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: Relaxin 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 $\pm$ 18 mm Hg to 10 $\pm$ 4.5 mm Hg after TAVI and maintained at 11.8 $\pm$ 5.7 mm Hg at 5 years (p for post-TAVI trend = 0.06). Mean aortic valve area increased from 0.62 $\pm$ 0.17 cm^2 to 1.67 $\pm$ 0.41 cm^2 after TAVI and 1.40 $\pm$ 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 $\leq$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 $\leq$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 $\leq$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 $\pm$ 12% to 56 $\pm$ 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 endsystolic 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 foramen 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)