

Special article

Summary of the Clinical Studies Reported in the Annual Scientific Sessions of the American College of Cardiology (Chicago, Illinois, United States, March 24-27, 2012)

Resumen de los ensayos clínicos presentados en las Sesiones Científicas Anuales del *American College of Cardiology* (Chicago, Illinois, Estados Unidos, 24-27 de marzo de 2012)

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Article history:

Available online 10 May 2012

Following its policy of disseminating scientific information to the cardiology community,¹⁻¹⁰ *Revista Española de Cardiología* offers a selection of the most relevant studies presented at the Scientific Sessions of the American College of Cardiology 2012 in Chicago, Illinois, specifically the *Late Breaking Clinical Trials*.

A summary of each selected study is presented, briefly outlining the objectives, methods, and results based on what was presented orally or simultaneously published in scientific journals in electronic format. Given that most of these studies have yet not been published in their final version, the information offered should be interpreted as preliminary.

SUMMARY BY TOPIC

Interventional Cardiology

CPORT-E: Outcomes of Non-Primary PCI at Hospitals With and Without On-site Cardiac Surgery: Final Medical Outcomes.

INFUSE-AMI: A 2x2 Factorial, Multicenter, Prospective, Randomized Evaluation of Intracoronary Abciximab and Aspiration Thrombectomy in Patients Undergoing Primary PCI for Anterior STEMI.

HOST-ASSURE: Randomized Comparison of Adding Cilostazol Versus Doubling the Dose of Clopidogrel after Receiving Percutaneous Coronary Intervention: The HOST-ASSURE Randomized Trial.

PARTNER: Late (≥ 2 years) Clinical and Echocardiographic Outcomes after Transcatheter versus Surgical Aortic Valve Replacement: Results from the High-Risk Cohort of the PARTNER Trial.

Prevention

TRA 2°P-TIMI 50: Evaluation of a Novel Antiplatelet Agent for Secondary Prevention in Patients With Atherosclerotic Disease: Results of the Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events.

STAMPEDE: Comparison of Bariatric Surgical Procedures and Advanced Medical Therapy for the Treatment of Type 2 Diabetes in Patients With Moderate Obesity: 1-year Trial Results.

A Mendelian Randomized Controlled Trial of Long-Term Reduction in Low-Density Lipoprotein Cholesterol Beginning Early in Life.

A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients With Primary Hypercholesterolemia.

Acute Coronary Syndromes

BRIDGE-ACS: A Multifaceted Intervention to Narrow the Evidence-Based Gap in the Treatment of Acute Coronary Syndromes: Main Results from the Cluster Randomized Trial.

ACRIN PA 4005: Multicenter Randomized Controlled Study of a Rapid "Rule Out" Strategy Using CT Coronary Angiogram Versus Traditional Care for Low-Risk ED Patients With Potential Acute Coronary Syndromes.

ROMICAT II: Results from the Multicenter Randomized Comparative Effectiveness Trial of Cardiac CT vs Alternative Triage Strategies in Acute Chest Pain Patients in the Emergency Department.

IMMEDIATE: Results of the Immediate Myocardial Metabolic Enhancement During Initial Assessment and Treatment in Emergency Care Trial: A Double-Blind Randomized Controlled Trial of Intravenous Glucose, Insulin, and Potassium (GIK) for Acute Coronary Syndromes in Emergency Medical Services.

Cardiac Surgery

CORONARY: The Coronary Artery Bypass Grafting Surgery Off or On Pump Revascularization Study.

ACCF-STACS: Survival after PCI or CABG in Older Patients With Stable Multivessel Coronary Disease: Results from the Database Collaboration on the Comparative Effectiveness of Revascularization Strategies.

Pulmonary Embolism

EINSTEIN PE: Oral Rivaroxaban Alone for Symptomatic Pulmonary Embolism.

MOPETT: Moderate Pulmonary Embolism Treated With Thrombolysis.

Heart Failure

FOCUS-CCTR: Results from the Effect of Transendocardial Autologous Bone Marrow Mononuclear Cell Delivery on Functional Capacity, Left Ventricular Function and Perfusion in Chronic Ischemic Heart Failure Randomized Trial.

Arrhythmias

ISSUE-3: Pacemaker Therapy in Patients With Neurally Mediated Syncope and Documented Asystole.

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stenosis, the 1-year survival rates are similar with transcatheter aortic valve replacement (TAVR) and surgical replacement. However, longer-term follow-up is necessary to determine whether TAVR has prolonged benefits.

Methods. At 25 centers, we randomly assigned 699 high-risk patients with severe aortic stenosis to undergo either surgical aortic-valve replacement or TAVR. All patients were followed for at least 2 years, with assessment of clinical outcomes and echocardiographic evaluation.

Results. The rates of death from any cause were similar in the TAVR and surgery groups (hazard ratio with TAVR=0.90; 95% confidence interval [CI], 0.71 to 1.15; $P=.41$) and at 2 years (Kaplan–Meier analysis) were 33.9% in the TAVR group and 35.0% in the surgery group ($P=.78$). The frequency of all strokes during follow-up did not differ significantly between the two groups (hazard ratio, 1.22; 95% CI, 0.67 to 2.23; $P=.52$). At 30 days, strokes were more frequent with TAVR than with surgical replacement (4.6% vs 2.4%, $P=.12$); subsequently, there were 8 additional strokes in the TAVR group and 12 in the surgery group. Improvement in valve areas was similar with TAVR and surgical replacement and was maintained for 2 years. Paravalvular regurgitation was more frequent after TAVR ($P<.001$), and even mild paravalvular regurgitation was associated with increased late mortality ($P<.001$).

Conclusions. A 2-year follow-up of patients in the PARTNER trial supports TAVR as an alternative to surgery in high-risk patients. The 2 treatments were similar with respect to mortality, reduction in symptoms, and improved valve hemodynamics, but paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality.

PREVENTION

Vorapaxar in the Secondary Prevention of Atherothrombotic Events¹⁵

Presented by David A Morrow, Boston, Massachusetts, United States.

Background. Thrombin potently activates platelets through the protease-activated receptor PAR-1. Vorapaxar is a novel antiplatelet agent that selectively inhibits the cellular actions of thrombin through antagonism of PAR-1.

Methods. We randomly assigned 26,449 patients who had a history of myocardial infarction, ischemic stroke, or peripheral arterial disease to receive vorapaxar (2.5 mg daily) or matching placebo and followed them for a median of 30 months. The primary efficacy end point was the composite of death from cardiovascular causes, myocardial infarction, or stroke. After 2 years, the data and safety monitoring board recommended discontinuation of the study treatment in patients with a history of stroke owing to the risk of intracranial hemorrhage.

Results. At 3 years, the primary end point had occurred in 1028 patients (9.3%) in the vorapaxar group and in 1176 patients (10.5%) in the placebo group (hazard ratio for the vorapaxar group, 0.87; 95% confidence interval [CI], 0.80 to 0.94; $P<.001$). Cardiovascular death, myocardial infarction, stroke, or recurrent ischemia leading to revascularization occurred in 1259 patients (11.2%) in the vorapaxar group and 1417 patients (12.4%) in the placebo group (hazard ratio, 0.88; 95% CI, 0.82 to 0.95; $P=.001$). Moderate or severe bleeding occurred in 4.2% of patients who received vorapaxar and 2.5% of those who received placebo (hazard ratio, 1.66; 95% CI, 1.43 to 1.93; $P<.001$). There was an increase in the rate of intracranial hemorrhage in the vorapaxar group (1.0%, vs 0.5% in the placebo group; $P<.001$).

Conclusions. Inhibition of PAR-1 with vorapaxar reduced the risk of cardiovascular death or ischemic events in patients with stable

atherosclerosis who were receiving standard therapy. However, it increased the risk of moderate or severe bleeding, including intracranial hemorrhage.

Bariatric Surgery versus Intensive Medical Therapy in Obese Patients With Diabetes. The STAMPEDE Trial¹⁶

Presented by Philip Raymond Schauer, Cleveland, Ohio, United States.

Background. Observational studies have shown improvement in patients with type 2 diabetes mellitus after bariatric surgery.

Methods. In this randomized, nonblinded, single-center trial, we evaluated the efficacy of intensive medical therapy alone versus medical therapy plus Roux-en-Y gastric bypass or sleeve gastrectomy in 150 obese patients with uncontrolled type 2 diabetes. The mean (\pm SD) age of the patients was 49 \pm 8 years, and 66% were women. The average glycated hemoglobin level was 9.2 \pm 1.5%. The primary end point was the proportion of patients with a glycated hemoglobin level of 6.0% or less at 12 months after treatment.

Results. Of the 150 patients, 93% completed 12 months of follow-up. The proportion of patients with the primary end point was 12% (5 of 41 patients) in the medical-therapy group versus 42% (21 of 50 patients) in the gastric-bypass group ($P=.002$) and 37% (18 of 49 patients) in the sleeve-gastrectomy group ($P=.008$). Glycemic control improved in all 3 groups, with a mean glycated hemoglobin level of 7.5 \pm 1.8% in the medical-therapy group, 6.4 \pm 0.9% in the gastric-bypass group ($P<.001$), and 6.6 \pm 1.0% in the sleeve-gastrectomy group ($P=.003$). Weight loss was greater in the gastric-bypass group and sleeve-gastrectomy group (-29.4 ± 9.0 kg and -25.1 ± 8.5 kg, respectively) than in the medical-therapy group (-5.4 ± 8.0 kg) ($P<.001$ for both comparisons). The use of drugs to lower glucose, lipid, and blood-pressure levels decreased significantly after both surgical procedures but increased in patients receiving medical therapy only. The index for homeostasis model assessment of insulin resistance (HOMA-IR) improved significantly after bariatric surgery. Four patients underwent reoperation. There were no deaths or life-threatening complications.

Conclusions. In obese patients with uncontrolled type 2 diabetes, 12 months of medical therapy plus bariatric surgery achieved glycemic control in significantly more patients than medical therapy alone. Further study will be necessary to assess the durability of these results.

A Mendelian Randomized Controlled Trial of Long Term Reduction in Low-Density Lipoprotein Cholesterol Beginning Early in Life¹⁷

Presented by Brian Anthony Ference, Detroit, Michigan, United States.

Background. Randomized controlled trials demonstrate that lowering low-density lipoprotein cholesterol (LDL-C) with a statin started in middle and later life reduces the risk of major coronary events, but residual risk persists. The purpose of the study was to make causal inferences about the association between a biomarker and a disease; to determine if lowering LDL-C earlier ($n=326$ 443) in life versus later ($n=169$ 138), before the development of atherosclerosis, prevents or delays the progression of coronary atherosclerosis, improving the clinical benefit of therapies that lower LDL-C.

Methods. Mendelian randomized controlled trial to study effects of 9 single-nucleotide polymorphisms (SNPs), or single-letter changes in DNA sequence that are each associated with lower LDL-C. SNPs allocation is determined randomly at conception; inheriting one of them is equal to being randomly assigned to treatment that lowers

LDL-C at birth. The primary end point was coronary heart disease (CHD): cardiovascular death, myocardial infarction, coronary revascularization.

Results. All 9 SNPs were associated with a 50% to 60% reduction in CHD risk for each 1 mmol/L (38.67 mg/dL) LDL-C lower lifetime exposure.

Conclusions. An 80% reduction in CHD risk could occur by lowering LDL by 2 mmol/L (77.34 mg/dL). Focusing on reductions in LDL-C beginning early in life has the potential to substantially reduce CHD burden globally.

A Randomized, Double-blind, Placebo-controlled Trial of the Safety and Efficacy of a Monoclonal Antibody to Proprotein Convertase Subtilisin/Kexin Type 9 Serine Protease, REGN727/SAR236553, in Patients With Primary Hypercholesterolemia (NCT: 01288443)¹⁸

Presented by James McKenney, Richmond, Virginia, United States.

Background. Serum proprotein convertase subtilisin kexin 9 (PCSK9) binds to low-density lipoprotein receptors, increasing serum low-density lipoprotein cholesterol (LDL-C). SAR236553 is a fully human monoclonal antibody to PCSK9. The primary objective of this study was to evaluate the LDL-C-lowering efficacy of 5 REGN727/SAR236553 (SAR236553) dosing regimens versus placebo at week 12 in patients with LDL-C 100 mg/dl on stable atorvastatin therapy. Secondary objectives included evaluation of effects on other lipid parameters and the attainment of LDL-C treatment goals of 100 mg/dl (2.59 mmol/l) and 70 mg/dl (1.81 mmol/l).

Methods. This double-blind, parallel-group, placebo-controlled trial randomized 183 patients with LDL-C 100 mg/dl (2.59 mmol/l) on stable-dose atorvastatin at 10, 20, or 40 mg for 6 weeks to subcutaneous placebo every 2 weeks (Q2W); SAR236553 50, 100, or 150 mg Q2W; or SAR236553 200 or 300 mg every 4 weeks (Q4W), alternating with placebo for a total treatment period of 12 weeks.

Results. SAR236553 demonstrated a clear dose-response relationship with respect to percentage LDL-C lowering for both Q2W and Q4W administration: 40%, 64%, and 72% with 50, 100, and 150 mg Q2W, respectively, and 43% and 48% with 200 and 300 mg Q4W. LDL-C reduction with placebo at week 12 was 5%. SAR236553 also substantially reduced non-high-dose lipoprotein cholesterol, apolipoprotein B, and lipoprotein(a). SAR236553 was generally well tolerated. One patient on SAR236553 experienced a serious adverse event of leukocytoclastic vasculitis.

Conclusions. When added to atorvastatin, PCSK9 inhibition with SAR236553 further reduces LDL-C by 40% to 72%. These additional reductions are both dose- and dosing frequency-dependent.

ACUTE CORONARY SYNDROMES

Effect of a Multifaceted Intervention on Use of Evidence-Based Therapies in Patients With Acute Coronary Syndromes in Brazil. The BRIDGE-ACS Randomized Trial¹⁹

Presented by Otavio Berwanger, São Paulo, Brazil.

Background. Studies have found that patients with acute coronary syndromes (ACS) often do not receive evidence-based therapies in community practice. This is particularly true in low- and middle-income countries. The aim of the study was to evaluate whether a multifaceted quality improvement (QI) intervention can improve the

use of evidence-based therapies and reduce the incidence of major cardiovascular events among patients with ACS in a middle-income country.

Methods. The BRIDGE-ACS (Brazilian Intervention to Increase Evidence Usage in Acute Coronary Syndromes) trial is a cluster-randomized (concealed allocation) trial conducted among 34 clusters (public hospitals) in Brazil and enrolling a total of 1150 patients with ACS from March 15, 2011, through November 2, 2011, with follow-up through January 27, 2012. Multifaceted QI intervention included educational materials for clinicians, reminders, algorithms, and case manager training, versus routine practice (control). Primary end point was the percentage of eligible patients who received all evidence-based therapies (aspirin, clopidogrel, anticoagulants, and statins) during the first 24 hours in patients without contraindications.

Results. Mean age of the patients enrolled was 62 (SD, 13) years; 68.6% were men, and 40% presented with ST-segment elevation myocardial infarction, 35.6% with non-ST-segment elevation myocardial infarction, and 23.6% with unstable angina. The randomized clusters included 79.5% teaching hospitals, all from major urban areas and 41.2% with 24-hour PCI capabilities. Among eligible patients (923/1150 [80.3%]), 67.9% in the intervention vs 49.5% in the control group received all eligible acute therapies (population average odds ratio [ORPA], 2.64 [95% CI, 1.28-5.45]). Similarly, among eligible patients (801/1150 [69.7%]), those in the intervention group were more likely to receive all eligible acute and discharge medications (50.9% vs 31.9%; ORPA, 2.49 [95% CI, 1.08-5.74]). Overall composite adherence scores were higher in the intervention clusters (89% vs 81.4%; mean difference, 8.6% [95% CI, 2.2%-15.0%]). In-hospital cardiovascular event rates were 5.5% in the intervention group vs 7.0% in the control group (ORPA, 0.72 [95% CI, 0.36-1.43]); 30-day all-cause mortality was 7.0% vs 8.4% (ORPA, 0.79 [95% CI, 0.46-1.34]).

Conclusions. Among patients with ACS treated in Brazil, a multifaceted educational intervention resulted in significant improvement in the use of evidence-based therapies.

Computed Tomographic Angiography for Safe Discharge of Patients With Possible Acute Coronary Syndromes. ACRI PA 4005²⁰

Presented by Harold Litt, Pennsylvania, Philadelphia, United States.

Background. Admission rates among patients presenting to emergency departments with possible ACS are high, although for most of these patients the symptoms are ultimately found not to have a cardiac cause. Coronary computed tomographic angiography (CCTA) has a very high negative predictive value for the detection of coronary disease, but its usefulness in determining whether discharge of patients from the emergency department is safe is not well established.

Methods. We randomly assigned low-to-intermediate-risk patients presenting with possible ACS, in a 2:1 ratio, to undergo CCTA or to receive traditional care. Patients were enrolled at 5 centers in the United States. Patients older than 30 years with a Thrombolysis in Myocardial Infarction (TIMI) risk score of 0 to 2 and signs or symptoms warranting admission or testing were eligible. The primary outcome was safety, assessed in the subgroup of patients with a negative CCTA examination, with safety defined as the absence of myocardial infarction and cardiac death during the first 30 days after presentation.

Results. We enrolled 1370 subjects: 908 in the CCTA group and 462 in the group receiving traditional care. The baseline characteristics were similar in the two groups. Of 640 patients with a negative CCTA examination, none died or had a myocardial infarction within 30 days (0%; 95% confidence interval [CI], 0 to 0.57). As compared with patients receiving traditional care, patients in the CCTA group had a higher rate of discharge from the emergency department (49.6% vs

22.7%; difference, 26.8 percentage points; 95% CI, 21.4 to 32.2), a shorter length of stay (median, 18.0 hours vs 24.8 hours; $P < .001$), and a higher rate of detection of coronary disease (9.0% vs 3.5%; difference, 5.6 percentage points; 95% CI, 0 to 11.2). There was one serious adverse event in each group.

Conclusions. A CCTA-based strategy for low-to-intermediate-risk patients presenting with a possible ACS appears to allow the safe, expedited discharge from the emergency department of many patients who would otherwise be admitted.

Multicenter Randomized Comparative Effectiveness Trial of Cardiac CT versus Alternative Triage Strategies in Acute Chest Pain Patients in the Emergency Department: Results from the ROMICAT II Trial²¹

Presented by Udo Hoffmann, Boston, Massachusetts, United States.

Background. The usefulness of coronary computed tomographic angiography (CCTA) in determining whether discharge of patients from the emergency department is safe is not well established. The objective of the study was to examine the effectiveness of CCTA versus the standard of care.

Methods. The study randomized 1000 chest-pain patients with suspected ACS on a 1:1 ratio to either a CCTA screening approach or standard care left to the discretion of the physician. The primary end point of ROMICAT II was length of stay in hospital.

Results. The average time to diagnosis was 10.4 hours in the CCTA group and 18.7 hours in the control group ($P = .001$). By reducing the time to diagnosis in the patients who were not suffering ACS, the CCTA-first approach reduced chest-pain patients' average hospital stay from about 31 hours to 23 hours ($P = .0002$) compared with the standard approach. About half the chest-pain patients scanned with CCTA to rule out possible noncardiac causes of their chest pain were safely discharged from the hospital within 9 hours of arriving at the emergency department. Only 15% of patients receiving standard care were in and out that fast. The hospital stay for patients with ACS was about 3.5 days in both groups. Patients in the CCTA group were much more likely to be discharged directly from the emergency department (46.7% vs 12.4%), but only slightly less likely to be admitted to the hospital (25.4% vs 31.7%). About half the patients in the control group were moved to an observation unit, compared with about a quarter of the CCTA patients. The safety of the CCTA-based approach was comparable to that of the standard approach. There were no missed ACS cases in either group, and major adverse events within 30 days were statistically similar in both the CCTA and standard-care groups (0.4 and 1.0, $P = .37$).

Conclusions. The CCTA-based strategy for screening chest-pain patients in the emergency department is safe and reduces overall patient time in the hospital but costs about the same overall as the current standard approach.

Out-of-Hospital Administration of Intravenous Glucose-Insulin-Potassium in Patients With Suspected Acute Coronary Syndromes. The IMMEDIATE Randomized Controlled Trial²²

Presented by Harry P. Selker, Boston, Massachusetts, United States.

Background. Laboratory studies suggest that in the setting of cardiac ischemia immediate intravenous glucose-insulin-potassium (GIK) reduces ischemia-related arrhythmias and myocardial injury. Clinical trials have not consistently shown these benefits, possibly due to delayed administration. The objective was to test out-of-hospital emergency medical service (EMS) administration of GIK in the first hours of suspected ACS.

Methods. Randomized, placebo-controlled, double-blind effectiveness trial in 13 US cities (36 EMS agencies), from December 2006 through July 31, 2011, in which paramedics, aided by electrocardiograph (ECG)-based decision support, randomized 911 (871 enrolled) patients (mean age, 63.6 years; 71.0% men) with high probability of ACS. Intravenous GIK solutions ($n = 411$) or identical-appearing 5% glucose placebo ($n = 460$) were administered by paramedics in the out-of-hospital setting and continued for 12 hours. The prespecified primary end point was progression of ACS to myocardial infarction (MI) within 24 hours, as assessed by biomarkers and ECG evidence. Prespecified secondary end points included survival at 30 days and a composite of prehospital or in-hospital cardiac arrest or in-hospital mortality, analyzed by intent-to-treat and by presentation with ST-segment elevation.

Results. There was no significant difference in the rate of progression to MI among patients who received GIK ($n = 200$; 48.7%) vs those who received placebo ($n = 242$; 52.6%) (odds ratio [OR], 0.88; 95% CI, 0.66-1.13; $P = .28$). Thirty-day mortality was 4.4% with GIK vs 6.1% with placebo (hazard ratio [HR], 0.72; 95% CI, 0.40-1.29; $P = .27$). The composite of cardiac arrest or in-hospital mortality occurred in 4.4% with GIK vs 8.7% with placebo (OR, 0.48; 95% CI, 0.27-0.85; $P = .01$). Among patients with ST-segment elevation (163 with GIK and 194 with placebo), progression to MI was 85.3% with GIK vs 88.7% with placebo (OR, 0.74; 95% CI, 0.40-1.38; $P = .34$); 30-day mortality was 4.9% with GIK vs 7.7% with placebo (HR, 0.63; 95% CI, 0.27-1.49; $P = .29$). The composite outcome of cardiac arrest or in-hospital mortality was 6.1% with GIK vs 14.4% with placebo (OR, 0.39; 95% CI, 0.18-0.82; $P = .01$). Serious adverse events occurred in 6.8% ($n = 28$) with GIK vs 8.9% ($n = 41$) with placebo ($P = .26$).

Conclusions. Among patients with suspected ACS, out-of-hospital administration of intravenous GIK, compared with glucose placebo, did not reduce progression to MI. Compared with placebo, GIK administration was not associated with improvement in 30-day survival but was associated with lower rates of the composite outcome of cardiac arrest or in-hospital mortality.

CARDIAC SURGERY

Off-Pump or On-Pump Coronary-Artery Bypass Grafting at 30 Days. CORONARY²³

Presented by Andre Lamy, Hamilton, Ontario, Canada.

Background. The relative benefits and risks of performing coronary artery bypass grafting (CABG) with a beating-heart technique (off-pump CABG), as compared with cardiopulmonary bypass (on-pump CABG), are not clearly established.

Methods. At 79 centers in 19 countries, we randomly assigned 4752 patients in whom CABG was planned to undergo the procedure off-pump or on-pump. The first co-primary outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis at 30 days after randomization.

Results. There was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (9.8% vs 10.3%; hazard ratio for the off-pump group, 0.95; 95% confidence interval [CI], 0.79 to 1.14; $P = .59$) or in any of its individual components. The use of off-pump CABG, as compared with on-pump CABG, significantly reduced the rates of blood-product transfusion (50.7% vs 63.3%; relative risk, 0.80; 95% CI, 0.75 to 0.85; $P < .001$), reoperation for perioperative bleeding (1.4% vs 2.4%; relative risk, 0.61; 95% CI, 0.40 to 0.93; $P = .02$), acute kidney injury (28.0% vs 32.1%; relative risk, 0.87; 95% CI, 0.80 to 0.96; $P = .01$), and respiratory complications (5.9% vs 7.5%; relative risk, 0.79; 95% CI, 0.63 to 0.98;

$P=.03$) but increased the rate of early repeat revascularizations (0.7% vs 0.2%; hazard ratio, 4.01; 95% CI, 1.34 to 12.0; $P=.01$).

Conclusions. There was no significant difference between off-pump and on-pump CABG with respect to the 30-day rate of death, myocardial infarction, stroke, or renal failure requiring dialysis. The use of off-pump CABG reduced the rates of transfusion, reoperation for perioperative bleeding, respiratory complications, and acute kidney injury but also resulted in an increased risk of early revascularization.

Comparative Effectiveness of Revascularization Strategies. ACCF-STS²⁴

Presented by William S Weintraub, Newark, Delaware, United States.

Background. Questions persist concerning the comparative effectiveness of PCI and coronary artery bypass grafting (CABG). The American College of Cardiology Foundation (ACCF) and the Society of Thoracic Surgeons (STS) collaborated to compare the rates of long-term survival after PCI and CABG.

Methods. We linked the ACCF National Cardiovascular Data Registry and the STS Adult Cardiac Surgery Database to claims data from the Centers for Medicare and Medicaid Services for the years 2004 through 2008. Outcomes were compared with the use of propensity scores and inverse-probability-weighting adjustment to reduce treatment-selection bias.

Results. Among patients aged 65 years or older who had 2-vessel or 3-vessel coronary artery disease without acute myocardial infarction, 86 244 underwent CABG and 103 549 underwent PCI. The median follow-up period was 2.67 years. At 1 year, there was no significant difference in adjusted mortality between the groups (6.24% in the CABG group as compared with 6.55% in the PCI group; risk ratio, 0.95; 95% confidence interval [CI], 0.90 to 1.00). At 4 years, there was lower mortality with CABG than with PCI (16.4% vs 20.8%; risk ratio, 0.79; 95% CI, 0.76 to 0.82). Similar results were noted in multiple subgroups and with the use of several different analytic methods. Residual confounding was assessed by means of a sensitivity analysis.

Conclusions. In this observational study of older patients with multivessel coronary disease that did not require emergency treatment there was a long-term survival advantage among patients who underwent CABG as compared with patients who underwent PCI.

PULMONARY EMBOLISM

Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism. EINSTEIN PE²⁵

Presented by Harry Roger Buller, Amsterdam, The Netherlands.

Background. A fixed-dose regimen of rivaroxaban, an oral factor Xa inhibitor, has been shown to be as effective as standard anticoagulant therapy for the treatment of deep-vein thrombosis, without the need for laboratory monitoring. This approach may also simplify the treatment of pulmonary embolism.

Methods. In a randomized, open-label, event-driven, noninferiority trial involving 4832 patients who had acute symptomatic pulmonary embolism with or without deep-vein thrombosis, we compared rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) with standard therapy with enoxaparin followed by an adjusted-dose vitamin K antagonist for 3, 6, or 12 months. The primary efficacy outcome was symptomatic

recurrent venous thromboembolism. The principal safety outcome was major or clinically relevant nonmajor bleeding.

Results. Rivaroxaban was noninferior to standard therapy (noninferiority margin, 2.0; $P=.003$) for the primary efficacy outcome, with 50 events in the rivaroxaban group (2.1%) versus 44 events in the standard-therapy group (1.8%) (hazard ratio, 1.12; 95% confidence interval [CI], 0.75 to 1.68). The principal safety outcome occurred in 10.3% of patients in the rivaroxaban group and 11.4% of those in the standard-therapy group (hazard ratio, 0.90; 95% CI, 0.76 to 1.07; $P=.23$). Major bleeding was observed in 26 patients (1.1%) in the rivaroxaban group and 52 patients (2.2%) in the standard-therapy group (hazard ratio, 0.49; 95% CI, 0.31 to 0.79; $P=.003$). Rates of other adverse events were similar in the two groups.

Conclusions. A fixed-dose regimen of rivaroxaban alone was noninferior to standard therapy for the initial and long-term treatment of pulmonary embolism and had a potentially improved benefit-risk profile.

Moderate Pulmonary Embolism Treated With Thrombolysis (MOPETT Study)²⁶

Presented by Mohsen Sharifi, Mesa, Arizona, United States.

Background. Currently massive pulmonary embolism is treated with thrombolytics. New data indicate that there could be a role for these drugs at lower doses in moderate PE. The aim of the study was to determine if reduced doses of the thrombolytic drug tissue plasminogen activator (tPA) could be used to treat moderate pulmonary embolism.

Methods. This prospective study enrolled 121 patients with moderate pulmonary embolism and were randomly assigned to tPA plus a modified regimen of anticoagulants versus just the anticoagulants. The dose of tPA used in this trial was 10 mg in 1 minute followed by 40 mg in 2 hours for patients who weighed 50 kg or more, or 0.5 mg/kg total dose given as 10 mg in 1 minute followed by the remainder in 2 hours for those weighing less than 50 kg. Patients were followed for a mean of 28 months. The 2 primary end points were pulmonary hypertension or pulmonary hypertension plus recurrent pulmonary embolism.

Results. The study group that received tPA did significantly better than the standard care group. In the tPA group, 16% had pulmonary hypertension at follow-up compared to 57% in the control group ($P<.001$), while 16% also developed pulmonary hypertension and recurrent pulmonary embolism compared to 63% of controls ($P<.001$). No cases of bleeding or intracranial hemorrhage were seen with thrombolysis and patients in this regimen had reduced hospital stay and a trend towards decreased mortality compared to those on anticoagulation therapy alone.

Conclusions. Use of a smaller tPA dose than that used in severe PE is effective and safe in moderate PE.

HEART FAILURE

Effect of Transendocardial Delivery of Autologous Bone Marrow Mononuclear Cells on Functional Capacity, Left Ventricular Function, and Perfusion in Chronic Heart Failure. The FOCUS-CTRN Trial²⁷

Presented by Emerson C. Perin, Houston, Texas, United States.

Background. Previous studies using autologous bone marrow mononuclear cells (BMCs) in patients with ischemic cardiomyopathy

have demonstrated safety and suggested efficacy. The objective was to determine if administration of BMCs through transcatheter injections improves myocardial perfusion, reduces left ventricular end-systolic volume (LVESV), or enhances maximal oxygen consumption in patients with coronary artery disease or LV dysfunction and limiting heart failure or angina.

Methods. A phase 2 randomized, double-blind, placebo-controlled trial of symptomatic patients (New York Heart Association classification II-III or Canadian Cardiovascular Society classification II-IV) with a left ventricular ejection fraction of 45% or less, a perfusion defect by single-photon emission tomography (SPECT), and coronary artery disease not amenable to revascularization who were receiving maximal medical therapy at 5 National Heart, Lung, and Blood Institute-sponsored Cardiovascular Cell Therapy Research Network (CCTRN) sites between April 29, 2009, and April 18, 2011. The intervention was bone marrow aspiration (isolation of BMCs using a standardized automated system performed locally) and transcatheter injection of 100 million BMCs or placebo (ratio of 2 for BMC group to 1 for placebo group). Co-primary end points were assessed at 6 months: changes in LVESV assessed by echocardiography, maximal oxygen consumption, and reversibility on SPECT. Phenotypic and functional analyses of the cell product were performed by the CCTRN biorepository core laboratory.

Results. Of 153 patients who provided consent, a total of 92 (82 men; average age: 63 years) were randomized (n=61 in BMC group and n=31 in placebo group). Changes in LVESV index (-0.9 mL/m² [95% CI, -6.1 to 4.3]; $P=.73$), maximal oxygen consumption (1.0 [95% CI, -0.42 to 2.34]; $P=.17$), and reversible defect (-1.2 [95% CI, -12.50 to 10.12]; $P=.84$) were not statistically significant. There were no differences in any of the secondary outcomes, including percent myocardial defect, total defect size, fixed defect size, regional wall motion, and clinical improvement.

Conclusions. Among patients with chronic ischemic heart failure, transcatheter injection of autologous BMCs compared with placebo did not improve LVESV, maximal oxygen consumption, or reversibility on SPECT.

ARRHYTHMIAS

Pacemaker Therapy in Patients With Neurally Mediated Syncope and Documented Asystole²⁸

Presented by Michele Brignole, Lavagna, Italy.

Background. Randomized controlled trials failed to prove superiority of cardiac pacing over placebo of unselected, neurally mediated syncope (NMS) in patients with positive tilt testing. The aim of the investigation was to assess the effectiveness of pacing therapy for preventing syncope recurrence in patients with a high probability of cardio-inhibitory NMS.

Methods. Multi-center, prospective, double-blind, randomized, placebo-controlled study. Eligible patients are at least 40 years of age and have suffered, in the prior 2 years, >3 syncope episodes of suspected NMS. Eligible patients (511) receive an implantable loop recorder and are followed until the first documented syncopal recurrence or a significant asystolic event. Those patients who have an asystolic pause (sinus arrest or AV block) >6 seconds or a syncopal asystolic pause >3 seconds receive a dual-chamber pacemaker implantation and are randomized to active therapy (Pm ON) or to placebo therapy (Pm OFF). The primary end point is the first syncope recurrence after pacemaker implant.

Results. The pacemaker-on group showed a 57% reduction in relative risk of fainting within 2 years of randomization ($P=.039$).

Conclusions. Dual-chamber permanent pacing is effective in reducing recurrence of syncope in patients aged ≥ 40 years with severe asystolic NMS.

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