Cardiology News / Recent Literature Review / Last Quarter 2017

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ACC.18 Congress: Orlando, FL, 10-12/3/2018

EHRA Meeting: Barcelona, 18-20/3/2018

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ESC Meeting: Munich, 25-29/8/2018

SPAIN Study: Dual-Chamber Pacing With Closed Loop Stimulation (DDD-CLS) Reduced Syncope Burden and Time to First Recurrence by 7-Fold, and Prolonged Time to First Syncope Recurrence in Patients Age≥40 Years With Tilt-Induced Cardio-inhibitory Vasovagal Syncope

DDD-CLS pacing is a rate-responsive mode that uses intracardiac impedance as a surrogate of cardiac contractility to adapt heart rate to patient needs. Among 46 patients, aged 56.30 ± 10.63 years, with tilt-induced cardioinhibitory vasovagal syncope, the proportion of patients with ≥50% reduction in the number of syncopal episodes was 72% with DDD-CLS compared with 28% with sham DDI mode (p=0.017). A total of 4 patients (8.7%) had events during DDD-CLS and 21 (45.7%) during sham DDI (hazard ratio: 6.7). Kaplan-Meier curve was significantly different between groups in time to first syncope: 29.2 months vs 9.3 months (p< 0.016); odds ratio: 0.11 (p< 0.0001) (Baron-Esquivias G et al, *J Am Coll Cardiol* 2017;70: 1720–28)**.**

PESA Study: Skipping Breakfast is Associated With an Increased Odds of Prevalent Noncoronary and Generalized Atherosclerosis Independently of the Presence of Conventional CV Risk Factors

Three patterns of breakfast consumption were studied: high-energy breakfast, when contributing to >20% of total daily energy intake (27% of the population); low-energy breakfast, when contributing between 5% and 20% of total daily energy intake (70% of the population); and skipping breakfast, when consuming <5% of total daily energy (3% of the population). Independent of the presence of traditional and dietary cardiovascular (CV) risk factors, and compared with high-energy breakfast, habitual skipping breakfast was associated with a higher prevalence of noncoronary (odds ratio-OR: 1.55) and generalized (OR: 2.57) atherosclerosis (Uzhova I et al, *J Am Coll Cardiol* 2017;70: 1833-42).

"Real life" Longevity of Implantable Cardioverter-Defibrillator Devices (ICDs) Turns out Much Shorter than Manufacturers' Projected Longevity

Manufacturers of implantable cardioverter-defibrillators (ICDs) promise a 5- to 9-year projected longevity; however, real-life data indicate otherwise. Over 20 years, among 685 ICD patients (601 men; age, 63.1 ± 13.3 years) with coronary (n = 396) or valvular (n = 15) disease, cardiomyopathy (n = 220), or electrical disease (n = 54) (mean ejection fraction 35%) and devices implanted for secondary (n = 562) or primary (n = 123) prevention (292 single-, 269 dual-chamber and 124 CRT devices implanted in the abdomen in 17 or chest in 668), ICD pulse generator replacements were performed in 238 patients. These were 209 men and 29 women, aged 63.7 ± 13.9 years, with ejection fraction of 37.7% ± 14.0%, who had an ICD for secondary (n = 210) or primary (n = 28) prevention. The mean ICD longevity was 58.3 ± 18.7 months. In 20 (8.4%) patients, devices exhibited premature battery depletion within 36 months. Most (94%) patients had none, minor, or modest use of ICD therapy. Longevity was longest for single-chamber devices and shortest for CRT devices. Latest-generation devices replaced over the second decade lasted longer compared with devices replaced during the first decade. When analyzed by manufacturer, Medtronic devices appeared to have longer longevity by 13 to 18 months. The authors concluded that ICDs continue to have limited longevity of 4.9 ± 1.6 years, and 8% demonstrate premature battery depletion by 3 years. CRT devices have the shortest longevity (mean, 3.8 years) by 13 to 17 months, compared with other ICD devices (Manolis AS et al, *Clin Cardiol* 2017;40:759-764).

CAMERA-MRI Study: AF is an Underappreciated Reversible Cause of Left Ventricular Systolic Dysfunction (LVSD) Despite Adequate Rate Control / Restoration of Sinus Rhythm With Catheter Ablation (CA) Results in Significant Improvements in Ventricular Function, Particularly in the Absence of Ventricular Fibrosis on Cardiac MRI (CMR)

Among patients (N=68) with persistent AF and idiopathic cardiomyopathy (LVEF ≤45%; average AF burden post-CA 1.6 ± 5.0% at 6 months), randomized to CA or medical therapy, absolute LVEF improved by 18 ± 13% in the CA group compared with 4.4 ± 13% in the medical group (p< 0.0001) and normalized (LVEF≥50%) in 58% vs 9% (p=0.0002). In those undergoing CA, the absence of late gadolinium enhancement predicted greater improvements in absolute LVEF (10.7%; p=0.0069) and normalization at 6 months (73% vs 29%; p=0.0093) (Prabhu S et al, *J Am Coll Cardiol* 2017;70:1949–61).

Brugada Syndrome (BrS): ICD Therapy is an Effective Therapy in High-Risk Patients With BrS, Albeit with a Significant Risk of Device-Related Complications

Among 104 patients with BrS having ICDs, for secondary prevention in 10 (9.6%) and primary prevention in 94 (90.4%), over 9.3 ± 5.1 years, 21 patients (20.2%) experienced 81 appropriate shocks. The rate of appropriate shocks was higher in secondary prevention patients ($p<0.01$). However, 4 of the 45 asymptomatic patients (8.9%) experienced appropriate ICD therapy, all with a spontaneous type 1 ECG and inducible ventricular arrhythmias. In multivariable analysis, type 1 ECG with syncope (hazard ratio -HR: 4.96; $p< 0.01$) and secondary prevention indication (HR: 6.85; $p< 0.01$) were significant predictors of appropriate therapy. A total of 37 inappropriate shocks occurred in 9 (8.7%), other ICD-related complications in 21 (20.2%), and deaths in 3 patients (2.9%) (1 electrical storm and 2 non-cardiovascular deaths) (Hernandez-Ojeda J et al, *J Am Coll Cardiol* 2017;70:1991-2002).

A High Percentage (49%) of 110 PFO/ASD Patients Were Also Migraine Sufferers / Percutaneous Closure Offered Migraine Relief in 83% of Patients, 82% in PFO Patients and 89% in ASD Patients

In 110 patients, the impact of PFO (n=75) /ASD (n=35) closure on migraine was investigated. Closure was effected with an Amplatzer occluder in a simplified procedure, performed under local anesthesia with use of fluoroscopy alone without intra-procedural echocardiographic guidance. Complete sealing was obtained in 98.7% of PFO and 94.3% of ASD patients. All patients received dual antiplatelet therapy for 6 months. Among 54 (49%) patients suffering from migraine before the procedures (45 PFO and 9 ASD patients), improvement (50%) or abolition (33.3%) of migraine occurred in 45 patients, 37 (82.2%) PFO and 8 (88.9%) ASD patients, yielding an overall favorable effect of 83.3%. An atrial septal aneurysm was present in 44 (58.7%) PFO patients, which has been considered an important predictor of migraine occurrence in PFO patients. Importantly, the favorable effect extended beyond the 6-month period when dual antiplatelet therapy was discontinued. Based on this experience and on literature review, a strategic approach for device closure is proposed for migraineurs with a PFO or ASD (Manolis AS, *Rev Recent Clin Trials* 2017;12:129-138).

BIOSTAT-CHF / PCSK9-LDL Receptor (LDLR) Axis: Heart Failure (HF) Risk was Positively Associated with Circulating PCSK9 and Negatively Associated with LDLR in Patients with Worsening HF

In 2,174 HF patients (aged 68±12 years; 53.2% with history of ischemic heart disease), during follow-up, multivariable analysis revealed a positive linear association between PCSK9 levels and risk of mortality (hazard ratio -HR: 1.24; $p=0.020$) and the composite endpoint (mortality or hospitalization for HF) (HR: 1.21; $p=0.010$). A similar analysis for LDLR revealed a negative association with mortality (HR: 0.86; $p=0.025$) and the composite endpoint (HR: 0.92; $p=0.087$). Including PCSK9 and LDLR improved risk score performance (Bayes-Genis A et al, *J Am Coll Cardiol* 2017;70:2128-36).

PARADIGM-HF and ATMOSPHERE: Among Heart Failure (HF) Patients With a History of AF, Those With Paroxysmal AF (PAF) were at Greater Risk of HF Hospitalization and Stroke than Patients with Persistent or Permanent AF, Underlining the Importance of Anticoagulant Therapy / New Onset AF was Associated With Increased Risk of All Outcomes

Among 15,415 HF patients (35.6% with history of AF, 30% of these with PAF), patients with PAF had a higher risk of the primary composite endpoint of CV death or HF hospitalization (HR: 1.20; $p< 0.001$), HF hospitalization (HR: 1.34; $p< 0.001$), and stroke (HR: 1.34; $p=0.037$), whereas the respective risks in patients with persistent or permanent AF were not elevated. Neither type of AF was associated with higher mortality. New onset AF was associated with the greatest risk of adverse outcomes: primary endpoint (HR: 2.21), HF hospitalization (HR: 2.11), stroke (HR: 2.20), and all-cause mortality (HR: 2.26), all $p < 0.001$, compared with patients without AF. Anticoagulants were used less often in patients with PAF (53%) and new-onset (16%) AF than in patients with persistent or permanent AF (71%). (Mogensen UM et al, *J Am Coll Cardiol* 2017;70: 2490-2500).

Among Patients Hospitalized With Heart Failure (HF), Ejection Fraction (EF) did not Influence a Poor 5-Year Survival and Elevated Risk for Cardiovascular and HF Admission

Among 39,982 patients admitted for HF, 18,299 (46%) had HF with preserved EF ≥50% (HFpEF), 3,285 (8.2%) had HF with borderline EF 41%-49% (HFbEF), and 18,398 (46%) had HF with reduced EF ≤40% (HFrEF). Overall, median survival was 2.1 years. In risk-adjusted survival analysis, all 3 groups had similar 5-year mortality (HFrEF 75.3% vs HFpEF 75.7%; hazard ratio-HR: 0.99; HFbEF 75.7% vs HFpEF 75.7%; HR: 0.99). The composite of mortality and rehospitalization was similar for all subgroups. Cardiovascular and HF readmission rates were higher in those with HFrEF and HFbEF compared with those with HFpEF (Shah KS et al, *J Am Coll Cardiol* 2017;70:2476-86).

COMPASS Trial: Patients with Stable Atherosclerotic Disease, Assigned to Rivaroxaban (2.5 mg bid) Plus Aspirin, Had Better CV Outcomes but More Major Bleeding Events Than Those Assigned to Aspirin Alone

Among 27,395 participants randomized to rivaroxaban (2.5 mg bid) plus aspirin (100 mg qd), rivaroxaban (5 mg bid), or aspirin (100 mg qd), the primary outcome (CV death, stroke, or MI) occurred in fewer patients in the rivaroxaban-plus-aspirin group than in the aspirin-alone group (379 patients -4.1% vs 496 patients -5.4%; hazard ratio-HR, 0.76; P<0.001), but major bleeding events occurred in more patients in the rivaroxaban-plus-aspirin group (288 patients -3.1% vs 170 patients -1.9%; HR, 1.70; P<0.001). There was no difference in intracranial or fatal bleeding. There were 313 deaths (3.4%) in the rivaroxaban-plus-aspirin group vs 378 (4.1%) in the aspirin-alone group (HR, 0.82; P=0.01). The primary outcome did not differ between patients in the rivaroxaban-alone group and the aspirin-alone group, but major bleeding events occurred in more patients in the rivaroxaban-alone group (Eikelboom JW et al, *N Eng J Med* 2017;377:1319-30).

RE-DUAL PCI: Among Patients With AF Having Had PCI, the Risk of Bleeding was Lower Among Those Who Received Dual Therapy With Dabigatran and a $P2Y_{12}$ Inhibitor Than Among Those Who Received Triple Therapy With Warfarin, a $P2Y_{12}$ Inhibitor, and Aspirin / Dual was Noninferior to Triple Therapy Regarding Thromboembolic Events

Among 2725 AF patients who had PCI, randomized to triple therapy (warfarin plus clopidogrel or ticagrelor) and aspirin (for 1-3 months) (triple-therapy group) or dual therapy with dabigatran (110 mg or 150 mg bid) plus a $P2Y_{12}$ inhibitor (clopidogrel or ticagrelor) and no aspirin (110-mg and 150-mg dual-therapy groups), the incidence of the primary end point was 15.4% in the 110-mg dual-therapy group vs 26.9% in the triple-therapy group (hazard ratio-HR, 0.52; P<0.001 for noninferiority & superiority) and 20.2% in the 150-mg dual-therapy group vs 25.7% in the triple-therapy group, which did not include elderly patients outside the United States (HR, 0.72; P<0.001 for noninferiority). The incidence of the composite efficacy end point was 13.7% in the two dual-therapy groups combined vs 13.4% in the triple-therapy group (HR, 1.04; P=0.005 for noninferiority). The rate of serious adverse events did not differ significantly among the groups. (Cannon CP et al, *N Engl J Med* 2017;377:1513-24).

PREMIUM: PFO Closure did not Meet the Primary Endpoint of 50% Reduction in Migraine Attacks and Adverse Events in Patients With Frequent Migraine

Among 230 PFO patients with migraine, there was no difference in responder rate in the PFO closure (45 of 117) vs control (33 of 103) groups. One serious adverse event (transient AF) occurred in 205 subjects who underwent PFO closure. Subjects in the PFO closure group had a significantly greater reduction in headache days (–3.4 vs –2.0 days/month, p=0.025). Complete migraine remission for 1 year occurred in 10 patients (8.5%) in the treatment group vs 1 (1%) in the control group (p=0.01) (Tobis JM et al, *J Am Coll Cardiol* 2017;70:2766-74).

The Long-Term Mortality Benefit Associated With a Mechanical vs a Biologic Prosthesis, Persisted Until Age 70 Among Patients Undergoing Mitral-Valve Replacement (MVR) and Until Age 55 Among Those Undergoing Aortic-Valve Replacement (AVR)

From 1996 through 2013, the use of biologic prostheses increased substantially for AVR and MVR, from 11.5% to 51.6% for AVR and from 16.8% to 53.7% for MVR. Among patients who underwent AVR, receipt of a biologic prosthesis was associated with higher 15-year mortality than receipt of a mechanical prosthesis among patients 45 to 54 years of age (30.6% vs. 26.4% at 15 years; hazard ratio-HR, 1.23; P=0.03) but not among patients 55 to 64 years of age. Among patients who underwent MVR, receipt of a biologic prosthesis was associated with higher mortality than receipt of a mechanical prosthesis among patients 40 to 49 years of age (44.1% vs 27.1%; HR, 1.88; P<0.001) and among those 50 to 69 years of age (50% vs. 45.3%; HR, 1.16; P=0.01). The incidence of reoperation was significantly higher among recipients of a biologic prosthesis than among recipients of a mechanical prosthesis. Patients who received mechanical valves had a higher cumulative incidence of bleeding and, in some age groups, stroke than did recipients of a biologic prosthesis. (Goldstone AB et al, *N Engl J Med* 2017;377:1847-57).

Compared With the Early-Generation Devices, TAVI Using the New-Generation Devices was Associated with Improved Procedural Outcomes in Patients With Pure Native Aortic Regurgitation (AR) / In Patients With Pure Native AR, Significant Post-Procedural AR was Independently Associated With Increased Mortality

A total of 331 patients with AR and mean STS score of 6.7 ± 6.7 underwent TAVI. The new-generation devices (n=212) were associated with a significantly higher device success rate (81.1% vs 61.3%; p< 0.001) due to lower rates of second valve implantation (12.7% vs 24.4%; p=0.007) and post-procedural AR ≥moderate (4.2% vs 18.8%; p< 0.001). There were no significant differences in major 30-day endpoints between the 2 groups. The cumulative rates of all-cause and cardiovascular death at 1-year follow-up were 24.1% and 15.6%, respectively. On multivariable analysis, post-procedural AR≥ moderate was independently associated with 1-year all-cause mortality

(hazard ratio: 2.85; p=0.001) (Yoon SH et al, *J Am Coll Cardiol* 2017; 70:2752-63).

ASSERT II: Subclinical Atrial Fibrillation (SCAF) Frequently Detected by Continuous ECG Monitoring in Older Patients Without a History of AF Attending Outpatient Cardiology and Neurology Clinics

Among 256 patients (aged ≥65; mean CHA_2DS_2-VASc score was 4.1±1.4; left atrium 4.7±0.8 cm; 48% with prior stroke, TIA, or systemic embolism) with an implanted s.c. ECG monitor, followed up for 16.3±3.8 months, SCAF ≥5 min was detected in 90 patients (detection rate, 34.4%/y). Baseline predictors of SCAF were increased age (hazard ratio -HR per decade, 1.55), left atrial dimension (HR per centimeter diameter, 1.43), and blood pressure (HR per 10 mm Hg, 0.87), but not prior stroke. The rate of occurrence of SCAF in those with a history of stroke, systemic embolism, or TIA was 39.4%/y vs 30.3%/y without (*P*=0.32). The cumulative SCAF detection rate was higher (51.9%/y) in those with left atrial volume above the median value of 73.5 mL (Healey JS et al, *Circulation* 2017;136:1276-83).

Cardiac Implantable Electronic Device (CIED) Lead Extraction Can be Successful with Mechanical Tools Using the Lead-Locking Device (LLD) Stylet Aided by Non-Powered Telescoping Sheaths Through a Simple, Safe, & Inexpensive Procedure Using Local Anesthesia

Among 54 patients (38 men and 16 women aged 68.9±13.1 years), 98 leads were percutaneously extracted (78 pacing (31 ventricular, 37 atrial, 4 VDD, 6 coronary sinus leads) and 20 defibrillating leads) for device infection (n=46) (more commonly due to Staphylococcus species, n=40), lead malfunction (n=5), or prior to defibrillator implant (n=3). Leads were in place for 6.7±4.3 years. Using simple traction (6 leads) and the LLD stylets (92 leads) aided with telescoping sheaths (15 patients), 96 (98%) leads in 52 (96.3%) patients were successfully removed, with all but one lead removed using a subclavian approach; in 1 patient, the right femoral approach was also required. In 2 patients, distal fragments from one ventricular pacing and one defibrillating lead could not be removed. Finally, lead removal was completely (52/54) (96.3%) or partially (2/54) (3.7%) successful in 54 patients for 96 of 98 leads (98%) without major complications (Manolis AS et al, *Anatol J Cardiol* 2017;18:289-295).

Lead Extraction for Noninfectious Indications Had Similar Long-Term Survival to That with Capping and Abandoning Leads / However, Extraction was Associated With Lower Risk of Device Infections at 5 Years

Among 6859 patients, 1113 (16.2%) undergoing extraction and 5746 (83.8%) capping and abandonment, the overall 1-year and 5-year mortality was 13.5% and 54.3%, respectively. Extraction was associated with a lower risk of device infection at 5 years relative to capping (adjusted hazard ratio, 0.78; *P*=0.027). There was no association between extraction and mortality, lead revision, or lead extraction at 5 years (Pokorney SD et al, *Circulation* 2017;136:1387-1395).

ELECTRa Study: Confirmed the Safety and Efficacy of Current Practice of Transvenous Lead Extraction (TLE)/Higher Success Rate With Lower Complications and Mortality in High vs Low Volume Centers

Among 3510 patients undergoing TLE, the primary endpoint of in-hospital procedure-related major complication rate was 1.7% (58/3510 pts) including a mortality of 0.5% (17/3510 pts). About two-thirds (37/58) of these complications occurred during the procedure and one-third (21/58) in the post-operative period. The most common procedure related complications were those requiring pericardiocentesis or chest tube and/or surgical repair (1.4%). Complete clinical and radiological success rates were 96.7% and 95.7%, respectively. The all cause in-hospital major complications and deaths were significantly lower in high (≥30 procedures/y) volume (HiV) centers vs low (<30/y) volume (LoV) centers (2.4% vs 4.1%, $P = 0.0146$; and 1.2% vs 2.5%, $P = 0.0088$), although those related to the procedure did not reach statistical significance. Radiological and clinical successes were more frequent in HiV vs LoV centers (Bongiorni MG et al; *Eur Heart J* 2017;38:2995-3005).

EARLY-MYO Trial: For Patients With STEMI Presenting ≤6h After Symptom Onset and With an Expected PCI-Related Delay, a Pharmacoinvasive (PhI) Strategy With Half-Dose Alteplase and Timely (3-24h) PCI Offers More Complete Reperfusion When Compared With Primary PCI (PPCI)

Among 344 patients randomized to PhI strategy (half-dose alteplase of 8-mg bolus followed by 42 mg in 90 min) (n=171) or PPCI (n=173), PhI was noninferior (and even superior) to PPCI for the primary end point (complete reperfusion) (34.2% vs 22.8%, $P_{noninferiority}<0.05$, $P_{superiority}=0.022$), with no significant differences in the frequency of: TIMI flow 3 (91.3% vs 89.2%, *P*=0.580), myocardial perfusion grade 3 (65.8% vs 62.9%, *P*=0.730), and ST-segment resolution ≥70% (50.9% vs 45.5%, *P*=0.377). Infarct size (23.3%±11.3% vs 25.8%±13.7%, *P*=0.101) and LVEF (52.2%±11.0% vs 51.4%±12.0%, *P*=0.562) were similar. No significant differences occurred in 30-day rates of total death (0.6% vs 1.2%, *P*=1.0), reinfarction (0.6% vs 0.6%, *P*=1.0), heart failure (13.5% vs 16.2%, *P*=0.545), major bleeding (0.6% vs 0%, *P*=0.497), or

intracranial hemorrhage (0% vs 0%), but minor bleeding (26.9% vs 11.0%, *P*<0.001) was observed more often in the PhI group (Pu J et al, *Circulation* 2017;136:1462-1473).

Cardiac Myosin-Binding Protein C (cMyC) at Presentation Provides Discriminatory Power Comparable to hs-cTn in the Diagnosis of Acute Myocardial Infarction (AMI) and May Perform Favorably in Patients Presenting Early After Symptom Onset

cMyC, a cardiac-restricted protein, more abundant than cardiac troponins (cTn), released more rapidly after acute myocardial infarction (AMI), was measured in 1954 patients presenting to the emergency department with symptoms suggestive of AMI (finally diagnosed in 340 patients or 17%). Concentrations of cMyC at presentation were significantly higher in those with vs without AMI (median, 237 ng/L vs 13 ng/L, *P*<0.001). Discriminatory power for AMI was comparable for cMyC, hs-cTnT, and hs-cTnI and superior to cTnI measured by a contemporary sensitivity assay. Use of cMyC more accurately classified patients with a single blood test into rule-out or rule-in categories. In early presenters (chest pain <3 h), the improvement in rule-in/rule-out classification with cMyC was larger compared with hs-cTnT and hs-cTnI (*P*<0.001). Comparing the C statistics, cMyC was superior to hs-cTnI and standard sensitivity cTnI (*P*<0.05 for both) and similar to hs-cTnT at predicting death at 3 years (Kaier TE et al, *Circulation* 2017;136:1495-1508).

Bilateral Internal Mammary Artery (BIMA) Grafting was Associated With a Reduced Risk of Repeat Revascularization and an Improvement in Long-Term Survival and Should be Considered More Frequently During Coronary Artery Bypass Grafting (CABG)

Amon 47,984 consecutive CABGs, over a median of 13.2 years, there was a higher freedom from repeat revascularization among patients receiving BIMA than those receiving single IMA (hazard ratio -HR, 0.78; *P*=0.009). Among the matched cohort, 19.4% (n=252) of patients receiving single IMA underwent repeat revascularization (majority PCI), whereas this frequency was 15.1% (n=196) among patients receiving BIMA (*P*=0.004). BIMA grafting was associated with a reduction in all-cause mortality at 12 years of follow-up (HR, 0.79; *P*=0.001), and there was no difference in in-hospital morbidity (Iribarne A et al, *Circulation* 2017;136:1676-85).

In Euthyroid Individuals, Higher Circulating Free T4 (fT4) Levels, but not TSH Levels, are Associated With Increased Risk of Incident AF

Of 30 085 participants from 11 cohorts, 1958 (6.5%) had subclinical hypothyroidism and 2574 individuals (8.6%) developed AF during follow-up. TSH at baseline was not significantly associated with incident AF in euthyroid participants or those with subclinical hypothyroidism. Higher fT4 levels at baseline in euthyroid individuals were associated with increased AF risk in age- and sex-adjusted analyses (hazard ratio, 1.45, for the highest quartile vs the lowest quartile of fT4; *P* for trend ≤0.001 across quartiles) (Baumgartner C et al, *Circulation* 2017;136:2100-16).

***TROPICAL-ACS:* Guided De-Escalation of Antiplatelet Treatment was Non-Inferior to Standard Treatment With Prasugrel at 1 Year After PCI**

Among 2610 ACS patients undergoing PCI, assigned to the guided de-escalation group (stage-adapted treatment with potent platelet inhibition in the acute phase and de-escalation to clopidogrel in the maintenance phase: 1 week prasugrel followed by 1 week clopidogrel and platelet function testing-guided maintenance therapy with clopidogrel or prasugrel from day 14 after hospital discharge) (N=1304), or to the control group (prasugrel for 12 months) (N=1306). The primary endpoint occurred in 95 patients (7%) in the guided de-escalation group and in 118 patients (9%) in the control group ($p_{non\text{-}inferiority}$=0.0004; hazard ratio -HR 0.81, $p_{superiority}$=0.12). Despite early de-escalation, there was no increase in the combined risk of CV death, MI, or stroke in the de-escalation group (32 patients [3%]) vs in the control group (42 patients - 3%; $p_{non\text{-}inferiority}$=0.0115). There were 64 bleeding events (5%) in the de-escalation group vs 79 events (6%) in the control group (HR 0.82; p=0.23) (Sibbin S et al, *Lancet* 2017;390: 1747-57).

PURE: Higher Fruit, Vegetable, and Legume Consumption (3-4 Servings or 375-500 g/d) was Associated With a Lower Risk of Non-Cardiovascular, and Total Mortality

Among 135 335 individuals aged 35-70 years without cardiovascular (CV) disease, over a median 7.4 years, higher total fruit, vegetable, and legume intake was inversely associated with major CV disease, MI, CV mortality, non-CV mortality, and total mortality by univariate analysis. The estimates were substantially attenuated in the multivariable adjusted models for major CV disease (hazard ratio - HR 0.90, p_{trend}=0.1301), MI (HR 0.99; p_{trend}=0.2033), stroke (HR 0.92; p_{trend}=0.7092), CV mortality (HR 0.73; p_{trend}=0.0568), non-CV mortality (HR 0.84; p_{trend}=0·0038), and total mortality (HR 0.81; p_{trend}<0·0001). The HR for total mortality was lowest for 3-4 servings per day (HR 0.78) compared with the reference group, with no further apparent decrease in HR with higher consumption. When examined separately, fruit

intake was associated with lower risk of CV, non-CV, and total mortality, while legume intake was inversely associated with non-CV death and total mortality. For vegetables, raw vegetable intake was strongly associated with a lower risk of total mortality, whereas cooked vegetable intake showed a modest benefit against mortality (Miller V et al, *Lancet* 2017;390:2037-49).

PURE: High Carbohydrate Intake was Associated With Higher Risk of Total Mortality, While Total Fat and Individual Types of Fat Were Related to Lower Total Mortality / Total Fat and Types of Fat Were not Associated With Cardiovascular Disease (CVD), MI, or CVD Mortality, Whereas Saturated Fat Had an Inverse Association With Stroke

Analysis of the dietary intake of 135 335 individuals indicated that higher carbohydrate intake was associated with an increased risk of total mortality (highest 5 *vs* lowest 1 quintile, HR 1.28, p_{trend}=0·0001) but not with the risk of CVD or CVD mortality. Intake of total fat and each type of fat was associated with lower risk of total mortality (quintile 5 *vs* quintile 1, total fat: HR 0.77, p_{trend}<0.0001; saturated fat, HR 0.86, p_{trend}=0·0088; monounsaturated fat: HR 0.81, p_{trend}<0·0001; and polyunsaturated fat: HR 0.80, p_{trend}<0·0001). Higher saturated fat intake was associated with lower risk of stroke (quintile 5 *vs* quintile 1, HR 0·79, p_{trend}=0.0498). Total fat and saturated and unsaturated fats were not significantly associated with risk of MI or CVD mortality (Dehghan M, et al, *Lancet* 2017;390:2050-62).

PURE: Higher Physical Activity Conferred a Lower Risk of Mortality and Cardiovascular Disease (CVD) Events in Individuals from Low-, Middle-, and High-Income Countries / Increasing Physical Activity is a Simple, Widely Applicable, Low Cost Global Strategy That Could Reduce Deaths and CVD in Middle Age

Among 130,843 participants without pre-existing CVD, compared with low physical activity (<600 MET × min/week or <150 min/w of moderate intensity physical activity), moderate (600–3000 MET × min or 150–750 min/w) and high physical activity (>3000 MET × min or >750 min/w) were associated with graded reduction in mortality (hazard ratio - HR 0·80, and 0·65; p<0·0001 for trend), and major CVD (HR 0.86; p<0·001 for trend). Higher physical activity was associated with lower risk of CVD and mortality in high-, middle-, and low-income countries. The adjusted population attributable fraction for not meeting the physical activity guidelines was 8% for mortality and 4.6% for major CVD, and for not meeting high physical activity was 13% for mortality and 9.5% for major CVD. Both recreational and non-recreational physical activity were associated with benefits (Lear SA et al, *Lancet* 2017;390:2643-54).

SPYRAL HTN-OFF MED: Results Provide Biological Proof of Principle for the Blood-Pressure-Lowering Efficacy of Renal Denervation

Results of prior randomized renal denervation studies were inconsistent. A new study evaluated the effect of renal denervation on blood pressure (BP) in the absence of antihypertensive medications in 80 patients with an office systolic BP (SBP) of ≥150 mmHg and <180 mmHg, diastolic BP (DBP) of ≥90 mmHg, and a mean 24-h ambulatory SBP of ≥140 mmHg and <170 mmHg, randomly assigned to renal denervation (n=38) or sham control (n=42) and followed up for 3 months. Office and 24-h ambulatory BP decreased significantly from baseline to 3 months in the renal denervation group: 24-h SBP −5.5 mmHg (p=0.0031), 24-h DBP −4.8 mm Hg (p<0.0001), office SBP −10 mmHg (p=0.0004), and office DBP −5.3 mmHg (p=0.0002). No significant changes were seen in the sham-control group. The mean difference between the groups favoured renal denervation for 3-month change in both office and 24-h BP from baseline. Baseline-adjusted analyses showed similar findings. There were no major adverse events in either group (Townsend RR et al, *Lancet* 2017;390:2160-70).

Everolimus-Eluting Bioresorbable Scaffolds (BVSs) vs Everolimus-Eluting Metallic Stents (EESs): BVSs Increased the Risks for Scaffold Thrombosis and Other Thrombotic Events at Mid- and Long-Term Follow-Up, and Risks Increased Over Time

Meta-analysis of 7 randomized and 38 observational studies indicated an incidence of definite or probable scaffold thrombosis after BVS implantation of 1.8% at a median of 1 year (41 studies, 21,884 patients) and 0.8% beyond 1 year (14 studies, 4688 patients). Seven trials involving 5578 patients that directly compared BVSs with EESs showed an increased risk for scaffold thrombosis (odds ratio - OR, 3.40) with BVSs at a median follow-up of 25 months. Increased risks were present at early (prominently subacute), late, and very late stages, and odds beyond 1 year were almost double those seen within 1 year. BVSs increased risks for MI (OR, 1.63), target lesion revascularization (OR, 1.31), and target lesion failure (OR, 1.37). Incidences of all-cause, cardiac, and noncardiac death and of target vessel and any revascularization did not differ (Zhang X-L et al, *Ann Intern Med* 2017;167:642-54).

Patients with non-STEMI (NSTEMI) Who Demonstrate a Totally Occluded Culprit Vessel on Coronary Angiography are at Higher Risk of Mortality and Major Adverse Cardiac Events

According to 7 studies with 40,777 NSTEMI patients, 10,415 (25.5%) had an occluded culprit artery with a predominant infero-lateral distribution (40% right

coronary and 33% left circumflex artery). There was an increased risk of both MACE (short-term RR: 1.41; $P = 0.0003$; medium- to long-term RR: 1.32; $P = 0.001$) and all-cause mortality (short-term RR: 1.67; $P < 0.0001$; medium to long-term RR: 1.42; $P = 0.01$) with total occlusion of the culprit artery (Khan AR et al, *Eur Heart J* 2017; 38:3082-89).

Greater Reductions in Left Ventricular (LV) Mass With Sacubitril/ Valsartan Compared to Olmesartan

Among 114 hypertensive patients receiving sacubitril/ valsartan (n=57) or olmesartan (n=57) (mean age 59.8 years; 67.5% male), LV mass index decreased to a greater extent in the sacubitril/valsartan group compared to the olmesartan group from baseline to 12 weeks (−6.36 vs. −2.32 g/m^2; $P = 0.039$) and from baseline to 52 weeks (−6.83 vs. −3.55 g/m^2; $P = 0.029$). These differences remained significant after adjustment for systolic blood pressure (SBP) at follow-up. There were no significant differences in local distensibility changes from baseline to 12 or 52 weeks between the two groups; however, there was a larger reduction in central pulse pressure for the sacubitril/valsartan group ($P = 0.010$) (Schmieder RE et al, *Eur Heart J* 2017; 38: 3308–3317).

PREVAIL & PROTECT AF Trials: 5-Year Outcomes After Left Atrial Appendage Closure (LAAC) in AF Patients Using the Watchman Device / Protection Against Ischemic Stroke and Systemic Embolism was Similar to Warfarin, but LAAC was Associated With Reductions in Hemorrhagic, Disabling and Fatal Stroke, Favorably Influencing Survival

For the PREVAIL trial, the first composite coprimary endpoint of stroke, systemic embolism (SE), or cardiovascular (CV)/unexplained death did not achieve noninferiority, whereas the second coprimary endpoint of post-procedure ischemic stroke/SE did achieve noninferiority; the warfarin arm maintained an unusually low ischemic stroke rate (0.73%). In the meta-analysis (1,114 patients), the composite endpoint was similar between groups (hazard ratio -HR: 0.82), as were all-stroke/SE (HR: 0.96). The ischemic stroke/SE rate was numerically but not statistically higher with LAAC (HR: 1.71; p=0.080). However, differences in hemorrhagic stroke, disabling/ fatal stroke, CV/unexplained death, all-cause death, and post-procedure bleeding favored LAAC (HR: 0.20; p=0.0022; HR: 0.45; p=0.03; HR: 0.59; p=0.027; HR: 0.73; p=0.035; HR: 0.48; p=0.0003, respectively) (Reddy VY et al, *J Am Coll Cardiol* 2017; 70:2964-75).

Hydroquinidine (HQ) Prevents Life-Threatening Arrhythmic Events (LAE) in Patients With Short QT Syndrome (SQTS)

Among 17 SQTS patients (82% male, age 29 ± 3 years, QTc before treatment 331±3 ms) receiving HQ therapy (584 ± 53 mg/day) (stopped in 2 cases due to gastrointestinal intolerance) for 6 ± 1 years, QTc was prolonged in all patients (by 60 ± 6 ms; p< 0.001). Patients on HQ experienced a reduction in both the rate of LAE from 40% to 0% (p=0.03) and the number of LAE per patient from 0.73 ± 0.3 to 0 (p=0.026). The annual rate of LAE in the 16 patients with a previous cardiac arrest dropped from 12% before HQ to 0 on therapy (p=0.028). (Mazzanti A et al, *J Am Coll Cardiol* 2017; 70:3010-5).

In 5 Patients with Refractory VT, Treatment with Noninvasive Electrophysiology (EP)-Guided Cardiac Radioablation Markedly Reduced the Burden of VT

Noninvasive mapping using multielectrode body-surface ECG (256 electrodes) to create a cardiac image and standard cardiac imaging (SPECT or CMR) was used to identify myocardial scar and the arrhythmogenic region ("exit site" of earliest electrical activation) during ventricular tachycardia (VT). This was combined with noninvasive ablation via stereotactic body radiation therapy (SBRT) (commonly used to treat tumors), which delivers precise, high-dose radiation to targets in the body (here a volumetric target for radioablation that targeted the area of the first 10 ms of VT, i.e. the exit site, and the full myocardial thickness of the associated ventricular scar) with minimal damage to normal adjacent tissue, to treat (with a single fraction of 25 Gy) 5 patients with refractory VT, induced and terminated with noninvasive program-med stimulation via an ICD. The mean ablation time was 14 min. During the 3 months before treatment, the patients had a combined history of 6577 episodes of VT. During a 6-week postablation "blanking period" (when arrhythmias may occur owing to postablation inflammation), there were 680 episodes of VT. After the 6-week blanking period, there were 4 episodes of VT over the next 46 patient-months, for a reduction from baseline of 99.9%. A reduction in episodes of VT occurred in all 5 patients. The mean LVEF did not decrease with treatment. At 3 months, adjacent lung showed opacities consistent with mild inflammatory changes, which had resolved by 1 year (Cuculich PS et al, *N Engl J Med* 2017;377:2325-36).

Systematic Review, Network Meta-Analysis, and Cost Effectiveness Analysis: Apixaban Ranks Higher Than Other Direct-Acting Oral Anticoagulants (DOACs) for Preventing Stroke in Atrial Fibrillation (AF) Patients

Analysis of 13 of 23 randomized trials involving 94 656 patients, comparing a DOAC with warfarin,

apixaban 5 mg bid (odds ratio – OR 0.79), dabigatran 150 mg bid (OR 0.65), edoxaban 60 mg qd (OR 0.86), and rivaroxaban 20 mg qd (OR 0.88) reduced the risk of stroke or systemic embolism. The risk of stroke or systemic embolism was higher with edoxaban 60 mg qd (OR 1.33) and rivaroxaban 20 mg qd (OR 1.35) than with dabigatran 150 mg bid. The risk of all-cause mortality was lower with all DOACs than with warfarin. Apixaban 5 mg bid (OR 0.71), dabigatran 110 mg bid (OR 0.80), edoxaban 30 mg qd (OR 0.46), and edoxaban 60 mg qd (OR 0.78) reduced the risk of major bleeding compared with warfarin. The risk of major bleeding was higher with 150 mg-dabigatran than apixaban (OR 1.33), rivaroxaban than apixaban (1.45), and rivaroxaban than 60 mg-edoxaban (OR 1.31). The risk of intracranial bleeding was substantially lower for most DOACs compared with warfarin, whereas the risk of gastrointestinal bleeding was higher with some DOACs than warfarin. Apixaban was ranked the highest for most outcomes, and was cost effective compared with warfarin (López-López JA et al, *BMJ* 2017;359:j5058).

Transseptal Puncture (TSP) for Access to the Left Atrium: Employing a Standardized Protocol with Use of Fluoroscopy Alone Minimized Serious Complications to 0.8% (2 Patients) Among 249 Consecutive Patients Undergoing TSP for Ablation of a Variety of Cardiac Arrhythmias

Among 249 patients (aged 41.6±17.4 years, 146 men, 33 children or young adolescents aged 7-18 years; 14 patients undergoing a repeat procedure) undergoing TSP by a single operator for ablation of a variety of arrhythmias, mostly related to left accessory pathways (n=145), left atrial tachycardias (n=33) or atrial fibrillation (AF) (n=70), TSP was guided by fluoroscopy alone in all patients without the use of echocardiography imaging. Patients with a manifest accessory pathway were the youngest (mean age 33.7±15.9) and patients with AF the oldest (mean age 56.0±10.8 years). A successful TSP was accomplished in 247 patients (99.2%). Two (0.8%) procedures were complicated by cardiac tamponade managed successfully with pericardiocentesis or surgical drainage. Review of the literature revealed no systematic reviews and meta-analyses of TSP studies; however, several patient series have documented that fluoroscopy-guided TSP, with various modifications in the technique employed in the present series, have been effective in 95-100% of the cases with a complication rate ranging from 0.0% to 6.7%, albeit with a mortality rate of 0.018%- 0.2%. Echo imaging techniques were employed in cases with difficult TSP. Based on this single-operator experience and review of the literature, a list of practical tips and tricks is provided for a successful and safe procedure, reserving the more expensive and patient inconveniencing echo-imaging techniques for difficult or failed cases (Manolis AS, *Curr Cardiol Rev* 2017;13: 305-318).

CULPRIT-SHOCK Trial: 30-Day Risk of Death or Severe Renal Failure was Lower Among MI Patients in Cardiogenic Shock Who Initially Underwent PCI of the Culprit Lesion Only Than Among Those Who Underwent Immediate Multivessel PCI

Among 706 patients who had multivessel disease, acute myocardial infarction (MI), and cardiogenic shock randomized to either PCI of the culprit lesion only, with the option of staged revascularization of nonculprit lesions, or immediate multivessel PCI, at 30 days, the composite primary end point of death or renal-replacement therapy had occurred in 158 of the 344 patients (45.9%) in the culprit-lesion-only PCI group and in 189 of the 341 patients (55.4%) in the multivessel PCI group (relative risk, 0.83; P=0.01). The relative risk of death in the culprit-lesion-only PCI group as compared with the multivessel PCI group was 0.84 (P=0.03), and the relative risk of renal-replacement therapy was 0.71 (P=0.07) (Thiele H et al, *N Engl J Med* 2017; 377:2419-32).

Legacy (Non-MRI Conditional) Devices Appear Safe During MRI / With Use of a Safety Protocol in 1509 Patients Undergoing MRI, no Long-Term Clinically Significant Adverse Events Were Reported

Among 1509 patients who had a pacemaker (58%) or an ICD (42%) that was not considered to be MRI-conditional (termed a "legacy" device) undergoing 2103 thoracic and nonthoracic MRI (1.5 Tesla) examinations with the pacing mode changed to asynchronous mode for pacing-dependent patients and to demand mode for other patients and the tachyarrhythmia functions disabled, no long-term clinically significant adverse events were reported. In 9 MRI examinations (0.4%), the patient's device reset (transiently in 8) to a backup mode. In 1 case, a pacemaker with <1 month left of battery life reset to ventricular inhibited pacing (non-reprogrammable/ was replaced). The most common notable change in device parameters (>50% change from baseline) immediately after MRI was a decrease in P-wave amplitude, which occurred in 1% of the patients. At long-term follow-up (results of which were available for 63% of the patients), the most common notable changes from baseline were decreases in P-wave amplitude (4%), and increases in atrial (4%), right ventricular (4%), and left ventricular capture thresholds (3%). The observed changes in lead parameters were not clinically significant and did not require device revision or reprogramming (Nazarian S et al, *N Engl J Med* 2017; 377:2555-64).

In High-Risk Patients With Renal Artery Stenosis (RAS) and Resistant Hypertension, Flash Pulmonary Edema, and/or Rapid Deterioration of Renal Function, Renal Artery Stenting (PRS), a Procedure With High Technical Success, May Constitute a Viable Option

In a series of 9 high-risk RAS patients with resistant hypertension (5 men, mean age 71 years), PRS was successful in all patients without complications and helped in bringing under control their elevated blood pressure (BP) and in maintaining their renal function over a mean of 21 months. Literature review of this controversial topic indicates that in carefully selected patients, PRS may play an important role in controlling BP, alleviating symptoms and perhaps preventing renal failure, albeit without concrete evidence of significantly affecting hard end-points of renal events, major cardiovascular events and death. Randomized controlled studies (RCTs), including the large CORAL trial, although heavily criticized, have not provided evidence in favor of revascularization. Although RCTs are rather neutral, many prospective, observational cohort studies, comparing the outcomes of patients after PRS have demonstrated significant improvement in systolic and diastolic BP in about two thirds and improvement and/or stabilization in renal function in 30-40% of patients undergoing PRS. Nevertheless, the issue remains unsolved and a subject of future studies for further more definitive settlement. There are suggestions to adopt physiological and functional renal lesion assessment that may enhance patient selection, at least for RAS cases of moderate lesion severity (Manolis AS et al, *Curr Hypertens Rev* 2017; *13:* 93-103).

Meta-analysis: The Most Commonly Found New-Onset Arrhythmia Following TAVI is Atrial Fibrillation (AF)

Among 65 studies (43 506 patients) reporting new-onset arrhythmias following TAVI, new-onset AF (2641 patients), bradyarrhythmias (182 patients; 4% prevalence at 1-year follow-up), supraventricular arrhythmias (29 patients), ventricular arrhythmias (28 patients) and non-specified major arrhythmias (855 patients) were reported. In most studies (52 out of 65), new-onset arrhythmia detection was limited to the first month following TAVI. The most frequently documented arrhythmia was AF with trend of increasing summary prevalence of 11%, 14%, 14% and 25% during inhospital, 30-day, 1-year and 2-year follow-ups, respectively (P for trend=0.011). Summary prevalence estimates of new-onset AF at 30-day follow-up differ significantly between studies of prospective and retrospective design (8% and 21%, respectively, P=0.002). New onset AF increased risk of death (relative risk 1.61) & cerebrovascular events (1.79) (Siontis GCM et al, *Heart* 2017 doi: 10.1136/heartjnl-2017-312310. Epub ahead of print)

Important Review and Other Articles

- 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death (Al-Khatib SM et al, *J Am Coll Cardiol* 2017 Oct 25. pii: S0735-1097(17) 41306-4),
- 2017 ACC/AHA/ Hypertension Guidelines (Whelton PK et al, *J Am Coll Cardiol* 2017, 24429; doi: 10.1016/j.jacc.2017.11.005)
- Obesity and atrial fibrillation (Lavie CJ et al, *J Am Coll Cardiol* 2017;70:2022-35),
- Interleukin-1 beta as a target for atherosclerosis therapy (Libby P, *J Am Coll Cardiol* 2017;70:2278-89),
- PCSK-9 inhibitors (Hlatky MA et al, *J Am Coll Cardiol* 2017;70: 2677-87),
- Sudden death risk stratification in dilated cardiomyopathy (Manolis AS, *Expert Rev Cardiovasc Ther* 2017;15:315-325),
- ACC Expert Consensus on management of mitral regurgitation (O'Gara PT et al, *J Am Coll Cardiol* 2017;70:2421-49),
- Cardiovascular complications of cancer therapy (Chang H-M et al, *J Am Coll Cardiol* 2017;70:2536-65),
- Appropriate use criteria for treatment of aortic stenosis (Bonow RO et al, *J Am Coll Cardiol* 2017;70:2566-98),
- VT ablation (Dukkipati SR et al, *J Am Coll Cardiol* 2017;70: 2909-41),
- Wine and cardiovascular health (Haseeb S et al, *Circulation* 2017;136:1434-48),
- Sleep apnea and cardiovascular disease (Drager LF et al, *Circulation* 2017;136: 1840-50),
- Risk stratification in arrhythmogenic right ventricular cardio-myopathy (Calkins H et al, *Circulation* 2017;136:2068-82),
- Handheld echocardiography (Chamsi-Pasha MA et al, *Circulation* 2017;136:2178-88),
- Diuretic treatment in heart failure (Ellison DH & Felker GM, *N Engl J Med* 2017; 377:1964-1975),
- Thrombo-embolic prevention after TAVI (Vranckx P et al, *Eur Heart J* 2017;38: 3341–3350),
- 2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants (Tomaselli GF et al, *J Am Coll Cardiol* 2017;70:3042-67),
- TAVI for severe AS in patients with heart failure & low ejection fraction (Steiner J et al, *J Am Coll Cardiol* 2017;70: 3026-41),
- Cardiac resynchronization therapy (Rao P & Faddis M, *Heart* 2017;103:2000–7),
- Transseptal puncture (Vahanian A & Brochet E*, Heart* 2017;103: 830–1837),
- Transseptal access to the left atrium: tips and tricks (Manolis AS, *Curr Cardiol Rev 2017;13:305-318*),
- TAVI in nonagenarians (Manolis AS & Manolis AA, *Ann Cardiothorac Surg* 2017;6:524-531),
- TAVI economics (Manolis AS, *Ann Cardiothorac Surg 2017;6:516-23*),
- Hypertension and cardiac arrhythmias (Lip G et al, *Europace 2017;19:891-911 & Eur Heart J Cardiovasc Pharmacother 2017;3:235-250*),
- Atrial flutter (Manolis AS, *Cardiol Rev* 2017;25:289-297*),*
- Structure & function of left atrium and left atrial appendage (Delgado V et al*, J Am Coll Cardiol* 2017;70:3157-72)