Highlights from the 59th Annual Scientific Sessions of the American College of Cardiology, March 13 to 17, 2010, Atlanta, Georgia

Frederic S. Resnic, MD, MSc, FACC, and Akshay Desai, MD, MPH, FACC

The 59th Annual Scientific Sessions of the American College of Cardiology (ACC), held March 13 to 17, 2010, in Atlanta, Georgia, provided a forum for the initial release of clinical trial data and a comprehensive review of many topics of significant interest to cardiothoracic surgeons. We provide a brief overview of the 5 most innovative and important developments from the ACC scientific sessions.

1. The EVEREST II Trial: Randomized Comparison of Catheter-based Treatment for Severe Mitral Regurgitation Versus Surgical Repair or Replacement. The results of the randomized trial of catheter-based treatment for severe mitral regurgitation (MR) and traditional mitral valve (MV) repair or replacement surgery, the EVEREST II study, were reported at the ACC Scientific Sessions on March 13, 2010, by Dr Ted Feldman. In this important study, patients with 3+ and 4+ MR, as assessed by a blinded core echocardiographic laboratory, were randomly assigned in a 2:1 manner to receive the MitraClip device (Abbott Laboratories, Abbott Park, IL) ($n = 184$) or open MV surgical repair or replacement ($n = 95$) and then followed clinically for 1 year.¹ The groups were well balanced for demographic and clinical features, although there was a slight excess of congestive heart failure in the clip group compared with the surgical group (90.8% vs 77.9%, $P < .001$). The majority of patients (86%) treated in the surgical arm underwent MV repair, with excellent clinical outcomes.

In the per-protocol analysis, major adverse events at 30 days, including death, myocardial infarction, reoperation for mitral disease, transfusion requirement more than 2 units, stroke, renal failure, sepsis, and deep wound infection, occurred in 9.6% of the clip group versus 57% of the control group ($P < .001$ for superiority of the clip treatment). This outcome was driven primarily by a significantly increased need for blood transfusion in the surgical group. Clinical success rate at 12 months, defined as freedom from death and reoperation for MV surgery and MR greater than 2+ grade, was 72.4% in the clip group versus 87.8% in the control group ($P < .001$ for

noninferiority of clip treatment). At 12 months in the per-protocol analysis, 82% in the clip group achieved 2+ or less MR versus 97% in the control group. Symptom control was excellent in both treated populations (New York Heart Association class I or II at follow-up was 98% in the clip group vs 88% in the surgical group). The results were unchanged when an intention-to-treat analytic framework was used. The echocardiographic results at 12 months also demonstrated significant improvements in left ventricular volumes and dimensions with either treatment (clip or surgery).²

These initial results of the EVEREST II trial are provocative and indicate that the percutaneous edge-to-edge treatment for significant MR afforded by the MitraClip device may be an important therapeutic option for selected patients given the demonstrated safety, effectiveness, and clinical benefit. Long-term follow-up data will be collected in these patients through 5 years of follow-up, at which time the durability and long-term efficacy of the procedure will be evaluated.

2. The Veterans Affairs Cooperative Trial CSP-474 of Radial Artery versus Saphenous Venous Grafting in Coronary Artery Bypass Surgery. The optimal choice of bypass conduit type beyond the routine use of the left internal thoracic artery graft during coronary artery bypass grafting (CABG) has been controversial. Therefore, the relative advantage of routine use of the radial artery (RA) as a conduit during CABG was evaluated in the Veterans Affairs cooperative study of the radial artery versus saphenous venous grafting in coronary bypass surgery. In this study performed at 11 VA cardiac surgical centers, Dr Steven Goldman presented the 1-year angiographic patency of RA conduits ($n = 366$) compared with the patency of saphenous vein (SV) grafts ($n = 367$). At 1 week, routine angiography demonstrated a patency rate of 99% for the RA grafts and 97% for the SV grafts. At 1 year, both conduit types achieved an angiographic patency rate of 89%. Secondary analyses demonstrated a lower rate of SV patency if endoscopic harvesting was used compared with open harvesting techniques (12-month patency rates: 78% vs 91%, $P < .001$). In addition, the RA grafts were more likely than SV grafts to fail because of diffuse disease at 1 year (ie, "string sign" failure; 8% vs 1.0%, $P < .001$). The target of the graft was not predictive of patency for the SV or RA graft. Although on-pump procedures were associated with higher patency rates for SV grafts compared with off-pump bypass surgeries (90% vs 78%, $P < .001$), there

From the Brigham and Women's Hospital and Harvard Medical School, Boston, Mass.

Address for reprints: Frederic S. Resnic, MD, MSc, FACC, Division of Cardiology, Brigham and Women's Hospital, 75 Francis St, Tower 3B, Boston, MA 02115 (E-mail: fresnic@partners.org).

J Thorac Cardiovasc Surg 2010;140:257-9

0022-5223/\$36.00

Copyright © 2010 by The American Association for Thoracic Surgery

doi:10.1016/j.jtcvs.2010.04.003

were no differences in the patency rates of RA grafts stratified by on- or off-pump procedures.³

This Veterans Affairs cooperative study demonstrated identical 12-month graft patency rates for RA versus SV grafts during elective CABG. Additional angiographic follow-up to 5 years is planned for patients treated during this study, which should help to answer whether longer-term patency rates remain similar between the 2 conduit types.

3. Additional Surgical Treatment of Ischemic Heart Failure Trial Data Find No Subset of Patients Who Benefit from Surgical Ventricular Reconstruction over Coronary Artery Bypass Grafting Alone. The primary results for “hypothesis 1” of the Surgical Treatment of Ischemic Heart Failure (STICH) trial revealed that among patients with left ventricular ejection fraction of 35% or less, coronary artery disease amenable to CABG, and predominant anterior left ventricular dysfunction amenable to surgical ventricular reconstruction (SVR), the combination of SVR and CABG resulted in significant reduction in left ventricular volumes but no improvement in anginal symptoms, exercise tolerance, or the composite of death or hospitalization for cardiovascular causes relative to CABG alone.⁴

New subgroup analyses from STICH presented at ACC 2010 shed additional light on this topic. Dr Robert Michler presented data on the subgroup of 595 STICH subjects with accurate measurements of preoperative and 4-month postoperative end-systolic volume index (ESVI). Among this subset (which had lower overall mortality than the STICH population as a whole), no group of patients deriving benefit from SVR could be identified on the basis of segregation by preoperative ESVI or achieved reduction in ESVI. As for the larger trial, the achieved reduction in ESVI was greater in patients receiving CABG + SVR versus CABG alone. Of note, however, CABG alone was associated with a mean 15% reduction in ESVI, with more than 20% of patients achieving a reduction of more than 30%. Relative to CABG alone, a nonsignificant trend toward enhanced mortality was seen with combined SVR + CABG for patients with preoperative ESVI greater than 90 mL/m². Despite a trend favoring the addition of SVR among those with an ESVI of 90 mL/m² or less, no statistically significant advantage over CABG alone could be identified. These results were not altered by confining the analysis to those with large achieved postoperative reductions in ESVI.⁵

Overall, these data, which complement previous subgroup analyses of global and regional left ventricular function from STICH arriving at similar conclusions, suggest that there is no definable subgroup of patients with ischemic cardiomyopathy who clearly benefit

from the addition of SVR to CABG alone. Results from hypothesis 1 of the STICH trial, investigating the benefits of CABG relative to optimal medical therapy in patients with coronary artery disease and left ventricular dysfunction, are expected in 2011.

4. Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery—Platelet Inhibition and Patient Outcomes Subanalysis. Although current guidelines support the use of clopidogrel as an adjunct to aspirin therapy in patients with acute coronary syndromes, recent data highlight that clopidogrel efficacy may be limited in practice by substantial variability in platelet inhibition, increased rates of bleeding (particularly after CABG), and a higher risk of stent thrombosis and myocardial infarction in nonresponders.⁶ Ticagrelor is a novel, reversible, oral antagonist of the adenosine diphosphate receptor P2Y₁₂ that provides faster, greater, and more consistent P2Y₁₂ inhibition than clopidogrel.⁷ The primary results of the Platelet Inhibition and Patient Outcomes (PLATO) study, initially reported in 2009,⁸ revealed that in patients presenting with an acute coronary syndrome, randomization to treatment with ticagrelor (180 mg loading dose, 90 mg twice daily thereafter) versus clopidogrel (300–600 mg loading dose, 75 mg daily thereafter) was associated with a statistically significant reduction in the rate of the composite end point of death from vascular causes, myocardial infarction, or stroke (9.8% vs 11.4%; hazard ratio [HR] 0.84; 95% confidence interval [CI], 0.77–0.92; $P < .001$). Remarkably, the benefit of ticagrelor over clopidogrel was not associated with an increase in the rate of major bleeding (11.6% for ticagrelor vs 11.2% for clopidogrel, $P = .43$).

At the ACC 2010 Scientific Sessions, Dr Claes Held and colleagues presented additional data regarding outcomes in the subgroup of 1260 patients randomized in PLATO who subsequently underwent CABG with cessation of study drug within 7 days of surgery. In this prespecified, but retrospective subgroup analysis, no difference was seen between ticagrelor and clopidogrel with regard to the primary composite PLATO outcome, the rates of myocardial infarction, or the rates of stroke. However, there was a striking, statistically significant 50% reduction in both all-cause (4.6% vs 9.2%, HR 0.49, $P = .002$) and cardiovascular (4.0% vs 7.5%, HR 0.52, $P = .009$) mortality in the ticagrelor-treated patients.⁹ Because no difference was seen between the 2 therapies with regard to the rates of post-CABG bleeding, myocardial infarction, or stroke, the mechanism of this substantial mortality reduction remains unclear. Overall, however, the promise of greater mortality reduction without an incremental risk of bleeding around the time of CABG heightens interest in ticagrelor as an alternative

to clopidogrel in the management of patients with acute coronary syndromes.

5. Five-Year Outcomes of the MAIN-COMPARE Registry of Left Main Coronary Artery Revascularization with Coronary Stenting versus Coronary Artery Bypass Grafting. Dr Seung-Yung Park reported the 5-year outcomes of the largest prospective registry of unprotected percutaneous coronary intervention versus CABG. Between January 2000 and June 2006, The Revascularization for Unprotected Left MAIN Coronary Artery Stenosis: COMparison of Percutaneous Coronary Angioplasty versus Surgical REvascularization from Multi-Center Registry (MAIN-COMPARE) collected detailed clinical and angiographic information on 1106 patients treated with coronary stenting compared with 1138 patients treated with CABG. Patients were followed for 5 years after their index procedure and evaluated for survival, Q-wave myocardial infarction, stroke, and target vessel revascularization using a propensity-matched algorithm. Before matching, the patients who received percutaneous coronary intervention were younger; less likely to have diabetes, hyperlipidemia, or renal insufficiency; less likely to be active smokers; and more likely to have had prior coronary interventional procedures.¹⁰ After the propensity match, 542 pairs of well-matched patients, without remaining baseline clinical or angiographic differences, were analyzed. At 3 years, there were no differences in survival or subsequent myocardial infarction between the treatment groups, although the stent group had a higher rate of repeat revascularization than the CABG group (12.6% vs 2.6%, $P < .001$).¹¹ At a median of 5.2 years of follow-up, the clinical results seen at 3 years were sustained. Although the rate of target vessel revascularization was significantly higher in the stent group (HR, 5.11; 95% CI, 3.52–7.42; $P < .001$), the risk of death for the stent group was not significantly different than that for the CABG group (HR 1.13; 95% CI, 0.88–1.44; $P = .35$). The combined risk of death, Q-wave myocardial infarction, and stroke (HR 1.07; 95% CI, 0.84–1.37; $P = .59$) was similar for both groups. Stent type (bare metal or drug eluting) did not significantly change these results. There was, however, a non-

significant trend toward an increase in the absolute mortality rate in the latter follow-up period (years 3–5) in the stent group compared with the CABG group.¹⁰

The 5-year MAIN-COMPARE results are consistent with the 1-year results of the SYNTAX trial, a prospective trial of 1800 patients with either left main or 3-vessel coronary artery disease undergoing revascularization who were randomized to drug-eluting stent treatment or CABG. The late separation of the mortality curves seen in the MAIN-COMPARE study warrant continued study through long-term follow-up of registry and randomized trial left main revascularization cohorts.

References

1. Feldman T, Kar S, Rinaldi M, et al. Percutaneous mitral repair with the Mitra-Clip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. *J Am Coll Cardiol*. 2009;54:686-94.
2. Feldman T. The Endovascular Valve Edge-to-Edge Repair Study (EVEREST II). Presented at the 59th Scientific Sessions of the American College of Cardiology: Late Breaking Clinical Trials, March 14, 2010, Atlanta, Georgia.
3. Goldman S. Radial artery grafts versus saphenous vein grafts in coronary artery bypass surgery: VA Cooperative Study (VA CABG) presented at the 59th Scientific Sessions of the American College of Cardiology: Late Breaking Clinical Trials, March 16, 2010, Atlanta, Georgia.
4. Jones RH, Velazquez EJ, Michler RE, et al. Coronary bypass surgery with or without surgical ventricular reconstruction. *N Engl J Med*. 2009;360:1705-17.
5. Michler RE. Influence of reduction of left ventricular volume on outcome after coronary artery bypass grafting with or without surgical ventricular reconstruction. Presented at the 59th Scientific Sessions of the American College of Cardiology: Late Breaking Clinical Trials, March 16, 2010, Atlanta, Georgia.
6. Mega JL, Close SL, Wiviott SD, et al. Cytochrome P-450 polymorphisms and response to clopidogrel. *N Engl J Med*. 2009;360:354-62.
7. Storey RF, Husted S, Harrington RA, et al. Inhibition of platelet aggregation by AZD6140, a reversible oral P2Y₁₂ receptor antagonist, compared with clopidogrel in patients with acute coronary syndromes. *J Am Coll Cardiol*. 2007;50:1852-6.
8. Wallentin L, Becker RC, Budahj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med*. 2009;361:1045-57.
9. Held C. Ticagrelor versus clopidogrel in patients with acute coronary syndromes undergoing coronary artery bypass surgery: results from the PLATO trial. Presented at the 59th Scientific Sessions of the American College of Cardiology: Late Breaking Clinical Trials, March 16, 2010, Atlanta, Georgia.
10. Park SJ. Five long-term safety and efficacy of stenting versus coronary-artery bypass grafting for unprotected left main coronary artery disease: 5-year results from the MAIN-COMPARE Registry. Presented at the 59th Scientific Sessions of the American College of Cardiology: Late Breaking Clinical Trials, March 14, 2010, Atlanta, Georgia.
11. Seung KB, Park DW, Kim YH, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med*. 2008;358:1781-92.