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Special article

Summary of the Clinical Studies Reported in the European Society of Cardiology Congress 2012 (August 25-29, 2012, Munich, Germany)

Resumen de estudios clínicos presentados en el Congreso de 2012 de la Sociedad Europea de Cardiología (25-29 de agosto de 2012, Múnich, Alemania)

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The European Society of Cardiology held its annual congress in Munich in 2012. The results of a selection of recently concluded clinical trials of outstanding importance were presented in special sections (Hot Lines).

Following recently established publishing policy,[1-8] *Revista Española de Cardiología* presents a summary of these studies which briefly outlines their objectives, methods, and results in line with the oral presentations. The information we offer should be considered preliminary because many of these studies have not yet been published in their final version.

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FAST-MI: Decrease in Early Mortality in STEMI Is Related to Changing Patient Profile and Behavior, as Well as Improved Organization of Care.

GRACE: Effects of Insulin Glargine and of Polyunsaturated Fatty Acids on Carotid Intima Media Thickness in High-Risk Diabetes.

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FAME II: Fractional Flow Reserve-Guided Percutaneous Coronary Intervention Plus Optimal Medical Treatment Versus Optimal Medical Treatment Alone in Patients with Stable Coronary Artery Disease.

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Interventional Cardiology

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PRAGUE-12: Randomized Open Multicenter Study Comparing Cardiac Surgery With MAZE Versus Cardiac Surgery Without MAZE in Patients With Coronary and/or Valvular Heart Disease and With Atrial Fibrillation.

AFib Ablation Pilot: One-year Follow-up of the Atrial Fibrillation Ablation Registry Conducted by the European Heart Rhythm Association.

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EPIDEMIOLOGY AND RISK FACTORS

PURE: Patterns of Risk Factor Prevalence for CVD Globally by Urbanization, Gender, and Economic Status of Countries and Individuals: The Prospective Urban Rural Epidemiologic (PURE) Study of 153 996 People from 628 Communities in 17 Countries[9]

Presented by Salim Yusuf (Hamilton, California, United States).

Introduction. The PURE study is a follow-up analysis showcasing the effect of macro- and microeconomic factors on lifestyle and dietary risk factors for cardiovascular disease. First presented last year at the ESC 2011 meeting and published in the Lancet, the PURE study has already shown that cardiovascular medications were underused in rural and poor populations. In PURE, one of the most devastating findings was the underuse of proven medical therapy for secondary prevention of cardiovascular diseases.

Material and methods. The PURE survey encompassed 153 996 adults from urban and rural communities in countries categorized as high-income (Canada, Sweden, and United Arab Emirates), upper-middle-income (Argentina, Brazil, Chile, Malaysia, Poland, South Africa, and Turkey), lower-middle-income (China, Colombia, and Iran), and low-income (Bangladesh, India, Pakistan, and Zimbabwe).

Results. In this newest analysis, energy from total fat, saturated fats, and protein increased almost linearly with increasing incomes. Carbohydrate intake, on the other hand, comprised approximately 65% of energy from diets in poor nations, with the percentage declining in wealthier nations. In terms of physical activity, the researchers observed that the amount of recreational physical activity increased with increasing GDP and wealth, but this increase was offset by a reduction in the amount of obligatory physical activity, such as activity required for physical labor.

Conclusions. There is a huge disparity between healthy diet and lifestyle behaviors between affluent and underdeveloped nations.

FAST-MI: Decrease in Early Mortality in STEMI Is Related to Changing Patient Profile and Behavior, as Well as Improved Organization of Care[10]

Presented by Nicolas Danchin (Paris, France).

Introduction. The contemporary decline in mortality reported in patients with ST-segment elevation myocardial infarction (STEMI) has been attributed mainly to improved use of reperfusion therapy. The aim was to determine potential factors (beyond reperfusion therapy) associated with improved survival in patients with STEMI over a 15-year period.

Material and methods. Four 1-month nationwide French registries, conducted 5 years apart (between 1995, 2000, 2005, 2010), including 6707 STEMI patients admitted to intensive care or coronary care units. Primary endpoint of the study: Changes over time in crude 30-day mortality, and mortality standardized to the 2010 population characteristics.

Results. Mean (SD) age decreased from 66.2 (14.0) to 63.3 (14.5) years, with a concomitant decline in history of cardiovascular events and comorbidities. The proportion of younger patients increased, particularly in women younger than 60 years (from 11.8% to 25.5%), in whom prevalence of current smoking (37.3% to 73.1%) and obesity (17.6% to 27.1%) increased. Time from symptom onset to hospital admission decreased, with a shorter time from onset to first call, and broader use of mobile intensive care units. Reperfusion therapy increased from 49.4% to 74.7%, driven by primary percutaneous coronary intervention (11.9% to 60.8%). Early use of recommended medications increased, particularly low-molecular-weight heparins and statins. Crude 30-day mortality decreased from 13.7% (95% CI, 12.0-15.4) to 4.4% (95% CI, 3.5-5.4), whereas standardized mortality decreased from 11.3% (95% CI, 9.5-13.2) to 4.4% (95% CI, 3.5-5.4). Multivariable analysis showed a consistent reduction in mortality from 1995 to 2010 after controlling for clinical characteristics in addition to the initial population risk score and use of reperfusion therapy, with odds mortality ratios of 0.39 (95%, 0.29-0.53, *P*<.001) in 2010 compared with 1995.

Conclusions. In France, the overall rate of cardiovascular mortality among patients with STEMI decreased from 1995 to 2010, accompanied by an increase in the proportion of women younger than 60 years with STEMI, changes in other population characteristics, and greater use of reperfusion therapy and recommended medications.

GRACE: Effects of Insulin Glargine and of Polyunsaturated Fatty Acids on Carotid Intima Media Thickness in High-Risk Diabetes [11]

Presented by Eva Lonn (Hamilton, California, United States).

Introduction. People with dysglycemia are at increased risk for atherosclerosis and cardiovascular events. Effects of basal insulin titrated to normalize fasting plasma glucose or with n-3 fatty acid supplements on atherosclerosis progression in this population are unknown. The objective of the study was to evaluate effects of insulin glargine and of n-3 fatty acid supplements on carotid intima media thickness (CIMT).

Material and methods. Randomized multicenter international 2×2 factorial design trial of 1184 people (mean age, 63 years) with known cardiovascular disease and/or cardiovascular risk factors plus impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes. Interventions: Participants received open label insulin glargine (with a target fasting blood glucose level of ≤95 mg per deciliter [5.3 mmol/l]), in addition to standard care or standard glycemic care alone and double-blind therapy with a 1-g capsule of ethyl esters of n–3 fatty acids or placebo. The primary outcome was the annualized rate of change in maximum CIMT for 12 carotid sites. Secondary outcomes were the annualized rates of change in maximum CIMT for the common carotid artery and for the common carotid plus bifurcation sites. Baseline, followed by annual, ultrasounds were obtained during a median follow-up of 4.9 years.

Results. Compared to standard care, insulin glargine reduced the primary CIMT outcome, but the difference was not statistically significant (difference =0.0030 ± 0.0021 mm/year; *P*=.145) and significantly reduced the secondary CIMT outcomes (differences of 0.0033 ± 0.0017 mm/year; *P*=.049 and 0.0045 ± 0.0021 mm/year; *P*=.032, respectively). There were no differences in the primary and secondary outcomes between the n-3 fatty acid supplement and placebo groups.

Conclusions. In people with known cardiovascular disease and/or cardiovascular risk factors and dysglycemia, insulin glargine used to target normoglycemia modestly reduced CIMT progression, while daily supplementation with 1 g of n-3 fatty acid supplements had no effect on CIMT progression.

ALTITUDE: ALiskiren Trial in Type 2 Diabetes Using cardio-renal Endpoints[12]

Presented by Hans Henrik Parving (Copenhagen, Denmark).

Introduction. Patients with type 2 diabetes are at increased risk of macro- and microvascular disease, and the presence of albuminuria and/or reduced kidney function further enhances macrovascular risk. Angiotensin-converting-enzyme inhibitors (ACE) reduce both macro- and microvascular events, yet the residual renal and cardiovascular risk still remains high. Aliskiren, a novel

oral direct renin inhibitor that unlike ACE and ARBs lowers plasma renin activity, angiotensin I and angiotensin II levels, may thereby provide greater benefit compared to ACE or ARB alone. The primary objective of the ALTITUDE trial is to determine whether aliskiren 300 mg once daily reduces cardiovascular and renal morbidity and mortality compared with placebo when added to conventional treatment (including ACE or ARB).

Material and methods. ALTITUDE is an international, randomized, double-blind, placebo-controlled, parallel-group study, which included three categories of high-risk patients with type 2 diabetes (aged>or=35 years): those with either urinary albumin/creatinine ratio (UACR) ≥200 mg/g; microalbuminuria (UACR) ≥20 <200 mg/g and eGFR≥30 <60 mL/min/1.73 m^2; and thirdly, those with a history of cardiovascular disease and eGFR≥30 <60 mL/min/1.73 m^2 with or without microalbuminuria. The ALTITUDE study enrolled 8561 subjects randomized to aliskiren 300 mg once daily or placebo on top of a single renin-angiotensin blockade. The data presented here represent a median patient follow-up of 32 months. The primary outcome measure is time to first event for the composite endpoint of cardiovascular death, resuscitated death, myocardial infarction, stroke, unplanned hospitalization for heart failure, onset of end-stage renal disease or doubling of baseline serum creatinine concentration. Secondary endpoints include a composite cardiovascular endpoint and a composite renal endpoint.

Results. The trial was halted prematurely due to absence of apparent benefit and an increase in adverse events. There was no difference in the composite endpoint and a 25% relative increase in stroke risk in the aliskiren group.

Conclusions. Adding aliskiren on top of ACE inhibitors/ARBs in the diabetic population is not recommended and may even be harmful.

The Great East Japan Earthquake Disaster and Cardiovascular Diseases[13]

Presented by Hiroaki Shimokawa (Sendai, Japan).

Introduction. While previous studies reported a short-term increase in individual cardiovascular disease after great earthquakes, mid-term occurrences of all types of cardiovascular disease after great earthquakes are unknown. We addressed this important issue in our experience with the Great East Japan Earthquake (11 March 2011).

Material and methods. We retrospectively examined the impact of the earthquake on the occurrences of cardiovascular disease and pneumonia by comparing the ambulance records made by doctors in our Miyagi Prefecture, the centre of the disaster area, during the periods of 2008–11 (n=124 152).

Results. The weekly occurrences of cardiovascular disease, including heart failure, acute coronary syndrome, stroke, cardiopulmonary arrest, and pneumonia were all significantly increased after the earthquake compared with the previous 3 years. The occurrences of acute coronary syndrome and cardiopulmonary arrest showed the rapid increase followed by a sharp decline, whereas those of HF and pneumonia showed a prolonged increase for more than 6 weeks and those of stroke and cardiopulmonary arrest showed a second peak after the largest aftershock (7 April 2011). Furthermore, the occurrence of cardiopulmonary arrest was increased in the first 24 hours after the earthquake, followed by other diseases later on. These increases were independent of age, sex, or residence area (seacoast vs inland).

Conclusions. These results indicate that the occurrences of all types of cardiovascular disease and pneumonia were increased in somewhat different time courses after the earthquake, including the first observation of the marked and prolonged increase in HF, emphasizing the importance of intensive medical management of all types of cardiovascular disease after great earthquakes.

ACUTE CORONARY SYNDROMES

TRILOGY-ACS: Prasugrel Versus Clopidodrel for Patients With Unstable Angina/Myocardial Infarction Without ST-Segment Elevation who are Medically Managed Without Revascularization[14]

Presented by Matthew Roe (Durham, United States).

Introduction. The effect of intensified platelet inhibition for patients with unstable angina or myocardial infarction without ST-segment elevation (NSTEMI) who do not undergo revascularization has not been delineated. Given the previously demonstrated benefits of prasugrel versus clopidogrel (both thienopyridine inhibitors of the platelet $P2Y_{12}$ receptor) among patients undergoing percutaneous coronary intervention (PCI), we evaluated whether aspirin plus prasugrel is superior to aspirin plus clopidogrel for long-term therapy in patients with unstable angina or NSTEMI who were younger than 75 years. We also undertook a concomitant and exploratory assessment of a lower prasugrel dose for patients aged 75 years or older.

Material and methods. In this double-blind, randomized trial, in a primary analysis involving 7243 patients younger than 75 years receiving aspirin, we evaluated up to 30 months of treatment with prasugrel (10 mg daily) versus clopidogrel (75 mg daily). In a secondary analysis involving 2083 patients aged 75 years or older, we evaluated 5 mg of prasugrel versus 75 mg of clopidogrel.

Results. At a median follow-up of 17 months, the primary end point of death from cardiovascular causes, myocardial infarction, or stroke among patients younger than 75 years occurred in 13.9% of the prasugrel group and 16.0% of the clopidogrel group (hazard ratio in the prasugrel group, 0.91; 95% confidence interval [CI], 0.79 to 1.05; *P*=.21). Similar results were observed in the overall population. The prespecified analysis of multiple recurrent ischemic events (all components of the primary end point) suggested a lower risk for prasugrel among patients younger than 75 years (hazard ratio, 0.85; 95% CI, 0.72 to 1.00; *P*=.04). Rates of severe and intracranial bleeding were similar in the two groups and for all age groups. There was no significant between-group difference in the frequency of nonhemorrhagic serious adverse events, except for a higher frequency of heart failure in the clopidogrel group.

Conclusions. Among patients with unstable angina or NSTEMI, prasugrel did not significantly reduce the frequency of the primary end point, as compared with clopidogrel, and similar risks of bleeding were observed.

IABP-SHOCK II: Randomized Comparison of Intraaortic Balloon Counterpulsation Versus Optimal Medical Therapy in Addition to Early Revascularization in Acute Myocardial Infarction Complicated by Cardiogenic Shock[15]

Presented by Holger Thiele (Leipzig, Germany).

Introduction. In current international guidelines, intraaortic balloon counterpulsation is considered to be a class I treatment for cardiogenic shock complicating acute myocardial infarction. However, evidence is based mainly on registry data, and there is a paucity of randomized clinical trials.

Material and methods. In this randomized, prospective, open-label, multicenter trial, we randomly assigned 600 patients with cardiogenic shock complicating acute myocardial infarction to intraaortic balloon counterpulsation (IABP group, 301 patients) or no intraaortic balloon counterpulsation (control group, 299 patients). All patients were expected to undergo early revascularization (by means of percutaneous coronary intervention or bypass surgery) and to receive the best available medical therapy.

The primary efficacy end point was 30-day all-cause mortality. Safety assessments included major bleeding, peripheral ischemic complications, sepsis, and stroke.

Results. A total of 300 patients in the IABP group and 298 in the control group were included in the analysis of the primary end point. At 30 days, 119 patients in the IABP group (39.7%) and 123 patients in the control group (41.3%) had died (relative risk with IABP, 0.96; 95% confidence interval, 0.79 to 1.17; *P*=.69). There were no significant differences in secondary end points or in process-of-care measures, including the time to hemodynamic stabilization, the length of stay in the intensive care unit, serum lactate levels, the dose and duration of catecholamine therapy, and renal function. The IABP group and the control group did not differ significantly with respect to the rates of major bleeding (3.3% and 4.4%, respectively; *P*=.51), peripheral ischemic complications (4.3% and 3.4%, *P*=.53), sepsis (15.7% and 20.5%, *P*=.15), and stroke (0.7% and 1.7%, *P*=.28).

Conclusions. The use of intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned.

IMAGING

DeFACTO: Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography[16]

Presented by James Min (Los Angeles, United States).

Introduction. Coronary computed tomographic (CT) angiography is a noninvasive anatomic test for diagnosis of coronary stenosis that does not determine whether a stenosis causes ischemia. In contrast, fractional flow reserve (FFR) is a physiologic measure of coronary stenosis expressing the amount of coronary flow still attainable despite the presence of a stenosis, but it requires an invasive procedure. Noninvasive FFR computed from CT (FFRCT) is a novel method for determining the physiologic significance of coronary artery disease (CAD), but its ability to identify ischemia has not been adequately examined to date. The aim of the study was to assess the diagnostic performance of FFRCT plus CT for diagnosis of hemodynamically significant coronary stenosis.

Material and methods. Multicenter diagnostic performance study involving 252 stable patients with suspected or known CAD from 17 centers in 5 countries who underwent CT, invasive coronary angiography (ICA), FFR, and FFRCT between October 2010 and October 2011. Computed tomography, ICA, FFR, and FFRCT were interpreted in blinded fashion by independent core laboratories. Accuracy of FFRCT plus CT for diagnosis of ischemia was compared with an invasive FFR reference standard. Ischemia was defined by an FFR or FFRCT of 0.80 or less, while anatomically obstructive CAD was defined by a stenosis of 50% or larger on CT and ICA. The primary study outcome assessed whether FFRCT plus CT could improve the per-patient diagnostic accuracy such that the lower boundary of the 1-sided 95% confidence interval of this estimate exceeded 70%.

Results. Among study participants, 137 (54.4%) had an abnormal FFR determined by ICA. On a per-patient basis, diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of FFRCT plus CT were 73% (95% CI, 67%-78%), 90% (95% CI, 84%-95%), 54% (95% CI, 46%-83%), 67% (95% CI, 60%-74%), and 84% (95% CI, 74%-90%), respectively. Compared with obstructive CAD diagnosed by CT alone (area under the receiver operating characteristic curve [AUC], 0.68; 95% CI, 0.62-0.74), FFRCT was associated with improved discrimination (AUC, 0.81; 95% CI, 0.75-0.86; P<.001).

Conclusions. Although the study did not achieve its prespecified primary outcome goal for the level of per-patient diagnostic accuracy, use of noninvasive FFR_{CT} plus CT among stable patients with suspected or known CAD was associated with improved diagnostic accuracy and discrimination vs CT alone for the diagnosis of hemodynamically significant CAD when FFR determined at the time of ICA was the reference standard.

CORE320: Diagnostic Performance of Combined Noninvasive Coronary Angiography and Myocardial Perfusion Imaging Using 320-row Detector Computed Tomography[17]

Presented by Joao A. Lima (Baltimore, United States).

Introduction. Computed tomography angiography (CTA) provides morphologic information of coronary anatomy and is capable of detecting the presence of atherosclerotic lesions. Morphologic information alone is, however, limited in its ability to predict physiological significance of coronary luminal stenosis. There is ample evidence that the benefit of revascularization is highest when stenoses are hemodynamically significant, as assessed by SPECT or by invasive measurement of fractional flow reserve. The aim of the present study was to evaluate the diagnostic performance of combined CTA and CT perfusion (CTP) study using a 320-row detector CT scanner to identify patients with flow limiting CAD, as compared to invasive angiography and SPECT.

Material and methods. This was a multicenter (16), multinational (8), prospective study which included 391 patients with suspected coronary artery disease who had been referred for clinically indicated coronary angiography. Noninvasive evaluation of coronary lesion severity (by CTA) + hemodynamic significance (by CTP) was compared to invasive angiography + SPECT and analyzed on a per patient and per vessel basis.

Results. Combined CTA and CTP was capable of detecting hemodynamically significant stenoses (50% or 70%), as defined by invasive angiography with an associated SPECT perfusion defect. Furthermore, combined CTA and CTP was found to be superior to CTA alone for correctly identifying flow limiting and functionally relevant obstructive coronary artery disease and predicted revascularization with accuracy similar to invasive coronary angiography + SPECT.

Conclusions. CORE320 shows that CTP added to CTA angiography accurately identifies flow-limiting coronary lesions that need to be treated.

FAME II: Fractional Flow Reserve-Guided Percutaneous Coronary Intervention plus Optimal Medical Treatment versus Optimal Medical Treatment Alone in Patients with Stable Coronary Artery Disease[18]

Presented by Bernard De Bruyne (Aalst, Belgium).

Introduction. The preferred initial treatment for patients with stable coronary artery disease is the best available medical therapy. We hypothesized that in patients with functionally significant stenoses, as determined by measurement of fractional flow reserve (FFR), percutaneous coronary intervention (PCI) plus the best available medical therapy would be superior to the best available medical therapy alone.

Material and methods. In patients with stable coronary artery disease for whom PCI was being considered, we assessed all stenoses by measuring FFR. Patients in whom at least one stenosis was functionally significant (FFR ≤0.80) were randomly assigned to FFR-guided PCI plus the best available medical therapy (PCI group) or the best available medical therapy alone (medical-therapy group).

Patients in whom all stenoses had an FFR of more than 0.80 were entered into a registry and received the best available medical therapy. The primary end point was a composite of death, myocardial infarction, or urgent revascularization.

Results. Recruitment was halted prematurely after enrollment of 1220 patients (888 who underwent randomization and 332 enrolled in the registry) because of a significant between-group difference in the percentage of patients who had a primary end-point event**.** 4.3% in the PCI group and 12.7% in the medical-therapy group (hazard ratio with PCI, 0.32; 95% confidence interval [CI], 0.19 to 0.53; *P*<.001). The difference was driven by a lower rate of urgent revascularization in the PCI group than in the medical-therapy group (1.6% vs 11.1%; hazard ratio, 0.13; 95% CI, 0.06 to 0.30; *P*<.001); in particular, in the PCI group, fewer urgent revascularizations were triggered by a myocardial infarction or evidence of ischemia on electrocardiography (hazard ratio, 0.13; 95% CI, 0.04 to 0.43; *P*<.001). Among patients in the registry, 3.0% had a primary end-point event.

Conclusions. In patients with stable coronary artery disease and functionally significant stenoses, FFR-guided PCI plus the best available medical therapy, as compared with the best available medical therapy alone, decreased the need for urgent revascularization. In patients without ischemia, the outcome appeared to be favorable with the best available medical therapy alone.

HEART FAILURE

PARAMOUNT: Efficacy and Safety of LCZ696, a First-in-Class Angiotensin Receptor Neprilysin Inhibitor, in Patients with Heart Failure and Preserved Ejection Fraction[19]

Presented by Scott Solomon (Boston, United States).

Introduction. Heart failure with preserved ejection fraction is associated with substantial morbidity and mortality, but effective treatments are lacking. We assessed the efficacy and safety of LCZ696, a first-in-class angiotensin receptor neprilysin inhibitor (ARNI), in patients with this disorder.

Material and methods. PARAMOUNT was a phase 2, randomised, parallel-group, double-blind multicentre trial in patients with New York Heart Association (NYHA) class II or III heart failure, left ventricular ejection fraction 45% or higher, and NT-proBNP greater than 400 pg/mL. Participants were randomly assigned (1:1) by central interactive voice response system to LCZ696 titrated to 200 mg twice daily or valsartan titrated to 160 mg twice daily, and treated for 36 weeks. Investigators and participants were masked to treatment assignment. The primary endpoint was change in NT-proBNP, a marker of left ventricular wall stress, from baseline to 12 weeks; analysis included all patients randomly assigned to treatment groups who had a baseline and at least one postbaseline assessment.

Results. We randomly assigned 149 patients to LCZ696 and 152 to valsartan; 134 in the LCZ696 group and 132 in the valsartan group were included in analysis of the primary endpoint. NT-proBNP was significantly reduced at 12 weeks in the LCZ696 group compared with the valsartan group (LCZ696: baseline, 783 pg/mL [95% CI, 670-914], 12 weeks, 605 pg/mL [512-714]; valsartan: baseline, 862 pg/mL [733-1012], 12 weeks, 835 [710-981]; ratio LCZ696/valsartan, 0.77, 95% CI, 0.64-0.92, *P*=.005). LCZ696 was well tolerated with adverse effects similar to those of valsartan; 22 patients (15%) on LCZ696 and 30 (20%) on valsartan had one or more serious adverse event.

Conclusions. In patients with heart failure with preserved ejection fraction, LCZ696 reduced NT-proBNP to a greater extent than did valsartan at 12 weeks and was well tolerated. Whether these effects would translate into improved outcomes needs to be tested prospectively.

Aldo-DHF: Aldosterone Receptor Blockade in Diastolic Heart Failure[20]

Presented by Burkert Mathias Pieske (Graz, Austria).

Introduction. The objective of the ALDO-DHF study is to investigate the significance of an aldosterone receptor blockade with spironolactone in the course of diastolic heart failure.

Material and methods. Aldo-DHF randomized 422 patients with heart failure and preserved ejection fraction to receive spironolactone 25 mg/day or placebo on top of other medical therapy. The primary end points are physical performance (quantified by spiroergometry) and Doppler-echocardiographic parameters for diastolic dysfunction. The secondary end points include quality of life and morbidity.

Results. The tissue Doppler echo measure improved significantly with spironolactone vs placebo at both six and 12 months (*P*<.001 for both differences), while there were no significant differences between treatment groups in peak VO_2 at either time point. As for secondary end points, left ventricular mass index as a measure of ventricular remodeling decreased similarly in the treatment groups at 6 months (*P*=.16) and continued to drop significantly out to 12 months in the spironolactone group but not in the control group (*P*=.009). Levels of N-terminal pro-brain-type natriuretic peptide (NT-proBNP) fell in both groups by 6 months, somewhat more so in the spironolactone group (*P*=.09). By one year, levels rose in both groups, but more so in the placebo group (*P*=.03). There were no significant differences in death or hospitalization rates.

Conclusions. Patients who received spironolactone for a year benefited with significantly improved diastolic function and ventricular remodeling as well as reduced levels of natriuretic peptides.

INTERVENTIONAL CARDIOLOGY

PROTECT: the Patient Related Outcomes with Endeavor Versus Cypher Stenting Trial[21]

Presented by William WIJNS (Aalst, Belgium).

Introduction. We sought to compare the long-term safety of two devices with different antiproliferative properties**.** the Endeavor zotarolimus-eluting stent (E-ZES; Medtronic, Inc) and the Cypher sirolimus-eluting stent (C-SES; Cordis, Johnson & Johnson) in a broad group of patients and lesions.

Material and methods. Between May 21, 2007 and December 22, 2008, we recruited 8791 patients from 36 recruiting countries to participate in this open-label, multicentre, randomised, superiority trial. Eligible patients were those aged 18 years or older undergoing elective, unplanned, or emergency procedures in native coronary arteries. Patients were randomly assigned to either receive E-ZES or C-SES (ratio 1:1). Randomisation was stratified per centre with varying block sizes of 4, 6, or 8 patients, and concealed with a central telephone-based or web-based allocation service. The primary outcome was definite or probable stent thrombosis at 3 years and was analysed by intention to treat. Patients and investigators were aware of treatment assignment.

Results. PROTECT randomised 8791 patients, of whom 8709 provided consent to participate and were eligible: 4357 were allocated to the E-ZES group and 4352 patients to the C-SES group. At 3 years, rates of definite or probable stent thrombosis did not differ between groups (1.4% for E-ZES [predicted: 1.5%] vs 1.8% [predicted: 2.5%] for C-SES; hazard ratio [HR], 0.81, 95% CI, 0.58-1.14, *P*=.22). Dual antiplatelet therapy was used in 8402 (96%) patients at discharge, 7456 (88%) at 1 year, 3041 (37%) at 2 years, and 2364 (30%) at 3 years.

Conclusions. No evidence of superiority of E-ZES compared with C-SES in definite or probable stent thrombosis rates was noted at 3 years. Time analysis suggests a difference in definite or probable stent thrombosis between groups is emerging over time, and a longer follow-up is therefore needed given the clinical relevance of stent thrombosis.

GARY: German Aortic Valve Registry - in hospital outcome[22]

Presented by Christian Hamm (Bad Nauheim, Germany).

Introduction. Standard treatment for aortic stenosis is surgical valve replacement. In recent years catheter based procedures have gained attention and are used in Germany in 30% of the cases. Randomized studies are still insufficient or ongoing. In order to assess the impact and role of these new technics in comparison to conventional surgery a nationwide registry was started in Germany in 2010 to capture all interventional and surgical procedures. Accordingly, this is the largest registry of its kind.

Material and methods. Prospective registry with follow-up for 5 years. The GARY registry is voluntary for the current 92 participating centers out of 99 in the country that do the procedures. It includes patients undergoing either conventional surgical aortic replacement or TAVI. The current analysis encompasses 13 860 patients treated during the last complete calendar year at 53 centers, but the registry had grown to >26 000 patients by July 2012, of whom 23% had TAVI.

Results. Eighty-five percent of all TAVI patients were over 75 years old and had a higher calculated peri-operative risk of mortality. The mean age of patients who received isolated elective and urgent conventional aortic valve replacement was 68.3±11.3 years, with a logistic EuroSCORE of 8.8%±9.7%. TAVI patients were on average significantly older (transfemoral 81.0±6.1 years, transapical 80.3±6.1 years) and with a higher operative risk. The reported in-hospital mortality for elective patients was 2.1% for conventional surgery, 5.1% for the transfemoral TAVI, and 7.7% for the transapical approach. There was a high procedural success (more than 97%) and a low rate of valve-related reinterventions (less than 0.5%). Stratification of the patients into risk groups revealed a particular benefit for people with high (EuroSCORE>20%) and very high (EuroSCORE>30%) risk when treated transfemorally, with mortality rates of 4.7% and 7.7%, respectively. The overall number of cerebrovascular events during hospital stay was low in the conventionally treated group (2.2%) and somewhat higher for TAVI patients (transfemoral 3.7%, transapical 3.5%). The rate of vascular complications was reported as 11.9% for the transfemoral, 2.5% for the transapical, and 1.0% for the conventional group. However, the number of patients who needed more than two units of packed red blood cells was 29.4% in conventional surgery and 25.4% with the transapical, but only 11.5% with the transfemoral approach. The number of postoperatively new pacemaker implants was 23.7% in the transfemoral group - significantly higher than in the transapical (9.9%) and in the conventional surgical groups (4.6%).

Conclusions. In the GARY registry, several forms of transcatheter aortic-valve implantation (TAVI) are being used primarily in high-risk patients, just as the guidelines recommend.

ACCESS-EUROPE: An Observational Study of the MitraClip® System in Europe[23]

Presented by Wolfgang Schillinger (Gottingen, Germany).

Introduction. ACCESS-EUROPE Phase I is a prospective, observational, multicenter study designed to gain information regarding the use of the MitraClip System in Europe in a commercial setting and to provide further evidence of the safety and effectiveness of the MitraClip System. As of April 13, 2011, the ACCESS-EUROPE study had completed enrollment of 567 patients in the MitraClip Device group. Complete 1-year safety and effectiveness results have not been reported.

Material and methods. Procedural data, 30-day safety results and clinical outcomes at 1 year will be presented. Outcomes defined by freedom from death, freedom from mitral valve surgery, and reduction in mitral regurgitation, as well as improvements in NYHA Functional Class, Six Minute Walk Test, and Quality of Life data, will be reported at 1 year.

Results. Patients enrolled in ACCESS-EUROPE were elderly (mean age 74±10 years) with significant baseline comorbidities including coronary artery disease in 63% and moderate to severe renal disease in 42%. At baseline, 77% of patients had functional MR, 85% were in NYHA Functional Class III/IV, 98% had ≥3+ mitral regurgitation and 53% had left ventricular ejection fraction <40%. The average logistic EuroSCORE was 23%±18. Results at 1 year are as follows: freedom from death was 82%, freedom from MR >2+ was 79%, freedom from mitral valve surgery was 94%, the majority of patients (72%) were in NYHA Class I/II, and median improvement of 60.5 meters in 6-minute walk distance was observed from baseline. Significant improvements in quality of life were also noted as evidenced by a median improvement of 14.0 points between baseline and 1 year scores on the Minnesota Living with Heart Failure Questionnaire.

Conclusions. One-year results of the ACCESS-EUROPE study demonstrate important clinical benefits in a real-world patient population with significant comorbidities who are at high surgical risk. Results from the complete 1-year cohort of MitraClip Device patients will be presented.

WOEST: First Randomised Trial that Compares two Different Regimens With and Without Aspirin in Patients on Oral Anticoagulant Therapy Undergoing Coronary Stent Placement[24]

Willem Dewilde (Nieuwegein, The Netherlands).

Introduction. Oral anticoagulants are obligatory in most patients with atrial fibrillation and those with mechanical heart valves. Over 30% of these patients have concomitant ischemic heart disease, and when they undergo percutaneous coronary intervention there is also an indication for aspirin and clopidogrel. While triple therapy is recommended in the guidelines, it is known to increase major bleeding, which could increase mortality, and there has been no prospective randomized data on the issue until now.

Material and methods. In the WOEST trial, 573 patients were randomized to dual therapy with oral anticoagulation and clopidogrel (75 mg daily) or to triple therapy with oral anticoagulation, clopidogrel, and aspirin 80 mg daily. Treatment was continued for 1 month after bare-metal stenting (35% of patients) and one year after drug-eluting-stent placement (65% of patients). Follow-up was for one year. The primary end point included minimal, minor, and major bleeding. Clinical ischemic events were a secondary end point.

Results. The primary end point of all TIMI bleeding was significantly reduced in the dual-therapy arm (44.9 vs 19.5%, $P<.001$). There was a significant reduction in minimal and minor bleeding, and while major bleeding was also numerically lower, this did not reach statistical significance ($P=.159$). There was no difference in intracranial bleeding, with three cases in each group. Regarding secondary end points, clinical ischemic events were a secondary end point, and results suggested these were not increased by dropping aspirin. Indeed, most end points showed lower numerical rates in the dual-therapy arm, and total mortality was actually significantly reduced.

Conclusions. According to WOEST trial, patients on oral anticoagulant therapy undergoing stenting should be treated with clopidogrel but not aspirin.

ARRYTHMIAS

PRAGUE-12: Randomized open multicenter study comparing cardiac surgery with MAZE versus cardiac surgery without MAZE in patients with coronary and/or valvular heart disease and with atrial fibrillation[25]

Presented by Petr Widimsky (Prague, Czech Republic).

Introduction. Surgical ablation procedure can restore sinus rhythm in patients with atrial fibrillation undergoing cardiac surgery. However, it is not known whether it has any impact on long-term clinical outcomes.

Material and methods. Open multicenter randomized prospective study. Primary efficacy outcome: presence of sinus rhythm (without any atrial fibrillation episode) during 24-hour ECG monitoring 1 year after surgery. Primary safety outcome: combined end point death, myocardial infarction, stroke or transient ischemic attack, new onset renal failure requesting hemodialysis at 30 days. Long-term outcome: combined end point death, major bleeding, stroke or transient ischemic attack, rehospitalization for heart failure at 1 and 5 years. Secondary outcomes: use of anticoagulation at 1 year, use of antiarrhythmia drugs at 1 year, pacemaker or cardioverter implantation, catheter ablation, operative data. Inclusion criteria: heart team indication for cardiac surgery (coronary bypass and/or valve replacement or repair), atrial fibrillation (paroxysmal, persistent or longstanding persistent) documented at least twice during the last 6 months before the operation, signed informed consent, age>18 years. Exclusion Criterion: emergency surgery. A total of 224 patients in three cardiac surgery centers were randomized by the envelope method into two groups: group A (cardiac surgery with the left atrial ablation procedure) included 117 patients, group B (cardiac surgery without the ablation procedure) included 107 patients.

Results. The ablation procedure prolonged the total surgical time by 20 minutes (220 min in group A vs 200 min in B). A Holter-ECG after one year revealed sinus rhythm in 60.2% of group A patients vs 35.5% in group B (P=.002). The combined safety end point at 30 days occurred in 10.3% (A) vs 14.7% (B, P=.411). There was neither change in the left ventricular ejection fraction nor in the left atrial diameter.

Conclusions. This multicenter randomized study confirmed that the left atrial ablation procedure performed during cardiac surgery improves the likelihood of sinus rhythm presence one year postoperatively without increasing perioperative complications. However, the higher prevalence of sinus rhythm did not translate to improved clinical outcomes at one year. Further follow-ups (e.g. 5 years) are warranted to show any potential clinical benefit which might occur later.

AFib Ablation Pilot: One Year Follow-up of the Atrial Fibrillation Ablation Registry Conducted by the European Heart Rhythm Association[26]

Presented by Elena Arbelo (Las Palmas de Gran Canaria, Spain).

Introduction. The Atrial Fibrillation Ablation Pilot Study is a prospective, multinational registry conducted by the European Heart Rhythm Association of the European Society of Cardiology in the context of the ESC EurObservational Research Programme. This study was designed to describe the clinical epidemiology of patients undergoing an atrial fibrillation (AFib) ablation procedure, and the diagnostic/therapeutic processes applied in these patients across Europe. We present the results of the 1-year follow-up analysis.

Material and methods. A total of 72 centres in 10 European countries (Belgium, France, Germany, The Netherlands, Czech Republic, Poland, Greece, Italy, Spain and Denmark) were asked to enroll 20 consecutive patients scheduled for a first AFib ablation procedure. Site selection targeted hospitals with a medium to high expertise (performing≥50 AFib ablation procedures/year). Between October 2010 and May 2011, 1410 patients were included, of which 1391 underwent an AFib ablation (98.7%). The median age was 60 years (IQR 52-66), and 28% females. Two thirds had paroxysmal AFib and 38% lone AFib. Symptoms were present in 86%. The indications for ablation were mostly symptomatic AFib, but in over a third of patients there was also a desire for a drug-free lifestyle and the maintenance of sinus rhythm. Pulmonary vein isolation was attempted in 97% of patients, the roof line in 19.3%, and the mitral isthmus line in 12.8%.

Results. The one-year rate of treatment success was defined as survival free from documented atrial arrhythmia, with or without antiarrhythmic drugs, starting from the end of the third month to 12 months. Recurrences in the first 3 months were not counted as failures. The rate of AF ablation success was 73.7%; 88% of patients were in sinus rhythm at 12 months. The readmission rate was 30%, which included admissions for atrial fibrillation, atrial flutter, or atrial tachycardia in 21% and from other cardiovascular causes in 4.4%. Four patients died during the year, including at least one from hemorrhagic stroke. About 65% of patients were on anticoagulation therapy during the follow-up, primarily on vitamin-K antagonists, and 32% were on antiarrhythmic agents.

Conclusions. About three-fourths of patients who underwent catheter ablation for atrial fibrillation in a European registry study were free of arrhythmia recurrences at one year. Almost 90% of patients had been symptomatic before atrial fibrillation ablation; a little less than half had symptoms a year after the procedure.

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