

# Summary of the Clinical Studies Reported in the Annual Scientific Sessions of the American Heart Association (Orlando, USA, November 14-18, 2009)

Leopoldo Pérez de Isla,<sup>a</sup> Antoni Bayes-Genis,<sup>a</sup> Juan Sanchis,<sup>a</sup> and Magda Heras<sup>b</sup>

<sup>a</sup>Editor Asociado, REVISTA ESPAÑOLA DE CARDIOLOGÍA

<sup>b</sup>Editora Jefe, REVISTA ESPAÑOLA DE CARDIOLOGÍA

Consistent with the objectives of REVISTA ESPAÑOLA DE CARDIOLOGÍA to facilitate the dissemination of scientific information among its readership, and following the precedent set in previous issues of the journal,<sup>1-6</sup> here we report a selection of the most significant studies presented during at the American Heart Association Scientific Sessions 2009 in Orlando (Florida, USA), specifically the so-called late-breaking clinical trials.

For each of the studies highlighted here, we provide a summary that includes a brief description of the objectives, methods, and results presented in the oral presentations or, where applicable, published simultaneously in electronic format in scientific journals. Given that complete reports have yet to be published for many of the studies, the information provided here should be considered preliminary.

## SUMMARY BY TOPIC

### Prevention

The ARBITER 6 study: extended-release niacin or ezetimibe and carotid intima-media thickness.

### Ischemic Heart Disease

CHAMPION-PCI study: platelet inhibition with cangrelor in patients undergoing PCI.

CHAMPION PLATFORM study: intravenous platelet blockade with cangrelor during PCI.

POPULAR study: do point-of-care platelet function assays predict clinical outcomes in clopidogrel pretreated patients undergoing elective PCI?

The RE-DEEM study: randomised dabigatran etexilate dose finding study in patients with acute coronary syndromes post index event.

### Cardiovascular Imaging

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### Heart Failure

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HEAAL study: effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure.

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PACE study: biventricular pacing in patients with bradycardia and normal ejection fraction.

### Cardiac Surgery

Bypassing the blues: telephone-delivered collaborative care for post-CABG depression.

OCTOPUS study: long-term cardiac and neurocognitive outcome after off-pump CABG versus PCI.

### Arrhythmias

The RECORD-AF registry: differences in clinical outcomes with rhythm- and rate-control therapies for atrial fibrillation in the RECORD-AF registry.

### Miscellaneous

EFFECT study: effectiveness of public report cards for improving the quality of cardiac care.

Correspondence: REVISTA ESPAÑOLA DE CARDIOLOGÍA. Sociedad Española de Cardiología. Nuestra Señora de Guadalupe, 5-7. 28028 Madrid. Spain. E-mail: rec@revespcardiologia.org

TREAT study: a trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease.

## PREVENTION

### Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness.<sup>7</sup> The ARBITER 6 Study

Presented by Dr Allen J. Taylor, Washington, DC, USA.

**Background.** Treatment added to statin monotherapy to further modify the lipid profile may include combination therapy to either raise the high-density lipoprotein cholesterol (HDL-C) level or further lower the low-density lipoprotein cholesterol (LDL-C) level.

**Methods.** We enrolled patients who had coronary heart disease or a coronary heart disease risk equivalent, who were receiving long-term statin therapy, and in whom an LDL-C level <100 mg/dL (2.6 mmol/L) and an HDLC level <50 mg/dL for men or 55 mg/dL for women (1.3 or 1.4 mmol/L, respectively) had been achieved. The patients were randomly assigned to receive extended-release niacin (target dose, 2000 mg/d) or ezetimibe (10 mg/d). The primary end point was the between-group difference in the change from baseline in the mean common carotid intima-media thickness after 14 months. The trial was terminated early, on the basis of efficacy, according to a prespecified analysis conducted after 208 patients had completed the trial.

**Results.** The mean HDL-C level in the niacin group increased by 18.4% over the 14-month study period, to 50 mg/dL ( $P<.001$ ), and the mean LDL-C level in the ezetimibe group decreased by 19.2%, to 66 mg/dL (1.7 mmol/L) ( $P<.001$ ). Niacin therapy significantly reduced LDL-C and triglyceride levels; ezetimibe reduced the HDL-C and triglyceride levels. As compared with ezetimibe, niacin had greater efficacy regarding the change in mean carotid intima-media thickness over 14 months ( $P=.003$ ), leading to significant reduction of both mean ( $P=.001$ ) and maximal carotid intima-media thickness ( $P\leq.001$  for all comparisons). Paradoxically, greater reductions in the LDL-C level in association with ezetimibe were significantly associated with an increase in the carotid intima-media thickness ( $R=-0.31$ ,  $P<.001$ ). The incidence of major cardiovascular events was lower in the niacin group than in the ezetimibe group (1% vs 5%,  $P=.04$  by the  $\chi^2$  test).

**Conclusions.** This comparative-effectiveness trial shows that the use of extended-release niacin causes a significant regression of carotid intima-media

thickness when combined with a statin and that niacin is superior to ezetimibe.

## ISCHEMIC HEART DISEASE

### CHAMPION PCI: Platelet Inhibition With Cangrelor in Patients Undergoing PCI.<sup>8</sup>

Presented by Dr Robert Harrington, Durham, NC, USA.

**Background.** Cangrelor, a nonthienopyridine adenosine triphosphate analogue, is an intravenous blocker of the adenosine diphosphate receptor P2Y<sub>12</sub>. This agent might have a role in the treatment of patients who require rapid, predictable, and profound but reversible platelet inhibition.

**Methods.** We performed a large-scale international trial comparing cangrelor with 600 mg of oral clopidogrel administered before percutaneous coronary intervention (PCI) in patients with acute coronary syndromes.

The primary efficacy end point was a composite of death from any cause, myocardial infarction, or ischemia-driven revascularization at 48 hours.

**Results.** We enrolled 8877 patients, and 8716 underwent PCI. At 48 hours, cangrelor was not superior to clopidogrel with respect to the primary composite end point, which occurred in 7.5% of patients in the cangrelor group and 7.1% of patients in the clopidogrel group (odds ratio, 1.05; 95% confidence interval [CI], 0.88-1.24;  $P=.59$ ). Likewise, cangrelor was not superior at 30 days. The rate of major bleeding (according to Acute Catheterization and Urgent Intervention Triage Strategy criteria) was higher with cangrelor, a difference that approached statistical significance (3.6% vs 2.9%; odds ratio, 1.26; 95% CI, 0.99-1.60;  $P=.06$ ), but this was not the case with major bleeding (according to the Thrombolysis in Myocardial Infarction criteria) or severe or life-threatening bleeding (according to Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries criteria). A secondary exploratory end point of death from any cause, Q-wave myocardial infarction, or ischemia-driven revascularization showed a trend toward a reduction with cangrelor, but it was not significant (0.6% vs 0.9%; odds ratio, 0.67; 95% CI, 0.39-1.14;  $P=.14$ ).

**Conclusions.** Cangrelor, when administered intravenously 30 minutes before PCI and continued for 2 hours after PCI, was not superior to an oral loading dose of 600 mg of clopidogrel, administered 30 minutes before PCI, in reducing the composite end point of death from any cause, myocardial infarction, or ischemia-driven revascularization at 48 hours.

## **CHAMPION PLATFORM: Intravenous Platelet Blockade with Cangrelor during PCI**

*Presented by Dr Deepak Bhatt, Boston, MA, USA.*

**Background.** Intravenous cangrelor, a rapid-acting, reversible adenosine diphosphate (ADP) receptor antagonist, might reduce ischemic events during percutaneous coronary intervention (PCI).

**Methods.** In this double-blind, placebo-controlled study, we randomly assigned 5362 patients who had not been treated with clopidogrel to receive either cangrelor or placebo at the time of PCI, followed by 600 mg of clopidogrel. The primary end point was a composite of death, myocardial infarction, or ischemia-driven revascularization at 48 hours. Enrollment was stopped when an interim analysis concluded that the trial would be unlikely to show superiority for the primary end point.

**Results.** The primary end point occurred in 185 of 2654 patients receiving cangrelor (7%) and in 210 of 2641 patients receiving placebo (8%) (odds ratio in the cangrelor group, 0.87; 95% confidence interval [CI], 0.71-1.07;  $P=.17$ ) (modified intention-to-treat population adjusted for missing data). In the cangrelor group, as compared with the placebo group, 2 prespecified secondary end points were significantly reduced at 48 hours: the rate of stent thrombosis, from 0.6% to 0.2% (odds ratio, 0.31; 95% CI, 0.11-0.85;  $P=.02$ ), and the rate of death from any cause, from 0.7% to 0.2% (odds ratio, 0.33; 95% CI, 0.13-0.83;  $P=.02$ ). There was no significant difference in the rate of blood transfusion (1% in the cangrelor group and 0.6% in the placebo group,  $P=.13$ ), though major bleeding on one scale was increased in the cangrelor group, from 3.5% to 5.5% ( $P<.001$ ), because of more groin hematomas.

**Conclusions.** The use of periprocedural cangrelor during PCI was not superior to placebo in reducing the primary end point. The prespecified secondary end points of stent thrombosis and death were lower in the cangrelor group, with no significant increase in the rate of transfusion. Further study of intravenous ADP blockade with cangrelor may be warranted.

## **The POPULAR Study: Do Point-of-Care Platelet Function Assays Predict Clinical Outcomes in Clopidogrel Pretreated Patients Undergoing Elective PCI?**

*Presented by Nicoline J. Breet, Nieuwegein, the Netherlands.*

**Background.** In patients undergoing elective PCI, several platelet function tests can help

predict 1-year thrombosis but not bleeding events. Dual antiplatelet therapy is indicated in patients undergoing PCI with stent implantation. Up to 36% of patients have decreased response to clopidogrel. The mechanism of clopidogrel resistance is multifactorial and includes alteration in drug metabolism due to genetic polymorphisms. Several studies have shown that platelet function testing is associated with clinical outcomes. However, it is unclear which platelet function test best predicts clinical events. The purpose of this study was to identify the platelet function test that best predicts clinical outcome.

**Methods.** This study performed a head-to-head comparison among seven platelet function tests: light transmittance aggregometry (LTA) (5 and 20  $\mu\text{mol/L}$  ADP), VerifyNow<sup>®</sup> P2Y<sub>12</sub>, Plateletworks<sup>®</sup>, IMPACT-R, IMPACT-R ADP, PFA-100 COL/ADP, and INNOVANCE<sup>®</sup> PFA P2Y. The 1-year primary endpoint was the composite of death, myocardial infarction, stent thrombosis and stroke. The 1-year primary safety endpoint was TIMI major and minor bleeding.

**Results.** A total of 1069 patients undergoing elective PCI with stent implantation treated with clopidogrel were included. The 7 platelet function tests were performed on the majority of patients. The mean age was 64 years, and 74% were men. Approximately 36% of patients were treated with bare-metal stents (BMS), and 64% treated with drug-eluting stents (DES).

At 1 year, LTA 5  $\mu\text{mol/L}$  ADP, LTA 20  $\mu\text{mol/L}$  ADP, VerifyNow<sup>®</sup>-P2Y<sub>12</sub>, Plateletworks<sup>®</sup> predicted primary endpoint. Patients with and without platelet inhibition had approximately 6% and 12% events at 1 year, respectively. Based on the 1-year primary endpoint, the area under the curve (AUC) for receiver operator characteristic for LTA 5  $\mu\text{mol/L}$  ADP, LTA 20  $\mu\text{mol/L}$  ADP, VerifyNow<sup>®</sup> P2Y<sub>12</sub>, Plateletworks<sup>®</sup>, IMPACT-R, IMPACT-R ADP, PFA-100 COL/ADP, and INNOVANCE<sup>®</sup> PFA P2Y was 0.63, 0.62, 0.62, 0.61, 0.56, 0.53, 0.50, and 0.56, respectively. Platelet reactivity did not predict 1-year bleeding events. Logistic regression modeling using clinical factors alone found an AUC of 0.64 in predicting 1-year primary endpoint. Adding procedural risk factors such as lesion and stent characteristics, the AUC increased to 0.72. Adding platelet reactivity resulted in a statistically significant increase in AUC for LTA 5  $\mu\text{mol/L}$  ADP, LTA 20  $\mu\text{mol/L}$  ADP, VerifyNow<sup>®</sup> P2Y<sub>12</sub>, Plateletworks<sup>®</sup>, although the absolute AUC was only modestly increased (0.74, 0.73, 0.74, and 0.78, respectively). The remainder platelet function tests did not provide additional value.

**Conclusions.** Some of the available platelet function tests added incremental value predicting clinical outcomes. However, of the tests with predictive value, only Plateletworks<sup>®</sup> and VerifyNow<sup>®</sup>-P2Y<sub>12</sub> are bedside assays. In addition, Plateletworks<sup>®</sup> is highly time-sensitive and must be performed <10 minutes from blood draw.

### The RE-DEEM Study: Randomised Dabigatran Etxilate Dose Finding Study in Patients With Acute Coronary Syndromes Post Index Event

*Presented by Dr Jonas Oldgren, Uppsala, Sweden.*

**Background.** The aim of this study was to compare different doses of dabigatran, an oral direct thrombin inhibitor, with placebo in patients with acute coronary syndrome. The study hypothesis was that dabigatran does not lead to an increase in clinically significant bleeding.

**Methods.** Following ST-elevation (STEMI) or non-ST-elevation myocardial infarction (NSTEMI), patients were randomized to dabigatran 50 mg twice daily (n=372), 75 mg twice daily (n=371), 110 mg twice daily (n=411), 150 mg twice daily (n=351), or placebo (n=373).

**Results.** A total of 1878 patients were randomized. The mean age was 62 years, 24% were women, 31% had diabetes, 29% had suffered a previous MI, and the index event was STEMI in 60% of cases and NSTEMI in 40%. PCI was performed during the index event in 54%. More than 90% received aspirin and clopidogrel. The mean time elapsed between index event and randomization was 7.4 days. Severe adverse events were recorded in 9% of the 50 mg group, 8% of the 75 mg group, 9% of the 110 mg group, 6% of the 150 mg group, and 9% of the placebo group. Treatment was discontinued in 20%, 16%, 19%, 18%, and 14%, respectively. Major bleeding and clinically relevant minor bleeding (by intention to treat) occurred in 3.5% of the 50 mg group, 4.3% of the 75 mg group, 7.8% of the 110 mg group, 7.7% of the 150 mg group, and 2.4% of the placebo group ( $P<.001$  for the trend). Major bleeding occurred in 0.8%, 0.3%, 2%, 1.2%, and 0.5% of patients, respectively. Cardiovascular death, infarction, or stroke occurred in 4.6%, 4.8%, 3.0%, 3.4%, and 3.8%, respectively.

**Conclusions.** Addition of dabigatran to conventional antiplatelet therapy was well tolerated in patients following STEMI and NSTEMI. Bleeding events were relatively infrequent and appeared to show a dose-dependent increase. New

studies are justified to assess the clinical efficacy of this drug.

## CARDIOVASCULAR IMAGING

### The CT-STAT Study: Coronary Computed Tomography for Systemic Triage of Acute Chest Pain Patients to Treatment

*Presented by Dr James Goldstein, Royal Oak, MI, USA.*

**Introduction and objectives.** The aim of this study was to compare coronary computed tomography (CT) angiography with standard stress testing in low-risk patients with acute chest pain. Coronary CT angiography would be expected to result in a reduction in the time and cost of diagnosis.

**Methods.** Low-risk patients with chest pain were randomized to coronary CT angiography (n=360) or risk assessment with standard stress testing (n=340).

**Results.** A total of 701 patients were randomized. Invasive coronary angiography was performed during the index hospitalization in 5.1% of patients who underwent coronary CT angiography compared with 4.6% in the standard stress testing group (no significant difference). The proportion of patients with a final diagnosis of acute coronary syndrome was 3.2% in patients who underwent coronary CT angiography compared with 3% in those in whom standard stress testing was used (no significant difference). In the CT angiography group, no significant stenosis was observed in 82% of patients, at least severe stenosis (>70%) in 7.5%, and moderate stenosis (25% to 75%) in 6.3%. Thirty-seven patients required additional stress tests that resulted in PCI in 9 and coronary artery bypass grafting (CABG) in 4. There were no cases of acute coronary syndrome without evidence of severe obstruction. In the patients who underwent standard stress tests, the results were normal in 90% of cases and abnormal or suspicious in 10%; PCI was ultimately performed in 8 patients and there were no cases of CABG. The time to diagnosis was reduced by 54% ( $P=.0001$ ) and cost was reduced by 38% ( $P=.0001$ ) in patients who underwent coronary CT angiography. Major adverse cardiac events (MACE) at 6-month follow-up were similar between the groups ( $P=.89$ ).

**Conclusions.** Among low-risk patients with acute chest pain, coronary CT angiography ruled out severe disease in 82%. This approach reduced the time and cost of diagnosis. The rate of adverse events was similar between groups. Further studies are required to address the long-term safety of this diagnostic technique.

## HEART FAILURE

### FAIR-HF (Ferinject Assessment in Patients With Iron Deficiency and Chronic Heart Failure): Ferric Carboxymaltose in Patients With Heart Failure and Iron Deficiency<sup>10</sup>

Presented by Dr Stefan Anker, Berlin, Germany.

**Background.** Iron deficiency may impair aerobic performance. This study aimed to determine whether treatment with intravenous iron (ferric carboxymaltose) would improve symptoms in patients who had heart failure, reduced left ventricular ejection fraction, and iron deficiency, either with or without anemia.

**Methods.** We enrolled 459 patients with chronic heart failure of New York Heart Association (NYHA) functional class II or III, a left ventricular ejection fraction of 40% or less (for patients with NYHA class II) or 45% or less (for NYHA class III), iron deficiency (ferritin level <100 µg/L or between 100 and 299 µg/L, if the transferrin saturation was <20%), and a hemoglobin level of 95 to 135 g/L. Patients were randomly assigned, in a 2:1 ratio, to receive 200 mg of intravenous iron (ferric carboxymaltose) or saline (placebo). The primary end points were the self-reported Patient Global Assessment and NYHA functional class, both at week 24. Secondary end points included the distance walked in 6 minutes and the health-related quality of life.

**Results.** Among the patients receiving ferric carboxymaltose, 50% reported being much or moderately improved, as compared with 28% of patients receiving placebo, according to the Patient Global Assessment (odds ratio for improvement, 2.51; 95% confidence interval [CI], 1.75-3.61). Among the patients assigned to ferric carboxymaltose, 47% had an NYHA functional class I or II at week 24, as compared with 30% of patients assigned to placebo (odds ratio for improvement by one class, 2.40; 95% CI, 1.55-3.71). Results were similar in patients with anemia and those without anemia. Significant improvements were seen with ferric carboxymaltose in the distance on the 6-minute walk test and quality-of-life assessments. The rates of death, adverse events, and serious adverse events were similar in the 2 study groups.

**Conclusions.** Treatment with intravenous ferric carboxymaltose in patients with chronic heart failure and iron deficiency, with or without anemia, improves symptoms, functional capacity, and quality of life; the side-effect profile is acceptable.

### The HEAL (Heart failure Endpoint Evaluation of Angiotensin II Antagonist Losartan) Study: Effects of High-dose Versus Low-dose Losartan on Clinical Outcomes in Patients With Heart Failure<sup>11</sup>

Presented by Dr Marvin Konstam, Boston, MA, USA

**Background.** Angiotensin-receptor blockers (ARBs) are effective treatments for patients with heart failure, but the relation between dose and clinical outcomes has not been explored. We compared the effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure.

**Methods.** This double-blind trial was undertaken in 255 sites in 30 countries; 3846 patients with heart failure of New York Heart Association class II-IV, left-ventricular ejection fraction 40% or less, and intolerance to angiotensin-converting-enzyme (ACE) inhibitors were randomly assigned to losartan 150 mg (n=1927) or 50 mg daily (n=1919). Allocation was by block randomisation stratified by centre and presence or absence of beta blocker therapy, and all patients and investigators were masked to assignment. The primary endpoint was death or admission for heart failure. Analysis was by intention to treat.

**Results.** Six patients in each group were excluded because of poor data quality. With 4.7-year median follow-up in each group (interquartile range [IQR], 3.7-5.5 for losartan 150 mg; 3.4-5.5 for losartan 50 mg), 828 (43%) patients in the 150 mg group versus 889 (46%) in the 50 mg group died or were admitted for heart failure (hazard ratio [HR], 0.90, 95% CI, 0.82-0.99; *P*=.027). For the 2 primary endpoint components, 635 patients in the 150 mg group versus 665 in the 50 mg group died (HR, 0.94, 95% CI, 0.84-1.04; *P*=.24), and 450 versus 503 patients were admitted for heart failure (HR, 0.87, 95% CI, 0.76-0.98; *P*=.025). Renal impairment (n=454 vs n=317), hypotension (203 vs 145), and hyperkalemia (195 vs 131) were more common in the 150 mg group than in the 50 mg group, but these adverse events did not lead to significantly more treatment discontinuations in the 150 mg group.

**Conclusions.** Losartan 150 mg daily reduced the rate of death or admission for heart failure in patients with heart failure, reduced left-ventricular ejection fraction, and intolerance to ACE inhibitors compared with losartan 50 mg daily. These findings show the value of up-titrating ARB doses to confer clinical benefit.

## The HEARTMATE II Trial: Advanced Heart Failure Treated With Continuous-flow Left Ventricular Assist Device<sup>12</sup>

Presented by Dr Joseph G. Rogers, Durham, NC, USA.

**Background.** Patients with advanced heart failure have improved survival rates and quality of life when treated with implanted pulsatile-flow left ventricular assist devices as compared with medical therapy. New continuous-flow devices are smaller and may be more durable than the pulsatile-flow devices.

**Methods.** In this randomized trial, we enrolled patients with advanced heart failure who were ineligible for transplantation, in a 2:1 ratio, to undergo implantation of a continuous-flow device (134 patients) or the currently approved pulsatile-flow device (66 patients). The primary composite end point was, at 2 years, survival free from disabling stroke and reoperation to repair or replace the device. Secondary end points included survival, frequency of adverse events, the quality of life, and functional capacity.

**Results.** Preoperative characteristics were similar in the 2 treatment groups, with a median age of 64 years (range, 26-81), a mean left ventricular ejection fraction of 17%, and nearly 80% of patients receiving intravenous inotropic agents. The primary composite end point was achieved in more patients with continuous-flow devices than with pulsatile-flow devices (62 of 134 [46%] vs 7 of 66 [11%];  $P<.001$ ; hazard ratio, 0.38; 95% confidence interval, 0.27-0.54;  $P<.001$ ), and patients with continuous-flow devices had superior actuarial survival rates at 2 years (58% vs 24%,  $P=.008$ ). Adverse events and device replacements were less frequent in patients with the continuous-flow device. The quality of life and functional capacity improved significantly in both groups.

**Conclusions.** Treatment with a continuous-flow left ventricular assist device in patients with advanced heart failure significantly improved the probability of survival free from stroke and device failure at 2 years as compared with a pulsatile device. Both devices significantly improved the quality of life and functional capacity.

## PACE (Pacing to Avoid Cardiac Enlargement): Biventricular Pacing in Patients With Bradycardia and Normal Ejection Fraction<sup>13</sup>

Presented by Dr Cheuk-Man Yu, Hong Kong.

**Background.** Observational studies suggest that conventional right ventricular apical pacing may have a deleterious effect on left ventricular

function. In this study, we examined whether biventricular pacing is superior to right ventricular apical pacing in preventing deterioration of left ventricular systolic function and cardiac remodeling in patients with bradycardia and a normal ejection fraction.

**Methods.** In this prospective, double-blind, multicenter study, we randomly assigned 177 patients in whom a biventricular pacemaker had been successfully implanted to receive biventricular pacing (89 patients) or right ventricular apical pacing (88 patients). The primary end points were the left ventricular ejection fraction and left ventricular end-systolic volume at 12 months.

**Results.** At 12 months, the mean left ventricular ejection fraction was significantly lower in the right-ventricular-pacing group than in the biventricular-pacing group (54.8 [9.1%] vs 62.2 [7%],  $P<.001$ ), with an absolute difference of 7.4 percentage points, whereas the left ventricular end-systolic volume was significantly higher in the right-ventricular-pacing group than in the biventricular-pacing group (35.7 [16.3] mL vs 27.6 [10.4] mL,  $P<.001$ ), with a relative difference between the groups in the change from baseline of 25% ( $P<.001$ ). The deleterious effect of right ventricular apical pacing occurred in prespecified subgroups, including patients with and patients without preexisting left ventricular diastolic dysfunction. Eight patients in the right-ventricular-pacing group (9%) and 1 in the biventricular-pacing group (1%) had ejection fractions of less than 45% ( $P=.02$ ). There was 1 death in the right-ventricular-pacing group, and 6 patients in the right-ventricular-pacing group and 5 in the biventricular-pacing group were hospitalized for heart failure ( $P=.74$ ).

**Conclusions.** In patients with normal systolic function, conventional right ventricular apical pacing resulted in adverse left ventricular remodeling and in a reduction in the left ventricular ejection fraction; these effects were prevented by biventricular pacing.

## CARDIAC SURGERY

### Bypassing the Blues: Telephone-Delivered Collaborative Care for Treating Post-CABG Depression.<sup>14</sup>

Presented by Dr Bruce Rollman, Pittsburgh, PA, USA.

**Background.** Depressive symptoms commonly follow CABG surgery and are associated with less positive clinical outcomes. The objective of this study was to test the effectiveness of telephone-delivered

collaborative care for post-CABG depression versus usual physician care.

**Methods.** Single-blind effectiveness trial at 7 university-based and community hospitals in or near Pittsburgh, Pennsylvania. Participants were 302 post-CABG patients with depression (150, intervention; 152, usual care) and a comparison group of 151 randomly sampled post-CABG patients without depression recruited between March 2004 and September 2007 and observed as outpatients until June 2008. The intervention consisted of 8 months of telephone-delivered collaborative care provided by nurses working with patients' primary care physicians and supervised by a psychiatrist and primary care physician from this study. The three main outcome measures were mental health-related quality of life (HRQL) measured by the Short Form-36 Mental Component Summary (SF-36 MCS) at 8-month follow-up; secondary outcome measures included assessment of mood symptoms (Hamilton Rating Scale for Depression [HRS-D]), physical HRQL (SF-36 PCS), and functional status (Duke Activity Status Index [DASI]); and hospital readmissions.

**Results.** The intervention patients reported greater improvements in mental HRQL (all  $P < .02$ ) (SF-36 MCS:  $\Delta$ , 3.2 points; 95% confidence interval [CI], 0.5-6), physical functioning (DASI:  $\Delta$ , 4.6 points; 95% CI, 1.9-7.3), and mood symptoms (HRS-D:  $\Delta$ , 3.1 points; 95% CI, 1.3-4.9); and were more likely to report a 50% or greater decline in HRS-D score from baseline (50.0% vs 29.6%; number needed to treat, 4.9 [95% CI, 3.2-10.4]) than usual care patients ( $P < .001$ ). Men with depression were particularly likely to benefit from the intervention (SF-36 MCS:  $\Delta$ , 5.7 points; 95% CI, 2.2-9.2;  $P = .001$ ). However, the mean HRQL and physical functioning of intervention patients did not reach that of the nondepressed comparison group.

**Conclusions.** Compared with usual care, telephone-delivered collaborative care for treatment of post-CABG depression resulted in improved HRQL, physical functioning, and mood symptoms at 8-month follow-up.

### **The OCTOPUS Study: Long-Term Cardiac and Neurocognitive Outcome After Off-Pump CABG Versus PCI**

*Presented by Dr Jakub Regieli, Utrecht, the Netherlands.*

**Background.** The aim of this study was to compare the effect of PCI versus off-pump CABG on long-term neurocognitive and cardiac outcomes. The hypothesis was that off-pump CABG would be

associated with better long-term neurocognitive and cardiac outcomes.

**Methods.** Patients with coronary heart disease were randomized to off-pump CABG (n=142) or PCI with conventional stenting (n=138).

**Results.** A total of 280 patients were randomized. There were no differences in baseline characteristics between the groups. In the group of patients randomized to off-pump CABG, the mean age was 59 years, 28% were women, 7% had a history of stroke or transient ischemic attack, 74% had coronary artery disease, and 79% had a normal ejection fraction. The primary cardiac endpoint at 7.5 years (death, myocardial infarction, stroke, or repeat revascularization) occurred in 31% of patients in the off-pump CABG group compared with 39.9% of the PCI group ( $P = .12$ ). The incidence of the combined endpoint of death, myocardial infarction, or cerebrovascular accident was 19.7% versus 17.4% ( $P = .62$ ); for death alone, 13.4% versus 8.7% ( $P = .21$ ); for myocardial infarction alone, 5.6% versus 8% ( $P = .44$ ); for stroke alone, 0.7% versus 0.7%; and for repeat revascularization, 11.3% versus 21.7% ( $P = .02$ ). Neurocognitive assessments were carried out in a subset of 200 patients. The off-pump CABG group achieved better results in 7 cognitive domains ( $P < .01$ ).

**Conclusions.** There were differences in cardiac and neurocognitive outcomes among patients with coronary artery disease following off-pump CABG compared with PCI. Results were similar for combined outcomes but repeat revascularization was more common in the PCI group. Off-pump CABG was associated with better long-term cognitive outcomes compared with PCI.

### **ARRHYTHMIAS**

#### **Record-AF Registry: Differences in Clinical Outcomes With Rhythm-and Rate-Control Therapies for Atrial Fibrillation in the Record-AF Registry.**

*Presented by Dr A. John Camm, London, England, UK.*

**Background.** In a registry study of patients with paroxysmal or persistent atrial fibrillation (AF), a rhythm-control strategy was the preferred therapeutic option (55%) among cardiologists. At 1 year, there was 18% occurrence of cardiovascular events and 3% mortality rate for both rate-control and rhythm-control strategies. Several large clinical trials have found that rate-control versus rhythm-control strategy for atrial fibrillation are similar with respect to major cardiovascular endpoints. However, "real-world" application of these strategies is not well known.

**Methods.** The Record-AF registry study was an international, observational, prospective 1-year longitudinal cohort study from 2007 to 2009 evaluating the management and clinical outcomes in paroxysmal and persistent AF patients. Patients were treated by cardiologists from 21 countries and 532 sites. Inclusion criteria included age  $\geq 18$  years, AF  $< 1$  year, and eligibility for pharmacologic treatment. Exclusion criteria included post-operative AF and AF due to reversible causes. Coprimary endpoints were therapeutic success and major adverse cardiac events (MACE). MACE was defined as cardiovascular death, myocardial infarction, stroke, transient ischemia attack leading to hospitalization, hospitalization or prolongation of hospitalization (arrhythmic or proarrhythmic events, other cardiovascular events, major complications of ablative procedure). Therapeutic success was defined as either sinus rhythm or controlled rate (depending on strategy) without MACE and without strategy switch.

**Results.** A total of 5604 patients were included in the study. Treating cardiologists chose the rate-control strategy in 45% of patients, rhythm-control strategy in 55%. At baseline, rate-control patients were significantly older (67 vs 64 years) and less Caucasian; had lower body mass index, lower systolic blood pressure, and faster resting heart rate; and were more likely to be in AF on baseline ECG. Approximately 50% of patients in each group had paroxysmal AF, and the remainder had persistent AF. As expected, rate-control patients were more likely treated with digoxin, calcium-channel blockers, and beta-blockers (excluding sotalol). Rhythm-control patients were more likely treated with antiarrhythmic drugs. In patients with CHAD<sub>2</sub> score of 2, approximately 55% and 45% were on oral vitamin K antagonist and aspirin, respectively. In patients with CHAD<sub>2</sub> score  $> 2$ , approximately 60% and 40% were on oral vitamin K antagonist and aspirin, respectively. Therapeutic success occurred in 60% and 47% of rhythm-control and rate-control strategy patients, respectively. MACE occurred in 17% and 18% of rhythm-control and rate-control strategy patients, respectively. Multivariate analysis showed that rhythm-control strategy predicted therapeutic success, with an odds ratio of 1.67 (95% CI, 1.45-1.91;  $P < .0001$ ), whereas clinical factors including coronary artery disease, heart failure, age  $> 75$ , and prior stroke or transient ischemic attack predicted therapeutic failure. Clinical factors, not treatment strategy, predicted MACE.

**Conclusions.** Rhythm-control strategy predicted therapeutic success, whereas clinical factors including coronary artery disease, heart failure, age  $> 75$ , and prior stroke or transient ischemic attack predicted

therapeutic failure. Clinical factors, not treatment strategy, predicted MACE.

## MISCELLANEOUS

### The EFFECT Study: Effectiveness of Public Report Cards for Improving the Quality of Cardiac Care<sup>15</sup>

*Presented by Dr Jack V. Tu, Toronto, Ontario, Canada.*

**Background.** Publicly released report cards on hospital performance are increasingly common, but whether they are an effective method for improving quality of care remains uncertain. The objective of this study was to evaluate whether the public release of data on cardiac quality indicators effectively stimulates hospitals to undertake quality improvement activities that improve health care processes and patient outcomes.

**Methods.** Population-based cluster randomized trial (Enhanced Feedback for Effective Cardiac Treatment [EFFECT]) of 86 hospital corporations in Ontario, Canada, with patients admitted for acute myocardial infarction (AMI) or congestive heart failure (CHF). Participating hospital corporations were randomized to early (January 2004) or delayed (September 2005) feedback of a public report card on their baseline performance (between April 1999 and March 2001) on a set of 12 process-of-care indicators for AMI and 6 for CHF. Follow-up performance data (between April 2004 and March 2005) also were collected.

**Results.** The coprimary outcomes were composite AMI and CHF indicators based on 12 AMI and 6 CHF process-of-care indicators. Secondary outcomes were the individual process-of-care indicators, a hospital report card impact survey, and all-cause AMI and CHF mortality. The publication of the early feedback hospital report card did not result in a significant systemwide improvement in the early feedback group in either the composite AMI process-of-care indicator (absolute change, 1.5%; 95% confidence interval [CI], 2.2-5.1;  $P = .43$ ) or the composite CHF process-of-care indicator (absolute change, 0.6%; 95% CI, -4.5 to 5.7;  $P = .81$ ). During the follow-up period, the mean 30-day AMI mortality rates were 2.5% lower (95% CI, 0.1-4.9;  $P = .045$ ) in the early feedback group compared with the delayed feedback group. The hospital mortality rates for CHF were not significantly different.

**Conclusions.** Public release of hospital-specific quality indicators did not significantly improve



composite process-of-care indicators for AMI or CHF.

### The TREAT (Trial to Reduce Cardiovascular Events With Aranesp Therapy) trial: A Trial of Darbepoetin Alfa in Type 2 Diabetes and Chronic Kidney Disease<sup>16</sup>

Presented by Dr Mark A. Pfeffer, Boston, MA, USA.

**Background.** Anemia is associated with an increased risk of cardiovascular and renal events among patients with type 2 diabetes and chronic kidney disease. Although darbepoetin alfa can effectively increase hemoglobin levels, its effect on clinical outcomes in these patients has not been adequately tested.

**Methods.** In this study involving 4038 patients with diabetes, chronic kidney disease, and anemia, we randomly assigned 2012 patients to darbepoetin alfa to achieve a hemoglobin level of approximately 13 g/dL and 2026 patients to placebo, with rescue darbepoetin alfa when the hemoglobin level was <9 g/dL. The primary end points were the composite outcomes of death or a cardiovascular event (nonfatal myocardial infarction, congestive heart failure, stroke, or hospitalization for myocardial ischemia) and of death or end-stage renal disease.

**Results.** Death or a cardiovascular event occurred in 632 patients assigned to darbepoetin alfa and 602 patients assigned to placebo (hazard ratio for darbepoetin alfa vs placebo, 1.05; 95% confidence interval [CI], 0.94-1.17;  $P=.41$ ). Death or end-stage renal disease occurred in 652 patients assigned to darbepoetin alfa and 618 patients assigned to placebo (hazard ratio, 1.06; 95% CI, 0.95-1.19;  $P=.29$ ). Fatal or nonfatal stroke occurred in 101 patients assigned to darbepoetin alfa and 53 patients assigned to placebo (hazard ratio, 1.92; 95% CI, 1.38-2.68;  $P<.001$ ). Red-cell transfusions were administered to 297 patients assigned to darbepoetin alfa and 496 patients assigned to placebo ( $P<.001$ ). There was only a modest improvement in patient-reported fatigue in the darbepoetin alfa group as compared with the placebo group.

**Conclusions.** The use of darbepoetin alfa in patients with diabetes, chronic kidney disease, and moderate anemia who were not undergoing dialysis did not reduce the risk of either of the 2 primary composite outcomes (death or a cardiovascular event, or death or a renal event) and was associated with an increased risk of stroke. For many persons involved in clinical decision making, this risk will outweigh the potential benefits.

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