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CARDIOLOGY CORNER

CARDIOLOGY NEWS

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Cardiology News/Recent Literature Review/First Quarter 2013

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HRS Meeting will take place in Denver, 8-11/5/13

EuroPCR to be held in Paris, 21-24/5/13

EuroPace will be held in Athens, 23-26/6/13

ESC Congress will be held in Amsterdam, 31/8-4/9/13

TCT Meeting: San Francisco, 28/10-1/11/13

AHA 2013: Dallas, 16-20/11/13

Pre-RELAX-AHF and RELAX-AHF Trials: Serelaxin Reduces 6-month Mortality in Acute Heart Failure Patients

In the Pre-RELAX-AHF (Relaxin in Acute Heart Failure) phase II study and RELAX-AHF phase III study patients hospitalized for acute heart failure were randomized within 16 h to IV placebo or serelaxin. Serelaxin reduced 6-month mortality in both studies (combined studies: N = 1,395; hazard ratio: 0.62; p = 0.0076). In RELAX-AHF, serelaxin improved the markers of cardiac (high-sensitivity cardiac troponin T), renal (creatinine/cystatin-C), and hepatic (AST/ALT) damage and of decongestion (N-T pro–BNP), while changes in these markers at day 2 and worsening heart failure during admission were associated with 6-month mortality. The authors concluded that early administration of serelaxin was associated with a reduction of 6-month mortality, while fewer signs of organ damage and more rapid relief of congestion were noted during the first days after admission (Metra et al, *J Am Coll Cardiol* 2013;61:196–206).

Favorable 5-Year Outcome after TAVI

The 5-year outcome was evaluated in 88 patients undergoing successful TAVI with a balloon-expandable valve. Mean aortic valve gradient decreased from 46 ± 18 mm Hg to 10 ± 4.5 mm Hg after TAVI and maintained at 11.8 ± 5.7 mm Hg at 5 years (p for post-TAVI trend = 0.06). Mean aortic valve area increased from 0.62 ± 0.17 cm^2 to 1.67 ± 0.41 cm^2 after TAVI and 1.40 ± 0.25 cm^2 at 5 years (p for post-TAVI trend <0.01). At 5 years, 3 patients (3.4%) had moderate prosthetic valve dysfunction. Survival rates at 1 to 5 years were 83%, 74%, 53%, 42%, and 35%, respectively. Median survival time after TAVI was 3.4 years, and the risk of death was significantly increased in patients with chronic obstructive pulmonary disease (hazard ratio [HR]: 2.17) and at least moderate paravalvular regurgitation (adjusted HR: 2.98). Thus, a favorable long-term outcome after TAVI was demonstrated. Signs of moderate prosthetic valve failure were observed in 3.4% of patients. No patients developed severe prosthetic regurgitation or stenosis. Comorbidities, mainly chronic lung disease and at least moderate paravalvular regurgitation, were associated with reduced long-term survival (Toggweiler et al, *J Am Coll Cardiol* 2013;61:413–419).

MADIT-CRT: Patients With Better Ejection Fraction Benefit the Most from Cardiac Resynchronization

In the MADIT-CRT study, among 1,809 patients, there were 696 (38%) patients with LVEF >30% (in the range of 30.1% to 45.3%); 914 patients (50.5%) with LVEF 26% to 30%; and 199 patients with LVEF ≤25% (11%). The mean reduction in LV end-diastolic volume with CRT-D therapy at the 1-year follow-up was directly related to increasing LVEF (LVEF >30%: 22.3%; LVEF 26% to 30%: 20.1%; and LVEF ≤25%: 18.7% reduction, respectively [p = 0.001]). CRT-D treatment similarly reduced the risk of HF/death in patients with LVEF >30% (hazard ratio [HR]: = 0.56, p = 0.003), LVEF 26% to 30% (HR: 0.67, p = 0.007), and LVEF ≤25% (HR: 0.57, p = 0.03; all p values for LVEF-by-treatment interactions >0.1). The authors concluded that the clinical benefit of CRT was evident regardless of baseline LVEF, including those with LVEF >30%, whereas the echocardiographic response was

increased with increasing LVEF, indicating that patients with better LVEF benefit the most (Kutyifa V et al, *J Am Coll Cardiol* 2013;61:936–944).

LBBB-Induced Cardiomyopathy Resolved with CRT

Among 375 candidates for CRT, 6 patients (1.6%) were identified who met all the following criteria for LBBB-induced cardiomyopathy: 1) history of typical LBBB for >5 years; 2) LV ejection fraction (EF) >50%; 3) decrease in LVEF to <40% and development of heart failure (HF) to NYHA functional class II to IV over several years; 4) major mechanical dyssynchrony; 5) no known etiology of cardiomyopathy; and 6) super-response to CRT with LVEF >45% and decrease in NYHA functional class at 1 year. Heart failure in these patients developed over a mean of 11.6 years. At the time of referral, Doppler echocardiograms showed major mechanical dyssynchrony. During CRT, NYHA functional class decreased, LV dimensions normalized and mechanical dyssynchrony was nearly resolved in all patients, and mean LVEF increased from 31 ± 12% to 56 ± 8% (p = 0.027). The authors concluded that these observations support the existence of a specific LBBB-induced cardiomyopathy resolved by CRT (Vaillant C et al, *J Am Coll Cardiol* 2013;61:1089–1095).

Dual Gene Therapy Provides Highly Efficient Biological Pacing

Dual gene therapy to effect biological pacing was tested by implanting either hyperpolarization-activated cyclic nucleotide–gated (HCN) channel 2 (*HCN2*), or the skeletal muscle sodium channel 1 (*SkM1*), or both with the appropriate adenovirus construct into the left bundle branches (LBB) or left ventricular (LV) epicardium of AV-blocked dogs. During stable peak gene expression on days 5 to 7, *HCN2*/*SkM1* LBB-injected dogs showed highly stable in vivo pacemaker activity superior to *SkM1* or *HCN2* alone and superior to LV-implanted dogs with regard to beating rates (resting ~80 bpm; max ~130 bpm), no dependence on electronic backup pacing, and enhanced modulation of pacemaker function during circadian rhythm or epinephrine infusion. In vitro isolated LV of dogs overexpressing *SkM1* manifested a more negative action potential (AP) threshold. The authors concluded that LBB-injected *HCN2*/*SkM1* potentially provides a more clinically suitable biological pacemaker strategy than other reported constructs, attributable to the more negative AP threshold and injection into the LBB (Boink GJJ et al, *J Am Coll Cardiol* 2013;61:1192–201).

Better Long-Term Outcome With Chest Compression Alone CPR

A retrospective cohort study combined 2 randomized trials comparing the short-term survival effects of CPR with chest compression alone or chest compression plus rescue breathing. Of the 2496 subjects, 1243 (50%) were randomly assigned to chest compression alone and 1253 (50%) to chest compression plus rescue breathing. Baseline characteristics were similar in the 2 groups. During the 1153.2 person-years of follow-up, there were 2260 deaths and 236 long-term survivors. Randomization to chest compression alone in comparison with chest compression plus rescue breathing was associated with a lower risk of death after adjustment for potential confounders (hazard ratio, 0.91; $P=0.02$). The authors concluded that there is long-term mortality benefit of dispatcher CPR instruction strategy consisting of chest compression alone rather than chest compression plus rescue breathing among adult patients with cardiac arrest (Dumas F et al, *Circulation* 2013;127:435-441).

Permanent Cardiac Pacing in Children: LV Apical and LV Lateral Wall Pacing are Associated With the Best Preservation of LV Function

Children (N=178; aged <18 years, median age 11.2 years) from 21 centers with AV block and no structural heart disease undergoing permanent pacing were followed up for a median of 5.4 years. Pacing sites were the free wall of the right ventricular (RV) outflow tract (n=8), lateral RV (n=44), RV apex (n=61), RV septum (n=29), left ventricular (LV) apex (n=12), LV midlateral wall (n=17), and LV base (n=7). LV synchrony, pump function, and contraction efficiency were better in children paced at the LV apex/LV midlateral wall. LV dyssynchrony correlated inversely with LV ejection fraction (EF) ($R=0.80$, $P=0.031$). Pacing from the RV outflow tract/lateral RV predicted significantly decreased LV function (LVEF <45%; odds ratio-OR, 10.72; $P=0.005$), whereas LV apex/LV midlateral wall pacing was associated with preserved LV function (LVEF ≥55%; OR, 8.26; $P=0.018$). The authors concluded that the site of ventricular pacing has a major impact on LV mechanical synchrony, efficiency, and pump function in children who require lifelong pacing. LV apex/LV midlateral wall pacing has the greatest potential to prevent pacing-induced LV dysfunction (Janousek J et al, *Circulation* 2013;127:613-623).

Infection Remains a Problem for Ventricular Assist Devices (VADs) Despite Use of Newer, Smaller Devices

Among 150 patients who received a VAD (2006–2008) at 11 US cardiac centers (86 or 57% receiving HeartMate II), 33 (22%) developed 34 device infections with an incidence rate of 0.10 per 100 person-days. The median time to infection was 68 days. The driveline was the most frequently infected site (n=28); 18 (64%) were associated with invasive disease. Staphylococci were the most common bacteria (47%); pseudomonas or other Gram-negative bacteria caused 32% of infections. A history of depression and elevated baseline serum creatinine were independent predictors of VAD infection (hazard ratio-HR=2.8; $P=0.007$ and 1.7; $P=0.023$, respectively). HeartMate II was also associated with an increased risk of infection. VAD infection

increased 1-year mortality (HR=5.6; $P<0.0001$). The authors concluded that infection frequently complicates VADs which adversely affects survival, and remains a problem despite the use of newer, smaller devices. Depression and renal dysfunction may increase the risk of VAD infection (Gordon RJ et al, *Circulation* 2013;127:691-702).

PROTECT AF Trial: Left Atrial Appendage (LAA) Closure is Noninferior to Anticoagulation

Patients (n=707) with nonvalvular atrial fibrillation and at least 1 risk factor were randomized to the Watchman LAA closure device (n=463) or continued warfarin (n=244) in a 2:1 ratio. Post-procedurally, warfarin was continued for ~45 days, followed by clopidogrel for 4.5 months and lifelong aspirin. Study discontinuation rates were 15.3% (71/463) and 22.5% (55/244) for the Watchman and warfarin groups, respectively. The time in therapeutic range for the warfarin group was 66%. After a mean follow-up of 2.3 years, the primary efficacy event (stroke, systemic embolism, and cardiovascular death) rates were 3.0% and 4.3% in the Watchman and warfarin groups, respectively (relative risk, 0.71 per year), which met the criteria for noninferiority. There were more primary safety events in the Watchman group (5.5% per year) than in the control group (3.6% per year; relative risk, 1.53). The authors concluded that left atrial appendage closure is noninferior to anticoagulation with warfarin (Reddy VY et al, *Circulation* 2013;127:720-729).

FREEDOM Trial: CABG is More Cost-effective Than DES PCI for Patients with Diabetes and Multivessel Coronary Artery Disease (CAD)

A total of 1900 patients with diabetes and multivessel CAD were randomized to PCI with DES (DES-PCI; n=953) or CABG (n=947) (2005-2010). Although initial procedural costs were lower for CABG, total costs for the index hospitalization were $8622 higher per patient. Over 5 years, follow-up costs were higher with PCI, owing to more frequent repeat revascularization and higher outpatient medication costs. However, cumulative 5-year costs remained $3641 higher per patient with CABG. There were only modest gains in survival with CABG, but when the results were projected to lifetime, CABG appeared economically attractive relative to DES-PCI, with substantial gains in both life expectancy and quality-adjusted life expectancy. The authors concluded that CABG, despite higher initial costs, is a cost-effective revascularization strategy compared with DES-PCI for patients with diabetes and multivessel CAD (Magnuson EA et al, *Circulation,* 2013;127:820-831).

LESSER EARTH Trial: CRT in Patients with Narrow QRS (<120 ms) Offers no Improvement and May be Harmful

The LESSER-EARTH trial, comparing the effects of cardiac resynchronization therapy (CRT) in patients with severe LV dysfunction and a QRS duration <120 ms, was interrupted prematurely by the Data Safety and Monitoring Board because of futility and safety concerns after 85 patients were randomized. Changes in exercise duration after 12 months were no different in patients with and without active CRT. Similarly, no significant differences were observed in LV end-systolic volumes and ejection fraction. CRT was rather associated with a significant reduction in the 6-minute walk distance, an increase in QRS duration and a nonsignificant trend toward an increase in heart failure–related hospitalizations (15 hospitalizations in 5 patients vs 4 in 4 patients). The authors concluded that in patients with heart failure and an ejection fraction ≤35%, and a QRS duration <120 ms, CRT did not improve clinical outcomes and was even associated with potential harm (Thibault B et al, *Circulation* 2013; 127:873-881).

Endovascular Reperfusion Therapy for Stroke: The Importance of Time From Initial CT to Groin Puncture ("Picture-to-Puncture" Time)

For acute stroke management, guidelines advocate the initiation of thrombolysis (IV tPA) within 60 minutes of patient arrival. However, <5% of all stroke patients receive tPA and <26.6% of tPA patients achieve this goal. The advent of endovascular reperfusion therapies has broadened the time window for treatment to 8 hours, rendering it possible to treat patients with larger clot burdens who do not qualify for tPA or patients in whom tPA has failed. A retrospective study evaluated 193 patients treated with endovascular therapy (2010 – 2012) at a single center. Patients transferred from outside hospitals were compared with locally treated patients. Good outcomes, as defined by 90-day modified Rankin Scale scores of 0 to 2, were analyzed by transfer status as well as time from initial CT to groin puncture ("picture-to-puncture" time). Outside transfers had longer picture-to-puncture times (205 min vs 89 min; $P<0.001$). This yielded fewer patients with favorable Alberta Stroke Program Early CT Scores on preprocedural CT imaging (Alberta Stroke Program Early CT Scores >7: 50% vs 76%; $P<0.001$) and significantly worse clinical outcomes (29% vs 51%; $P=0.003$). Picture-to-puncture times were independently associated with good outcomes (odds ratio, 0.994; $P=0.009$). The authors concluded that delays in picture-to-puncture times for interhospital transfers reduce the probability of good outcomes among stroke patients undergoing endovascular therapy (Sun CJ et al, *Circulation* 2013;127:1139-1148).

IMS III Study: A Combined Approach of Thrombolysis and Endovascular Therapy for Stroke is no Better than Thrombolysis

Patients with acute ischemic stroke who had received intravenous (IV) t-PA within 3 hours after symptom onset were randomly assigned to receive additional endovascular

therapy (n=434) or IV t-PA alone (n=222), in a 2:1 ratio. The study was stopped early because of futility after 656 participants had undergone randomization. The proportion of participants with a modified Rankin score of ≤2 at 90 days did not differ significantly according to treatment (40.8% with endovascular therapy and 38.7% with IV t-PA). Findings in the endovascular-therapy and IV t-PA groups were similar for mortality at 90 days (19.1% and 21.6%, respectively; P=NS) and number of patients with symptomatic intracerebral hemorrhage within 30 hours after initiation of t-PA (6.2% and 5.9%, respectively; P=NS). The authors concluded the similar safety outcomes and no significant difference in functional independence were observed with endovascular therapy after t-PA, as compared with t-PA alone (Broderick JP et al, *N Engl J Med* 2013;368:893-903).

SYNTHESIS Expansion Study: Endovascular Therapy for Stroke is not Superior to Thrombolysis

Patients (N=362) with acute ischemic stroke were randomly assigned, within 4.5 hours after onset, to endovascular therapy (intraarterial thrombolysis with t-PA, mechanical clot disruption or retrieval, or a combination) (n=181) or IV t-PA (n=181); therapies were effected within a median time of 3.75 h and 2.75 h, respectively (P<0.001). The primary outcome was survival free of disability at 3 months. At 3 months, 55 patients in the endovascular-therapy group (30.4%) and 63 in the t-PA group (34.8%) were alive without disability (odds ratio, 0.71; P=NS). Intracranial hemorrhage within 7 days occurred in 6% of the patients in each group, and there were no significant differences between groups in the rates of other serious adverse events or mortality. The authors concluded that in patients with acute ischemic stroke, endovascular therapy is not superior to standard treatment with IV t-PA (Ciccone A et al, *N Engl J Med* 2013;368:904-913).

Rekindled Interest in Pacemaker Reuse as a Feasible, Safe and Viable Option

Among 603 consecutive patients receiving a permanent pacemaker (2000–2010), 307 patients received resterilized pacemakers, and 296 control patients a new pacemaker. A total of 85 pacemakers had to be explanted, 31 in the control group (10.5%) and 54 in the study group (17.6%; relative risk-RR, 1.68; *P*=0.02). The primary end-point (unexpected battery depletion/ infection/ device dysfunction) was reached by 43 patients, 16 in the control group (5.5%) and 27 in the study group (7.2%; RR, 1.3; *P*=0.794). In terms of individual outcomes, 5 new pacemakers (1.7%) and 11 resterilized pacemakers (3.6%) had unexpected battery depletion (RR, 2.12; *P*=0.116); 3.7% new pacemakers and 3.2% reused pacemakers had a procedure-related infection (RR, 0.87; *P*=0.46); and 1 pacemaker in the study group malfunctioned. The authors concluded that pacemaker reuse is feasible and safe and is a viable option for patient with bradyarrhythmias. Other than an expected shorter pulse generator life, pacemaker reuse is not inferior to use of new devices (Nava S et al, *Circulation* 2013;127:1177-1183).

Persistent LBBB post TAVI is Associated With More Pacemaker Implants but no Worse Clinical Outcome

Among 1060 patients undergoing transcatheter aortic valve implantation (TAVI) with a CoreValve System (2007-2011), 818 patients (77%) without LBBB or pacemaker at admission or having a pacer implant within 48 h were analyzed. Among them, 224 patients (group A; 27.4%) developed a persistent LBBB vs 594 (group B; 72.6%) who did not. A low implantation of the valve was significantly more frequent in group A (15% vs 9.8%, *P*=0.02). During median follow-up of 438 days, LBBB was not associated with higher all-cause or cardiac mortality, or hospitalization for heart failure at 30 days or 1 year. At 30 days, but not at 1 year, group A had a significantly higher rate of pacemaker implantation. The authors concluded that persistent LBBB after CoreValve implantation showed no effect on hard end points, but led to a higher short-term rate of pacemaker implantation (Testa L et al, *Circulation* 2013;127:1300-1307).

PC Trial: PFO Closure for Cryptogenic Stroke not Superior to Medical Therapy per the Intention-to-Treat Analysis

In a multicenter trial, patients with a patent foramen ovale (PFO) and ischemic stroke, transient ischemic attack (TIA), or a peripheral thromboembolic event were randomly assigned to undergo closure of the PFO with the Amplatzer PFO Occluder or to receive medical therapy. At a mean follow-up of ~4 years, the primary end point (death, nonfatal stroke, TIA, or peripheral embolism) occurred in 7 of 204 patients (3.4%) in the closure group and in 11 of 210 patients (5.2%) in the medical-therapy group (hazard ratio-HR for closure vs. medical therapy, 0.63; P=NS). Nonfatal stroke occurred in 1 patient (0.5%) in the closure group and 5 patients (2.4%) in the medical-therapy group (HR, 0.20; P=NS), and TIA occurred in 5 (2.5%) and 7 patients (3.3%), respectively (HR, 0.71; P=NS). The authors concluded that according with an analysis performed on data for the intention-to-treat population, PFO closure for secondary prevention of cryptogenic embolism did not result in a significant reduction in the risk of recurrent embolic events or death as compared with medical therapy (Meier B et al, *N Engl J Med* 2013;368:1083-1091).

RESPECT Trial: PFO Closure Superior to Medical Therapy in the Per-Protocol and As-Treated Analyses, but not in Intention-To-Treat Analysis

A prospective, multicenter trial randomly assigned 980 patients (mean age, 45.9 years) with cryptogenic stroke, in a 1:1 ratio, to medical therapy alone or closure of the patent fora-

men ovale (PFO). The medical-therapy group received one or more antiplatelet medications (74.8%) or warfarin (25.2%). Follow-up was unequal in the 2 groups (1375 patient-years in the closure group vs. 1184 in the medical group, P=0.009) due to a higher dropout rate in the medical group. In the intention-to-treat cohort, 9 patients in the closure group and 16 in the medical group had a recurrence of stroke (hazard ratio-HR with closure, 0.49; P=0.08). The difference in the rate of recurrent stroke was significant in the prespecified per-protocol cohort (6 events in the closure group vs. 14 events in the medical group; HR, 0.37; P=0.03) and in the as-treated cohort (5 events vs. 16 events; HR, 0.27; P=0.007). Serious adverse events were similar, 23% in the closure group vs 21.6% in the medical-therapy group (P=NS). Procedure-related or device-related serious adverse events occurred in 21 of 499 patients in the closure group (4.2%), but the rate of atrial fibrillation or device thrombus was not increased. The authors concluded that in the primary intention-to-treat analysis, there was no significant benefit associated with closure of a PFO in patients with a cryptogenic ischemic stroke. However, closure was superior to medical therapy alone in the prespecified per-protocol and as-treated analyses, with a low rate of associated risks (Carroll JD et al, *N Engl J Med* 2013;368:1092-1100).

RED-HF Trial: No Benefit of Anemia Treatment With Darbepoetin in Patients With Systolic Heart Failure

In a randomized, double-blind trial, 2278 patients with systolic heart failure and mild-to-moderate anemia (hemoglobin, 9-12 g/dL) were assigned to receive either darbepoetin alfa (to achieve a hemoglobin target of 13 g/dL) or placebo. The primary outcome (death from any cause or hospitalization for worsening heart failure) occurred in 576 of 1136 patients (50.7%) in the darbepoetin group and 565 of 1142 patients (49.5%) in the placebo group (hazard ratio in the darbepoetin group, 1.01; P=NS). The neutral effect of darbepoetin alfa was consistent across all prespecified subgroups. Stroke occurred in 42 patients (3.7%) in the darbepoetin group and 31 patients (2.7%) in the placebo group (P=NS). Thromboembolic adverse events were noted in 153 patients (13.5%) in the darbepoetin group and 114 patients (10.0%) in the placebo group (P=0.01). Cancer-related adverse events were similar in the two groups. The authors concluded that darbepoetin alfa did not improve clinical outcomes in patients with systolic heart failure and mild-to-moderate anemia (Swedberg K et al, *N Engl J Med* 2013; 368:1210-1219).

AF Confers a Higher Risk for Cognitive Decline and Dementia, Regardless of Prior History of Stroke

A metaanalysis of 21 studies indicated that atrial fibrillation (AF) was associated with a higher risk for cognitive decline in patients with first or recurrent stroke (relative risk - RR, 2.70) and in a broader population including patients with or without a history of stroke (RR, 1.40). Analysis of prospective studies alone yielded similar results (RR, 1.36), and likewise the analysis of dementia which eliminated heterogeneity (RR, 1.38). The authors concluded that AF is associated with a higher risk for cognitive impairment and dementia, with or without a history of clinical stroke (Kalantarian S et al, *Ann Intern Med* 2013;158:338-346).

Important Review and Other Articles

Pathogenesis of acute coronary syndromes (Crea F & Liuzzo G, *J Am Coll Cardiol* 2013; 61:1-11), 2012 ACCF/AHA/HRS Focused Update for Device-Based Therapy of Cardiac Rhythm Abnormalities (Tracy CM et al, *J Am Coll Cardiol* 2013; 61:e6-e75), 2013 ACCF/AHA Guideline for the management of STEMI (O'Gara PT et al, *J Am Coll Cardiol* 2013; 61:485-510 & *Circulation* 2013;127:e362-e425), Inappropriate sinus tachycardia (Olshansky B & Sullivan RM, *J Am Coll Cardiol* 2013; 61:793-801), Sudden cardiac death in young athletes (Chandra N et al, *J Am Coll Cardiol* 2013; 61:1027-1040), Paravalvular leak after TAVI (Genereux P et al, *J Am Coll Cardiol* 2013; 61:1125-1136), Patient selection for ventricular assist devices (Miller LW & Guglin M, *J Am Coll Cardiol* 2013; 61:1125-1136), ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 Appropriate Use Criteria for ICDs & CRT (Russo AM, *J Am Coll Cardiol* 2013;61:1318-1368), Update on channelopathies (Webster G & Berul CI, *Circulation* 2013;127:126-140), Heart Disease & Stroke Statistics (AHA) (Go AS et al, *Circulation* 2013;127:e6-e245), Therapeutic hypothermia after cardiac arrest (Scirica BM, *Circulation* 2013;127:244-250), Childhood obesity (Li JS et al, *Circulation* 2013;127:260-267), Cost of ventricular assist devices (Miller LW et al, *Circulation* 2013;127:743-748), Wearable cardioverter-defibrillators (Adler A et al, *Circulation* 2013;127:854-860), Syncope (Saklani P et al, *Circulation* 2013; 127:1330-1339), Familial hypercholesterolemia (Hovingh GK et al, *Eur Heart J* 2013;34:962-971), DES (Stefanini GG & Holmes DR, *N Engl J Med* 2013;368:254-265), Adverse effects in TAVI (Khatri PJ et al, *Ann Intern Med* 2013;158:35-46), Heart failure with preserved ejection fraction (Meyer T et al, *Ann Intern Med* 2013;158:ITC1-1), Cardioprotection (Heusch G, *Lancet* 2013;381(9861): 166-175), Hypertrophic cardiomyopathy (Maron BJ & Maron MS, *Lancet* 2013;381(9862):242-255).

Cardiology News /Recent Literature Review / Second Quarter 2013

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ESC Congress will be held in Amsterdam, 31/8-4/9/13

HCS Meeting: Athens, 10-12/10/2013

TCT Meeting: San Francisco, 28/10-1/11/13

AHA 2013: Dallas, 16-20/11/13

ACC 2014: Washington, DC, 29-31/3/2014

Athens Cardiology Update 2014: Athens (Crown Plaza Hotel), 10-12/4/2014

HRS Meeting: San Francisco, 7-10/5/2014

EuroPCR: Paris, 20-23/5/2014

CardioStim 2014: Nice, 18-21/6/2014

ARMYDA-9 CAROTID: Clopidogrel Load & Atorvastatin Reload Prevent Ischemic Cerebral Events After Protected Carotid Stenting

A total of 156 patients undergoing protected carotid stenting were randomized to a 600-mg (n=78) or 300-mg (n=78) clopidogrel load given 6 h before intervention and either an atorvastatin reload (n=76; 80 mg + 40 mg initiating 12 h before the procedure) or no statin reload (n=80). Occurrence of the primary outcome (30-day incidence of TIA/stroke or new ischemic lesions on cerebral MRI performed at 24-48 h) was lower in the 600-mg clopidogrel arm (18% vs. 35.9% in the 300-mg group; p = 0.019) and in the atorvastatin reload arm (18.4% vs 35.0% in the no statin reload group; p=0.031). High-dose clopidogrel also significantly reduced the TIA/stroke rate at 30 days (0% vs 9%, p = 0.02), without an increase in bleeding risk. The authors concluded that in patients undergoing carotid stenting, a 600-mg clopidogrel load and a short-term reload with high-dose atorvastatin protects against early ischemic cerebral events (Patti G et al, *J Am Coll Cardiol* 2013;61:1379-1387).

MADIT CRT: Carvedilol Produces 30% Reduction in Hospitalizations for HF or Death When Compared With Metoprolol

The effects of metoprolol and carvedilol were compared in the MADIT-CR study. Hospitalization for HF or death occurred in 23% on carvedilol and 30% on metoprolol (hazard ratio-HR: 0.70, p=0.001), further attenuated in the subgroup of CRT-D patients (HR: 0.61, p = 0.001) and CRT-D patients with LBBB (HR: 0.51, p <0.001). Ventricular arrhythmias occurred in 22% and in 26%, respectively, of the patients receiving carvedilol or metoprolol (HR: 0.80, p = 0.050). A dose-dependent relationship was found in carvedilol, but not in metoprolol. The authors concluded that in HF patients in NYHA class I/II & wide QRS, carvedilol was associated with a 30% reduction in hospitalizations for HF or death when compared with metoprolol. A novel beneficial and synergistic effect of carvedilol was seen in patients with CRT-D & LBBB. Finally, a dose-dependent effect was apparent in carvedilol, but not in metoprolol (Ruwald et al, *J Am Coll Cardiol* 2013;61:1518–1526).

Colchicine Reduces In-Stent Restenosis (ISR) in Diabetic Patients Receiving a Bare-Metal Stent

A total of 196 diabetic patients, aged 64±7 years, with contraindication to a drug-eluting stent, undergoing PCI with a bare-metal stent (BMS), were randomized to receive colchicine 0.5 mg twice daily or placebo for 6 months. The angiographic in-stent restenosis (ISR) was 16% in the colchicine group and 33% in the control group (p = 0.007; odds ratio: 0.38). The number needed to treat to avoid 1 case of angiographic ISR was 6. The results were similar for IVUS-defined ISR (odds ratio: 0.42; number needed to treat = 5). Lumen area loss was 1.6 mm^2 in colchicine-treated patients and 2.9 mm^2 in the control group (p = 0.002). Adverse events from colchicine were limited to gastrointestinal symptoms. The authors concluded that colchicine is associated with less neointimal hyperplasia and decreased ISR in diabetic patients after PCI with a BMS (Deftereos S et al, *J Am Coll Cardiol* 2013;61:1679–1685).

Cryoballoon PVI Comparable to RFC Ablation in AF

Cryoballoon ablation was used for pulmonary vein isolation (PVI) in 605 patients with paroxysmal (n=579) or persistent (n=26) AF. PVI was achieved in 91%. At median follow-up of 30 months (n=451), 278 (~62%) patients were free of AF recurrence with no need for repeat procedures. Rates of freedom from AF after 1, 2, & 3 repeat procedures (using cryoballoon and/or radiofrequency catheter-RFC ablation) were 75%, 76%, and 77%, respectively. Use of the smaller balloons or both balloons produced the highest rates of long-term freedom from AF. Phrenic nerve palsy was noted in 12 patients (2%), resolving within 3-9 months. The authors concluded that long-term freedom from AF after cryoballoon ablation is similar to that reported for radio-frequency ablation. A choice between balloons may improve outcomes (Vogt et al, *J Am Coll Cardiol* 2013;61:1707–1712).

STOP-AF Trial: Cryoballoon Ablation a Safe and Effective Alternative to Antiarrhythmic Drugs for Symptomatic Paroxysmal AF

Patients with symptomatic paroxysmal AF and previously failed drug therapy underwent 2:1 randomization to either cryoballoon ablation (n=163) or drug therapy (n=82). In 160 (98.2%) patients, 3 or more pulmonary veins (PVs) were

isolated. All 4 major PVs were isolated in 97.6% of patients, as were 21 of 21 left common PVs and 10 of 13 right middle PVs. In 83% of patients, cryoballoon alone was sufficient for PV isolation (PVI). At 12 months, treatment success was 70% compared with 7.3% of antiarrhythmic drug patients. Sixty-five (79%) drug-treated patients crossed over to cryoablation during 12 months of study follow-up due to recurrent, symptomatic AF. Twenty-nine of 259 procedures (11.2%) were associated with phrenic nerve palsy; 25 of these had resolved by 12 months. Cryoablation patients had significantly improved symptoms at 12 months. The authors concluded that cryoballoon ablation is a safe and effective alternative to antiarrhythmic medication for patients with symptomatic paroxysmal AF, for whom at least one drug has failed, with acceptable risks (Packer et a, *J Am Coll Cardiol* 2013;61: 1713–23).

Substitution of Prasugrel for Clopidogrel in Patients on Triple Therapy Increases the Risk of Bleeding

About 10% of patients who receive dual antiplatelet therapy after PCI have an indication for oral anticoagulation. In a consecutive series of 377 patients who underwent PCI with DES and had an indication for oral anticoagulation were treated with a 6-month regimen of aspirin and oral anticoagulation with either prasugrel or clopidogrel. A total of 21 patients (5.6%) received prasugrel instead of clopidogrel. TIMI major and minor bleeding occurred significantly more often in the prasugrel compared with the clopidogrel group: 6 (28.6%) vs. 24 (6.7%); adjusted hazard ratio (HR): 3.2, p = 0.03). There was no significant difference regarding the secondary endpoint (composite of death, myocardial infarction, ischemic stroke, or definite stent thrombosis): 2 (9.5%) vs. 25 (7.0%). The authors concluded that substitution of prasugrel for clopidogrel in patients needing triple therapy increases the risk of bleeding (Sarafoff et al, *J Am Coll Cardiol* 2013;61:2060–2066).

CARE-HF Trial: RV Dysfunction (TAPSE ≤14 mm) is a Prognostic Determinant Among CRT Patients

Of 813 patients in the CARE-HF trial, 688 had tricuspid plane systolic excursion (TAPSE) measured at baseline, and 345 of them were assigned to CRT. Median age was 66 years, LVEF 24%, and TAPSE 19 mm. Those with worst TAPSE (<17.4 mm) were more likely to have ischemic heart disease. Overall, CRT improved LV but not RV structure and function. At median follow-up of 2 years, 213 deaths occurred. Patients with lower TAPSE had a higher mortality, regardless of assigned treatment (p<0.001). Greater inter-ventricular delay, NYHA class, mitral regurgitation, and NT pro–B-NP, lower TAPSE, and assignment to control group were independently associated with higher mortality. Reduction in mortality with CRT was similar in each tertile of TAPSE. The authors concluded that right ventricular (RV) dysfunction is a powerful determinant of prognosis among candidates for CRT, regardless of treatment assigned, but did not diminish the benefit of CRT (Damy et al, J *Am Coll Cardiol* 2013;61:2153–2160).

"Real-World" Experience With Dabigatran: No Evidence of Excess Bleeding or MI

Concerns have been raised about an excess of bleeding or myocardial infarction (MI) among patients treated with dabigatran. From a Danish Registry, a dabigatran-treated group (n=4978) and a 1:2 propensity-matched warfarin-treated group (n=8,936) were compared. Stroke and systemic embolism were not significantly different between the 2 groups. Adjusted mortality was significantly lower with both dabigatran doses (110 mg bid, hazard ratio-HR: 0.79; 150 mg bid, HR: 0.57). Pulmonary embolism was lower compared with warfarin for both doses of dabigatran. Less intracranial bleeding was seen with both dabigatran doses (110 mg, HR: 0.24; 150 mg, HR: 0.08). The incidence of MI was lower with both dabigatran doses (110 mg, HR: 0.30; 150 mg, HR: 0.40). Gastrointestinal bleeding was lower with the lower dose of dabigatran 110 mg (HR: 0.60) but not with the higher dose. The authors concluded that in this "everyday clinical practice", there were similar stroke/systemic embolism and major bleeding rates with both doses of dabigatran compared with warfarin. Mortality, intracranial bleeding, pulmonary embolism, and MI were lower with dabigatran, compared with warfarin (Larsen et al, *J Am Coll Cardiol* 2013;61:2264–2273).

Direct Transaortic Approach for TAVI is Feasible

Initial US experience with direct transaortic approach to transcatheter aortic valve implantation (TAVI) was reported in 44 patients with inoperable, severe aortic stenosis, ineligible for transfemoral access. Data were compared with those from 76 patients who underwent transapical TAVI. Device implantation success (89% vs. 84%) and 30-day combined safety endpoint of all-cause mortality, MI, major stroke, disabling bleeding, severe acute kidney injury, and valve reintervention (20% vs. 33%) were similar. The transaortic approach was associated with lower combined bleeding and vascular event rate (27% vs. 46%; p = 0.05), shorter median ICU stay (3 vs. 6 days; p = 0.01), and a favorable learning curve. The authors concluded that the transaortic approach is technically feasible and seems to be associated with favorable outcome (Lardizabal et al, *J Am Coll Cardiol* 2013;61:2341–5).

Northern Manhattan Study (NOMAS): Incidentally Detected PFO by Transthoracic Echocardiography has Very Low Prevalence and is not Associated With an Increased Risk of Clinical or Subclinical Stroke

Patent foramen ovale (PFO) presence was assessed by transthoracic echocardiography with saline contrast injection in 1,100 stroke-free individuals aged >39 of a community-based sample followed for a mean of 11 years. Also, 360 participants

had MRI for silent brain infarct (SBI) detection. PFO was present in 164 (14.9%). Over a mean follow-up of 11.0 ± 4.5 years, 111 ischemic strokes occurred (10.1%), 15 (9.2%) in the PFO and 96 (10.3%) in the non-PFO group. The 12.5-year cumulative risk of stroke was 10.1% in the PFO and 10.4% in the non-PFO group (p=NS). The adjusted hazard ratio for PFO and stroke was 1.10. In the MRI subcohort, PFO was not associated with SBI. The authors concluded that in this community-based cohort, PFO was not associated with an increased risk of clinical or subclinical stroke (Di Tullio et al, *J Am Coll Cardiol* 2013;62:35–41).

Pregnancy Loss is Associated With an Increased Risk of MI, Stroke, and Renovascular Hypertension: A Possible Risk Factor for Atherosclerotic Disease in Women?

Among women pregnant at least once, a cohort of women was identified with miscarriages, stillbirths, or live singleton births. Among 1,031,279 such women followed for an average of 15 years per woman, 2798 myocardial infarctions (MIs), 4053 strokes, and 1269 cases of renovascular hypertension were detected. Women with stillbirths had 2.7, 1.7, and 2.4 times the rates of MI, strokes, and renovascular hypertension, respectively, as women with no stillbirths. Compared with women with no miscarriages, women with miscarriages had 1.13, 1.16, and 1.20 times the rates of these same outcomes, respectively; these associations were dose dependent, with each additional miscarriage increasing the rates of MI, strokes and renovascular hypertension by 9%, 13%, and 19%, respectively. Associations were strongest in younger women (<35 years). The authors concluded that pregnancy losses were associated with subsequent risks of MI, strokes, and renovascular hypertension, conditions linked to atherosclerosis, making pregnancy loss a possible candidate risk factor for atherosclerotic disease in women, with possible inflammatory processes being the common denominator (Ranthe et al, *Circulation* 2013;127:1775-1782).

Swedish Study: AF is an Independent Risk Factor of All-Cause Mortality in Patients Hospitalized With Incident AF and Relative Risk is Higher in Women and Highest in the Youngest Patients

A total of 272,186 patients (≤85 years; 44% women) hospitalized with incidental AF (1995–2008) and 544,344 matched controls were compared. The adjusted long-term relative all-cause mortality risk in women vs. controls was 2.15, 1.72, and 1.44 (P<0.001) in the age categories ≤65, 65–74, and 75–85 years, respectively. These figures for men were 1.76, 1.36, and 1.24 (P<0.001). Among comorbidities, neoplasm, chronic renal failure, and chronic obstructive pulmonary disease contributed most to the increased mortality vs. controls. In patients with AF as the primary diagnosis, the relative risk of mortality was 1.63, 1.46, and 1.28 (P<0.001) in women and 1.45, 1.17, and 1.10 (P<0.001) in men. The authors concluded that AF was an independent risk factor of all-cause mortality in patients with incident AF. Although the actual risk was consistently lower in women, the highest relative risk of mortality was seen in women and in the youngest patients compared with controls (Andersson et al, *Eur Heart J* 2013;34:1061–1067).

AFFIRM Study/ Propensity-Adjusted Analysis: Increased Mortality Among Patients Taking Digoxin

The association between digoxin and mortality was assessed in patients enrolled in the AFFIRM trial. Analyses were conducted in all patients and in subsets according to the presence or absence of heart failure (HF). Digoxin was associated with an increase in all-cause mortality (hazard ratio-HR 1.41; P<0.001), cardiovascular mortality (HR 1.35, P = 0.016), and arrhythmic mortality (HR 1.61, P = 0.009). The all-cause mortality was increased with digoxin in patients without or with HF. There was no significant digoxin–gender interaction for all-cause or cardiovascular mortality. The authors concluded that digoxin was associated with a significant 41% increase in all-cause mortality in patients with AF after correcting for clinical characteristics and comorbidities, regardless of gender or of the presence or absence of HF (Whitbeck et al, *Eur Heart J* 2013;34: 1481-1488).

AFFIRM Study/ Post Hoc Propensity-Matched Analysis: Lack of Evidence of Increased Mortality Among Patients Taking Digoxin

In the AFFIRM study, 4060 patients with paroxysmal and persistent AF were randomized to rate (n=2027) vs. rhythm (n=2033) control strategies. Of these, 1377 received digoxin as initial therapy. A cohort was assembled of 878 pairs of patients receiving and not receiving digoxin, who were balanced on baseline characteristics. During the 3.4 years of the mean follow-up, all-cause mortality occurred in 14 and 13% of matched patients receiving and not receiving digoxin, respectively (hazard ratio-HR associated with digoxin use: 1.06; P = NS). Also, no association with all-cause hospitalization or incident non-fatal cardiac arrhythmias could be found. The authors concluded that in patients with paroxysmal and persistent AF, no evidence was found of increased mortality or hospitalization in those taking digoxin as baseline initial therapy (Gheorghiade et al, *Eur Heart J* 2013;34:1489-1497).

The Post-Hoc Non-Randomized Observational Design of Both the AFFIRM Trial Analyses May Explain the Conflicting Results About the Risk of Digoxin

The editorial comments that accompany the above 2 studies, which are two different analyses of the AFFIRM trial, point to the different design of the studies in order to explain the conflicting results of analysis of the same data. The first edi-

torial indicates that "In the article by Whitbeck et al, digoxin use was assessed at randomization and during follow-up. The association of digoxin use with mortality was evaluated treating digoxin as a time-dependent covariate in a Cox proportional hazard model. By using digoxin as a time-dependent covariate, patients changed from being in the 'on-digoxin' group to the 'not on-digoxin' group if their medication use changed over time in the study, and their associated time at risk for death contributed to each respective group". On the other hand "In the article by Gheorghiade et al, digoxin use was assessed at a fixed time point only, at the time of randomization". The first commenter concludes that "Given the non-randomized, observational design of both studies, the findings should be considered hypothesis generating. Even sophisticated statistical methods such as propensity analysis cannot replace randomization" (Murphy S, *Eur Heart J* 2013;34:1465-1467).

The commenters in the second editorial also point to the post hoc and non-randomized design of the analyses, but focus on the high dose of digoxin used indicating that "patients in AFFIRM were receiving high doses of digoxin, since they were encouraged to have an serum level ≥1.0 ng/mL", which "may have contributed to the observed increased mortality". Their concluding remark is that "With regard to the place of digoxin in AF, it is likely that this will further diminish in the future, because of its inefficacy to reduce heart rate during exercise on the one hand, and the outcome of studies such as the study of Whitbeck et al", albeit "low-dose digoxin may still be useful, but trials examining this question are urgently needed" (van Veldhuisen et al, *Eur Heart J* 2013;34:1468-1470).

Adding a New Oral Anticoagulant to Antiplatelet Therapy Results in a Modest Reduction in Cardiovascular Events but a Substantial Increase in Bleeding

A meta-analysis was performed of 7 randomized studies evaluating the efficacy and safety of adding a novel oral anticoagulant to single (aspirin) or dual (aspirin and clopidogrel) antiplatelet therapy in patients with acute coronary syndromes (ACS). The analysis comprised 30 866 patients, 4135 (13.4%) on single, and 26 731 (86.6%) on dual antiplatelet therapy, with an ACS within the last 7–14 days. When compared with aspirin alone, the addition of an oral anticoagulant reduced the incidence of major adverse cardiac events (MACE) (hazard ratio-HR 0.70), but increased clinically significant bleeding (HR: 1.79). Compared with dual antiplatelet therapy with aspirin and clopidogrel, adding an oral anticoagulant decreased the incidence of MACE (HR: 0.87), but more than doubled the bleeding (HR: 2.34). The authors concluded that in patients with a recent ACS, the addition of a new oral anticoagulant to antiplatelet therapy results in a modest reduction in MACE but a substantial increase in bleeding, most pronounced with triple therapy (Oldgren et al, *Eur Heart J* 2013;34:1670-1680).

CHAMPION PHOENIX: Intravenous Cangrelor Significantly Reduced the Rate of Ischemic Events in Patients Undergoing PCI

A total of 11,145 patients who were undergoing percutaneous coronary intervention (PCI) were randomly assigned to receive a bolus and infusion of cangrelor or a loading dose of 600 mg or 300 mg of clopidogrel. The primary efficacy end point (death, myocardial infarction, ischemia-driven revascularization, or stent thrombosis at 48 hours) occurred in 4.7% in the cangrelor group and 5.9% in the clopidogrel group (odds ratio-OR, 0.78; P=0.005). Stent thrombosis developed in 0.8% in the cangrelor group and in 1.4% in the clopidogrel group (OR, 0.62; P=0.01); this rate at 48 hours was 0.16% in the cangrelor group and 0.11% in the clopidogrel group (OR, 1.50; P=NS). Adverse events were infrequent except for transient dyspnea which occurred more frequently with cangrelor (1.2% vs. 0.3%). The authors concluded that cangrelor significantly reduced the rate of ischemic events, including stent thrombosis, during PCI, with no significant increase in severe bleeding (Bhatt et al, *N Engl J Med* 2013;368:1303-1313).

STREAM: Prehospital or Early Fibrinolysis Followed by Timely Coronary Angiography Resulted in Effective Reperfusion in Patients With STEMI Presenting Within 3 Hours and Who Could not Undergo PCI Within 1 Hour, Albeit With a Slightly Increased Risk of Intracranial Bleeding

A total of 1892 patients with STEMI, who presented within 3 hours and who were unable to undergo primary PCI within 1 hour, were randomized to primary PCI or fibrinolytic therapy (tenecteplase) before transport to a PCI-capable hospital. Coronary angiography was performed emergently if fibrinolysis failed; otherwise within 6-24 hours. The primary end point (death, shock, congestive heart failure, or 30-day reinfarction) occurred in 116 of 939 patients (12.4%) in the fibrinolysis group and in 135 of 943 patients (14.3%) in the primary PCI group (relative risk, 0.86; P = NS). Emergency angiography was required in 36.3% of patients in the fibrinolysis group; the remainder underwent angiography at a median of 17 hours. More intracranial hemorrhages occurred in the fibrinolysis group (1.0% vs. 0.2%, P = 0.04; after protocol amendment, 0.5% vs. 0.3%, P = 0.45). The rates of nonintracranial bleeding were similar. The authors concluded that prehospital fibrinolysis with timely coronary angiography resulted in effective reperfusion in patients with early STEMI who could not undergo primary PCI within 1 hour after the first medical contact. However, fibrinolysis was associated with a slightly increased risk of intracranial bleeding (Armstrong et al, *N Engl J Med* 2013;368:1379-87).

BLOCK HF Trial: Biventricular is Better than Right Ventricular Pacing in Patients With AV Block and LV Dysfunction With NYHA Class I-III Heart Failure

A total of 691 patients with AV block requiring pacing, NYHA class I-III heart failure and a left ventricular (LV) ejection fraction ≤50% were randomly assigned to right ventricular (RV) or biventricular (BiV) pacing and were followed for an average of 37 months. The primary outcome (death, urgent care visit for heart failure requiring IV therapy, or a ≥15% increase in the LV end-systolic volume index) occurred in 190 of 342 patients (55.6%) in the RV-pacing group, compared with 160 of 349 (45.8%) in the BiV-pacing group (hazard ratio, 0.74). LV lead–related complications occurred in 6.4% of patients. The authors concluded that BiV pacing was superior to conventional RV pacing in patients with AV block and LV systolic dysfunction with NYHA class I-III heart failure (Curtis et al, *N Engl J Med* 2013; 368:1585-1593).

BRUISE CONTROL: No Need to Interrupt Warfarin Therapy Before Pacemaker or ICD Implantation

Patients with an annual risk of thromboembolic events of ≥5% were randomized to continue warfarin or to stop it and receive bridging therapy with heparin. The safety monitoring committee asked for termination of the trial after the second prespecified interim analysis. Clinically significant device-pocket hematoma occurred in 12 of 343 patients (3.5%) in the continued-warfarin group, as compared with 54 of 338 (16.0%) in the heparin-bridging group (relative risk, 0.19; P<0.001). Major surgical and thromboembolic complications were rare and similar in the 2 groups (1 tamponade and 1 myocardial infarction in the heparin-bridging group and 1 stroke and 1 TIA in the continued-warfarin group). The authors concluded that compared with bridging therapy with heparin, a strategy of uninterrupted warfarin treatment at the time of pacemaker or ICD implantation significantly reduced the incidence of device-pocket hematomas (Birnie et al, *N Engl J Med* 2013; 368:2084-2093).

ADVANCE III Trial: Using More Intervals to Detect Ventricular Tachyarrhythmias Reduces Electrical Therapy and Inappropriate ICD Shocks

A total of 1902 patients (mean age 65 years) with ischemic or nonischemic cardiomyopathy receiving an implantable cardioverter defibrillator (ICD) for primary (75%) or secondary prevention were randomized 1:1 to programming with long- (30/40 intervals; n=948) or standard-detection (18/24; n=954) intervals. During a median follow-up of 12 months, long-detection group had 346 delivered therapies vs 557 in the standard-detection group (incident rate ratio - IRR, 0.63; $P<0.001$). The long- vs the standard-detection group experienced 23 vs 37 ATPs per 100 person-years (IRR, 0.58; $P<0.001$); 19 vs 30 shocks per 100 person-years (IRR, 0.77; $P=0.06$), with a significant difference in the probability of therapy occurrence ($P<0.001$); and a reduction in first occurrence of inappropriate shock (5.1 per 100 patient-years vs 11.6; IRR, 0.55; $P=0.008$). Mortality and arrhythmic syncope rates did not differ between groups. The authors concluded that the use of a long- vs standard-detection interval may be preferable as it results in a lower rate of electrical therapy, and inappropriate ICD shocks (Gasparini et al, *JAMA* 2013;309:1903-1911).

Receiving a Dual-Chamber ICD for Primary Prevention When there is no Indication for Pacing Confers Similar Mortality at One Year but a Higher Complication Rate

Among 32,034 patients who received an implantable cardioverter defibrillator (ICD) for primary prevention and lacked an indication for pacing, 12,246 (38%) received a single-chamber and 19,788 (62%) a dual-chamber device. Rate of complications was lower for single-chamber devices (3.51% vs 4.72%; $P<0.001$), but 1-year mortality, 1-year all-cause hospitalization or hospitalization for heart failure were similar. The authors concluded that when used for primary prevention without indication for pacing, dual-chamber ICDs compared with single-chamber devices are associated with a higher risk of device-related complications and similar 1-year mortality and hospitalization outcomes (Peterson et al, *JAMA* 2013;309(19):2025-2034).

Multivessel CABG Confers Lower Long-Term Mortality than Multivessel PCI When Comorbidities Exist

Over 5 years of follow-up, among 105,156 propensity score–matched patients (aged >65years) with multivessel coronary disease undergoing revascularization (1992-2008), coronary artery bypass surgery (CABG) was associated with lower mortality than percutaneous coronary intervention (PCI) (hazard ratio-HR, 0.92; $P<0.001$). The difference was greater among patients with diabetes (HR, 0.88), tobacco use (HR, 0.82), heart failure (HR, 0.84), and peripheral arterial disease (HR, 0.85). However, patients with none of these factors had slightly better survival after PCI. The authors concluded that multivessel CABG is associated with lower long-term mortality than multivessel PCI, an association considerably modified by presence of comorbidities, with improvement in survival mainly in patients with diabetes, tobacco use, heart failure, or peripheral arterial disease (Hlatky et al, *Ann Intern Med* 2013;158:727-734).

ROCKET AF: Patients Transitioned From Warfarin to Rivaroxaban Had More Bleeding in First 7 Days Atoned After 30 Days

In ROCKET AF, 7897 (~55%) patients were warfarin-experienced (at least 6 weeks of prior treatment) and 6367 (~45%) were warfarin-naive. The effect of rivaroxaban vs warfarin on stroke was consistent: 2.32 rates per 100 patient-years

of follow-up vs 2.87 for warfarin-naive patients (hazard ratio-HR, 0.81) and 1.98 vs 2.09 for warfarin-experienced patients (HR, 0.94; *P=NS*). During the first 7 days, rivaroxaban was associated with more bleeding than warfarin (HR in warfarin-naive patients 5.83, and in warfarin-experienced patients, 6.66). After 30 days, rivaroxaban had less bleeding than warfarin in warfarin-naive patients (HR, 0.84) and similar bleeding in warfarin-experienced patients (HR, 1.06; $P = 0.003$). The authors concluded that the efficacy of rivaroxaban in warfarin-experienced and warfarin-naive patients was similar but there were more bleeding events in the first 7 days; after 30 days, rivaroxaban was associated with less bleeding in warfarin-naive patients and similar bleeding in warfarin-experienced patients. Patients enrolled with INRs of 2.0-3.0 had outcomes similar to those with INRs <2.0. The authors recommend that patients who are going to switch from warfarin to rivaroxaban should start 20 mg of rivaroxaban and stop warfarin only when the INR is <3.0 (Mahaffey et al, *Ann Intern Med* 2013;158:861-868).

Important Review and Other Articles

Guidelines for the management of patients with peripheral artery disease (Anderson et al, *J Am Coll Cardiol* 2013; 61:1555-1570), Management of type B aortic dissection (Fattori et al, *J Am Coll Cardiol* 2013; 61:1661-1678), Management of patients with AF (Anderson et al, *J Am Coll Cardiol* 2013;61:1935-1944), Genetics of ARVC (Marcus et al, *J Am Coll Cardiol* 2013;61:1945-1948), Genomics in cardiovascular disease (Roberts et al, *J Am Coll Cardiol* 2013;61:2029-2037), Platelet function tests (Gorog & Fuster, *J Am Coll Cardiol* 2013;61:2115-2129), Appropriate utilization of cardiovascular imaging (Carr et al, *J Am Coll Cardiol* 2013;61:2199-2206 & Patel et al, *J Am Coll Cardiol* 2013;61:2207-2231), Cardiac complications of thoracic irradiation (Jaworski et al, *J Am Coll Cardiol* 2013;61:2319-2328), Guidelines for non-STE ACS (Anderson et al, *J Am Coll Cardiol* 2013;61:e179-e347), Cardio-hepatic interactions in heart failure (Samski et al, *J Am Coll Cardiol* 2013;61:2397-2405), In-hospital cardiac arrest (Morrison et al, *Circulation* 2013;127:1538-1563), Early repolarization (Obeyesekere et al, *Circulation* 2013; 127;1620-1627), Air pollution and cardiovascular system (Manolis et al, *Hosp Chronicles* 2013;8:103-111 & Gold et al, *Circulation* 2013; 127:1903-1913), Williams syndrome (Collins II, *Circulation* 2013; 127:2125-2134), Pet ownership and cardiovascular risk (Levine et al, *Circulation* 2013;127:2353-2363), Valve-in-valve procedure (Webb & Dvir, *Circulation* 2013;127: 2542-2550), IVUS (Bangalore & Bhatt, *Circulation* 2013;127:e868-e874), Cancer drugs and the heart (Suter & Ewer, *Eur Heart J* 2013;34:1102-1111), Management of pericardial effusion (Imazio & Adler, *Eur Heart J* 2013; 34:1186-1197), CRT update (Yu & Hayes, *Eur Heart J* 2013; 34:1396-1403), Cardiomyopathy work-up (Rapezzi et al, *Eur Heart J* 2013; 34:1448-1458), Biomarkers in AF (Hijazi et al, *Eur Heart J* 2013;34:1474-1480), Use of PPIs in cardiac patients (Agewall et al, *Eur Heart J* 2013;34:1708-1715), Myocardial perfusion injury (Froehlich et al, *Eur Heart J* 2013;34:1714-1724), Telemedicine and cardiac implants (Varma & Ricci, *Eur Heart J* 2013;34:1885-1893), Acute coronary syndromes (Libby, *N Engl J Med* 2013; 368:2004-2013), Management of asymptomatic carotid stenosis (Raman et al, *Ann Intern Med* 2013;158:676-685).

Cardiology News /Recent Literature Review / Third Quarter 2013

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HCS Meeting: Athens, 10-12/10/2013

TCT Meeting: San Francisco, 28/10-1/11/13

AHA 2013: Dallas, 16-20/11/13

ACC 2014: Washington, DC, 29-31/3/2014

Athens Cardiology Update 2014: Athens (Crown Plaza Hotel), 10-12/4/2014

HRS Meeting: San Francisco, 7-10/5/2014

EuroPCR: Paris, 20-23/5/2014

CardioStim 2014: Nice, 18-21/6/2014

Percutaneous Left Atrial Appendage Closure May be a Therapeutic Alternative in Patients with Atrial Fibrillation (AF) and Absolute Contraindications to Anticoagulation Therapy

Left atrial appendage closure (LAAC) with the AMPLATZER Cardiac Plug (ACP) was successfully performed in 51 of 52 (98%) patients (aged 74±8 years) with AF and absolute contraindications to anticoagulation therapy. Most patients received dual-antiplatelet therapy after the procedure for 1-3 months and single antiplatelet therapy thereafter. Main complications were device embolization (1.9%) and pericardial effusion (1.9%), with no cases of periprocedural stroke. At follow-up (20±5 months), death rate was 5.8%, stroke 1.9%, systemic embolism 0%, pericardial effusion 1.9%, and major bleeding 1.9%. The presence of mild peridevice leak was observed in 16.2% of patients at the 6-month follow-up as evaluated by transesophageal echo. There were no cases of device thrombosis. The authors concluded that in patients with nonvalvular AF at high risk of cardioembolic events and absolute contraindications to anticoagulation, LAAC using the ACP device followed by dual-/single-antiplatelet therapy was associated with a low rate of embolic and bleeding events and no device thrombosis at short and midterm follow-up (Urena M et al, *J Am Coll Cardiol* 2013;62:96–102).

Preliminary Favorable Experience With Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation

Percutaneous ligation of the left atrial appendage (LAA) with the LARIAT device (a snare with a pre-tied suture guided epicardially over the LAA) was success-fully performed in 85 of 89 (96%) patients with complete closure achieved in 81 patients, while 4 had a ≤2-3-mm residual LAA leak. There were 3 complications (during pericardial access, n=2; & transseptal catheterization, n=1). Adverse events included severe pericarditis post-operatively (n=2), late pericardial effusion (n=1), sudden death (n=2), & late strokes (n=2). At 1 (81 of 85) & 3 months (77 of 81) post-ligation, 95% of the patients had complete LAA closure by transesophageal echo (TEE). Of the 65 patients undergoing 1-year TEE, there was 98% complete LAA closure, including patients with previous leaks. The authors concluded that LAA closure with the LARIAT device can be performed effectively with acceptably low complication rate (Bartus et al, *J Am Coll Cardiol* 2013;62:108–118).

NEXT Trial: Low Rate of Restenosis and Stent Thrombosis With the Biodegradable Polymer Biolimus-Eluting Stent

A biodegradable polymer biolimus-eluting stent-BES (Nobori) (n=1617) was compared with a durable polymer cobalt-chromium everolimus-eluting stent-EES (Xience/ Promus) (n=1618). The primary efficacy endpoint (target lesion revascularization-TLR at 1 year) occurred in 67 patients (4.2%) in the BES group, and in 66 patients (4.2%) in the EES group, demonstrating noninferiority of BES over EES. Cumulative incidence of definite stent thrombosis was low and similar between the 2 groups (0.25% vs. 0.06%, p=NS). An angiographic substudy enrolling 528 patients (BES: n=263, and EES: n=265) demonstrated noninferiority of BES over EES regarding the primary angiographic endpoint of in-segment late loss (0.03±0.39 mm vs. 0.06±0.45 mm) at 266±43 days after stent implantation. The authors concluded that 1-year clinical and angiographic outcome after BES implantation was noninferior to and not different from that after EES implantation. Both BES and EES had a low rate of TLR and extremely low rate of stent thrombosis (Natsuaki et al, *J Am Coll Cardiol* 2013;62:181–190).

ATLAS-ACS 2 TIMI 51: Reduction of Stent Thrombosis in Patients With Acute Coronary Syndromes (ACS) Treated With Rivaroxaban

A total of 15,526 patients with recent ACS were randomized to receive either 2.5 mg or 5 mg bid of rivaroxaban or placebo for a mean of 13 months and up to 31 months. Among patients who had a stent placed before or at the time of the event (n=9,631 or 63%), rivaroxaban significantly reduced definite and probable stent thrombosis in the pooled (1.9% vs 1.5%; hazard ratio -HR: 0.65; p=0.017) and the 2.5 mg bid (1.9% vs 1.5%; HR: 0.61; p=0.023) treatment groups when compared with placebo, with a trend toward a reduction in the 5 mg bid group (1.9% vs. 1.5%; HR: 0.70; p = 0.089). Among patients who received dual antiplatelet therapy (DAPT) with both aspirin and a thienopyridine, the benefit of rivaroxaban emerged during the period of active treatment with DAPT (HR: 0.68; combined rivaroxaban group vs. placebo). Among stented patients treated with DAPT, there was a mortality reduction among those treated with rivaroxaban 2.5 mg bid (HR: 0.56; p=0.014), but not with the 5 mg bid dose. The authors concluded that among stented patients with ACS treated with DAPT, administration of rivaroxaban 2.5 mg bid was associated with a reduction in stent thrombosis and mortality (Gibson et al, *J Am Coll Cardiol* 2013;62:286–290).

PLATO Trial: Ticagrelor Compared With Clopidogrel Reduces the Incidence of Stent Thrombosis in Acute Coronary Syndromes Patients

Of 18 624 patients hospitalized for acute coronary syndromes (ACS), 11289 (61%) had ≥1 intracoronary stent. Ticagrelor reduced stent thrombosis compared with clopidogrel across all definitions: definite, 1.37% (n=71) vs 1.93% (n=105; hazard ratio-HR, 0.67; *P*=0.009); definite or probable, 2.21% (n=118) vs 2.87% (n=157; HR, 0.75; *P*=0.017); and definite, probable, and possible, 2.94% (n=154) vs 3.77 (n=201; HR, 0.77). The reduction in definite stent thrombosis was consistent regardless of ACS type, presence of diabetes mellitus, stent type, CYP2C19 genetic status, loading dose of aspirin, dose of clopidogrel, and use of glycoprotein IIb/IIIa inhibitors. The reduction in stent thrombosis with ticagrelor was greater for late (>30 days; HR, 0.48) and subacute (4 hours–30 days; HR, 0.60) compared with acute (<24 hours; HR, 0.94) stent thrombosis or for patients compliant to therapy compared with less compliant patients. Randomization to ticagrelor was a strong independent inverse predictor of definite stent thrombosis (HR, 0.65). The authors concluded that ticagrelor compared with clopidogrel reduces stent thrombosis in patients with ACS, with consistent benefit across a broad range of patient, stent, and treatment characteristics (Steg et al, *Circulation* 2013;128:1055-1065).

GENERATIONS Trial: Prasugrel 5 mg in the Elderly Despite Lower Platelet Inhibition Maintains Non-inferiority to Prasugrel 10 mg in Nonelderly Patients

Prasugrel 5 mg in the elderly (≥75 years, n=73; aged 79±3 years) met the primary pharmacodynamic non-inferiority criterion vs prasugrel 10 mg in non-elderly (≥45 to <65 years; n=82; aged 56±5 years) stable coronary artery disease (CAD) patients receiving background aspirin. For prasugrel 5 mg, maximum platelet aggregation (MPA) was significantly lower (57 ± 14%) than clopidogrel (63 ± 14%; p <0.001) in elderly

but higher than prasugrel 10 mg in non-elederly (46± 12%; p <0.001). Pharmacodynamic response by 3 different assays during all treatments appeared similar between age cohorts. Prasugrel 5 mg resulted in fewer elderly poor responders than clopidogrel. Rates of mild bleeding were higher with prasugrel 10 mg but similar for prasugrel 5 mg vs clopidogrel 75 mg. The authors concluded that in aspirin-treated stable CAD patients, prasugrel 5 mg in the elderly had lower platelet inhibition but met the noninferiority criterion vs prasugrel 10 mg in no-elderly, with significantly better pharmacodynamic response and fewer poor responders compared to clopidogrel 75 mg in the elderly (Erlinge et al, *J Am Coll Cardiol* 2013;62:577–583).

Continuous Positive Airway Pressure (CPAP) Therapy of Obstructive Sleep Apnea Reduces Atrial Fibrillation (AF) Recurrences After Catheter Ablation

Among 62 patients with obstructive sleep apnea (OSA) out of 426 patients with AF undergoing pulmonary vein isolation (PVI), 32 were "CPAP users" and 30 "CPAP nonusers." CPAP therapy resulted in higher AF-free survival rate (72% vs. 37%; p = 0.01) and AF-free survival off antiarrhythmic drugs or repeat ablation following PVI (66% vs. 33%; p = 0.02). AF recurrence rate of CPAP-treated patients was similar to a group of patients without OSA (HR: 0.7, p = 0.46). AF recurrence following PVI in CPAP nonuser patients was significantly higher (HR: 2.4, p < 0.02) and similar to that of OSA patients managed medically without ablation (HR: 2.1, p=NS). The authors concluded that CPAP is an important therapy in OSA patients undergoing PVI that improves arrhythmia free survival, while PVI offers limited value to OSA patients not treated with CPAP (Fein et a, *J Am Coll Cardiol* 2013; 62:300–305).

Obstructive Sleep Apnea: a Novel Risk Factor for Sudden Cardiac Death?

During a 5-year follow-up of 10,701 consecutive adults undergoing polysomnography for obstructive sleep apnea (OSA), 142 patients had sudden cardiac death (SCD) (annual rate 0.27%). In multivariate analysis, independent risk factors for SCD were age, hypertension, coronary artery disease, cardiomyopathy or heart failure, ventricular ectopy or nonsustained ventricular tachycardia, and lowest nocturnal O2sat (per 10% decrease, hazard ratio-HR: 1.14; p=0.029). SCD was best predicted by age >60 years (HR: 5.53), apnea-hypopnea index >20 (HR: 1.60), mean nocturnal O2sat <93% (HR: 2.93), and lowest nocturnal O2sat <78% (HR: 2.60; all p <0.0001). The authors conclude that among adults referred for polysomnography, OSA predicted incident SCD. Nocturnal hypoxemia strongly predicted SCD independently of well-established risk factors. These findings implicate OSA as a novel risk factor for SCD (Gami et al, *J Am Coll Cardiol* 2013;62:610–616).

Air Pollution is an Acute Trigger of Atrial Fibrillation

Among 300 eligible patients out of 1143 screened, 200 with dual-chamber implantable cardioverter defibrillator (ICD) devices were enrolled and 176 were followed for at least 90 days. The association of AF onset with air quality including ambient particulate matter <2.5 mm aerodynamic diameter ($PM_{2.5}$), black carbon, sulfate, particle number, NO_2, SO_2, and O_3 in the 24 h prior to the arrhythmia was examined utilizing a case-crossover analysis. Of 176 patients followed for an average of 1.9 years, 49 patients had 328 episodes of AF lasting ≥30 s. Positive but nonsignificant associations were found for $PM_{2.5}$ in the prior 24 h, but stronger associations were found with shorter exposure windows. The odds of AF increased by 26% for each 6.0 mg/m^3 increase in $PM_{2.5}$ in the 2 h prior to the event (p=0.004). The authors concluded that particulate matter was associated with increased odds of AF onset within hours following exposure in patients with known cardiac disease, indicating that acute exposure to air pollution triggers AF (Link et al, *J Am Coll Cardiol* 2013;62:816–825).

Community Study: Patients With Heart Failure are at Increased Risk of Cancer

A case-control community study compared patients newly diagnosed with heart failure (HF) and age-, sex-, and date-matched controls without HF (961 pairs); also patients and individuals without cancer at the index date (596 pairs) were followed for development of cancer. Before the index date, 22% of HF cases and 23% of controls had a history of cancer (odds ratio - OR: 0.94). During 9,203 person-years of follow-up (7.7 ± 6.4 years), 244 new cancer cases were identified; HF patients had a 68% higher adjusted risk of developing cancer (hazard ratio - HR: 1.68). The HRs were similar for men and women, with a trend toward a stronger association among subjects ≤75 years of age (p = 0.22) and during the most recent time period (p = 0.075). Among HF cases, incident cancer increased the adjusted risk of death (HR: 1.56). The authors concluded that HF patients are at increased risk of cancer, which appears to have increased over time, while cancer further increases mortality in HF patients (Hasin et al, *J Am Coll Cardiol* 2013;62:881–886).

RE-LY: Integrating Ischemic and Bleeding Events as "Ischemic Stroke Equivalents" Indicates Similar Benefits of the 2 Doses of Dabigatran Over Warfarin

In patients with AF, although the higher dose (150 mg bid) of dabigatran reduces ischemic stroke and increases bleeding compared with the lower dose (110 mg bid), the 2 doses confer similar mortality. Ischemic and bleeding events were integrated as "ischemic stroke equivalents" in an analysis of the 18,113 AF patients in the RE-LY trial, in order to compare a weighted benefit of the 2 doses of dabigatran with each other, and with that of warfarin. The analysis indicated that, compared with

warfarin, there was a significant decrease in ischemic stroke equivalents with both dabigatran doses: –0.92 per 100 patient years (p = 0.02) with dabigatran 110 mg bid and –1.08 (p = 0.01) with dabigatran 150 mg bid, while there was no difference between the 2 doses. The authors concluded that both doses of dabigatran as compared with warfarin have similar benefits when considering a weighted estimate of efficacy and safety, supporting the individualization of the dose based on patient characteristics and physician and patient preferences (Eikelboom et al, *J Am Coll Cardiol* 2013;62:900–908).

Triple Antithrombotic Therapy May be Replaced by Oral Anticoagulant + Clopidogrel Without Additional Thrombotic Risk and With a Lower Risk of Bleeding

Among 12,165 AF patients hospitalized with myocardial infarction (MI) and/or undergoing PCI, within 1 year, MI or coronary death occurred in 2,255 patients (18.5%), ischemic stroke in 680 (5.6%), and bleeding events in 769 (6.3%). Compared to triple therapy (oral anticoagulant-OAC +aspirin +clopidogrel), no increased risk of recurrent coronary events was seen for dual therapy (OAC +clopidogrel: hazard ratio-HR: 0.69; OAC + aspirin: HR: 0.96; or aspirin + clopidogrel: HR: 1.17), but aspirin plus clopidogrel was associated with a higher risk of ischemic stroke (HR: 1.50). Also, OAC + aspirin (HR: 1.52) and aspirin +clopidogrel (HR: 1.60) were associated with a significantly increased risk of all-cause death. When compared to triple therapy, bleeding risk was nonsignificantly lower for OAC + clopidogrel (HR: 0.78) and significantly lower for OAC + aspirin and aspirin + clopidogrel. The authors concluded that AF patients with indication for triple antithrombotic therapy after MI/PCI, OAC and clopidogrel may be equal or better on both benefit and safety issues compared to triple therapy (Lamberts et al, *J Am Coll Cardiol* 2013;62:981–989).

Left Atrial Pouch Thrombus Mimics Myxoma

A 70-year-old woman with chronic atrial fibrillation underwent echocardiography which showed a large ovoid mass attached to the interatrial septum in the left atrium; the mass was further characterized by transesophageal echocardiography and was diagnosed as a myxoma. She was placed on anticoagulant therapy with warfarin before elective cardiac surgery and had no thromboembolic event during a 2.5-month period. Preoperative transesophageal echo showed the disappearance of the intracardiac mass and the presence of a left atrial septal pouch, suggesting that the mass was a thrombus originating from the left atrial septal pouch (Shimamoto K et al, *J Clin Ultrasound* 2013 Aug 27. doi: 10.1002/jcu.22087).

Malignant Bileaflet Mitral Valve Prolapse Syndrome

Among 24 victims of idiopathic out-of-hospital cardiac arrest (i.e., no ischemia, cardiomyopathy, or channelopathy) having an implantable cardioverter defibrillator (ICD) (16 women, median age 33.5 years), bileaflet mitral valve prolapse (MVP) was found in 10 (42%). Compared with patients with normal mitral valves, patients with bileaflet MVP were predominantly women (9 of 10 or 90% vs. 7 of 14 or 50%, p = 0.04); had a higher prevalence of biphasic or inverted T waves (7 of 9 or 78% vs. 4 of 14 or 29%, p =0.04); and on Holter monitoring had more frequent ventricular ectopy (ventricular bigeminy 100% vs 10%, p<0.0001; ventricular tachycardia 78% vs 10%, p=0.006, and premature ventricular contractions - PVCs originating from the outflow tract alternating with the papillary muscle or fascicular region 78% vs 20%, p=0.02). Over a median 1.8 years, 13 of 24 patients (54%) received appropriate ICD shocks. Only bileaflet MVP was associated with ventricular fibrillation recurrences requiring ICD therapy on follow-up (odds ratio: 7.2; p = 0.028). The authors concluded that a "malignant" subset of patients with MVP may experience life-threatening ventricular arrhythmias and is characterized by bileaflet MVP, female sex, and frequent complex ventricular ectopic activity, including PVCs of the outflow tract alternating with papillary muscle or fascicular origin (Sriram et al, *J Am Coll Cardiol* 2013;62:222–230).

"Low-Adenosine Syncope": a Distinct Entity With Recent Sudden Onset in Middle/Old Age (>40 Years) Without Prodromes, Normal Heart and Normal ECG

A group of 15 patients with sudden-onset syncope without prodromes with normal heart and normal ECG were compared with 31 patients with established vasovagal syncope (VVS). Patients in the study group were older than those with VVS (age 61±12 vs 46± 17 years) and had a history of fewer episodes of syncope (median of 2 vs 9 years) that were of more recent onset (median of 1 vs 10.5 years). The study group had lower median baseline adenosine plasma levels than the VVS group (0.25 vs 0.85 mmol/l). Adenosine plasma level of ≤0.36 best discriminated between groups, displaying 73% sensitivity and 93% specificity. Tilt table testing was more frequently positive in patients with VVS than in the study group (74% vs. 33%), with a similarly high positivity rate of adenosine/ATP testing in both groups (33-60% vs 37-43%). The authors concluded that clinical features and a low adenosine level define a distinct type of syncope, different from VVS, and suggest a causal role of the adenosine pathway (Deharo et al, *J Am Coll Cardiol* 2013;62:1075–1080).

EnligHTN I: A New Multi-Electrode Ablation Catheter is Effective for Renal Denervation

A novel multi-electrode system (EnligHTN™) was employed for catheter-based renal artery denervation in 46 patients (67% male, mean age 60 years, and mean baseline office blood pressure 176/96 mmHg) with drug-resistant hypertension. Office blood pressure was significantly reduced from

baseline to 1, 3, and 6 months by 228/10, 227/10 and 226/10 mmHg, respectively (P <0.0001). No acute renal artery injury or other serious vascular complications occurred, with small, non-relevant, changes in average estimated glomerular filtration rate. The authors concluded that renal sympathetic denervation, using the new catheter resulted in a rapid and significant office blood pressure reduction that was sustained through 6 months (Worthley et al, *Eur Heart J* 2013; 34: 2132–2140).

Pulmonary Artery Denervation (PADN): a First-in-Man Application to Treat Idiopathic Pulmonary Artery Hypertension (IPAH)/Feasible and Efficacious at Short-Term Follow-up

Of 21 patients with IPAH, 13 underwent the PADN procedure and were compared with the other 8 who refused (control group). PADN was performed at the bifurcation of the main pulmonary artery (PA), and at the ostial right & left PA. At 3 months, PADN patients showed significant reduction of mean PA pressure (from 55±5 mmHg to 36±5 mmHg, p<0.01), and improvement of the 6-min walk test (from 324± 21 m to 491±38 m, p < 0.006) and of the tricuspid excursion (Tei) index (from 0.7±0.04 to 0.50±0.04, p<0.001). The authors concluded that PADN had a beneficial effect on functional capacity and hemodynamics in patients with drug-refractory IPAH (Chen et al, *J Am Coll Cardiol* 2013;62:1092–100).

FinCV Study: High Thromboembolic Risk After Cardioversion of Acute Atrial Fibrillation (AF) in Patients with Conventional Risk Factors

There were 38 (0.7%) definite thromboembolic events (31 strokes) and 4 TIAs within 30 days (median 2 days) after 5,116 successful cardioversions (CV) in 2,481 patients with AF lasting <48 h who received neither oral anticoagulation nor peri-procedural heparin therapy. Age (odds ratio-OR: 1.05), female sex (OR: 2.1), heart failure (OR: 2.9), and diabetes (OR: 2.3) were the independent predictors of definite embolic events. The highest risk of thromboembolism (9.8%) was observed among patients with heart failure and diabetes, whereas patients with no heart failure and age <60 years had the lowest risk of thromboembolism (0.2%). The authors concluded that the post-CV thromboembolic complications were increased in certain subgroups of patients when no anticoagulation is used after CV of acute AF (Airaksinen et al, *J Am Coll Cardiol* 2013;62:1187–1192).

Residual SYNTAX Score: a Powerful Predictor of 5-Year Mortality in the SYNTAX Trial

In the PCI group of the SYNTAX Trial (n=903), 5-year clinical outcomes were stratified by complete (CR) (residual SYNTAX Score 0) and incomplete revascularization (ICR) (residual SYNTAX Score >0). The mean baseline SYNTAX Score was 28.4±11.5 and residual SYNTAX Score was 4.5±6.9. A progressively higher residual SYNTAX Score (CR 0, n=386, 42.7%; ICR >0-4, n=184, 20.4%; ICR >4-8, n=167, 18.5%; ICR>8, n=153, 16.9%) was shown to be a marker of increasing clinical comorbidity and anatomic complexity. Subjects with CR or residual SYNTAX Scores ≤8 had comparable 5-year mortality (CR, 8.5%; residual SYNTAX Score >0–4, 8.7%; >4–8, 11.4%; *P*=0.60). A residual SYNTAX Score >8 was associated with 35% all-cause mortality at 5-years (*P*<0.001). Similar results were obtained from the analysis of the medically treated diabetic and left main subgroups. The authors concluded that residual SYNTAX Score was a powerful indicator of 5-year mortality by determining the completeness of revascularization (Farooq et al, *Circulation* 2013;128:141-151).

RELY-ABLE: a Higher Rate of Major Bleeding With the Higher Dabigatran Dose

A total of 5851 patients (48%) enrolled in the RE-LY trial continued to receive dabigatran for up to 28 months after RE-LY (median follow-up, 2.3 years). Rates of stroke or systemic embolism were 1.46% and 1.60%/y on dabigatran 150 and 110 mg bid, respectively (hazard ratio - HR, 0.91). Rates of major hemorrhage were 3.74% and 2.99%/y on dabigatran 150 & 110 mg (HR, 1.26). Rates of death were 3% & 3.1%/y (HR, 0.97). Rates of hemorrhagic stroke were 0.13% & 0.14%/y. The authors concluded that during 2.3 years of continued treatment with dabigatran after RE-LY, there was a higher rate of major bleeding with dabigatran 150 mg bid in comparison with 110 mg, and similar rates of stroke and death (Connolly et al, *Circulation* 2013;128:237–243).

ARISTOTLE Secondary Analysis: Stroke, Mortality, & Major Bleeding Risks are Lower With Apixaban than Warfarin Regardless of AF Type and Duration

A secondary analysis of the ARISTOTLE trial which included 18201 patients with atrial fibrillation (AF) (2786 or 15.3% paroxysmal and 15412 or 84.7% persistent or permanent) comparing apixaban with warfarin indicated a consistent reduction in stroke or systemic embolism (P for interaction = 0.71), all-cause mortality (P for interaction = 0.75), and major bleeding (P for interaction = 0.50) with apixaban compared with warfarin for both AF types. Rate of stroke or systemic embolism was significantly higher in patients with persistent or permanent AF than patients with paroxysmal AF (1.52 vs. 0.98%; P = 0.003, adjusted P = 0.015) with a trend towards higher mortality in patients with persistent or permanent AF (3.90 vs. 2.81%; P = 0.0002, adjusted P = 0.066). The authors concluded that the risks of stroke, mortality, and major bleeding were lower with apixaban than warfarin regardless of AF type and duration (Al-Khatib et al, *Eur Heart J* 2013; 34: 2464–2471).

Atrial Fibrillation (AF) Epidemic: Prevalence of 8.8 Million Adults >55 Years in 2010 in the European Union Estimated to Double by 2060 to 17.9 Million

According to estimates from the Rotterdam Study and projections from the European Union's statistics office, prevalence of AF for the group 55–59 years was 1.3% in men and 1.7% in women and increased to 24.2% in men, and 16.1% in women, for ages >85 years. Furthermore, it is estimated that in the European Union, 8.8 million adults over 55 years had AF in 2010 and projected that this number will double by 2060 to 17.9 million. The authors conclude that from 2010 to 2060, the number of adults >55 years with AF in the European Union will more than double with major public health implications (Krijthe et al, *Eur Heart J* 2013; 34: 2746–2751).

Totally Subcutaneous ICD: a Viable Alternative to Conventional ICD?

A subcutaneous implantable cardioverter defibrillator (ICD) was successfully implanted in 314 of 321 patients in whom it was attempted (74% male, mean age 52±16 years and mean left ventricular ejection fraction of 36±16%; 13% had a previous transvenous ICD). The 180-day system complication-free rate was 99%, and sensitivity analysis of the acute ventricular fibrillation conversion rate was >90% in the entire group. Over a mean of 11 months, there were 38 discrete spontaneous episodes of ventricular tachycardia/ventricular fibrillation recorded in 21 patients (6.7%), all of which successfully converted. A total of 41 patients (13.1%) received an inappropriate shock. The authors concluded that these findings support the efficacy and safety of the subcutaneous ICD System for the treatment of life-threatening ventricular arrhythmias (Weiss et al, *Circulation* 2013;128:944-953).

Brugada Syndrome Behind Complete RBBB

A group of 11 patients with no structural heart disease who had Brugada syndrome (BS) and complete right bundle branch block (CRBBB) were studied. In 7 patients, BS was diagnosed before the development of CRBBB. BS was diagnosed upon spontaneous resolution of CRBBB (n=1) or by right ventricular pacing (n=3). On repeated ECGs, new additional upward-convex ST-segment elevation was found in V2 or V3 in 3 patients. In 2 patients, new ST-segment elevation was induced by class IC drugs. The QRS duration was more prolonged in patients with BS and CRBBB compared with age- and sex-matched controls: 170±13 vs 145±15 ms in V1 and 144±19 vs 128±7 ms in V5 (both $P<0.0001$). The amplitude of R in V1 was larger in BS patients than in the controls ($P=0.03$), but that of R′ was similar ($P=0.056$). The authors concluded that BS can coexist behind CRBBB, and CRBBB can completely mask BS. BS might be demonstrated by resolution of CRBBB or by spontaneous or drug-induced ST-segment elevation (Aizawa et al, *Circulation* 2013;128:1048-1054).

Greatest Benefit from Cardiac Resynchronization Therapy (CRT): Patients with LBBB & QRS >150 ms

Among 24169 patients receiving CRT-D, 1-year and 3-year mortality rates were 9.2% and 25.9%, respectively. Risk of 3-year mortality was lowest among patients with LBBB and QRS duration of ≥150 ms (21%), compared with LBBB and QRS duration of 120-149 ms (26.5%; hazard ratio - HR, 1.30), no LBBB and QRS ≥150 ms (~31%; HR, 1.34), and no LBBB and QRS of 120-149 ms (32%; HR, 1.52). Risk of 1-year all-cause readmission was also lowest among patients with LBBB and QRS ≥150 ms (~39%), compared with LBBB and QRS of 120-149 ms (45%; HR, 1.18), no LBBB and QRS ≥150 ms (~46%; HR, 1.16), and no LBBB and QRS of 120-149 ms (49.6%; HR, 1.31). There were no observed associations with complications. The authors concluded that LBBB and QRS ≥150 ms, compared with LBBB and QRS <150 ms or no LBBB regardless of QRS duration, was associated with lower risk of all-cause mortality and of all-cause, cardiovascular, and heart failure readmissions (Peterson et al, *JAMA* 2013;310:617-626).

REVERSE Study: Beneficial Effects of Cardiac Resynchronization Therapy (CRT) in Patients with Mild Heart Failure (HF) are Sustained Over 5 Years

According to the 5-year results of the REVERSE study on CRT in 419 NYHA Class I-II HF patients with QRS ≥120 ms and left ventricular (LV) ejection fraction (LVEF) ≤40%, maximal improvement in function and LV remodeling were achieved at 2 years, with an increase of the 6-min walk test by mean of 18 m and quality of life by 8 units. There was a mean decrease in LV end-systolic volume index by ~23 mL/m^2 and in end-diastolic volume index by 25 mL/m^2; the mean increase in LVEF was 6% ($P < 0.0001$) with sustained improvement thereafter. The annual and 5-year mortality was 2.9 and 13.5% and the annual and 5-year rate of death or first HF hospitalization 6.4, and 28%. The 5-year LV lead-related complication rate was 12.5%. The authors concluded that in patients with mild HF, CRT produced reverse LV remodelling and very low mortality and need for heart failure hospitalization. These effects were sustained over 5 years (Linde et al, *Eur Heart J* 2013; 34: 2592–2599).

CHANCE: Clopidogrel plus Aspirin is Superior to Aspirin Alone for Secondary Prevention in Minor Stroke or TIA Without Further Hemorrhagic Risk

A total of 5170 patients within 24 hours after the onset of minor ischemic stroke or high-risk transient ischemic attack (TIA) were assigned to combination therapy with clopidogrel and aspirin (clopidogrel initially 300 mg, followed by 75 mg qd for 90 days, plus aspirin at a dose of 75 mg qd for the first 21 days) or to placebo plus aspirin (75 mg qd for 90 days). Stroke recurred in 8.2% of patients in the clopidogrel–aspirin group, as compared with 11.7% of those in the aspirin group

(hazard ratio, 0.68; P<0.001). Hemorrhage developed in 7 patients (0.3%) in the clopidogrel–aspirin group and in 8 (0.3%) in the aspirin group (P=NS); the rate of hemorrhagic stroke was 0.3% in each group. The authors concluded that in patients with TIA or minor stroke treated within 24 hours, the combination of clopidogrel and aspirin is superior to aspirin alone for reducing the risk of stroke in the first 90 days and does not increase the risk of hemorrhage (Wang et al, *N Engl J Med* 2013;369:11-19).

ACCOAST: Pretreatment With Prasugrel has no Effect on Ischemic Events But Increases Major Bleeding

A total of 4033 patients with non-ST elevation acute coronary syndromes (ACS) received prasugrel (30-mg loading dose) before coronary angiography (pretreatment group) or placebo (control group), with an additional 30 mg of prasugrel given in the pretreatment group and 60 mg in the control group at time of PCI. The rate of the primary efficacy end point (death, myocardial infarction, stroke, urgent revascularization, or glycoprotein IIb/IIIa inhibitor rescue therapy) through day 7, did not differ significantly between the two groups. The rate of the key safety end point of all major bleeding episodes, whether related or not related to coronary-artery bypass grafting (CABG), through day 7 was increased with pretreatment (hazard ratio, 1.90; P=0.006). The authors concluded that among patients with ACS who were scheduled to undergo catheterization, pretreatment with prasugrel did not reduce the rate of major ischemic events up to 30 days but increased the rate of major bleeding complications (Montalescot et al, *N Engl J Med* 2013; 369:999-1010).

PRAMI: Dilating NonCulprit Lesions in Acute Myocardial Infarction Confers Significant Benefit (Preventive Angioplasty)

A total of 465 patients with ST elevation myocardial infarction (STEMI), undergoing primary angioplasty (PCI) of the infarct-related artery (2008-2013), were randomly assigned to either preventive PCI (234 patients) or no preventive PCI (231 patients). Over a mean of 23 months, the primary outcome (cardiac death, nonfatal myocardial infarction, or refractory angina) occurred in 21 patients in the preventive PCI group and in 53 patients in the control group (infarct-artery-only PCI) (overall hazard ratio-HR, 0.35; P<0.001 / HR 0.34 for cardiac death, 0.32 for nonfatal myocardial infarction, and 0.35 for refractory angina). The authors concluded that in patients with STEMI and multivessel coronary artery disease undergoing infarct-artery PCI, preventive PCI in noninfarct vessel stenoses significantly reduced the risk of adverse cardiovascular events, compared with PCI limited to the culprit lesion (Wald et al, *N Engl J Med* 2013; 369:1115-1123).

Combined Therapy With Vasopressin-Epinephrine + Methylprednisolone During CPR and Stress-Dose Hydrocortisone in Postresuscitation Shock Confers Improved Survival in Cardiac Arrest Victims

Cardiac arrest victims (n=268) received either vasopressin plus epinephrine (VSE group, n = 130) or saline placebo plus epinephrine (control group, n = 138) for the first 5 CPR cycles after randomization, followed by additional epinephrine if needed. During the first CPR cycle after randomization, patients in the VSE group additionally received methylprednisolone (40 mg). Shock after resuscitation was treated with stress-dose hydrocortisone (300 mg daily for 7 days maximum and gradual taper) (VSE group, n = 76) or saline placebo (control group, n = 73). Patients in the VSE group vs patients in the control group had higher probability for return of spontaneous circulation (ROSC) of 20 min or longer (84% vs 66%; odds ratio-OR, 2.98; $P=0.005$) and survival to hospital discharge (14% vs 5%; OR, 3.28; $P=0.02$). Patients in the VSE group with post-resuscitation shock vs respective patients in the control group had higher probability for survival to hospital discharge with adequate neurological function (21%] vs ~8%; OR, 3.74; $P=0.02$. Adverse events were similar in the 2 groups. The authors concluded that combined vasopressin-epinephrine and methylprednisolone during CPR and stress-dose hydrocortisone in postresuscitation shock resulted in improved survival to hospital discharge with favorable neurological status (Mentzelopoulos et al, *JAMA* 2013;310:270-279).

MIDA Registry: Early Surgical Intervention is Superior to Watchful Waiting for Mitral Regurgitation Due to Flail Mitral Valve Leaflets

Among 1021 patients with flail mitral valve regurgitation, 575 patients were initially medically managed and 446 underwent mitral valve surgery within 3 months. There was no significant difference in early mortality (1.1% for early surgery vs 0.5% for medical management, P=NS) and new-onset heart failure rates (0.9% for early surgery vs 0.9% for medical management, P=NS) between treatment strategies at 3 months. In contrast, long-term survival rates were higher for patients with early surgery (86% vs 69% at 10 years, $P<0.001$); 5-year mortality was reduced by 52.6% ($P<0.001$). Long-term heart failure risk was also lower with early surgery (7% vs 23% at 10 years, $P<0.001$). Reduction in late-onset atrial fibrillation was not observed. The authors concluded that patients with mitral valve regurgitation due to flail mitral leaflets, performance of early mitral surgery compared with initial medical management was associated with greater long-term survival and a lower risk of heart failure, with no difference in new-onset atrial fibrillation (Suri et al, *JAMA* 2013;310:609-616).

Greater than 3-Fold Higher Risk of Stroke or TIA Following Device Implantation in Patients with a PFO in Comparison with Those without a PFO

In a retrospective analysis of 6075 patients having endocardial leads of cardiac implantable electronic devices (CIEDs), among whom 364 patients had a patent foramen ovale (PFO) as detected by echocardiography, followed for a mean 4.7±3.1 years, stroke and/or a transient ischemic attack (TIA) occurred in 30/364 (8.2%) PFO vs 117/5711 (2.0%) non-PFO patients (hazard ratio-HR, 3.49; $P<0.0001$). After adjusting for age, gender, history of stroke/TIA, atrial fibrillation, and aspirin/warfarin use, the association of PFO with stroke/TIA remained significant (HR, 3.30; $P<0.0001$). All-cause mortality was similar between the two groups. The authors concluded that in patients with endocardial leads, the presence of a PFO, as detected by echocardiography, is associated with an increased risk of embolic stroke/TIA. The authors suggest screening for PFOs in patients who require CIEDs, and, when detected, consideration should be given for PFO closure, anticoagulation, or nonvascular lead placement (DeSimone et al, *Circulation* 2013;128:1433-1441).

Daily Increases in Gaseous and Particulate Air Pollutant Concentrations Have a Marked and Close Temporal Link with Heart Failure Hospitalizations & Heart Failure Mortality

A systematic review and meta-analysis was conducted of studies investigating the association between daily increases in gaseous (carbon monoxide, sulphur dioxide, nitrogen dioxide, ozone) and particulate matter of diameter <2.5 μm ($PM_{2.5}$) or <10 μm (PM_{10}) air pollutants, and heart failure hospitalizations or heart failure mortality. This literature search revealed that heart failure hospitalization or death was associated with increases in carbon monoxide (3.52% per 1 part per million-ppm), sulphur dioxide (2.36% per 10 parts per billion-ppb), and nitrogen dioxide (1.70% per 10 ppb), but not ozone (0.46% per 10 ppb) concentrations. Increases in particulate matter concentration were associated with heart failure hospitalization or death ($PM_{2.5}$ 2.12% per 10 μg/m^3; PM_{10} 1.63% per 10 μg/m^3). Strongest associations were seen on the day of exposure, with more persistent effects for $PM_{2.5}$. The authors estimate that a mean reduction in $PM_{2.5}$ of 3.9 μg/m^3 would prevent 7978 heart failure hospitalizations and save a third of a billion US dollars a year. They concluded that air pollution has a close temporal association with heart failure hospitalization and heart failure mortality, rendering air pollution a public health hazard with grave cardiovascular and economic health consequences (Shah et al, *Lancet* 2013; 382:1039–1048).

PRAIS-UK: Early Revascularization Significantly Improves 10-Year Mortality of Non-ST Elevation Acute Coronary Syndrome

A group of 493 out of 1046 patients with non-ST-elevation acute coronary syndrome (ACS) (mean age 66 years; 40% women) surviving to 6 months, were followed for a median of 11.6 years. Total mortality was 46% (225) with 55% of total deaths classified as cardiovascular. Variables associated with higher mortality comprised age (10 years increase hazard ratio-HR 2.14), ST depression or bundle branch block (compared to normal ECG) with HR 1.68, and history of heart failure (compared to no HF) with HR 1.81. The HR for risk of death in patients who received a revascularization procedure (versus those who did not) in the first 6 months was 0.41. The authors concluded that **n**on-ST elevation ACS is associated with about 50% mortality over 10 years that may be improved by early revascularization (Erdem et al, *Int J Cardiol* 2013;168:490–494).

Important Review and Other Articles

Genetics in channelopathies (Schwartz et al, J Am Coll Cardiol 2013;62:169-180), TAVI in Europe (Mylotte et al, J Am Coll Cardiol 2013;62:210-219), Renal denervation (Davis et al, J Am Coll Cardiol 2013;62:231-241), Heart failure with preserved ejection fraction (Paulus et al, J Am Coll Cardiol 2013;62:263-271), ACCF/AHA/SCAI 2013 Update of the Clinical Competence Statement on Coronary Artery Interventional Procedures (Harold et al, J Am Coll Cardiol 2013;62:357–396), Obstructive sleep apnea (Drager et al, J Am Coll Cardiol 2013;62:569–576), Early repolarization (Adler et al, J Am Coll Cardiol 2013;62:863-868), ICD use (Hohnloser & Israel Circulation 2013; 128:172-183), Cognitive function after CABG (Hogan et al, Circulation 2013; 128:162-171), Cardiovascular function and treatment in β-thalassemia major (Pennell et al, Circulation 2013; 128:281-308), Device infections (Mulpuru et al, Circulation 2013;128:1031-1038), Acute aortic syndrome (Sheikh et al, Circulation 2013; 128:1122-1127), ARVC (Saguner et al, Circulation 2013;128:1381-1386), Telemedicine & cardiac implants (Varma & Ricci, Eur Heart J 2013;34:1885-1893), Practical guide on use of new oral anticoagulants (Heidbuchel et al, Eur Heart J 2013;34:2094-2106), Catheter based renal denervation (Mahfoud et al, Eur Heart J 2013;34:2149-2157), 2013 ESH/ESC Guidelines for the management of arterial hypertension (Mancia et al, Eur Heart J 2013;34:2159-2219), 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy (Brignole et al, Eur Heart J 2013;34:2281-2329), Diabetes & vascular disease (Paneni et al, Eur Heart J 2013;34:2436-2443 / Beckman et al, Eur Heart J 2013;34:2444-2452), Myocarditis (Caforio et al, Eur Heart J 2013;34:2636-2648), Coronary collaterals (Seiler et al, Eur Heart J 2013;34:2674-2682), STEMI: adjunctive reperfusion strategy (Curzen et al, *Lancet* 2013; 382:633-643).

2013 European Society of Cardiology Congress News

In a Hot Line session the results from the phase II **REALIGN** study were presented, indicating that the oral anticoagulant dabigatran failed to protect patients with mechanical valves from thromboembolic events. Rather, a higher number of thromboembolic and bleeding complications occurred in these patients compared to standard treatment with warfarin. This was the reason that prompted the early termination of this study after enrolment of 252 patients. The composite of stroke, TIA, systemic embolism, MI or death occurred in 15 patients (9%) in the dabigatran group and in 4 patients (5%) in the warfarin group. Major bleeding occurred in 7 patients (4%) on dabigatran and 2 (2%) on warfarin.

The factor Xa inhibitor edoxaban was found to be non-inferior to standard therapy with warfarin for the prevention of venous thromboembolism (VTE) in the **Hokusai-VTE** trial. The study included 4921 patients with deep vein thrombosis and 3319 patients with pulmonary embolism, who were randomized to 60 mg edoxaban daily (or 30 mg for those considered at higher risk of bleeding) or warfarin for 3-12 months. The primary end-point (recurrent symptomatic VTE) occurred in 3.2% of patients on edoxaban and 3.5% of patients on warfarin. In the subgroup with pulmonary embolism, recurrent events were reported in 3.3% on edoxaban and 6.2% on warfarin. Bleeding occurred in 8.5% for edoxaban and 10.3% for warfarin.

The investigational anticoagulant otamixaban had increased rates of bleeding with no reduction noted in mortality or MI events in patients with non-ST elevation ACS, according with the results of the phase III **TAO** study. Another negative study was presented, the **TASTE** trial, whereby aspiration of thrombus prior to angioplasty and stenting in STEMI patients did not improve survival compared with primary PCI and stenting alone.

Patients with STEMI who have additional preventive angioplasty have significantly better outcomes than thos who only undergo to primary PCI of the infarct-artery, according to the **PRAMI** trial. STEMI patients after completion of infarct-artery PCI were randomized to either preventive (additional) PCI of other significant coronary stenosis (n=234) or no further PCI (n=231). At 23 months, the primary outcome (cardiac death, non-fatal MI, or refractory angina) occurred in 21 patients assigned to preventive PCI and in 53 patients assigned to no preventive PCI, an absolute risk reduction of 14% and a relative risk reduction of 65% (hazard ratio 0.35).

According with the results of the **ACCOAST** trial, pretreatment with prasugrel in patients with non-ST elevation ACS was associated with an increased (almost double) risk of major bleeding (2.6% vs 1.4% at 7 days and 2.9% vs 1.5% at 30 days).

Two trials of oral anti-hyperglycemic agents, dipeptidyl peptidase 4 (DPP-4) inhibitors saxagliptin and alogliptin, were reported to meet the non-inferiority criterion for ischemic target. According to the results of the phase IV **SAVOR-TIMI 450** (saxagliptin) and the **EXAMINE** (alogliptin) studies, diabetic patients receiving these drugs did not have any increase or decrease of major adverse cardiac events. In another negative trial, the **ASSURE** study, the apoA-1 inducer RVX-208 did not raise HDL levels and failed to promote atheromatous plaque regression. A rather neutral study (**AQUARIUS**) was also reported, which showed that the renin inhibitor, aliskiren, neither improves nor slows the progression of coronary atherosclerosis. Another phase II trial (**ATOMIC-AHF**) testing the cardiac myosin activator omecamtiv mecarbil in heart failure reported that the drug did not achieve its primary efficacy endpoint in reducing dyspnea in patients with acute heart failure.

An important study for cardiac resynchronization therapy (CRT), the **Echo-CRT study**, included 809 patients with narrow QRS, NYHA class III-IV heart failure, left ventricular ejection fraction ≤35%, who were randomized 1:1 to CRT (n=404) or control (n=405) with the device turned off in the control group. At a mean follow-up of 19.4 months, the primary endpoint (death or first hospitalization for worsening heart failure) occurred in 28.7% of patients in the CRT group and 25.2% in the control group. In addition, 11.1% of CRT patients died vs 6.4% in the control group, with cardiovascular mortality in 9.2% of CRT patients vs 4.2% in the control group. Thus, the conclusion was that CRT in patients with narrow QRS has no benefit and may even harm patients with heart failure, results which are quite similar with the recently reported findings of the LESSER EARTH study.

New **ESC guidelines** (2013) were reported: Guidelines for *Cardiac Pacing & CRT*, Guidelines on *Diabetes & Cardiovascular Disease* (in collaboration with the European Association for the Study of Diabetes-EASD), Guidelines on *Hypertension* (developed with the European Society of Hypertension), & Guidelines on *Stable Coronary Artery Disease* (http://www.escardio.org/guidelines-surveys/esc-guidelines/Pages/GuidelinesList.aspx).