more advanced acute decompensated heart failure and low cardiac output or will translate to meaningful improvements in clinical outcomes remains a subject for future study.

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