Cardiology News / Recent Literature Review / Last Quarter 2015

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Boston AF Symposium: Orlando, 14-16/1/2016

ACC 65th Annual Session: Chicago, 2-4/4/2016

HRS 37th Annual Meeting: San Francisco, 4-7/5/16

CardioStim/Europace: Nice, 8-11/6/2016

Euro PCR: Paris, 17-20/5/2016

ESC Meeting: Rome, 27-31/8/2016

Targeting Ablation to the Distal Segment of the Main Renal Artery and Post-Bifurcation Branches May Optimize Renal Denervation (RDN)

Insufficient procedural efficacy has been proposed to explain nonresponse to renal denervation (RDN). The impact of different patterns of lesion placements on the efficacy and consistency of catheter-based radiofrequency (RF) RDN was examined in pigs. Increasing the number of RF lesions (4, 8, and 12) in the main renal artery was not sufficient, but targeted treatment of the renal artery branches or distal segment of the main renal artery resulted in markedly less variability of response and significantly greater reduction of both norepinephrine (NE) and axon density than conventional treatment of only the main renal artery. Combination treatment (main artery plus branches) produced the greatest change in renal NE and axon density with the least heterogeneity. The changes lasted through 28 days post-treatment (Mahfoud F et al, *J Am Coll Cardiol* 2015;66:1766-1775).

High Levels of Cardiorespiratory Fitness in Midlife Confer Lower Mortality, Use of Health Care Resources, and Health Care Costs Later in Life

Among 19,571 healthy individuals who underwent cardiorespiratory fitness assessment at a mean age of 49 years, over 126,388 person-years of follow-up, average annual health care costs were significantly lower for participants aged ≥65 years with high than low midlife fitness in both men and women. Average annual health care costs in later life were incrementally lower per MET achieved in midlife in men and women. The authors concluded that higher cardiorespiratory fitness in middle age is strongly associated with lower health care costs at an average of 22 years later in life, independent of cardiovascular risk factors (Bachmann JM et al, *J Am Coll Cardiol* 2015;66:1876-1885).

Moderate Physical Activity is Associated with a Reduced Risk of Atrial Fibrillation (AF) in Middle-Aged and Elderly Women

According to a Swedish study comprising 36,513 AF-free women (aged 49–83, median 60 years) during a median of 12 years, 2915 cases of AF were diagnosed. The risk of AF decreased with increasing levels of leisure-time exercise at study entry (relative risk - RR 0.85, for ≥4 h/week vs <1 h/week) and walking/bicycling (RR 0.81, for ≥40 min/day vs almost never) (Drca N et al, *Heart* 2015;101:1627-1630).

Very Late Thrombosis of Bioresorbable Coronary Scaffolds Despite Antiplatelet Therapy, Possibly Related to Scaffold Discontinuity and Restenosis, Implies an Extended Period of Vulnerability to Ischemic Events

Four patients presented with very late scaffold thrombosis (VLScT) at 44, 19 (2 cases), and 21 months, after implantation of an Absorb Bioresorbable Vascular Scaffold. At the time of VLScT, all patients were taking low-dose aspirin, and 2 patients were also taking prasugrel. Optical coherence tomography (OCT) showed malapposed scaffold struts surrounded by thrombus in 7.1%, 9%, and 8.9% of struts in 3 cases. Scaffold discontinuity with struts in the lumen center was the cause of malapposition in 2 cases. Uncovered scaffold struts with superimposed thrombus were the predominant findings in 1 case. OCT percent area stenosis at the time of VLScT was high in 2 cases (71-75%) without evidence of excessive neointimal hyperplasia. Thrombus aspirate analysis showed persistence of intracoronary polymer fragments in 1 case (Räber L et al, *J Am Coll Cardiol* 2015;66:1901-1914).

Meta-Analysis: Macrolide Antibiotics Increase Rates of Ventricular Tachyarrhythmias, Sudden Cardiac Death, and Cardiovascular Death, but not All-Cause Deaths

Meta-analysis of 33 studies involving 20,779,963 participants indicated that patients who took macrolides, compared with those who did not, experienced an increased risk of developing sudden cardiac death (SCD) or ventricular tachyarrhythmias (VTAs) (relative risk - RR: 2.42), SCD (RR: 2.52), and cardiovascular death (RR: 1.31). No association was found between macrolides use and all-cause death or any cardiovascular events. The RRs associated with SCD or VTAs were 3.40 for azithromycin, 2.16 for clarithromycin, and 3.61 for erythromycin, respectively. RRs for cardiovascular death were 1.54 for azithromycin and 1.48 for clarithromycin. No association was noted between roxithromycin and adverse cardiac outcomes (Cheng Y-J et al, *J Am Coll Cardiol* 2015;66: 2173-2184).

Most Patients With Symptomatic Carcinoid Valvular Heart Disease Have Symptom and Survival Benefit from Valve Replacement Especially when Operated Before Advanced Right-Sided Heart Failure Develops

Among 195 patients with carcinoid heart disease (CaHD) (70% NYHA class III or IV), all having tricuspid valve replacement (159 bioprostheses, 36 mechanical), and 157 pulmonary valve operation, with 4-23% also having other concomitant operations, there were 20 perioperative deaths (10%). After year 2000, perioperative mortality was 6%. Survival rates at 1, 5, and 10 years were 69%, 35%, and 24%, respectively. Overall mortality was associated with older age, cytotoxic chemotherapy, and tobacco use; 75% of survivors had symptomatic improvement at follow-up (Connolly HM et al, *J Am Coll Cardiol* 2015;66:2189-2196).

ROCKET AF: In Patients With Atrial Fibrillation (AF) and Additional Stroke Risk Factors, Anti-coagulation With Rivaroxaban is Associated With a Higher Rate of Major or Non-Major GI Bleeding than Warfarin, but Similar Rate of Most Severe GI Bleeding

Among 14,236 patients, 684 experiencing gastrointestinal (GI) bleeding during follow-up, there was a significantly higher rate of major or non-major clinical GI bleeding in rivaroxaban- vs warfarin-treated patients (3.61 events/100 patient-years vs 2.60 events/100 patient-years; hazard ratio: 1.42). Severe GI bleeding rates were similar between treatment arms, and fatal GI bleeding events were rare. Independent clinical factors most strongly associated with GI bleeding were baseline anemia, history of GI bleeding, and long-term aspirin use (Sherwood MW et al, *J Am Coll Cardiol* 2015;66:2271-2281).

In Patients With Severe, Symptomatic Secondary Tricuspid Regurgitation (TR) at High Risk for Surgery, Transcatheter Reduction Therapy May be an Acceptable Alternative Strategy

The transcatheter Forma Repair System (Edwards Lifesciences, Irvine, Ca, USA), designed to provide a surface for native leaflet coaptation to reduce TR by occupying the regurgitant orifice area, was employed via the left axillary vein in 7 high-risk patients with severe TR and clinical signs of heart failure (NYHA class II-IV) who were declined for surgery (logistic EuroSCORE 25.7 ± 17.4%). The device consists of a spacer (a foam-filled polymer balloon) and a rail that is anchored at the right ventricular apex. Device implantation was successful without procedural complications in all patients, with significant reductions in TR severity (moderate in 3 and mild in 4 patients). Median hospital stay was 4 days. At 30 days, all patients but 1 had improvement in NYHA status (to class II) with marked reduction in peripheral edema and moderate TR (Campelo-Parada F et al, *J Am Coll Cardiol* 2015;66:2475-2483).

CRT-D is Associated with a Lower Risk of Heart Failure Hospitalization or Death Among Patients With Stages 3-5 Chronic Kidney Disease, Including Those on Dialysis, Than Management With Defibrillators Alone

Among 10,946 cardiac resynchronization therapy (CRT)-eligible patients (ejection fraction<35%, QRS >120 ms, NYHA class III/IV) with stage 3 to 5 chronic kidney disease (CKD), CRT-D use (n=9,525) compared with ICD only (n=1421) was associated with a reduction in heart failure (HF) hospitalization or death (hazard ratio - HR: 0.84; p< 0.0001), death (HR: 0.85; p<0.0004), and HF hospitalization alone (HR: 0.84; p< 0.009). Subgroup analyses suggested that CRT was associated with a reduced risk of HF hospitalization and death across CKD classes. The incidence of in-hospital, short-term, and mid-term device-related complications did not vary across CKD stages (Friedman DJ et al, *J Am Coll Cardiol* 2015;66:2618-2629).

NORDIC ICD Trial: Defibrillation Testing During Initial ICD Implantation is no Longer Required for Routine Left-Sided ICD Implantation

Among 1077 patients having initial ICD implantation with (n = 540) or without (n = 537) defibrillation (DF) testing (all ICD shocks programmed to 40 J irrespective of DF test results), over a mean of 22.8 months, first shock efficacy (FSE) was found to be non-inferior in patients with an ICD implanted without a DF test, with a difference in FSE of 3% in favour of the no-DF test ($P_{\text{non-inferiority}}$ <0.001 for the pre-defined non-inferiority margin of −10%). A total of 112 procedure-related serious adverse events occurred within 30 days in 94 patients (17.6%) tested compared with 89 events in 74 patients (13.9%) not tested (P = 0.095) (Bänsch D et al, *Eur Heart J* 2015; 36: 2500-2507).

In Patients With Ventricular Arrhythmias (VAs) that Exhibit LBBB and Inferior Axis, Pace Mapping in the RV Outflow Tract (RVOT) May not Identify the VA Focus. In Such Patients, Particularly When Ablation Has Failed, Mapping Performed at the Pulmonary Sinus Cusp (PSC) Identifies VAs that Can be Successfully Ablated

Among 218 patients undergoing successful endocardial ablation of idiopathic VAs with a left bundle branch block (LBBB) morphology and inferior axis, 24 patients had VAs originating from the PSC. In the first 7, initial ablation performed in the RVOT failed but produced a small change in the QRS morphology in 3 patients. In all 24 patients, the earliest activation was eventually identified in the PSC, where a sharp potential was recorded preceding

the QRS onset by 28.2 ± 2.9 ms. The successful ablation site was in the right cusp (RC) in 10 patients (42%), the left cusp (LC) in 8 (33%), and the anterior cusp (AC) in 6 (25%). ECG analysis showed that RC-VAs had unique ECG characteristics (larger R-wave in lead I and a smaller aVL/aVR ratio of Q-wave amplitude compared with AC-VAs and LC-VAs; R-wave amplitude in inferior leads was smaller in VAs localized in the RC than in the LC but did not differ between VAs from the AC and LC (Liao Z et al, *J Am Coll Cardiol* 2015;66:2633-2644).

Revascularization, not Necessarily by PCI, of Chronic Total Occlusion (CTO), is Associated with Improved Long-Term Survival Relative to Medical Therapy

Among 1957 patients, a CTO was treated by PCI in 405 (20.7%), medical therapy in 667 (34.1%), and coronary bypass in 885 (45.2%) patients. Of those treated by PCI or medical therapy, propensity score matching identified 294 pairs of patients; PCI was successful in 177 patients (60.2%). All-cause mortality at 5 years was 11.6% for CTO PCI and 16.7% for medical therapy, hazard ratio-HR 0.63 (p=0.052). The composite of 5-year death or MI occurred in 13.9% of the CTO PCI group and 19.6% in the medical therapy group, HR 0.64 (p=0.043). Among the CTO PCI group, if CTO was revascularized by any means, 5-year mortality was 10.6% vs 18.3% in those not revascularized in the medical therapy group, HR 0.50 (p=0.016) (Ladwiniec A et al; *Heart* 2015;101:1907-1914).

CvLPRIT Cardiovascular Magnetic Resonance (CMR) Substudy: In Patients With STEMI and Multivessel Disease, Complete Revascularization is Associated with a Small Increase (12%) in the Risk of Type 4a MIs, but Similar Total Infarct Size, Compared With a Strategy Addressing Only the Infarct-Related Artery (IRA)

Among 203 of the 296 patients in the main trial (98 complete revascularization and 105 IRA-only), having a pre-discharge CMR, total infarct size was similar in the two groups. The complete revascularization group had an increase in non-IRA MI on the pre-discharge CMR (22 of 98 vs 11 of 105, p= 0.02). There was no difference in total infarct size or ischemic burden between treatment groups at follow-up CMR (McCann GP et al, *J Am Coll Cardiol* 2015;66:2713-2724).

CHASE-AF: Pulmonary Vein Isolation (PVI) Should be the Initial Strategy of Ablation in Patients With Persistent AF, Because More Extensive Ablation Has no Better Rhythm Control Outcomes

Two strategies of catheter ablation were compared in 205 patients (mean age 62 years) with persistent atrial fibrillation (AF): pulmonary vein isolation (PVI) and a stepwise approach (full defrag) of PVI, ablation of complex fractionated electrograms, and additional linear ablation lines for atrial tachycardias in patients with persistent AF after PVI. Patients were prospectively randomized to either PVI alone (n = 78) or full defrag (n = 75), with 52 patients not randomized due to AF termination with the original PVI. A total of 241 ablations were performed (mean: 1.59 in the PVI-alone group, 1.55 in the full-defrag group). With the stepwise approach, termination of AF occurred in 45 (60%) patients. However, arrhythmia-free survival did not differ whether patients underwent single or multiple procedures (p=NS). Procedure duration, fluoroscopy time, and radiofrequency duration were significantly longer in the full-defrag group (all p<0.001) (Vogler J et al, *J Am Coll Cardiol* 2015;66: 2743-2752).

New Oral Anticoagulants (NOACs) and Left Atrial Appendage Closure (LAAC) are Cost-Effective Over Warfarin for Stroke Risk Reduction in Patients With Nonvalvular AF / LAAC Proved to be the Most Cost-Effective Treatment

Using a Markov model and information from PROTECT AF 4-year data and meta-analyses of warfarin and NOACs, it was shown that relative to warfarin, LAAC was cost-effective at 7 years ($42,994/quality-adjusted life-years - QALY), and NOACs were cost-effective at 16 years ($48,446/QALY). LAAC was dominant over NOACs by year 5 and warfarin by year 10. At 10 years, LAAC gave more QALYs than warfarin and NOACs (5.855 vs 5.601 vs 5.751, respectively). In sensitivity analyses, LAAC remained cost-effective relative to warfarin ($41,470/QALY at 11 years) and NOACs ($21,964/QALY at 10 years) (Reddy VY et al, *J Am Coll Cardiol*. 2015;66:2728-2739).

VISTA Trial: Substrate-Based Ablation is Superior to Targeting Only Clinical and Stable Ventricular Tachycardias (VTs) in Ischemic Cardiomyopathy, and Confers a Significant Reduction of Combined Incidence of Rehospitalization and Mortality

Subjects with ischemic cardiomyopathy and hemodynamically stable VT were randomized to clinical ablation (n= 60) vs substrate-based ablation that targeted all "abnormal" electrograms in the scar (n= 58). At 1 year, 9 (15.5%) in the substrate-based and 29 (48.3%) patients in the clinical VT ablation group had VT recurrence (p< 0.001). More patients undergoing clinical VT ablation (58%) were on antiarrhythmic drugs after ablation vs substrate-based ablation (12%; p< 0.001). Seven (12%) patients with substrate ablation and 19 (32%) with clinical ablation required rehospitalization (p= 0.014). Mortality at 1 year was 11.9%; 8.6% in the substrate ablation and 15% in the clinical ablation group (p = 0.21). Combined incidence of rehospitalization and mortality was

significantly lower with substrate ablation (p = 0.003). Periprocedural complications were similar (p=NS) (Di Biase L et al, *J Am Coll Cardiol* 2015;66:2872-2882).

EVEREST II: The 5-Year Results Support the Superiority of Surgery in Reducing Mitral Regurgitation (MR) but Also the Long-Term Safety of the Mitraclip and the Durability of MR Reduction After Percutaneous Repair / Although Patients Treated With Percutaneous Repair More Commonly Required Surgery for Residual MR in the First Year, Between Years 1-5, there were Comparably Low Rates of Surgery for Valve Dysfunction

In EVEREST II, treatment of MR with the MitraClip showed superior safety compared with surgery, but less effective reduction in MR at 1 year. At 5 years, the rate of the composite endpoint of freedom from death, surgery, or 3+/4+ MR in the as-treated population was 44.2% in the percutaneous repair and 64.3% in the surgical group (p= 0.01); difference driven by increased rates of 3+ to 4+ MR (12.3% vs 1.8%; p= 0.02) and of surgery (27.9% vs 8.9%; p=0.003) with percutaneous repair. After percutaneous repair, 78% of surgeries were performed within the first 6 months. Beyond 6 months, rates of surgery and moderate-to-severe MR were comparable between groups; as well as 5-year mortality rates (20.8% and 26.8%) (Feldman T et al, *J Am Coll Cardiol* 2015;66:2844-2854).

CURRENT AS Registry: Earlier Aortic Valve Replacement (AVR) in Patients With Asymptomatic Severe Aortic Stenosis (AS) is Associated with Lower Long-Term Risk of Hospitalization for HF or All-Cause Mortality Compared With Currently Recommended by Guidelines to Await Symptom Onset

Data from 1,808 asymptomatic severe AS patients having AVR (n=291) or conservative strategies (n=1,517) and from a propensity score–matched cohort of 582 patients (n= 291 in each group) indicated that the cumulative 5-year incidences of all-cause death (15.4% vs 26.4%, p= 0.009) and heart failure (HF) hospitalization (3.8% vs 19.9%, p< 0.001) were significantly lower in the initial AVR group. In the conservative group, AVR was performed in 41% of patients during follow-up (Taniguchi T et al, *J Am Coll Cardiol* 2015;66:2827-2838).

STS/ACC TVT Registry: Technological Advances in Device Configuration, Smaller Catheter Sizes, and Patient-Specific Access Site Selection Can Lower Risk of Extracardiac Complications in Patients Undergoing TAVI/ However, these Patients Have Multiple Co-morbidities, Including Advanced Age, and the Risk of Periprocedural Stroke Remains an Important Concern

Comparison of 2 time periods (2012 & 2013) among 26,414 TAVI procedures (by 31/12/2014) in TVT Registry revealed that TAVI patients remain elderly (mean age 82), with multiple comorbidities reflected by a high mean STS score (8.34%), were highly symptomatic (NYHA class III/IV in ~83%), frail (slow 5-m walk test in ~82%), and have poor self-reported health status. Procedure performance is changing, with an increased use of moderate sedation (from 1.6% to 5.1%) and increase in femoral access (~67% in 2014). Vascular complication rates are decreasing (from 5.6% to 4.2%), whereas site-reported stroke rates remain stable at 2.2% (Holmes DR et al, *J Am Coll Cardiol* 2015;66:2813-2823).

FreezeAF Study: Noninferiority of Cryoballoon (CB) Versus Open Irrigated Radiofrequency (RF) Ablation in Patients With Paroxysmal Atrial Fibrillation (PAF)

A total of 315 PAF patients were randomly assigned to RF (n=159) or CB (n=156) ablation. Freedom from arrhythmia with absence of persistent complications at 1 year was achieved by 70.7% with RF and 73.6% with CB (multiple procedure success), including 31 redo procedures in each group (19.5% of RF vs 19.9% of CB; *P*=NS). Rates at 6 months were 63.1% and 64.1% for the RF and CB groups (single procedure success), and noninferiority was confirmed (risk difference, 0.010; *P*=0.002). Periprocedural complications for the index procedure were more frequent in the CB group (5% RF, 12.2% CB; *P*=0.022) with a significant difference in phrenic nerve palsies (0% RF, 5.8% CB; *P*=0.002) (Luik A et al, *Circulation* 2015**;** 132: 1311-1319).

Meta-Analysis of Case-Control Studies: Significant Association Between Recent Respiratory Infection and Acute Myocardial Infarction (AMI) / Estimated Vaccine Effectiveness Against AMI was Comparable with the Efficacy of Currently Accepted Therapies for Secondary Prevention of AMI

According with 16 case–control studies (8 on influenza vaccination, 10 on influenza infection and AMI), recent influenza infection, influenza-like illness or respiratory tract infection was more likely in AMI cases, with a pooled odds ratio - OR 2.01. Influenza vaccination was associated with AMI, with a pooled OR of 0.71, equating to an estimated vaccine effectiveness of 29% against AMI (Barnes M et al, *Heart* 2015;101:1738-1747).

Treatment With Colchicine in Patients With STEMI Undergoing Primary PCI is Associated With Smaller Infarct Size, as Defined by Both Biomarker Release and MRI-Late Gadolinium Enhancement (LGE)

Patients (n=151) presenting with ST-segment–elevation myocardial infarction (STEMI) ≤12 hours from pain onset (treated with primary PCI) were randomly assigned to colchicine (n=77) or placebo (n=74) for 5 days. A subset of patients (n=60) underwent cardiac MRI-LGE

6-9 days after the index STEMI. The area under the CK-MB curve was 3144 $ng \cdot h^{-1} \cdot mL^{-1}$ in the colchicine group vs 6184 $ng \cdot h^{-1} \cdot mL^{-1}$ in controls (P<0.001). Indexed MRI–LGE defined infarct size was 18.3 mL/1.73 m^2 in the colchicine group (n=31) vs 23.2 mL/1.73 m^2 in controls (n=29) (P=0.019). The relative infarct size (as a proportion to left ventricular myocardial volume) was 13% and 19.8%, respectively (P=0.034) (Deftereos S et al, *Circulation* 2015; 132: 1395-1403).

Taiwanese Database: Risk of Mortality was Lower for AF Patients Receiving Rate-Control With B-Blockers or Calcium Channel Blockers (B-Blockers Conferred the Largest Risk Reduction), While Digoxin Use was Associated With Greater Mortality

Over a mean of ~5 years, among 43,879 patients with atrial fibrillation (AF) receiving β-blockers, 18,466 receiving calcium blockers, and 38,898 receiving digoxin, 88,263 patients (32.7%) died. Compared to a reference group of 168,678 subjects who did not receive any rate-control drug, the risk of mortality was lower in patients receiving β-blockers (hazard ratio – HR =0.76) and calcium channel blockers (HR=0.93). On the contrary, the digoxin group had a higher risk of mortality with an HR of 1.12 (Chao T-F et al, *Circulation* 2015; 132: 1604-1612).

WEARIT-II Registry: High Rate of Sustained Ventricular Tachyarrhythmias (VTAs) at 3 Months in Patients At-Risk Who are not Eligible for an ICD / The Wearable Cardioverter Defibrillator (WCD) Can Protect Patients During this Period

A total of 2000 patients (median age 62 years; median ejection fraction 25%) with ischemic (n=805, 40%), or nonischemic cardiomyopathy (n=927, 46%), or congenital /inherited heart disease (n=268) received a wearable cardioverter defibrillator (WCD) for a median of 90 days, with median daily use of 22.5 h. There was a total of 120 sustained VTAs in 41 patients, of whom 54% received appropriate WCD shock (10 patients or 0.5% received inappropriate therapy). Rate of sustained VTAs by 3 months was 3% among patients with ischemic cardio-myopathy and congenital/inherited heart disease, and 1% among nonischemic patients (P=0.02). Finally, 840 patients (42%) were implanted with an ICD. The most frequent reason not to implant an ICD following WCD use was improvement in ejection fraction (Kutyifa V et al, *Circulation* 2015; 132: 1613-1619).

Descending Thoracic or Thoracoabdominal Aortic Aneurysm: Risk of Rupture Starts to Increase With a Diameter >5.0 - 5.5 cm / Uncertain Whether Aneurysm Repair in this Range Leads to Overall Benefit

Of 257 patients (age, 72.4±10.5 years; 143 women) with descending thoracic or thoracoabdominal aortic aneurysm (baseline mean maximal diameter 52.4±10.8 mm, with 103 patients having diameters ≥55 mm) without a history of aortic dissection in whom surgical intervention was not undertaken, over 2 years, definite and possible aortic events occurred in 19 (7.4%) and 31 (12.1%) patients, respectively. Maximal aortic diameter at baseline was the only significant predictor of aortic events (hazard ratio=1.12). Estimated rates of definite aortic events within 1 year were 5.5%, 7.2%, and 9.3% for aortic diameters of 50, 55, and 60 mm, respectively (Kim JB et al, *Circulation* 2015; 132: 1620-1629).

Meta-analysis: Doses of Physical Activity (PA) in Excess of the Guideline-Recommended Minimum PA Levels May be Required for More Substantial Reductions in Heart Failure (HF) Risk

In 12 prospective cohort studies with 20,203 HF events among 370,460 patients (53.5% women; median follow-up, 13 years), the highest levels of PA were associated with reduced risk of HF (hazard ratio – HR for highest vs lowest PA, 0.70). Compared with patients reporting no leisure-time PA, those who engaged in guideline-recommended minimum levels of PA (500 MET-min/wk; 2008 US guidelines) had modest reductions in HF risk (HR, 0.90). However, a higher risk reduction was observed among patients who engaged in PA at twice (HR for 1000 MET-min/wk, 0.81) and 4 times (HR for 2000 MET-min/wk, 0.65) the minimum guideline-recommended levels (Pandey A et al, *Circulation* 2015; 132: 1786-1794**).**

CARDIA Study: Higher Intake of Fruits and Vegetables (F/V) During Young Adulthood was Associated With Lower Odds of Prevalent Coronary Artery Calcium After 20 Years of Follow-Up / Important to Establish a High Intake of F/V as Part of a Healthy Dietary Pattern Early in Life

Among the study participants (n=2506) (mean age at baseline 25.3 years; 62.7% female), higher intake of F/V was associated with a lower prevalence of coronary artery calcium (measured at year 20 using computed tomography): odds ratio - OR, 0.78, and 0.74, from the lowest to the highest tertile of F/V, P value for trend <0.001. There was attenuation of the association between F/V and coronary artery calcium after adjustment for other dietary variables, but the trend remained significant: OR, 0.84, and 0.92, P value for trend <0.002 (Miedema MD et al, *Circulation* 2015; 132: 1990-1998).

PATH Registry: Better Survival and Neurological Outcome With Therapeutic Hypothermia for Post–Cardiac Arrest Patients with an Initial Nonshockable Rhythm

Among 519 patients after in- and out-of-hospital cardiac arrest with nonshockable initial rhythms, 201

propensity score–matched pairs (mean age 63±17 years, 51% male; 60% with initial pulseless electric activity) were compared. Survival to hospital discharge was greater in patients who received therapeutic hypothermia (TH) (17.6% vs 28.9%; $P<0.01$), as was a discharge Cerebral Performance Category of 1 to 2 (13.7% vs 21.4%; $P=0.04$). Patients who received TH were more likely to survive (odds ratio, 2.8) and to have better neurological outcome (odds ratio, 3.5) than those that did not receive TH (Perman SM et al, *Circulation* 2015; 132: 2146-2151).

Outcomes are Better with Basic (BLS) than Advanced Life Support (ALS) for Several Out-of-Hospital Medical Emergencies

In a 20% random sample of Medicare beneficiaries from non-rural areas with major trauma, stroke, acute myocardial infarction (AMI), or respiratory failure, except in cases of AMI, patients showed superior outcomes with BLS despite being older and having more comorbidities. In propensity score analysis, survival to 90 days among patients with trauma, stroke, and respiratory failure was higher with BLS than ALS (6.1% points for trauma; 7% points for stroke; and 3.7% points for respiratory failure). Patients with AMI did not have differences in survival at 30 days but had better survival at 90 days with ALS (1% point). Neurologic functioning favored BLS for all diagnoses. Instrumental variable analysis for trauma and stroke had similar results, showed no survival differences between BLS and ALS for respiratory failure, and showed better survival at all time points with BLS than ALS for patients with AMI (Sanghavi P et al, *Ann Intern Med.* 2015;163:681-690).

Potassium Channel Blockade May Enhance Atrial Fibrillation (AF)–Selective Antiarrhythmic Effects of Optimized State-Dependent Sodium Channel Blockade

In a mathematical model, combining optimized Na^+-channel blocker with I_{Kr} block increased rate-dependent and atrium-selective peak I_{Na} reduction, increased AF selectivity, and more effectively terminated AF compared with optimized Na^+-channel blocker alone. Combining optimized Na^+-channel blocker with I_{Kur} block had similar effects but without I_{Kr} block–induced ventricular action potential prolongation. Consistent with the mathematical model, in coronary-perfused canine hearts, the addition of dofetilide (selective I_{Kr} blocker) to pilsicainide (selective I_{Na} blocker) produced enhanced atrium-selective effects on maximal phase 0 upstroke and conduction velocity. Furthermore, pilsicainide plus dofetilide had higher AF termination efficacy than pilsicainide alone. Pilsicainide alone had no significant effect on AF inducibility, whereas pilsicainide plus dofetilide rendered AF noninducible (Aguilar M et al, *Circulation* 2015; 132: 2203-2211**).**

3 Large Prospective Cohorts: Higher Consumption of Coffee, either Caffeinated or Decaffeinated, was Associated With Lower Risk of Total Mortality

The associations of consumption of total, caffeinated, and decaffeinated coffee with risk of subsequent total and cause-specific mortality were examined among 74,890 women in the Nurses' Health Study (NHS), 93,054 women in the Nurses' Health Study II, and 40,557 men in the Health Professionals Follow-up Study. During 4,690,072 person-years of follow-up, 19,524 women and 12,432 men died. Compared with nondrinkers, coffee consumption of 1-5 cups/day was associated with lower risk of mortality, whereas coffee consumption of >5 cups/day was not. However, when restricting to never smokers compared with nondrinkers, the hazard ratios of mortality were 0.94 for ≤1 cup/day, 0.92 for 1.1 to 3.0 cups/day, 0.85 for 3.1-5.0 cups/day, and 0.88 for >5 cups per day (P value for trend < 0.001). Significant inverse associations were observed for caffeinated ($P < 0.001$) and decaffeinated coffee ($P = 0.022$). Significant inverse associations were observed between coffee consumption and deaths attributed to cardiovascular disease, neurologic diseases, and suicide. No significant association between coffee consumption and total cancer mortality was found (Ding M et al, *Circulation* 2015; 132: 2305-2315**).**

Among Patients With Continuous-Flow Left Ventricular Assist Devices, Restoration of Pulsatile Flow Through Modulations in Pump Speed Leads to Decline in Muscle Sympathetic Nerve Activity (MSNA)

Reductions in pump speed in 13 patients (10 men / 3 women, 54±14 years) with Heartmate II continuous-flow left ventricular assist devices led to increases in pulse pressure (high vs low speed: 17±7 vs 26±12 mm Hg; $P<0.01$), distension of the carotid artery, and carotid arterial wall tension ($P<0.05$ for all measures). In addition, MSNA was reduced (high vs low speed: 41±15 vs 33±16 bursts/minute; $P<0.01$) despite a reduction in mean arterial pressure and was inversely related to pulse pressure ($P=0.037$) (Cornwell WK et al, *Circulation* 2015; 132: 2316-2322).

40-Year Analysis of >500 Patients With Primary Malignant Cardiac Tumors (PMCTs): MPCTs are Extremely Rare and Continue to be Associated With Poor Prognosis / Over the Past 5 Decades, Incidence and Survival Appear to Have Increased

From a total of 7,384,580 cases of cancer registered in the National Cancer Institute, 551 PMCTs (0.008%) were identified with an incidence of 34 cases per 100 million persons, increased over time (25.1 in 1973–1989, 30.2 in 1990–1999, and 46.6 in 2000–2011). Most patients are female (54.1%) and white (78.6%) with median age at diagnosis of 50 years. The most common PMCTs are

sarcomas (n=357, 64.8%), lymphomas (n=150, 27%) and mesotheliomas (n=44, 8%), mostly diagnosed with biopsy (96.8%). Use of chemotherapy is not documented; 19% received radiation and 44% had surgery. After a median of 80 months, 413 patients had died. The 1-, 3-, and 5-year survival rates were 46%, 22%, and 17% and have improved over the eras, with 1-, 3-, and 5-year survival rates of 32%, 17%, and 14% for 1973-1989 and 50%, 24%, and 19% for 2000-2011 (*P*=0.009). Cardiac sarcomas and mesotheliomas are the most lethal PMCTs. Patients with cardiac lymphomas and sarcomas are younger and have worse survival than patients with extracardiac disease of similar histopathology (*P*<0.001) (Oliveira GH et al, *Circulation* 2015; 132: 2395-2402**).**

Transvenous Lead Removal (TLR): Complication Rate in Patients Undergoing TLR was Higher Than Previously Reported Related to Female Gender and Device Infections but not to Hospital Volume

Among 91,890 TLR procedures in the US, in-hospital death (2.2%), hemorrhage requiring transfusion (2.6%), vascular complications (2.0%), pericardial complications (1.4%), open heart surgery (0.2%), and postoperative respiratory failure (2.4%) were recorded. Independent predictors of complications were female gender and device infections. Hospital volume was not independently associated with higher complications. There was a significant rise in overall complication rates over the study period (Deshmukh A et al, *Circulation* 2015; 132: 2363-2371).

TUXEDO–India Trial: In Patients With Diabetes and Coronary Artery Disease Undergoing PCI, Paclitaxel-Eluting Stents were Inferior to Everolimus-Eluting Stents, with Higher Rates of Target-Vessel Failure, Myocardial Infarction, Stent Thrombosis, and Target-Vessel Revascularization at 1 Year

Among 1830 patients with diabetes and coronary artery disease who were undergoing PCI randomly assigned to receive either a paclitaxel-eluting stent or an everolimus-eluting stent, at 1 year, paclitaxel-eluting stents did not meet the criterion for noninferiority to everolimus-eluting stents with respect to the primary end point (rate of target-vessel failure, 5.6% vs 2.9%; relative risk, 1.89; P=0.38 for noninferiority). There was a higher 1-year rate in the paclitaxel-eluting stent group of target-vessel failure (P=0.005), spontaneous myocardial infarction (3.2% vs 1.2%, P=0.004), stent thrombosis (2.1% vs 0.4%, P=0.002), target-vessel revascularization (3.4% vs 1.2%, P=0.002), and target-lesion revascularization (3.4% vs 1.2%, P=0.002) (Kaul U et al, *N Engl J Med* 2015; 373:1709-1719).

ABSORB III Study: Everolimus-Eluting Bioresorbable Scaffolds are Non-Inferior to Everolimus-Eluting Cobalt–Chromium Stents with Respect to Target-Lesion Failure (Cardiac Death, Target-Vessel Myocardial Infarction, or Ischemia-Driven Target-Lesion Revascularization) at 1 Year

Among 2008 patients with stable or unstable angina assigned to receive an everolimus-eluting bioresorbable vascular (Absorb) scaffold (n=1322) or an everolimus-eluting cobalt–chromium (Xience) stent (n=686), target-lesion failure at 1 year occurred in 7.8% in the Absorb and 6.1% in the Xience group (P=0.007 for noninferiority; P=0.16 for superiority). There was no significant difference between the Absorb and the Xience group in cardiac death (0.6% vs 0.1%; P=NS), target-vessel MI (6.0% vs 4.6%; P=NS), or ischemia-driven target-lesion revascularization (3% vs 2.5%; P=NS). Device thrombosis within 1 year occurred in 1.5% in the Absorb group and in 0.7% in the Xience group (P=NS) (Ellis SG et al, *N Engl J Med* 2015; 373:1905-1915).

BIOSOLVE-II First-In-Man Trial: Implantation of the Second-Generation Drug-Eluting Absorbable Metal Scaffold (DREAMS 2G Device) in De-Novo Coronary Lesions is Feasible, With Favourable Safety and Performance Outcomes at 6 Months, and Could be an Alternative to Absorbable Polymeric Scaffolds

In 123 patients (123 lesions) receiving a novel second-generation drug-eluting absorbable metal scaffold (DREAMS 2G), at 6 months, in-segment late lumen loss was 0.27 ± 0.37 mm, and angiographically discernable vasomotion was documented in 20 (80%) of 25 patients. Intravascular ultrasound showed a preservation of the scaffold area (6.24 ± 1.15 mm^2 post-procedure *vs* 6.21 ± 1.22 mm^2 at 6 months) with a low neointimal area (0.08 ± 0.09 mm^2), and optical coherence tomography did not detect any intraluminal mass. Target lesion failure occurred in 4 (3%) patients: one (<1%) patient died from cardiac death, 1 (<1%) patient had periprocedural MI, and 2 (2%) patients needed clinically driven target lesion revascularization. No definite or probable scaffold thrombosis was observed (Haude M et al, *Lancet* 2016; 387, No. 10013:31–39).

A Cohort US Study on Early Repolarization: J Waves and QRS Slurs did not Exhibit an Increased Risk for Cardiovascular Death in Long-Term Follow-up

In veterans <56 years (~90% men) who had resting 12-lead ECG, over a median follow-up of 17.5 years, 859 cardiovascular deaths occurred. Of 20,661 ECGs, 4219 (20%) had J waves or QRS slurs in the inferior (3318 or 78.6%) and/or lateral leads (1701 or 40.3%). The upper bound of differences in risk for cardiovascular death from any of the J-wave or QRS slur patterns suggests that an increased risk can be safely ruled out (inferior, −0.77%;

lateral, −1.07%) (Pargaonkar VS et al, *Ann Intern Med* 2015;163:747-755).

COURAGE Trial (15-Year Follow-up): Among Patients With Stable Ischemic Heart Disease, Objective Evidence of Ischemia, Significant Coronary Disease, and a Substantial Risk of Death (Mortality ~4%/Year), there was no Difference in Long-Term Survival With an Initial Strategy of Optimal Medical Therapy Plus PCI Compared With Optimal Medical Therapy Alone

In the COURAGE trial, an initial management strategy of optimal medical therapy alone compared with optimal medical therapy plus PCI among 2287 patients with stable ischemic heart disease did not differ in clinical outcome over a median follow-up period of 4.6 years. Extended (15-year) survival information was available for 1211 patients (53% of the original group). The median follow-up for all patients was 6.2 years (range, 0-15). A total of 561 deaths (180 during the follow-up period in the original trial and 381 during the extended follow-up period) occurred: 284 deaths (25%) in the PCI group and 277 (24%) in the medical-therapy group (adjusted hazard ratio, 1.03; P=NS) (Sedlis SP et al, *N Engl J Med* 2015; 373:1937-1946).

LEADERS FREE: Among Patients at High Bleeding Risk Who Underwent PCI, a Polymer-Free Umirolimus (Biolimus A9)-Coated Stent was Superior to a Bare-Metal Stent When Used With a 1-Month Course of Dual Antiplatelet Therapy

A total of 2466 patients at high bleeding risk undergoing PCI, were randomized to a drug-coated stent or a bare-metal stent. The drug-coated stent was a polymer-free drug-coated stent that transfers umirolimus (biolimus A9), a highly lipophilic sirolimus analogue, into the vessel wall over 1 month. All patients received 1 month of dual antiplatelet therapy. At 390 days, the primary safety end point (cardiac death, MI, or stent thrombosis) occurred in 112 patients (9.4%) in the drug-coated–stent group and in 154 patients (12.9%) in the bare-metal–stent group (hazard ratio - HR, 0.71; P<0.001 for noninferiority; P=0.005 for superiority). During the same period, clinically driven target-lesion revascularization was needed in 59 patients (5.1%) in the drug-coated–stent group and in 113 patients (9.8%) in the bare-metal–stent group (HR, 0.50; P<0.001) (Urban P et al, *N Engl J Med* 2015; 373:2038-2047).

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves Suspected from Reduced Leaflet Motion Detected by 4-Dimensional, Volume-Rendered CT / Therapeutic Anticoagulation With Warfarin, but not Therapy With Antiplatelet Drugs, Prevented and Effectively Treated This Phenomenon

Data obtained from 55 patients in a clinical trial of TAVI and from 2 registries that included 132 patients who were undergoing either transcatheter (TAVI) or surgical aortic-valve bioprosthesis implantation showed reduced leaflet motion noted on computed tomography (CT) in 22 of 55 patients (40%) in the clinical trial and in 17 of 132 patients (13%) in the 2 registries. Therapeutic anticoagulation with warfarin, as compared with dual antiplatelet therapy, decreased the incidence of reduced leaflet motion (0% and 55%, respectively, P=0.01 in the clinical trial; and 0% and 29%, respectively, P=0.04 in the pooled registries). In patients who were reevaluated with follow-up CT, restoration of leaflet motion was noted in all 11 patients who were receiving anticoagulation and in 1 of 10 patients who were not (P<0.001). There was no significant difference in the incidence of stroke or TIA between the two groups in the clinical trial (2 of 22 patients and 0 of 33 patients, respectively; P=NS), but in the registries, a significant difference was detected (3 of 17 patients and 1 of 115 patients, respectively; P=0.007) (Makkar RR et al, *N Engl J Med* 2015; 373:2015-2024).

SPRINT Trial: Intensive (<120 mmHg) vs Standard (<140 mmHg) Blood-Pressure (BP) Control is Superior in Patients at High Risk for Cardiovascular Events but Without Diabetes, Albeit With Higher Rates of Some Adverse Events

Patients (n=9361) with a systolic BP of ≥130 mmHg and an increased cardiovascular risk, but without diabetes, were randomized to a systolic BP target of <120 mmHg (n=4678, intensive treatment) or a target of <140 mmHg (n=4683, standard treatment). At 1 year, the mean systolic BP was 121.4 mm Hg in the intensive-treatment and 136.2 mmHg in the standard-treatment group. Trial was stopped early (median 3.26 years) due to significantly lower rate of the primary composite outcome (myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes) in the intensive-treatment group (1.65% vs 2.19%/year; hazard ratio - HR, 0.75; P<0.001). All-cause mortality was also significantly lower in the intensive-treatment group (HR, 0.73; P=0.003). Rates of serious adverse events (hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of traumatic falls) were higher in the intensive-treatment group (SPRINT Research Group, *N Engl J Med* 2015; 373:2103-2116).

EMPA-REG OUTCOME Trial: Empagliflozin (Inhibitor of Sodium–Glucose Cotransporter 2) Added to Standard Care Confers Cardiovascular Benefit in Patients with Type 2 Diabetes

A total of 7020 patients were randomly treated with 10 mg or 25 mg of empagliflozin or placebo (median observation time, 3.1 years). The primary outcome (death from cardiovascular causes, nonfatal MI, or nonfatal stroke) occurred in 490 of 4687 patients (10.5%) in the

pooled empagliflozin group and in 282 of 2333 patients (12.1%) in the placebo group (hazard ratio, 0.86; P=0.04 for superiority). There were no significant between-group differences in the rates of MI or stroke, but in the empagliflozin group there were significantly lower rates of death from cardiovascular causes (3.7%, vs 5.9% in the placebo group; 38% relative risk reduction), hospitalization for heart failure (2.7% and 4.1%, respectively; 35% relative risk reduction), and death from any cause (5.7% and 8.3%, respectively; 32% relative risk reduction). There was no significant between-group difference in the secondary outcome (primary outcome plus hospitalization for unstable angina) (P=0.08 for superiority). Among patients receiving empagliflozin, there was an increased rate of genital infection but no increase in other adverse events (Zinman B et al, *N Engl J Med* 2015; 373:2117-2128).

Toxic Central Obesity (NHANES III): Normal-Weight Central Obesity is associated with Higher Mortality than BMI-Defined (but no Central) Obesity

Among 15,184 adults (aged 18-90 years; 52% women), persons with normal-weight central obesity had the worst long-term survival: a man with a normal BMI (22 kg/m^2) and central obesity had greater total mortality risk than one with similar BMI but no central obesity (hazard ratio - HR, 1.87), and this man had twice the mortality risk of those who were overweight or obese by BMI only (HR, 2.24 & 2.42, respectively). Women with normal-weight central obesity also had a higher mortality risk than those with similar BMI but no central obesity (HR, 1.48) and those who were obese according to BMI only (HR, 1.32). Expected survival estimates were consistently lower for those with central obesity when age and BMI were controlled for (Sahakyan KR et al, *Ann Intern Med.* 2015;163:827-835).

ROC Trial: In Patients With Out-Of-Hospital Cardiac Arrest, Continuous Chest Compressions During CPR did not Result in Significantly Higher Rates of Survival or Favorable Neurologic Function than did Interrupted Chest Compressions

Of 23,711 adults with non–trauma-related cardiac arrest, 12,653 were assigned to continuous chest compressions (intervention group) and 11,058 to interrupted chest compressions at a ratio of 30 compressions to 2 ventilations (control group). A total of 1129 of 12,613 patients with available data (9%) in the intervention group and 1072 of 11,035 (9.7%) in the control group survived until discharge (P=0.07); 7% of the patients in the intervention group and 7.7% of those in the control group survived with favorable neurologic function at discharge (P=0.09). Hospital-free survival was significantly shorter in the intervention group than in the control group (P=0.004) (Nichol G et al, *N Engl J Med* 2015; 373:2203-2214).

ANNEXA-A and ANNEXA-R Trials: Andexanet Alfa Reversed the Anticoagulant Activity of Factor Xa Inhibitors, Apixaban and Rivaroxaban, in Older Healthy Participants Within Minutes After Administration and for the Duration of Infusion, Without Evidence of Clinical Toxic Effects

Healthy older (mean age 58 years) volunteers were given 5 mg of apixaban bid or 20 mg of rivaroxaban qd. Andexanet was administered as a bolus or as a bolus plus a 2-h infusion. Among the *apixaban*-treated participants, anti–factor Xa activity was reduced by 94% with andexanet bolus (n=24), vs 21% with placebo (n=9) (P<0.001), and unbound apixaban concentration was reduced by 9.3 ng/ml vs 1.9 ng/ml (P<0.001); thrombin generation was fully restored in 100% vs 11% of the participants (P<0.001) within 2-5 min. Among the *rivaroxaban*-treated participants, anti–factor Xa activity was reduced by 92% with andexanet bolus (n=27) vs 18% with placebo (n=14) (P<0.001), and unbound rivaroxaban concentration was reduced by 23.4 ng/ml vs 4.2 ng/ml (P<0.001); thrombin generation was fully restored in 96% vs 7% of the participants (P<0.001). These effects were sustained with andexanet bolus plus infusion. In a subgroup, transient increases in levels of D-dimer and prothrombin fragments 1 and 2 were observed, which resolved within 24-72 h. No serious adverse or thrombotic events were reported (Siegal DM et al, *N Engl J Med* 2015; 373:2413-2424).

IPD-Work Consortium: Long Working Hours Increase Risk of Stroke and Less So Coronary Heart Disease Risk / More Attention Should Be Paid to the Management of Vascular Risk Factors in Individuals Who Work Long Hours

Meta-analysis of 25 studies comprised data for 603,838 men and women who were free from coronary heart disease at baseline, and data for 528,908 men and women who were free from stroke at baseline. Mean follow-up for coronary heart disease was 8.5 years, in which 4768 events were recorded, and for stroke 7.2 years, in which 1722 events were recorded. Compared with standard hours (35–40 h/week), working long hours (≥55 h/week) was associated with an increase in risk of coronary heart disease (relative risk - RR 1.13; p=0.02) and stroke (1.33; p=0.002). A dose–response association was recorded for stroke, with RR estimates of 1.10 (p=0.24) for 41–48 working hours, 1.27 (p=0.03) for 49–54 working hours, and 1.33 (p=0.002) for ≥55 working hours/week compared with standard working hours (p_{trend}<0·0001) (Kivimaki M et al, *Lancet* 2015; 386 (No. 10005):1739–1746).

REVERT Trial: Postural Modification of Valsalva Maneuver Increases Conversion of Supraventricular Tachycardias (SVT) from 17% to 43%

A modified Valsalva maneuver (done semi-recumbent with supine repositioning and passive leg raise immediately after the Valsalva strain) (n=214) was compared with a nonmodified version of the maneuver (n=214) in 428 patients presenting with SVT. 37 (17%) of those assigned to standard Valsalva achieved sinus rhythm compared with 93 (43%) of 214 in the modified Valsalva maneuver group (odds ratio 3.7; p<0·0001) (Appelboam A et al, *Lancet* 2015; 386, No. 10005:1747–1753).

FAME Study 5-Year Follow-Up: Fractional Flow Reserve (FFR)-Guided PCI Conferred a Decrease of Major Adverse Cardiac Events for up to 2 Years, at 2-5 Years the Risks Were Similar / This Outcome was Achieved With a Lower Number of Stented Arteries and Less Resource Use / FFR Guidance of Multivessel PCI Could be the Standard of Care in Most Patients

In FAME, fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) (PCI done only if FFR was ≤0.80) improved outcome compared with angiography-guided PCI for up to 2 years of follow-up. After 5 years, major adverse cardiac events occurred in 31% of patients (154 of 496) in the angiography-guided group vs 28% (143 of 509 patients) in the FFR-guided group (relative risk 0.91; p=NS). The number of stents placed per patient was significantly higher in the angiography-guided than in the FFR-guided group (mean 2.7 *vs* 1.9, p<0.0001) (van Nunen LX et al, *Lancet* 2015; 386, No. 10006:1853–1860).

Spironolactone vs Placebo, Bisoprolol, and Doxazosin for Drug-Resistant Hypertension (PATHWAY-2): Spironolactone was the Most Effective Add-On Drug, Supporting a Primary Role of Sodium Retention in Resistant Hypertension

Patients (n=335), aged 18–79 years with seated clinic systolic blood pressure (BP) ≥140 mmHg (or ≥135 mm Hg for patients with diabetes) and home systolic BP (18 readings over 4 days) ≥130 mmHg, despite treatment for at least 3 months with maximally tolerated doses of 3 drugs, were rotated, in a preassigned, randomized order, through 12 weeks of once daily treatment with each of spironolactone (25–50 mg) (n=285), bisoprolol (5–10 mg) (n=285), doxazosin modified release (4–8 mg) (n=282), and placebo (n=274), in addition to their baseline BP drugs. The dose was doubled after 6 weeks of each cycle; 230 patients completed all treatment cycles. The average reduction in home systolic BP by spironolactone was superior to placebo (–8.70 mmHg; p<0·0001), superior to the mean of the other 2 active treatments (doxazosin and bisoprolol; −4.26; p<0.0001), and superior when compared with the individual treatments; vs doxazosin (–4.03; p<0.0001) and vs bisoprolol (–4.48; p<0.0001). Spironolactone was the most effective BP-lowering treatment, throughout the distribution of baseline plasma renin; but its margin of superiority and likelihood of being the best drug for the individual patient were many-fold greater in the lower than higher ends of the distribution. All treatments were well tolerated. In 6 of the 285 patients who received spironolactone, serum potassium exceeded 6 mmol/L on one occasion (Williams B et al, *Lancet* 2015; 386, No. 10008:2059–2068).

CLEAN Trial: Chlorhexidine–Alcohol Appears More Effective than Povidone Iodine–Alcohol as a Skin Antiseptic to Prevent Intravascular-Catheter-Related Infections, Albeit With More Severe Skin Reactions

A total of 1181 patients (2547 catheters) were randomly assigned to 2% chlorhexidine–70% alcohol (594 patients with scrubbing, 587 without) and 1168 (2612 catheters) to 5% povidone iodine–69% alcohol (580 patients with scrubbing, 588 without). Chlorhexidine–alcohol was associated with lower incidence of catheter-related infections (0.28 *vs* 1.77 per 1000 catheter-days with povidone iodine–alcohol; hazard ratio 0.15; p=0.0002). Scrubbing was not associated with a significant difference in catheter colonization (p=NS). No systemic adverse events were reported, but severe skin reactions occurred more frequently in those assigned to chlorhexidine–alcohol (27 or 3% patients *vs* 7 or 1% with povidone iodine–alcohol; p=0.0017) and led to chlorhexidine discontinuation in 2 patients (Mimoz O et al, *Lancet* 2015; 386, No. 10008:2069–2077).

Review & Meta-Analysis: Transradial Access for Coronary Angiography and Percutaneous Coronary Intervention (PCI) is Associated with a Small but Significant Increase in Radiation Exposure in Both Diagnostic and Interventional Procedures Compared With Transfemoral Access / Differences in Radiation Exposure Narrowed Over Time

Data from 24 randomized controlled trials (RCTs) for 19,328 patients showed that transradial access was associated with a small but significant increase in fluoroscopy time for coronary angiograms (weighted mean difference - WMD, fixed effect: 1.04 min; p<0.0001) and PCI (1.15 min; p<0.0001), compared with transfemoral access. Transradial access was also associated with higher kerma (gray-Gy)-area product for coronary angiograms (WMD, fixed effect: 1.72 Gy·cm^2; p=0.06), and higher kerma-area product for PCI (0.55 Gy·cm^2; p=0.02). Operator radiation doses for PCI with basic protection were 107±110 μSv with transradial and 74±68 μSv with transfemoral access; with supplementary protection, the doses decreased to 21±17 μSv with transradial access and

46±9 μSv with transfemoral. Overall difference in fluoroscopy time between the 2 procedures has decreased significantly by 75% over the past 20 years from 2 min in 1996 to ~30 s in 2014 (p<0.0001) (Plourde G et al, *Lancet* 2015; 386, No. 10009: 2192–2203).

High-STEACS Trial: Low Plasma Levels of High-Sensitivity Troponin at Presentation in Patients With Suspected Acute Coronary Syndrome Identify Two-Thirds of Patients at Very Low Risk of Cardiac Events Who Could be Discharged From Hospital

According to a prospective study of 6304 consecutive patients with suspected acute coronary syndrome, 782 (16%) of 4870 patients in the derivation cohort having MI, with a further 32 (1%) re-presenting with MI and 75 (2%) cardiac deaths at 30 days, in patients without MI at presentation, troponin concentrations were <5 ng/L in 2311 (61%) of 3799 patients, with a negative predictive value of 99.6% for the primary outcome (MI or subsequent MI or cardiac death at 1 month). The negative predictive value was consistent across groups stratified by age, sex, risk factors, and previous cardiovascular disease. In two independent validation cohorts, troponin concentrations were <5 ng/L in 594 (56%) of 1061 patients, with an overall negative predictive value of 99.4%. At 1 year, these patients had a lower risk of MI and cardiac death than did those with a troponin concentration of ≥5 ng/L (0.6% *vs* 3.3%; adjusted hazard ratio 0.41; p<0.0001) (Shah ASV et al, *Lancet* 2015; 386, No. 10012: 2481–2488).

Danish Cohort Study: In a Real-World Cohort of Patients with a First Hospitalization for an Acute Coronary Syndrome (ACS), Early Invasive Treatment Strategy was Associated With a Lower Risk for Cardiac Death and Rehospitalization for MI Compared with a Conservative Invasive Approach

In 19,704 propensity score–matched patients hospitalized with a first ACS, compared with a conservative approach, early invasive strategies were associated with a lower risk for cardiac death (cumulative incidence, 5.9% vs 7.6%; hazard ratio - HR, 0.75; *P*< 0.001). Similar results were found for rehospitalization for MI (cumulative incidence, 3.4% vs 50%; HR, 0.67; *P*< 0.001) and all-cause death (cumulative incidence, 7.3% vs. 10.6%; HR, 0.65; *P*< 0.001) (Hansen KW et al, *Ann Intern Med* 2015;163: 737-746).

In Digoxin Users Variant Alleles at Each of the 3 Loci in the *ABCB1* Gene were Associated with an Increased Risk of SCD Compared With those with None or One T Allele, Implying that the *ABCB1* Genotype Modifies the Risk of Cardiac Toxicity by Digoxin

The ATP-binding cassette B1 (*ABCB1*) gene encodes P-glycoprotein, a transport protein playing an important role in the bioavailability of digoxin. In a total of 10,932 persons (≥45 years), 419 sudden cardiac deaths (SCDs) occurred during a median of 9.8 years. In non-users of digoxin, the risk of SCD was not different across genotypes. In digoxin users, homozygous T allele carriers of C1236T (HR 1.90; allele frequency 0.43), G2677T (HR 1.89; allele frequency 0.44) and C3435T (HR 1.72; allele frequency 0.53) had a significantly increased risk of SCD (Niemeijer MN et al, *Heart* 2015;101: 1973-1979).

Sweetened Beverage Consumption is Associated With Higher Risk of Heart Failure (HF), Possibly Having Implications for HF Prevention Strategies

Among 42,400 Swedish men, aged 45-79 years, during a mean follow-up of 11.7 years, a total of 4113 HF events were identified. A positive association was observed between sweetened beverage consumption and risk of HF after adjustment for other risk factors (p for trend <0.001). Men who consumed ≥2 servings of sweetened beverages per day had a significantly higher risk of developing HF (23%) compared to men who were non-consumers (Rahman I et al, *Heart* 2015;101:1961-1965).

Micra Pacing Study: Transcatheter Leadless Pacing Can Safely and Effectively be Applied

Patients (n=140) requiring a VVI pacer underwent implantation of the Micra transcatheter pacing system, from the femoral vein, fixed in the right ventricle using 4 protractible nitinol tines. Over 1.9 ± 1.8 months, 30 adverse events related to the system or procedure occurred, mostly due to transient dysrhythmias or femoral access complications. One pericardial effusion without tamponade occurred after 18 device deployments. In 60 patients followed to 3 months, mean pacing threshold was 0.51 ± 0.22 V, and no threshold was ≥2 V. Average R-wave was 16.1 ± 5.2 mV and impedance was 650.7 ± 130 ohms (Ritter P et al, *Eur Heart J* 2015; 36: 2510-2519).

Long-Term Exposure to Road Traffic Noise was Associated with Small Increased Risks of All-Cause and Cardiovascular Mortality and Morbidity in the General Population, Particularly for Stroke in the Elderly

Median daytime exposure to road traffic noise in London (8.6 million inhabitants) was 55.6 dB. Daytime road traffic noise increased risk of hospital admission for stroke with relative risk (RR) 1.05 in adults, and 1.09 in the elderly in areas >60 vs <55 dB. Nighttime noise was associated with stroke admissions only among the elderly. Daytime noise was associated with all-cause mortality in adults (RR 1.04 in areas >60 vs <55 dB). Positive but non-significant associations were seen with mortality for cardiovascular and ischemic heart disease, and stroke (Halonen JI et al, *Eur Heart J* 2015; 36: 2653-2661).

Normalization of Testosterone Level is Associated with Reduced Incidence of Myocardial Infarction, Stroke and Mortality in Men

Of 3 groups (Gp) among 83,010 male veterans with low total testosterone (TT) levels, Gp1 with testosterone replacement therapy (TRT) and normalization of TT levels (n = 43,931, median age = 66 years, mean follow-up = 6.2 years), Gp2 with TRT but without normalization of TT levels (n = 25,701, median age = 66 years, mean follow-up = 4.6 years), and Gp3 without TRT (n = 13,378, median age = 66 years, mean follow-up = 4.7 years), all-cause mortality (hazard ratio - HR: 0.44), risk of MI (HR: 0.76), and stroke (HR: 0.64) were lower in Gp1 vs Gp3. Also, all-cause mortality (HR: 0.53), risk of MI (HR: 0.82), and stroke (HR: 0.70) were lower in Gp1 vs Gp2. There was no difference in MI or stroke risk between Gp2 and Gp3 (Sharma R et al, *Eur Heart J* 2015; 36: 2706-2715).

Reduced Appropriate Implantable Cardioverter-Defibrillator (ICD) Therapy after Cardiac Resynchronization Therapy (CRT)-Induced Left Ventricular Function Recovery

In 6 retrospective cohort studies (n = 1740), in patients with post-CRT LVEF ≥35%, rate of ICD therapy was significantly lower than patients with post-CRT LVEF <35%. Similarly, patients with post-CRT LVEF ≥45% had lower estimated rates of ICD therapy. Limiting analysis to studies discounting ICD therapies during LVEF recovery, patients with LVEF recovery (≥35 or ≥45%) had significantly lower rates of ICD therapy (Chatterjee NA et al, *Eur Heart J* 2015; 36: 2780-2789).

CONTROL Study: Prostar XL-Based Vascular Closure in TAVI Procedures was Associated with More Major Vascular Complications Compared with ProGlide; However, In-Hospital Mortality was Similar

Among 3138 transfemoral TAVI patients (944 matched / 472 pairs), major vascular complications or in-hospital mortality occurred more frequently in Prostar vs ProGlide group (9.5 vs 5.1%, P = 0.016), driven by higher rates of major vascular complication (7.4 vs 1.9%, P < 0.001) in the Prostar group. However, in-hospital mortality was similar (4.9 vs 3.5%, P = 0.2). Femoral artery stenosis occurred less frequently in the Prostar group (3.4 vs 0.5%, P = 0.004), but overall, Prostar use was associated with higher rates of major bleeding (16.7 vs 3.2%, P < 0.001), acute kidney injury (17.6 vs 4.4%, P < 0.001) and with longer hospital stay (median 6 vs 5 days, P = 0.007) (Barbash IM et al, *Eur Heart J* 2015; 36: 3370-3379).

Important Review and Other Articles

2015 International Consensus on Cardiopulmonary Resuscitation (*Circulation* 2015;132:S2-S268), ***2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation*** (*Circulation* 2015;132:S315-S573), ***AHA/ACC Scientific Statement on Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities*** (*Circulation* 2015;132: e256-e349 and *J Am Coll Cardiol* 2015;66:2343-2450), Arrhythmia-induced cardiomyopathies (Gopinathannair R et al, *J Am Coll Cardiol* 2015;66:1714-1728), Percutaneous pulmonary valve implantation (Ansari MM et al, *J Am Coll Cardiol* 2015;66:2246-2255), Transthyretin amyloidosis (Gertz MA et al, *J Am Coll Cardiol* 2015;66:2451-2466), Hemodynamics of mechanical circulatory support (Burkhoff *D et al, J Am Coll Cardiol* 2015;66:2663-2674), 2015 ACC/AHA/HRS Advanced Training Statement on Clinical Cardiac Electrophysiology (Zipes DP et al, *J Am Coll Cardiol* 2015;66:2767-2802), Risk factor modification in AF (Miller JD et al, *J Am Coll Cardiol* 2015;66:2899-2906), Cardiovascular management in pregnancy: antithrombotic agents and antiplatelet agents (Yarrington CD et al, *Circulation* 2015;132:1354-1364), AHA Statement on infective endocarditis (*Circulation* 2015; 132:1435-1486 & 1487-1515), PCSK-9 inhibitors (Bergeron N et al, *Circulation* 2015;132:1648-1666), Cardiac arrest in pregnancy (Jeejeebhoy FM et al, *Circulation* 2015;132:1747-1773), Contrast-induced nephropathy (Wichmann JL et al, *Circulation* 2015;132:1931-1936,), Pediatric pulmonary hypertension (Abman SH et al, *Circulation* 2015;132:2037-2099), Cardio-Oncology (Bellinger AM et al, *Circulation* 2015;132:2248-2258), Cardiovascular implications of hypoglycemia (Connelly KA et al, *Circulation* 2015;132:2345-2350), Idarucizumab (Eikelboom JW et al, *Circulation* 2015;132:2412-2422), Cardiac complications in non-cardiac surgery (Devereaux PJ & Sessler DI, *N Engl J Med* 2015; 373: 2258-2269), Resistant hypertension in chronic kidney disease (Rossignol P et al, *Lancet* 2013; 386:1588–1598), Role of ambulatory and home blood pressure monitoring in clinical practice (Shimbo D et al, *Ann Intern Med* 2015;163:691-700), Pulmonary embolism guidelines (Raja AS et al, *Ann Intern Med* 2015;163:701-711), Blood pressure screening (Siu AL et al, *Ann Intern Med* 2015;163:778-786), Radial vs femoral access in ACS (Ando G & Capodanno D et al, *Ann Intern Med* 2015;163:932-940), Patent foramen ovale (Asrress KN et al, *Heart* 2015; 101:1916-1925), When to consider an ICD following MI (Szwejkowski BR et al, *Heart* 2015; 101:1996-2000), Resistant hypertension (Rimoldi SF et al, *Eur Heart J* 2015; 36 : 2686-2695), 2015 ESC guidelines for the management of infective endocarditis (Habib G et al, *Eur Heart J* 2015; 36:3075-3128), Treatment of arrhythmogenic right ventricular dysplasia (Corrado D et al, *Eur Heart J* 2015; 36:3227-3237).