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Antonis S. Manolis, MD, Hector Anninos, MD
Athens University School of Medicine, Athens, Greece

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

HCS Panhellenic Congress**:** Athens, 20-22/10/2016

TCT Conference: Washington, DC, 29/10-2/11/2016

AHA Scientific Sessions: New Orleans, 12-16/11/2016

AF Symposium: Orlando, 12-14/1/2017

ACC.17: Washington, DC, 17-19/3/2017

HONEST Study: Morning Home Blood Pressure (BP) May be Superior to Clinic BP as a Predictor of Coronary Events and Stroke in Patients With Hypertension

In 21,591 hypertensive patients (mean age ~65 years), having 127 stroke and 121 CAD events over a mean follow-up of 2 years, the incidence of stroke events was significantly higher in patients with morning home systolic blood pressure (HSBP) ≥145 mmHg compared with <125 mmHg (hazard ratio -HR ~6.0), and in patients with clinic systolic blood pressure (CSBP) ≥150 mmHg compared with <130 mmHg (HR 5.82); morning HSBP predicted stroke events similarly to CSBP. Incidence of CAD events was significantly higher in patients with morning HSBP ≥145 mmHg compared with <125 mmHg (HR 6.24) and in patients with CSBP ≥160 mmHg compared with <130 mmHg (HR 3.51). Thus, compared with morning HSBP predicted CAD events more strongly than CSBP (Kario K et al, *J Am Coll Cardiol* 2016;67:1519-1527).

A 1-h Combination Algorithm Allows Fast Rule-Out/ Rule-In of Major Adverse Cardiac Events (MACE): In Patients with Chest Pain Presenting to Emergency Department (ED), Combining hs-cTnT Levels on Arrival and 1 h Later With the Patient History and ECG More Effectively Identified MACE Within 30 Days Than Screening Based on hs-cTnT Alone

In a prospective observational study enrolling 1,038 patients presenting to the emergency department (ED) with chest pain, an extended algorithm comprising hs-cTnT results at 1 h combined with history and ECG, identified 60% of all patients for rule-out and had a higher sensitivity than the troponin algorithm alone (97.5% vs 87.6%; p< 0.001). The negative predictive value was 99.5% and the likelihood ratio was 0.04 with the extended algorithm vs 97.8% and 0.17, respectively, with the troponin algorithm. The extended algorithm ruled-in 14% of patients with a higher sensitivity (75.2% vs 56.2%; p< 0.001) but a slightly lower specificity (94.0% vs 96.4%; p< 0.001) than the troponin algorithm. The rule-in arms of both algorithms had a likelihood ratio >10 (Mokhtari A et al, *J Am Coll Cardiol* 2016;67:1531-1540).

CTSN Trial: Strategies for Rate and Rhythm Control to Treat Postoperative Atrial Fibrillation (AF): Neither Treatment Strategy Showed a Net Clinical Advantage Over the Other / They were Associated With Equal Numbers of Days of Hospitalization, Similar Complication Rates, and Similarly Low Rates of Persistent AF 60 Days After Onset

Among 695 of 2109 patients (33%) who had AF after cardiac surgery, 523 underwent randomization to heart-rate or rhythm control. The total numbers of hospital days were similar in the 2 groups (median, 5.1 and 5 days, respectively; P = NS). There were no significant between-group differences in the rates of death (P = NS) or overall serious adverse events (24.8 per 100 patient-months in the rate-control group and 26.4 per 100 patient-months in the rhythm-control group, P = NS), including thromboembolic and bleeding events. About 25% of patients in each group deviated from the assigned therapy, mainly because of drug ineffectiveness (in the rate-control group) or amiodarone side effects or adverse drug reactions (in the rhythm-control group). At 60 days, 93.8% of the patients in the rate-control group and 97.9% of those in the rhythm-control group had had a stable heart rhythm without AF for the previous 30 days (P = 0.02), and 84.2% and 86.9%, respectively, had been free from AF from discharge to 60 days (P = NS) (Gillinov AM et al, *N Engl J Med* 2016; 374:1911-1921).

COGENT: Gastroprotection With Proton Pump Inhibitors (PPIs) Should be Utilized in Appropriately Selected Patients With Coronary Artery Disease Requiring Dual Antiplatelet Therapy (DAPT), Even if Patients are on Low-Dose Aspirin

High-dose aspirin users (n= 1,272 or 34%; higher rates of hyperlipidemia, smoking and history of PCI) had similar 6-month Kaplan-Meier estimates of adjudicated composite gastrointestinal (GI) events (1.7% vs 2.1%; hazard ratio - HR: 0.88) and major adverse cardiac events (4.8% vs 5.5%; HR: 0.73) compared with low-dose aspirin users (n= 2,480 or 66%; older, female, and with higher rates of peripheral artery disease, prior stroke, and hypertension). Randomization to PPI therapy reduced 6-month Kaplan-Meier estimates of the primary GI endpoint in low-dose (1.2% vs 3.1%) and high-dose aspirin subsets (0.9% vs 2.6%), and did not adversely affect the primary cardiovascular endpoint in either group (Vaduganathan M et al, *J Am Coll Cardiol* 2016;67:1661-1671).

Left Ventricular Assist Device (VAD) May Improve Clinical Outcomes of Patients With Acute Myocardial Infarction (AMI) and Heart Failure Who do not Respond Adequately to Conventional Therapy

VAD were implanted in 502 patients with AMI and 66% were INTERMACS profile 1 in 66% (median age 58.3 years, 77% male): 443 left VADs; 33 bi-VADs; and 26 total artificial hearts. A higher proportion of AMI than non-AMI patients had pre-operative intra-aortic balloon pumps (57.6% vs 25.3%; p< 0.01), intubation (58% vs 8.3%; p< 0.01), extracorporeal membrane oxygenation (17.9% vs 1.7%, p< 0.01), cardiac arrest (33.5% vs 3.3%, p< 0.01), and higher-acuity INTERMACS profiles. At 1 month post-VAD, 91.8% of AMI patients were alive with ongoing device support, 7.2% had died on device, and 1% had been transplanted. At 1-year post-VAD, 52% of AMI patients were alive with ongoing device support, 25.7% had been transplanted, 1.6% had left VAD explanted for recovery, and 20.7% had died on device. The AMI group had higher early phase hazard (hazard ratio - HR: 1.24; p= 0.04) and reduced late-phase hazard of death (HR: 0.57; p= 0.04) than the non-AMI group did. After accounting for established risk factors, the AMI group no longer had higher early mortality hazard (HR: 0.89; p= 0.30), but it had lower late mortality hazard (HR: 0.55; p= 0.02) (Acharya D et al, *J Am Coll Cardiol* 2016;67:1871-1880).

ALBATROSS Trial: A Mineralocorticoid Receptor Antagonist (MRA) Given Early After Myocardial Infarction (MI) did not Reduce the Composite of Death, Ventricular Arrhythmia, Cardiac Arrest, Need for Implantable Defibrillator, or New or Worsening Heart Failure (HF) at 6 Months, but Seemed to Lower Mortality Among Those Presenting With ST-Segment Elevation MI (STEMI)

Among 1,603 patients presenting with acute MI (92% of whom presented without HF) and randomized to receive an MRA regimen with a single intravenous bolus of potassium canrenoate (200 mg) followed by oral spironolactone (25 mg once daily) for 6 months in addition to standard therapy or standard therapy alone, the primary outcome occurred in 95 (11.8%) and 98 (12.2%) patients in the treatment and control groups, respectively (hazard ratio - HR: 0.97). Death occurred in 11 (1.4%) and 17 (2.1%) patients in the treatment and control groups, respectively (HR: 0.65). The odds of death were reduced in the treatment group (3 or 0.5% vs 15 or 2.4%; HR: 0.20) in the subgroup of STEMI (n = 1,229), but not in non–STEMI (p for interaction = 0.01). Hyperkalemia >5.5 mmol/l–1 occurred in 3% and 0.2% of patients in the treatment and standard therapy groups, respectively (p < 0.0001) (Beygui F et al, *J Am Coll Cardiol* 2016;67:1917-1927).

Takotsubo (TS) Registry: Patients Predisposed To TS Stress Cardiomyopathy Typically Have a Low Cardiovascular Risk Profile But Increased COPD, Migraine and Affective Disorders. Risk is Increased in Those Using B_2-Adrenergic Agonist Agents and Medications for Migraine / Mortality Rate is Similar to Patients With Acute Coronary Syndromes

Of the 505 patients with TS cardiomyopathy (TSC), 442 (87.5%) were women (mean age of 67 ± 10 years). The largest age group was between 60 and 69 years old with one-fifth of the patients <60 years of age. Compared with CAD control subjects (n= 1,010), patients with TSC were characterized by a low cardiovascular risk factor profile but with increased chronic obstructive pulmonary disease (COPD), migraine, and affective disorders. The use of beta-blockers was less common but use of β2-adrenergic agonist agents was more common in patients with TSC compared with either of the control groups. Being a patient with TSC was associated with a hazard ratio of 2.1 for death compared with the control subjects without CAD (n= 1,007). This was similar to the excess mortality risk seen among the CAD control subjects compared with control subjects without CAD (hazard ratio: 2.5) (Tornvall P et al, *J Am Coll Cardiol* 2016;67:1931-1936).

UK Registry: Causes of Sudden Cardiac Death (SCD) in Athletes Vary With Age. Sudden Arrhythmic Death Syndrome (SADS) is Prevalent in Children and Adolescents, Whereas Cardiomyopathies are the Most Common Cause in Adults. Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is Strongly Associated With SCD During Exertion

Autopsies were performed in 357 consecutive cases of athletes who died suddenly (mean 29 ± 11 years of age, 92% males, 76% Caucasian, 69% competitive). Sudden arrhythmic death syndrome (SADS) was the most prevalent cause of death (n= 149 or 42%), mostly in young athletes. This was a diagnosis of exclusion, defined as a structurally normal heart with no evident abnormality on macroscopic and histological evaluation and a negative result for toxicology screening, underscoring the importance of inherited primary arrhythmia syndromes as a major cause of SCD in athletes. Myocardial disease was detected in 40% of cases (mostly older athletes), including idiopathic left ventricular hypertrophy (LVH) and/or fibrosis (n= 59, 16%); ARVC (13%); and hypertrophic cardiomyopathy (HCM) (6%). Coronary artery anomalies occurred in 5% of (mostly young) cases. SCD during intense exertion occurred in 61% of cases (particularly in ARVC and left ventricular fibrosis). Almost 40% of athletes die at rest, highlighting the need for complementary preventive strategies (Finocchiaro G et al, *J Am Coll Cardiol* 2016;67:2108-2115).

BLOCK HF Trial: In Patients With AV Block (AVB) & Heart Failure, Biventricular Compared With RV Pacing is Associated With Improvement in Survival, Heart Failure-Related Urgent Care, and Adverse Ventricular Remodeling, Better Functional Capacity and Quality of Life

Among 691 patients with AVB, NYHA symptom class I to III heart failure, and left ventricular ejection fraction≤50% randomized to biventricular (n=349) or right ventricular (RV) pacing (n=342), biventricular pacing conferred greater improvement in NYHA class at 12 months, with 19% improved, 61% unchanged, and 17% worsened, compared with 12%/62%/ 23% in the RV arm. QOL was improved through 12 months. At 6 months, clinical composite score was improved/unchanged/ worsened in 53%/24%/24% in the biventricular arm compared with 39%/33%/28% in the RV arm. This improvement was sustained through 24 months (Curtis AB et al, *J Am Coll Cardiol* 2016;67:2148-2157).

OBSERVANT Study: In Patients With Low Operative Risk, Significantly Better 3-Year Survival and Freedom From Major Adverse Cardiac And Cerebrovascular Events (MACCE) were Observed after Surgical Aortic Valve Replacement (SAVR) Compared With Transcatheter Aortic Valve Implantation (TAVI)

One month survival was 97.1% after SAVR and 97.4% after TAVI (P=NS) among 355 low-risk patients in each group (EuroSCORE II <4%). Cardiac tamponade, pacemaker implantation, major vascular damage, and moderate-to-severe paravalvular regurgitation were significantly more frequent after TAVI compared with SAVR. Stroke rates were equal. SAVR was associated with higher risk of cardiogenic shock, severe bleeding, and acute kidney injury. At 3 years, survival was 83.4% after SAVR and 72% after TAVI (*P*=0.0015), and freedom from MACCE was 80.9% after SAVR and 67.3% after TAVI (*P*<0.001) (Rosato S et al, *Circ Cardiovasc Interv* 2016;9:e003326).

PARTNER II: In Intermediate-Risk Patients, TAVI was Similar to Surgical Aortic-Valve Replacement (AVR) With Respect to Death or Disabling Stroke

Among 2032 intermediate-risk (STS risk score of ≥4% & <8%) patients with severe aortic stenosis, randomly assigned to TAVI or surgical AVR, the rate of death from any cause or disabling stroke was similar (P=0.001 for noninferiority). At 2 years, the Kaplan–Meier event rates were 19.3% in the TAVI and 21.1% in the surgery group (hazard ratio – HR in TAVI, 0.89; P=NS). In the transfemoral-access cohort, TAVI resulted in a lower rate of death or disabling stroke than surgery (HR, 0.79; P=0.05), whereas in the transthoracic-access cohort, outcomes were similar in the two groups. TAVI resulted in larger aortic-valve areas and also in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation (Leon MB et al, *N Engl J Med* 2016; 374:1609-1620).

Propensity Score Analysis: TAVI With SAPIEN 3 in Intermediate-Risk Severe Aortic Stenosis Patients is Confers Low Mortality, Strokes, & Regurgitation at 1 Year & Appears Superior to Surgery

At 1 year follow-up of the SAPIEN 3 observational study, 79 of 1077 intermediate-risk patients had died (all-cause mortality 7·4%; 6·5% in the transfemoral access subgroup), and disabling strokes had occurred in 24 (2%), aortic valve re-intervention in 6 (1%), and moderate or severe paravalvular regurgitation in 13 (2%). In the propensity-score analysis comprising 963 TAVI patients receiving SAPIEN 3 and 747 with surgical valve replacement (PARTNER 2A trial), for the primary composite endpoint of mortality, strokes, and moderate or severe aortic regurgitation, TAVI was both non-inferior (pooled weighted proportion difference of −9·2%; p<0.0001) and superior (−9·2%; p<0.0001) to surgical valve replacement (Thourani VH et al, *Lancet* 2016; 387 (10034):2218–2225).

A Case–Control Study: Deficiency of the Aortic or any Rim, Device >5 mm Larger than ASD Diameter, and Weight: Device Size Ratio are Risk Factors for Cardiac Erosion Following Transcatheter Closure of Atrial Septal Defects (ASDs)

Among 125 erosions reported after ASD closure with an Amplatzer septal occlude, the median duration from implant to erosion was 14 days, but was >1 year in 16 patients. Nine patients (aged ≥17 years) who died were more likely to have an oversized device, and to have erosion into the aorta, than survivors. Aortic or superior vena cava rim deficiencies were more common in cases than in controls. In addition, larger balloon-sized ASD diameter, Amplatzer septal occluder device size, and device size–ASD diameter difference, and smaller weight-to-device size ratio were associated with erosion. On multivariable analysis, deficiency of any rim, device >5 mm larger than ASD diameter, and weight:device size ratio were associated with erosion (McElhinney DB et al, *Circulation* 2016; 133:1738-1746.

The ABC (Age, Biomarkers, Clinical History) Stroke Risk Score: A Better Biomarker-Based Risk Score for Predicting Stroke in Atrial Fibrillation?

A new risk score, the ABC (*A*ge, *B*iomarkers, *C*linical history) score, was developed and validated in 14,701 AF patients, with further external validation in another 1400 AF patients. The most important predictors were prior

stroke/transient ischemic attack, NT-proBNP, cTn-hs, and age. The ABC-stroke score was well calibrated and yielded higher c-indices than the widely used CHA_2DS_2-VASc score in both the derivation cohort (0.68 vs. 0.62, $P < 0.001$) and the external validation cohort (0.66 vs. 0.58, $P < 0.001$) (Hijazi Z et al, *Eur Heart J* 2016; 37:1582-1590).

ARISTOTLE /RE-LY Investigators: ABC-Bleeding Score, Using Age, Bleeding History, & 3 Biomarkers (Hemoglobin, cTn-hs, and GDF-15 or Cystatin C/CKD-EPI) Performed Better than HAS-BLED & ORBIT Scores in Patients with Atrial Fibrillation (AF)

The ABC-bleeding score (age, biomarkers [growth differentiation factor-15 or GDF-15, high-sensitivity cardiac troponin T or cTnT-hs, and hemoglobin], and clinical history of previous bleeding) yielded a higher c-index than HAS-BLED and ORBIT scores for major bleeding in both the derivation (n=14,537, ARISTOTLE trial) cohort (0.68 *vs* 0.61 *vs* 0.65, respectively; ABC-bleeding *vs* HAS-BLED p<0.0001 and ABC-bleeding *vs* ORBIT p=0.0008), and in the external validation (n=8468, RE-LY trial) cohort (0.71 *vs* 0.62 for HAS-BLED *vs* 0.68 for ORBIT; ABC-bleeding *vs* HAS-BLED p<0.0001 and ABC-bleeding *vs* ORBIT p=0.0016). A modified ABC-bleeding score using alternative biomarkers (hematocrit, cTnI-hs, cystatin C, or creatinine clearance) also outperformed the HAS-BLED and ORBIT scores (Hijazi Z et al, *Lancet* 2016; 387 (10035): 2302–2311).

ACC PINNACLE Registry: High Undertreatment Rate (38-40%) With Aspirin Alone Instead of Oral Anticoagulant (OAC) in Atrial Fibrillation Patients at Risk for Stroke, Usually Associated With Conditions Related to Coronary Disease (CAD)

Among 210,380 AF patients with CHADS2 score ≥2, 80,371 (38.2%) were treated with aspirin alone, and 130,009 (61.8%) with warfarin or non-vitamin K antagonist OACs. In another cohort of 294,642 patients with CHA2DS2-VASc ≥2, 118,398 (40.2%) were treated with aspirin alone, and 176,244 (59.8%) with warfarin or non-vitamin K antagonist OACs. After multivariable adjustment, hypertension, dyslipidemia, CAD, prior MI, unstable and stable angina, recent CABG, and peripheral arterial disease were associated with prescription of aspirin only, whereas male gender, higher body mass index, prior stroke/TIA, prior systemic embolism, and congestive heart failure were associated with more frequent prescription of OAC (Hsu J et al; *J Am Coll Cardiol* 2016; 67:2913-2923).

Non-Paroxysmal (NPAF) Compared to Paroxysmal Atrial Fibrillation (PAF) is Associated With a Highly Significant Increase in Thromboembolism and Death

According to 12 studies comprising 99,996 patients, the unadjusted risk ratio (RR) for thromboembolism in NPAF vs PAF was 1.355 ($P< 0.001$). In the study subset off oral anticoagulation, unadjusted RR was 1.689 ($P= 0.007$). The overall multivariable adjusted hazard ratio (HR) for thromboembolism was 1.384 ($P< 0.001$). The overall unadjusted RR for all-cause mortality was 1.462 ($P< 0.001$)and the adjusted HR for all-cause mortality was 1.217 ($P< 0.001$). Rates of bleeding were similar (Ganesan AN et al, *Eur Heart J* 2016;37:1591-1602).

VINDICATE Study: In Patients With Chronic Heart Failure (HF), Vitamin D Deficiency is Common, and High-Dose Vitamin D_3 Supplementation is Safe, Well Tolerated, and Associated With a Favorable Effect on Cardiac Function

Among 229 patients (179 men) with chronic HF and vitamin D deficiency (cholecalciferol<50 nmol/l or <20 ng/ml), randomized to 1 year of vitamin D3 (4,000 IU or 100 μg daily) or matching non−calcium-based placebo, the 6-min walk distance at 1 year did not improve, but there was a significant improvement in cardiac function (ejection fraction +6.07%; p< 0.0001); and a reversal of LV remodeling (LV end diastolic diameter -2.49 mm and LV end systolic diameter -2.09 mm (p= 0.043) (Witte KK et al, *J Am Coll Cardiol* 2016;67:2593-2603.).

Percutaneous Mitral Valve Plication With the Mitral Clip May be Effective for Symptom Relief in Patients With Obstructive Hypertrophic Cardiomyopathy (HCM) via Reduction of Systolic Anterior Motion (SAM) and Mitral Regurgitation (MR)

Percutaneous mitral valve leaflet plication to reduce SAM and MR using the transcatheter mitral clip system was completed in 5 of 6 referred patients (age 83 ± 8 years; 5 women) (one patient had cardiac tamponade and the procedure was aborted). SAM was eliminated and the intraoperative LVOT gradient (91 ± 44 mmHg to 12 ± 6 mmHg; p= 0.007), left atrial pressure (29 ± 11 mmHg to 20 ± 8 mmHg; p= 0.06), and MR grade (3.0 ± 0 vs. 0.8 ± 0.4; p= 0.0002) were decreased, associated with improved cardiac output (in n= 4; 3.0 ± 0.6 l/min to 4.3 ± 1.2 l/min; p= 0.03). Over 15 ± 4 months, symptom improvement to NYHA class I or II occurred in all patients. Follow-up echocardiography demonstrated continued absence of SAM and significant reduction in MR, although high systolic LVOT velocities (i.e., >4 m/s) were evident in 3 of the 5 treated patients (Sorajja P et al, *J Am Coll Cardiol* 2016;67:2811-2818).

EARLY-BAMI Trial: In Patients With Acute STEMI Given IV Metoprolol within 12 h Before Primary Angioplasty, Infarct Size Measured by CMR was not Significantly Different Than in Those Given a Placebo

A total of 683 STEMI patients (mean age 62 ± 12 years; 75% male) presenting within 12 h were randomized to IV

metoprolol (n= 336) or placebo (n= 346). Infarct size by cardiac magnetic resonance (CMR) (performed in 342 patients) did not differ between the metoprolol (15.3 ± 11%) and placebo groups (14.9 ± 11.5%; p= 0.616). Peak and area under the creatine kinase curve did not differ between groups. LV ejection fraction by CMR did not differ. Incidence of malignant arrhythmias was 3.6% in the metoprolol group vs 6.9% in placebo (p= 0.050). Incidence of adverse events was not different between groups (Roolvink V et al, *J Am Coll Cardiol* 2016; 67:2705-2715).

Trimethylamine N-oxide (TMAO), an Intestinal Microbe-Generated Phosphatidylcholine Metabolite is Related to the Pathogenesis of Atherosclerotic CAD

TMAO arises from gut microbiota metabolism following ingestion of diets rich in phosphatidylcholine (or lecithin), the major dietary source of choline, and carnitine, an abundant nutrient in red meat. In 353 consecutive stable patients with angiographic evidence of CAD, the median TMAO level was 5.5 μM, the median SYNTAX score was 11, and 289 (81.9%), 40 (11.3%), and 24 (6.8%) patients had low (0 to 22), intermediate (23 to 32), and high (≥33) SYNTAX scores, respectively. Plasma TMAO levels correlated (all p<0.0001) with the SYNTAX score (r= 0.61), SYNTAX score II (r= 0.62), and hs-cTnT (r= 0.29). After adjustment, elevated TMAO levels remained independently associated with a higher SYNTAX score (odds ratio - OR: 4.82; p< 0.0001), SYNTAX score II (OR: 1.88; p= 0.0001), but were not associated with subclinical myonecrosis (OR: 1.14; p= 0.3147). Elevated TMAO level was an independent predictor of the presence of diffuse lesions, even after adjustments for traditional risk factors and for hs-cTnT (OR: 2.05; p= 0.0001) (Senthong V et al, *J Am Coll Cardiol* 2016;67:2620-2628).

The Stepathlon Cardiovascular Health Study: Light Weight, Low-Cost, Noninteractive Pedometers Can Promote Modest Improvements in Physical Activity, Sitting, and Weight Among Private and Public Sector Employees

Stepathlon, a low-cost, pedometer-based, workplace physical activity and wellness program, which utilized an mHealth technology-based approach to facilitate large-scale implementation and program delivery, was conducted annually as a 100-day event, aiming to encourage participants to increase step counts and physical activity. After Stepathlon completion, participants (N=69,219, age 36 ± 9 years, 23.9% female, 92% lower-middle income countries) recorded improved step count (+3,519 steps/day; p< 0.0001), exercise days (+0.89 days; p < 0.0001), sitting duration (−0.74 h; p< 0.0001) and weight (−1.45 kg; p< 0.0001). Improvements occurred in women and men, in all geographic regions, and in both high and lower-middle income countries, with reproducible annual results. Predictors of weight loss included step increase, sitting duration decrease, and increase in exercise days (all p< 0.0001) (Ganesan AN et al, *J Am Coll Cardiol* 2016; 67:2453-2463).

A Study of 1.5 Million Blood Donors: Non-O Blood Groups Explain >30% of Venous Thromboembolic Events

in Denmark and Sweden (1987-2012), a total of 9170 venous and 24,653 arterial thromboembolic events occurred in 1,112,072 blood donors; compared with blood group O, non-O blood groups were associated with higher incidence of both venous and arterial events. The highest rate ratios (RR) were observed for pregnancy-related venous thromboembolism (RR, 2.22), deep vein thrombosis (RR, 1.92), and pulmonary embolism (RR, 1.80) (Vasan SK et al, *Circulation* 2016;133:1449-1457).

CMR Study in Male Elite Master Athletes: the Hypothesis of an Exercise-Induced Arrhythmogenic Right Ventricular (RV) Cardiomyopathy is Questioned

Among 33 healthy white competitive elite male master endurance athletes (age 30–60 years) with a training history of 29±8 years, and 33 pair-matched white controls, undergoing cardiopulmonary exercise testing, Doppler and speckle tracking echocardiography, and cardiovascular magnetic resonance (CMR), indexed left ventricular (LV) (96±13 and 62±10 g/m^2; *P*<0.001), and RV mass (36±7 and 24±5 g/m^2; *P*<0.001) and indexed LV (104±13 and 69±18 mL/m^2; *P*<0.001) and RV end-diastolic volume (110±22 and 66±16 mL/m^2; *P*<0.001) were significantly increased in athletes in comparison with control subjects. RV ejection fraction did not differ between athletes and controls (52±8 and 54±6%; *P*=NS). Pathological late enhancement was detected in 1 athlete. No correlations were found for LV and RV volumes and ejection fraction with NT-proBNP, and high-sensitive troponin was negative in all subjects (Bohm P et al, *Circulation* 2016;133:1927-1935).

STICHES Trial: Coronary Artery Bypass (CABG) Improves Survival in Ischemic Cardiomyopathy

Among 1212 coronary artery disease patients with an ejection fraction of ≤35%, randomly assigned to CABG plus medical therapy (CABG group, n=610) or medical therapy alone (medical-therapy group, n=602), over 9.8 years, death occurred in 359 patients (58.9%) in the CABG group and in 398 patients (66.1%) in the medical group (hazard ratio – HR with CABG vs medical therapy, 0.84; P=0.02). A total of 247 patients (40.5%) in the CABG group and 297 patients (49.3%) in the medical-therapy group died from cardiovascular causes (HR, 0.79; P=0.006). Death from any cause or hospitalization for cardiovascular causes occurred in 467 patients (76.6%) in

the CABG and in 524 patients (87.0%) in the medical group (HR, 0.72; P<0.001) (Velazquez EJ et al, *N Engl J Med* 2016; 374:1511-1520).

Resuscitation Outcomes Consortium (ROC): In Out-Of-Hospital Cardiac Arrest (OOHCA) Due to Shock-Refractory VF or Pulseless VT, Neither Amiodarone Nor Lidocaine Resulted in a Higher Rate of Survival or Favorable Neurologic Outcome Than Placebo

Among 3026 OOHCA patients, randomly assigned to amiodarone (974), lidocaine (993), or placebo (1059), 24.4%, 23.7%, and 21%, respectively, survived to hospital discharge. The difference in survival rate for amiodarone vs placebo was 3.2% (P=0.08); for lidocaine vs placebo, 2.6%; and for amiodarone vs lidocaine, 0.7% (P=0.70). Neurologic outcome at discharge was similar in the 3 groups. There was heterogeneity of treatment effect with respect to whether the arrest was witnessed (P=0.05); both drugs were associated with a higher survival rate than placebo among patients with bystander-witnessed arrest but not among those with unwitnessed arrest. More amiodarone recipients required temporary cardiac pacing (Kudenchuk PJ et al, *N Engl J Med* 2016; 374:1711-1722).

HOPE-3 Trials: Among Persons at Intermediate Risk With no Cardiovascular Disease, Antihypertensive Therapy With Candesartan plus Diuretic Does not Protect from Major Cardiovascular Events, but Therapy With Rosuvastatin or Combined Rosuvastatin and Candesartan plus Hydrochlorothiazide Does

Among 12,705 participants at intermediate risk with no cardiovascular disease (mean baseline blood pressure 138.1/81.9 mm Hg) randomly assigned to candesartan (16 mg/d) plus hydrochlorothiazide (12.5 mg/d) or placebo, over a median follow-up of 5.6 years, the decrease in blood pressure was 6/3 mm Hg greater in the active-treatment group. The first coprimary outcome (composite of cardiovascular death, nonfatal MI, or stroke) occurred in 260 participants (4.1%) with active-treatment and in 279 (4.4%) with placebo (hazard ratio-HR, 0.93; P=NS); the second coprimary outcome (heart failure, cardiac arrest, or revascularization) occurred in 312 participants (4.9%) and 328 participants (5.2%), respectively (HR, 0.95; P=NS) (Lonn EM et al, *N Engl J Med* 2016; 374:2009-2020).

In the same cohort, random assignment to rosuvastatin (10 mg/d) or placebo led to 26.5% lower LDL cholesterol in the active treatment group. The first coprimary outcome occurred in 235 participants (3.7%) in the rosuvastatin group and in 304 participants (4.8%) in the placebo group (HR, 0.76; P=0.002). The results for the second coprimary outcome were consistent with the results for the first (occurring in 277 participants or 4.4% in the rosuvastatin group and in 363 participants or 5.7% in the placebo group; HR, 0.75; P<0.001). In the rosuvastatin group, there was no excess of diabetes or cancers, but there was an excess of cataract surgery (3.8% vs 3.1%; P=0.02) and muscle symptoms (5.8% vs 4.7%; P=0.005) (Yusuf S et al, *N Engl J Med* 2016; 374:2021-2031).

Finally, among those (n=3180) assigned to combined therapy (rosuvastatin and the 2 antihypertensive agents) compared with the 3168 assigned to dual placebo, the first coprimary outcome occurred in 113 participants (3.6%) in the combined-therapy group and in 157 (5%) in the dual-placebo group (HR, 0.71; P=0.005). The second coprimary outcome occurred in 136 participants (4.3%) and 187 participants (5.9%), respectively (HR, 0.72; P=0.003). Muscle weakness and dizziness were more common in the combined-therapy than in the dual-placebo group, but the overall discontinuation rate was similar in the two groups (Yusuf S et al, *N Engl J Med* 2016; 374:2032-2043).

FIRE AND ICE: Cryoballoon Ablation Noninferior to Radiofrequency Ablation With Respect to Efficacy and Safety in Patients With Drug-Refractory Paroxysmal Atrial Fibrillation (PAF)

Among 762 PAF patients randomized to cryoballoon (n=378) or radiofrequency ablation (n=384), over mean follow-up of 1.5 years, the primary efficacy end point (first documented clinical failure, i.e. recurrence of AF, occurrence of atrial flutter or atrial tachycardia, use of antiarrhythmic drugs, or repeat ablation following a 90-day period after the index ablation, occurred in 138 patients in the cryoballoon group and in 143 in the radiofrequency group (1-year event rates, 34.6% and 35.9%, respectively; hazard ratio-HR, 0.96; P<0.001 for noninferiority). The primary safety end point (composite of death, cerebrovascular events, or serious treatment-related adverse events) occurred in 40 patients in the cryoballoon group and in 51 patients in the radiofrequency group (1-year event rates, 10.2% and 12.8%, respectively; hazard ratio, 0.78; P=NS) (Kuck K_H et al, *N Engl J Med* 2016; 374:2235-2245).

HERMES Collaboration Meta-Analysis of 5 Randomized Trials: Endovascular Thrombectomy After Large-Vessel Ischemic Stroke is of Benefit to Most Patients / Timely Treatment should be Provided to These Patients

In 2015, 5 randomized trials showed efficacy of endovascular thrombectomy over medical care in patients with acute ischemic stroke caused by occlusion of proximal anterior cerebral arteries. Patient data for 1287 patients (634 assigned to endovascular thrombectomy, 653 assigned to control), pooled from these trials (MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA), indicated that endovascular thrombectomy led to significantly reduced disability at 90 days compared with control (adjusted common odds ratio-cOR 2·49;

p<0.0001). The number needed to treat with endovascular thrombectomy to reduce disability by at least one level on modified Rankin scale-mRS for one patient was 2.6. Effect sizes favouring endovascular thrombectomy over control were present in several strata of special interest, including in patients aged ≥80 years (cOR 3.68), those randomized >5h after symptom onset (cOR 1.76), and those not eligible for intravenous alteplase (2.43). Mortality at 90 days and risk of parenchymal hematoma and symptomatic intracranial hemorrhage did not differ between populations (Goyal M et al, *Lancet* 2016; 387 (10029):1723–1731).

DANAMI 3-DEFER: No advantage of Deferred Stent Implantation vs Standard PCI in Patients With ST-Segment Elevation Myocardial Infarction (STEMI)

Among 1215 patients with STEMI randomized to primary PCI with immediate stent implantation (n=612) or deferred stent implantation 48 h after the index procedure if a stabilized flow could be obtained in the infarct-related artery (n=603), at a median follow-up of 42 months, the primary endpoint (all-cause mortality, hospital admission for heart failure, recurrent infarction, and any unplanned revascularization of the target vessel) occurred in 109 (18%) patients who had standard PCI and in 105 (17%) patients who had deferred stent implantation (hazard ratio 0·99; p=NS). Procedure-related MI, bleeding requiring transfusion or surgery, contrast-induced nephropathy, or stroke occurred in 28 (5%) vs 27 (4%) patients, with no significant differences between groups (Kelbæk H et al, *Lancet* 2016; 387 (10034):2199–2206).

ixCELL-DCM: Transendocardial Delivery of Cellular Therapy with Ixmyelocel-T in Patients With Reduced-Ejection Fraction Ischemic Heart Failure Resulted in Significant Reduction in Cardiac Events Compared With Placebo Leading to Improved Patient Outcomes

Ixmyelocel-T is an expanded, multicellular therapy produced from a patient's own bone marrow by selectively expanding two key types of bone marrow mononuclear cells: CD90+ mesenchymal stem cells and CD45+ CD14+ auto-fluorescent+ activated macrophages. Randomized catheter-based transendocardial injection of ixmyelocel-T cell therapy in 66 patients with heart failure and reduced ejection fraction compared with placebo (n=60) led to primary efficacy endpoint (all-cause death, cardiovascular admission, and unplanned clinic visits to treat acute heart failure) being observed in 47 patients: 50 events in 25 (49%) of 51 patients in the placebo group and 38 events in 22 (38%) of 58 patients in the ixmyelocel-T group, which represents a 37% reduction in cardiac events compared with placebo (risk ratio 0.63; p=0.0344). 41 (75%) of 51 participants in the placebo group had serious adverse events vs 31 (53%) of 58 in the ixmyelocel-T group (p=0.02) (Patel AN et al, *Lancet* 2016; 387:2412–2421).

GAUSS-3: Among Patients With Statin Intolerance Due to Muscle-Related Adverse Effects, Use of Evolocumab Compared With Ezetimibe Resulted in a Significantly Greater Reduction in LDL-Cholesterol Levels After 24 Weeks

Of the 491 patients who entered phase A (20 mg atorvastatin vs placebo) (age 60.7±10.2 years; 50% women; 34.6% with coronary heart disease; entry mean LDL-C level, 212.3 ±67.9 mg/dL), muscle symptoms occurred in 209 (42.6%) while taking atorvastatin but not while taking placebo. Of these, 199 entered phase B, along with 19 who proceeded directly to phase B (randomization 2:1 to subcutaneous evolocumab 420 mg monthly or 10 mg daily of oral ezetimibe) due to elevated creatine kinase (n = 218, with 73 randomized to ezetimibe and 145 to evolocumab; entry mean LDL-C level, 219.9 ±72 mg/dL). For the mean of weeks 22 and 24, LDL-C with ezetimibe was 183 mg/dL (mean percent LDL-C change, −16.7%), and with evolocumab 103.6 mg/dL (mean percent change, −54.5%) ($P < .001$). LDL-C level at week 24 with ezetimibe was 181.5 mg/dL (mean percent change, −16.7%) and with evolocumab was 104.1 mg/dL (mean percent change, −52.8%) ($P < .001$). For the mean of weeks 22 and 24, between-group difference in LDL-C was −37.8%. For week 24, between-group difference in LDL-C was −36.1%. Muscle symptoms were reported in 28.8% of ezetimibe-treated patients and 20.7% of evolocumab-treated patients (log-rank P = NS). Active study drug was stopped for muscle symptoms in 5 of 73 ezetimibe-treated patients (6.8%) and 1 of 145 evolocumab-treated patients (0.7%) (Nissen SE et al, *JAMA* 2016; 315:1580-1590**).**

SPRINT Trial for the Subgroup of Hypertensive Patients Aged ≥75 Years: Treating to a Systolic BP (SBP) Target of <120 mmHg Compared With <140 mmHg Resulted in Significantly Lower Rates of Fatal and Nonfatal Major Cardiovascular Events and Death From Any Cause

Among 2636 participants (mean age ~80 years; ~38% women; 2510 or ~95% providing complete follow-up data) randomized to an SBP target of <120 mmHg (intensive treatment group, n = 1317) or an SBP target of <140 mmHg (standard treatment group, n = 1319), at a median follow-up of 3.14 years, there was a lower rate of the primary composite outcome (nonfatal MI, other acute coronary syndrome, nonfatal stroke, nonfatal acute decompensated heart failure, and cardiovascular death) (102 vs 148 events; hazard ratio - HR, 0.66) and all-cause mortality (73 deaths vs 107 deaths, respectively; HR, 0.67). The overall rate of serious adverse events was not different between treatment groups (48.4% vs 48.3%). Absolute rates of hypotension were 2.4% in the intensive treatment group vs 1.4% in the standard treatment group

(HR, 1.71), 3% vs 2.4% for syncope (HR, 1.23), 4% vs 2.7% for electrolyte abnormalities (HR, 1.51), 5.5% vs 4.0% for acute kidney injury (HR, 1.41), and 4.9% vs 5.5% for injurious falls (HR, 0.91) (Williamson JD et al, *JAMA* 2016;315:2673-2682).

Quitting Smoking Abruptly vs Gradually is More Likely to Lead to Lasting Abstinence, Even for Those Who Initially Prefer to Quit by Gradual Reduction

Among 697 adult smokers with tobacco addiction, all receiving behavioral support from nurses and nicotine replacement before and after quit day, at 4 weeks, 39.2% of the participants in the gradual-cessation group (reduced smoking gradually by 75% in the 2 weeks before quitting) were abstinent compared with 49% in the abrupt-cessation group (relative risk, 0.80). At 6 months, 15.5% of the participants in the gradual-cessation group were abstinent compared with 22% in the abrupt-cessation group (relative risk, 0.71). Participants who preferred gradual cessation were significantly less likely to be abstinent at 4 weeks than those who preferred abrupt cessation (38.3% vs 52.2%; *P*= 0.007) (Lindson-Hawley N et al, *Ann Intern Med* 2016;164:585-592).

Systematic Review and Meta-Analysis: Compared With Everolimus-Eluting Metallic Stents (EESs), Everolimus-Eluting Bioresorbable Vascular Scaffold (BVSs) do not Eliminate and Might Increase Risks for Stent Thrombosis and MI in Adults Having PCI

According to 6 randomized, controlled trials and 38 observational studies, each involving at least 40 patients with BVS implantation, the pooled incidence of definite or probable stent thrombosis after BVS implantation was 1.5 events per 100 patient-years (PYs) (126 events during 8508 PYs). In 6 randomized trials directly comparing BVSs with EESs, a non–statistically significant increased risk for stent thrombosis (odds ratio - OR, 2.05; *P*= 0.067) and myocardial infarction (MI) (OR, 1.38; *P*= 0.064) was observed with BVSs. The 6 observational studies that compared BVSs with EESs showed increased risk for stent thrombosis (OR, 2.32; *P*= 0.035) and MI (OR, 2.09; *P*= 0.007) with BVSs. The relative rates of all-cause and cardiac death, revascularization, and target lesion failure were similar for BVSs and EESs (Zhang X-L et al, *Ann Intern Med* 2016;164:752-763.).

Systematic Evidence Review: The Beneficial Effect of Aspirin for the Primary Prevention of CVD is Modest and Occurs at Doses of ≤100 mg/d / Older Adults Seem to Achieve a Greater Relative MI Benefit / Consider Bleeding Risk which May Vary Considerably

According to 2 good-quality and 9 fair-quality randomized, controlled trials, aspirin reduced the risk for nonfatal myocardial infarction (MI) (relative risk - RR, 0.78) but not nonfatal stroke; aspirin showed little or no benefit for all-cause or cardiovascular mortality. Benefits began within the first 5 years. Older adults achieved greater relative MI reduction, but no other effect modifications were found in analyzed subpopulations. In trials with aspirin doses of ≤100 mg/d, the reduction in nonfatal MI benefit persisted (absolute risk reduction, 0.15 to 1.43 events per 1000 person-years) and a 14% reduction in nonfatal stroke benefit was noted, but no benefit was found for all-cause mortality (RR, 0.95) or cardiovascular mortality (RR, 0.97) (Guirguis-Blake JM et al, *Ann Intern Med* 2016;164:804-813).

However, in CVD primary prevention studies, low-dose aspirin use (≤100 mg daily or every other day) increased major gastrointestinal (GI) bleeding risk by 58% (odds ratio - OR, 1.58) and hemorrhagic stroke risk by 27% (OR, 1.27). Estimated excess major bleeding events were 1.39 for GI bleeding and 0.32 for hemorrhagic stroke per 1000 person-years of aspirin exposure using baseline bleeding rates from a community-based observational sample. Such events could be greater among older persons, men, and those with CVD risk factors that also increase bleeding risk (Whitlock EP et al, *Ann Intern Med* 2016;164:826-835).

Prolonged PR interval is Associated with Significant Increases in Atrial Fibrillation, Heart Failure and Mortality

The results of a review and meta-analysis of 14 studies comprising 400,750 participants suggest an increased risk of mortality with prolonged PR interval risk ratio (RR) 1.24 (5 studies). Prolonged PR interval was associated with significant risk of heart failure or left ventricular dysfunction (RR 1.39, 3 studies) and atrial fibrillation (RR 1.45, 8 studies) but not cardiovascular mortality, coronary heart disease or myocardial infarction or stroke or TIA. Similar observations were recorded when limited to studies of first-degree heart block (Kwok CS et al, *Heart* 2016;102:672-680).

Atrial Fibrillation (AF) in the Setting of Myocardial Infarction (MI) (STEMI or NSTEMI) is Associated With Impaired 3-Month Outcome

Among 155,071 hospital survivors of MI, AF was documented in 24,023 (15.5%) cases. The AF subtypes were new-onset AF with sinus rhythm at discharge (3.7%), new-onset AF with AF at discharge (3.9%), paroxysmal AF (4.9%) and chronic AF (3%). The event rate per 100 person-years for the composite cardiovascular outcome (all-cause mortality, MI or ischemic stroke) was 90.9 in patients with any type of AF vs 45.2 in patients with sinus rhythm, adjusted hazard ratio (HR) 1.28. The composite cardiovascular outcome was similar among AF subtypes and between NSTEMI and STEMI. AF was associated

with higher risk of mortality (HR 1.59), reinfarction (HR 1.14) and ischemic stroke (HR 2.29) (Batra G et al, *Heart* 2016;102:926-933).

XANTUS Study: Patients with Non-Valvular Atrial Fibrillation (AF) Receiving Rivaroxaban, Had 2.1 Major Bleeding Events per 100 Patient-Years, 1.9 Deaths per 100 Patient-Years, and 0.7 Stroke Events per 100 Patient-Years

Among 6784 patients treated with rivaroxaban (mean patient age 71.5 years, range 19–99; 41% female, and 9.4% with documented severe or moderate renal impairment, i.e. creatinine clearance <50 mL/min), the mean $CHADS_2$ was 2.0 and CHA_2DS_2-VASc score 3.4; 859 (12.7%) patients had a CHA_2DS_2-VASc score of 0 or 1. The mean treatment duration was 329 days. Treatment-emergent major bleeding occurred in 128 patients (2.1 events per 100 patient-years), 118 (1.9 events per 100 patient-years) died, and 43 (0.7 events per 100 patient-years) suffered a stroke (Camm AJ et al, *Eur Heart J* 2016; 37:1145-1153).

EMPA-REG OUTCOME® Trial: In Patients With Type 2 Diabetes and High Cardiovascular (CV) Risk, Empagliflozin Reduced Heart Failure Hospitalization and Cardiovascular Death

The initial EMPA-REG OUTCOME® trial reported that empagliflozin added to standard of care reduced major adverse CV events in patients with diabetes and high CV risk. In this analysis heart failure outcomes were investigated among 7020 patients randomized to receive empagliflozin 10 mg, empagliflozin 25 mg, or placebo; 706 (10.1%) had heart failure at baseline. Heart failure hospitalization or CV death occurred in a lower percentage of patients treated with empagliflozin (5.7%) than with placebo (8.5%) (hazard ratio, HR: 0.66; $P< 0.001$); number needed to treat to prevent one heart failure hospitalization or CV death: 35 over 3 years. Empagliflozin improved other heart failure outcomes, including hospitalization for or death from heart failure (2.8 vs 4.5%; HR: 0.61; $P< 0.001$) and was associated with a reduction in all-cause hospitalization (36.8 vs 39.6%; HR: 0.89; $P = 0.003$) (Fitchett D et al, *Eur Heart J* 2016;37:1526-1534).

Danish Databases: All NOACs Safe and Effective Alternatives to Warfarin with no Significant Difference Between NOACs and Warfarin for Ischemic Stroke / Risks of Death or Bleeding Lower for Apixaban and Dabigatran vs Warfarin

Among 61678 anticoagulant naïve patients with atrial fibrillation (AF) receiving warfarin (n=35436, 57%), dabigatran 150 mg (n=12701, 21%), rivaroxaban 20 mg (n=7192, 12%), and apixaban 5 mg (n=6349, 10%), NOACs were not significantly different from warfarin with regards to ischemic stroke. At 1 year, rivaroxaban was associated with lower annual rates of ischemic stroke or systemic embolism (3% vs 3.3%, respectively) compared with warfarin: hazard ratio – HR 0.83. HRs for dabigatran and apixaban (2.8% and 4.9% annually, respectively) were non-significant compared with warfarin. The annual risk of death was significantly lower with apixaban (5.2%) and dabigatran (2.7%) (HR 0.65 and 0.63, respectively) compared with warfarin (8.5%), but not with rivaroxaban (7.7%). For the combined endpoint of any bleeding, annual rates for apixaban (3.3%) and dabigatran (2.4%) were significantly lower than for warfarin (5%) (HR 0.62). Warfarin and rivaroxaban had comparable annual bleeding rates (5.3%) (Larsen TB et al, *BMJ* 2016;353:i3189).

ORBIT-AF registry: Patients With a Family History of AF Developed AF at a Younger Age, had Less Comorbidity, and were more Symptomatic. Once AF Developed, No Significantly Increased Risks

Among 9,999 US patients with AF, 1,481 (14.8%) had a family history of AF. Relative to those without, those with a family history of AF developed AF 5 years earlier (median age 65 vs 70 years, $P<0.01$), with less comorbidity, and had more severe AF-related symptoms. No differences were found between the 2 groups in the risk of AF progression, stroke, non–central nervous system embolism, or TIA, all-cause hospitalization, and all-cause death (Gundlund A et al, *Am Heart J* 206;175:28–35).

CHARGE & FORCe: Consumption of Omega 3s Linked to Lower Risk of Fatal Coronary Heart Disease (CHD)

Analysis of 19 cohort studies evaluating biomarkers of seafood-derived eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) and plant-derived α-linolenic acid (ALA) for incident CHD, in 45 637 individuals (median age at baseline 59 years; ~63% male) documented 7973 total CHD, 2781 fatal CHD, and 7157 nonfatal MI events. The ω-3 biomarkers ALA, DPA, and DHA were associated with a lower risk of fatal CHD, with relative risks (RRs) of 0.91 for ALA, 0.90 for DPA, and 0.90 for DHA. Although DPA was associated with a lower risk of total CHD (RR, 0.94), ALA (RR, 1.00), EPA (RR, 0.94), and DHA (RR, 0.95) were not. Significant associations with nonfatal MI were not evident. Associations appeared generally stronger in phospholipids and total plasma (Del Gobbo LC et al, dx.doi.org/10.1001/jamainternmed.2016.2925).

Influenza Infection is Associated with AF (18% Increased Risk), which is Reduced with Vaccination

Among 11,374 patients with newly diagnosed AF, those with compared with those without influenza infection or vaccination (n = 38,353), patients with influenza infection without vaccination (n = 1369) were

associated with a significantly higher risk of AF with an odds ratio of 1.182 (P = 0.032) after adjustment for baseline differences. The risk of AF was lower in patients receiving influenza vaccination without influenza infection (n = 16,452) with an odds ratio - OR of 0.881 (P < 0.001). In patients who received vaccination and experienced influenza infection (n = 696), the risk of AF was similar to that in the reference group (OR 1.136; P = NS) (Chang T-Y et al, *Heart Rhythm* 2016; 13:1189–94).

ARISTOTLE trial: A History of Bleeding is Associated With Several Risk Factors for Stroke and Higher Risk of Major—but not Intracranial—Bleeding, During Anticoagulation / The Beneficial Effects of Apixaban over Warfarin for Stroke, Hemorrhagic Stroke, Death, or Major Bleeding Remain Consistent Regardless of History of Bleeding

Among 18,140 patients receiving apixaban or warfarin, a bleeding history was reported at baseline in 3,033 patients (16.7%), who more often were male, with a history of prior stroke/TIA/systemic embolism and diabetes; higher $CHADS_2$ scores, age, and body weight; and lower creatinine clearance and mean systolic blood pressure. Major (but not intracranial) bleeding occurred more frequently in patients with vs without a history of bleeding (hazard ratio 1.35). There were no significant interactions between bleeding history and treatment for stroke/embolism, hemorrhagic stroke, death, or major bleeding, with fewer outcomes with apixaban vs warfarin for all of the outcomes independent of a bleeding history (De Katerina R et al, *Am Heart J* 2016; 175:175–183).

Meta-Analysis: Left Atrial Appendage Occlusion (LAAO) is not Superior over NOACs for Stroke Prevention, but consistently has Lower Thromboembolic & Bleeding events

Per 6 RCTs and 27 observational studies LAAO was less effective than NOACs for stroke prevention (odds ratio 0.86), but had a lower rate of hemorrhagic events during follow-up. However, a meta-proportion analysis of observational studies revealed that LAAO was associated with a lower rate of both thromboembolic events (1.8 vs 2.4 events per 100 patient-years) and major bleeding events during follow-up (2.2 vs 2.5 events per 100 patient-years) as compared with NOACs. With prolonged follow-up duration after LAAO implantation, the rate of thromboembolic events decreased (Li X et al, *Heart Rhythm* 2016;13:1203–1214).

Drug-Induced Brugada Synrome from Noncardiac Drugs Occurs Predominantly in Adult Males, Usually Late after the Onset of Therapy

A total of 74 cases of drug-induced Brugada syndrome from 27 noncardiac medications were identified: 77% were male, and drug toxicity was involved in 46%. It generally occurred weeks after the initiation of therapy. Mortality was 13%. All cases had a type I Brugada pattern during drug therapy. Nevertheless, their ECG in the absence of drugs was more frequently abnormal than the ECG of controls (56% vs 33%, P = o.04). Among the cases, 36 (49%) were induced by psychotropic drugs, 20 (27%) were induced by analgesic–anesthetic drugs, and 18 (24%) were induced by other noncardiac drugs. The most frequently reported agent was intravenous propofol (20% of cases). The most frequently reported oral agents were lithium (20%) and amitriptyline (16%). The complete list of drugs can be found at www.brugadadrugs.org (Konigstein M et al, *Heart Rhythm* 2016; 13:1083–1087).

Important Review and Other Articles

- 2015 ACC/AHA/HRS Guideline for the management of supraventricular tachycardia (Page RL et al, *J Am Coll Cardiol* 2016;67:1575-1623), Risk stratification for arrhythmic events in patients with asymptomatic pre-excitation (Al-Khatib SM et al, *J Am Coll Cardiol* 2016;67:1624-1638), Drug-induced QT prolongation and torsade de pointes (Schwartz PJ, Woosley RL, *J Am Coll Cardiol* 2016;67:1639-1650), Kawasaki disease (Newburger JW et al, *J Am Coll Cardiol* 2016;67:1738-1749), Treatment of venous thromboembolism with new anticoagulants (Becattini C & Agnelli G, *J Am Coll Cardiol* 2016;67:1941-1955), Constrictive pericarditis vs restrictive cardiomyopathy (Garcia MJ, *J Am Coll Cardiol* 2016;67:2061-2076), Asymptomatic severe aortic stenosis (Généreux *P et al, J Am Coll Cardiol* 2016;67:2263-2288), Sinus node and atrial arrhythmias (John RM & Kumar S, *Circulation* 2016;133:1892-1900), Dilated cardiomyopathy (Japp AG et al, *J Am Coll Cardiol.* 2016;67:2996-3010), Acute ischemic stroke intervention (Khandelwal P et al, *J Am Coll Cardiol* 2016;67:2631-2644), Statin-associated side effects (Thompson *PD et al, J Am Coll Cardiol* 2016;67:2395-2410), Heavy metals, cardiovascular disease, and the unexpected benefits of chelation therapy (Lamas GA et al, *J Am Coll Cardiol* 2016;67:2411-2418), Heparin-induced thrombocytopenia (Salter *BS et al, J Am Coll Cardiol* 2016;67:2519-2532), Peripartum cardiomyopathy (Arany Z & Elkayam U, Circulation 2016;133:1397-1409), Early repolarization (Patton KK et al, *Circulation* 2016;133:1520-1529), AHA advisory for the wearable cardioverter defibrillator (Piccini JP et al, Circulation 2016;133:1715-1727), Ivabradine (Psotka MA & Teerlink JR, *Circulation* 2016;133:2066-2075), Coronary artery bypass (Alexander JH & Smith PK, *N Engl J Med* 2016; 374:1954-1964), Aspirin for primary prevention of CVD (Guirguis-Blake JM, *Ann Intern Med* 2016;164:804-13), The role of obesity in atrial fibrillation (Nalliah CJ et al, *Eur Heart J* 2016; 37:1565-1572), Updated EHRA practical guide on use of NOACs (Heidbuchel H et al, *Europace* 2015;17:1467–1507), How to perform His bundle pacing (Dandamudi G & Vijayaraman P, *Heart Rhythm* 2016;13:1362–1366).