Cardiology News / Recent Literature Review / First Quarter 2020

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?ESC Meeting: Amsterdam, 29/8-2/9/2020

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?HCS/Panhellenic (41st) Congress of Cardiology: Athens, 22-24/10/20

Persistent Proarrhythmic Neural Remodeling (Characterized by Extracardiac Sympathetic Hyperinnervation and Sympathetic Neural Hyperactivity) Despite Recovery from Premature Ventricular Contraction-Induced Cardiomyopathy (PVC-CM)

In 12 canines, with pacing-applied PVC-CM, after 12 weeks of PVCs, LVEF and dP/dT decreased significantly. Resting sympathetic nerve activity (SNA) and vagal nerve activity (VNA), exercise SNA, SNA response to evoked PVCs, heart rate (HR) at rest, and exercise increased, whereas HR variability (HRV) decreased. There was increased spontaneous atrial and ventricular arrhythmias in PVC-CM. Increased SNA preceded both atrial and ventricular arrhythmia onset. Clonidine suppressed SNA and abolished all arrhythmias. After stopping PVC for 4 weeks, LVEF, dP/dT, and resting VNA recovered to baseline levels. However, SNA, resting HR, HRV, and atrial and ventricular proarrhythmia persisted. Sympathetic hyperinnervation was found in stellate ganglia but not ventricles of PVC-CM and recovered animals versus sham controls. The authors concluded that neural remodeling in PVC-CM is characterized by extracardiac sympathetic hyperinnervation and sympathetic neural hyperactivity that persists despite normalization of LVEF, constituting an important trigger and substrate for atrial and ventricular proarrhythmia (Tan AY et al, *J Am Coll Cardiol* 2020; 75:1-13).

PARAGON-HF: The Benefits of Sacubitril/Valsartan in HFpEF are Present When Initiated in the High-Risk Window Within 180 Days of a Recent Hospitalization

Among 4,796 randomized patients in PARAGON-HF, over a median follow-up of 35 months, risk of total HF hospitalizations and cardiovascular death was inversely and nonlinearly associated with timing from prior HF hospitalization ($p<0.001$). Compared with valsartan, absolute risk reductions with sacubitril/valsartan were more prominent in patients enrolled early after hospitalization: 6.4% (≤1 month), 4.6% (1-3 months), and 3.4% (3-6 months), whereas no risk reduction was observed in patients screened >6 months or who were never hospitalized (trend in absolute risk reduction: $p_{interaction}=0.050$) (Vaduganathan M et al, *J Am Coll Cardiol* 2020; 75:245-54).

Oral Anticoagulation (OAC) for Patients With Atrial Fibrillation (AF) on Long-Term Dialysis: Not Associated With a Reduced Risk of Thromboembolism / Warfarin, Dabigatran, and Rivaroxaban Were Associated With Higher Bleeding Risk Compared With Apixaban and no Anticoagulant

Of 16 observational studies (N=71,877) regarding patients on long-term dialysis who had AF, only 2 studies investigated direct OACs. Outcomes for dabigatran and rivaroxaban were limited to major bleeding events. Compared with no anticoagulants, apixaban and warfarin were not associated with a significant decrease in stroke and/or systemic thromboembolism (apixaban 5 mg, hazard ratio -HR: 0.59; apixaban 2.5 mg, HR: 1.00; warfarin, HR: 0.91). Apixaban 5 mg was associated with a significantly lower risk of mortality (vs. warfarin, HR: 0.65; vs. apixaban 2.5 mg, HR: 0.62; vs. no anticoagulant, HR: 0.61). Warfarin was associated with a significantly higher risk of major bleeding than apixaban 5 mg/2.5 mg and no anticoagulant (vs. apixaban 5 mg, HR: 1.41; vs. apixaban 2.5 mg, HR: 1.40; vs. no anticoagulant, HR: 1.31). Dabigatran and rivaroxaban were also associated with significantly higher risk of major bleeding than apixaban and no anticoagulant (Kuno T et al, *J Am Coll Cardiol* 2019; 75:273-85).

Left Ventricular Septal (LVs) Pacing Provides Short-Term Hemodynamic Improvement and Electrical Resynchronization as Good as Biventricular (Biv) and Possibly His Bundle (HB) Pacing / LVs Pacing May Serve as an Alternative for CRT

Temporary LVs pacing (transaortic approach) alone or in combination with right ventricular (RV) (LVs+RV), BiV, and HB pacing was performed in 27 patients undergoing CRT implantation. As compared with baseline, LVs pacing resulted in a larger reduction in QRS area (to 73 ± 22 μVs) than BiV (to 93 ± 26 μVs; $p<0.05$) and LVs+RV pacing (to 108 ± 37 μVs; $p<0.05$). The increase in LVdP/dtmax was similar during LVs and BiV pacing (17±10% vs. 17±9%, respectively) and larger than during LVs+RV pacing (11±9%; $p<0.05$) (Salden FCWM et al, *J Am Coll Cardiol* 2020;75: 347-59).

Global Longitudinal Strain (GLS) Decreases With Immune Checkpoint Inhibitor (ICI) Myocarditis in either Preserved or Reduced EF and is Strongly Associated With MACE

At presentation with myocarditis, 61 of 101 cases (60%) had a normal ejection fraction (EF). Pre-ICI, GLS was similar between cases and control subjects (n=92) (20.3±2.6% vs. 20.6±2.0%; p=0.60). There was no change in GLS among control subjects on an ICI without myocarditis (pre-ICI vs. on ICI, 20.6±2.0% vs. 20.5±1.9%; p=0.41); in contrast, among cases, GLS decreased to 14.1±2.8% (p<0.001). The GLS at presentation with myocarditis was lower among cases presenting with either a reduced (12.3±2.7%) or preserved EF (15.3±2.0%; p<0.001). Over a median follow-up of 162 days, 51 (51%) experienced MACE. The risk of MACE was higher with a lower GLS among patients with either a reduced or preserved EF (Awadalla M et al, *J Am Coll Cardiol* 2020;75:467-78).

Large-Scale, Individual Patient Data Pooled Study: Very-Late Stent-Related Events Occurred Between 1 and 5 Years after Percutaneous Coronary Intervention (PCI) at a Rate of ~2%/Year with All Stent Types

Data from 19 prospective, randomized stent trials indicated that among 25,032 total patients, 3,718, 7,934, and 13,380 were treated with BMS, DES1, and DES2, respectively. MACE rates within 1 year after PCI were progressively lower after treatment with BMS vs DES1 vs DES2 (17.9% vs 8.2% vs 5.1%, respectively, p<0.0001). Between years 1 and 5, very-late MACE occurred in 9.4% of patients (including 2.9% cardiac death, 3.1% MI, and 5.1% TLR). Very-late MACE occurred in 9.7%, 11%, and 8.3% of patients treated with BMS, DES1, and DES2, respectively (p<0.0001), linearly increasing between 1 and 5 years (Madhavan MV et al, *J Am Coll Cardiol* 2020;75:590-604).

Multi-Ethnic Study of Atherosclerosis (MESA): Irregular Sleep Duration and Timing are Novel Risk Factors for CVD, Independent of Traditional CVD Risk Factors and Sleep Quantity and/or Quality

Among 1,992 participants free of CVD who completed 7-day wrist actigraphy for sleep assessment, over a median follow-up of 4.9 years, 111 participants developed CVD events. The multivariable-adjusted HRs for CVD across categories of sleep duration standard deviation (SD) (SD of actigraphy-measured sleep duration and sleep-onset timing across 7 days) were 1.00 (reference) for≤60 min, 1.09 for 61-90 min, 1.59 for 91-120 min, and 2.14 for >120 min (p trend = 0.002). Similarly, compared with participants with a sleep timing SD≤30 min, the HRs for CVD were 1.16 for 31-60 min, 1.52 for 61-90 min, and 2.11 for >90 min (p trend=0.002). Exclusion of current shift workers yielded similar results (Huang T et al, *J Am Coll Cardiol* 2020; 74:991-9).

Young (≤50 Years) Patients Who Experience a Type 2 MI Have Higher Long-Term All-Cause and CV Mortality Than Those Who Experience Type 1 MI, With Nearly 1/2 of Patients With Myocardial Injury and >1/3 of Patients With Type 2 MI Dying Within 10 Years

Among 3,829 patients (median age 44 years; 30% women); 55% had type 1 MI, 32% had type 2 MI, and 13% had myocardial injury. Over a median follow-up of 10.2 years, mortality was highest for myocardial injury (45.6%), followed by type 2 MI (34.2%) and type 1 MI (12%) (p<0.001). In an adjusted model, type 2 MI was associated with higher all-cause (hazard ratio-HR: 1.8; p=0.004) and CV mortality (HR: 2.7; p=0.003) compared with type 1 MI. Those with type 2 MI or myocardial injury were younger and had fewer CV risk factors but had more non-CV comorbidities. They were significantly less likely to be prescribed CV medications at discharge (Singh A et al, *J Am Coll Cardiol* 2020; 75:1003-13).

LEADER: Liraglutide Should Be Considered Suitable for Patients With Type 2 Diabetes (T2D) with or without a History of NYHA Functional Class I-III HF

Among 9,340 patients with T2D and high CV risk assigned 1:1 to liraglutide (up to 1.8 mg daily) or placebo plus standard care, at baseline, 18% of patients had a history of NYHA functional class I-III HF. Effects of liraglutide vs placebo on major adverse CV events were consistent in patients with (hazard ratio -HR: 0.81) and without (HR: 0.88) a history of HF (p interaction=0.53). In both subgroups, fewer deaths were observed with liraglutide (HR: 0.89 with HF; HR: 0.83 without HF; p interaction=0.63) vs placebo. No increased risk of HF hospitalization was observed with liraglutide, regardless of HF history. Effects of liraglutide on the composite of HF hospitalization or CV death were consistent in patients with (HR: 0.92) and without (HR: 0.77) a history of HF (Marso SP et al, *J Am Coll Cardiol* 2020; 75:1128-41).

Transcatheter Correction of Sinus Venosus (SV) ASD is an Alternative to Surgery in a Substantial Proportion of Patients

The superior sinus venosus atrial septal defect (SVASD) is characterized by deficiency of the common wall between the SVC and the right upper (RU) pulmonary vein (PV). Transcatheter correction with implantation of a covered stent in the SVC was performed in 25 patients.

Only 8 patients were deemed technically unsuitable. The procedure involved balloon test inflation in the anticipated stent landing zone with simultaneous TEE and pulmonary venography to confirm defect closure and unobstructed PV drainage, followed by deployment of a 10-zig covered Cheatham platinum stent. Stents of lengths between 5 and 8 cm were implanted. A second, uncovered stent was used for anchoring in 9 patients. The RUPV was protected with a high-pressure balloon during stent implantation to prevent PV obstruction in 4 patients. The median follow-up period was 1.4 years, with no mortality. Stent embolization occurred in 1 patient; another required drainage of hemopericardium. Cardiac computed tomography after 3 months confirmed unobstructed PV return. At latest follow-up, a residual shunt was present in 1 patient (Hansen JH et al, *J Am Coll Cardiol* 2020;74:1266–78).

DAPA-HF: Dapagliflozin Reduced CV Death and Worsening Heart Failure (HF), Improved Symptoms, Physical Function, and Quality of Life

Among 4443 patients having available Kansas City Cardiomyopathy Questionnaire (KCCQ) at baseline, the effects of dapagliflozin vs placebo on reducing CV death or worsening HF were consistent across the range of KCCQ-total symptom score (TSS). Patients treated with dapagliflozin had greater improvement in mean KCCQ-TSS, clinical summary score, and overall summary score at 8 months. Fewer patients treated with dapagliflozin had a deterioration in KCCQ-TSS; and more patients had at least small, moderate, and large improvements (Kosiborod MN et al, *Circulation* 2020; 141:90–99).

DAPA-HF: Dapagliflozin Reduced the Risk of Death and Worsening Heart Failure and Improved Symptoms Across the Broad Spectrum of Age Studied in DAPA-HF

Among 4744 patients 22 to 94 years of age (mean age, 66.3 years) who were randomized, 636 patients (13.4%) were <55 years of age, 1242 (26.2%) were 55-64 years of age, 1717 (36.2%) were 65-74 years of age, and 1149 (24.2%) were ≥75 years of age. The rate of the primary outcome (per 100 person-years, placebo arm) in each age group was 13.6, 15.7, 15.1, and 18 with corresponding dapagliflozin/placebo hazard ratios of 0.87, 0.71, 0.76, and 0.68 (*P* for interaction=0.76). Consistent benefits were observed for the components of the primary outcome, all-cause mortality, and symptoms. Although adverse events and study drug discontinuation increased with age, neither was significantly more common with dapagliflozin in any age group (Martinez FA et al, *Circulation* 2020; 141:100–111).

International, Multicentered, Evidence-Based Reappraisal of 17 Genes Reported to Cause Congenital Long QT Syndrome (LQTS), Indicates Only 3 Genes (*KCNQ1, KCNH2*, *SCN5A*) Causing Typical LQTS and Another 4 Genes (*CALM1-3* and *TRDN*) Responsible for Rare Cases of Infantile/Pediatric LQTS With Atypical Features

Only 3 genes (*KCNQ1, KCNH2*, and *SCN5A*) were found to have definitive evidence for causation of typical LQTS. Four other genes (*TRDN* and *CALM1-3*) were classified as having strong or definitive evidence supporting an etiology for LQTS with atypical features. 9 genes were found to have limited or disputed evidence for disease causation. The final gene studied, *CACNA1C*, was found to have a definitive association with Timothy syndrome but only moderate evidence supporting a cardiac-only phenotype concordant with LQTS (Adler A et al, *Circulation* 2020; 141:418–428).

Coconut Oil Consumption Results in Significantly Higher LDL-Cholesterol Than Nontropical Vegetable Oils

A meta-analysis of 16 articles indicated that coconut oil consumption significantly increased LDL-cholesterol by 10.47 mg/dL and HDL-cholesterol by 4 mg/dL as compared with nontropical vegetable oils. These effects remained significant after excluding nonrandomized trials, or trials of poor quality. Coconut oil consumption did not significantly affect markers of glycemia, inflammation, and adiposity as compared with nontropical vegetable oils (Neelakantan N et al, *Circulation* 2020;141:803–814).

BERLIN VT study: Preventive VT Ablation Before ICD Implantation Did Not Reduce Mortality or Hospitalization for Arrhythmia or Worsening Heart Failure During 1 Year of Follow-Up Compared With the Deferred Ablation Strategy

Patients with stable ischemic cardiomyopathy, a LVEF 30-50%, and documented VT were randomly assigned 1:1 to a preventive (n=76) or deferred (n=83) ablation strategy. During a mean follow-up of 396±284 days, the primary end point (all-cause death and hospitalization for either symptomatic ventricular arrhythmia or worsening heart failure) occurred in 32.9% vs 27.7% (hazard ratio, 1.09; *P*=0.77). On the basis of prespecified criteria for interim analyses, the study was terminated early for futility. In the preventive vs deferred ablation group, 6 vs 2 patients died (7.9% vs 2.4%; *P*=0.18), 8 vs 2 patients were admitted for worsening heart failure (10.4% vs 2.3%; *P*=0.062), and 15 vs 21 patients were hospitalized for symptomatic ventricular arrhythmia (19.5% vs 25.3%; *P*=0.27). Among secondary outcomes,

the proportions of patients with sustained ventricular tachyarrhythmia (39.7% vs 48.2%; *P*=0.050) and appropriate ICD therapy (34.2% vs 47.0%; *P*=0.020) were numerically reduced in the preventive ablation group (Willems S et al *Circulation* 2020;141: 1057–1067).

TAVI for Bicuspid Aortic Valve (AoV): Using Current-Generation Devices, Procedural, Postprocedural, and 1-Year Outcomes Were Comparable with TAVI of Tricuspid AoV Disease / With Newer-Generation Devices, TAVR is a Viable Treatment Option for Patients With Bicuspid AoV Disease

Of 170 959 TAVI procedures at 593 sites 5412 (3.2%) were performed in patients with bicuspid AV, including 3705 with current-generation devices. In comparison with patients with tricuspid valves, patients with bicuspid AoV were younger and had a lower STS score. When current-generation devices were used to treat patients with bicuspid AoV, device success increased (93.5 vs 96.3; *P*=0.001) and the incidence of 2+ aortic insufficiency declined (14% vs 2.7%; *P*<0.001) in comparison with older-generation devices. With current-generation devices, device success was slightly lower in the bicuspid (vs tricuspid) AoV group (96.3% vs 97.4%, *P*=0.07), with a slightly higher incidence of residual moderate or severe aortic insufficiency among patients with bicuspid AoV (2.7% vs 2.1%; *P*<0.001). A lower 1-year adjusted risk of mortality (hazard ratio-HR, 0.88) was observed for patients with bicuspid AV vs patients with tricuspid AoV, whereas no difference was observed in the 1-year adjusted risk of stroke (HR, 1.14) (Halim SA et al, *Circulation* 2020;141:1071–1079)

Treat Stroke To Target: After an Ischemic Stroke or TIA With Evidence of Atherosclerosis, Patients Who Had a Target LDL Cholesterol Level of <70 mg/dl Had a Lower Risk of Subsequent Cardiovascular Events Than Those Who Had a Target Range of 90-110 mg/dl

Among 2860 patients followed for a median of 3.5 years, with 1430 assigned to each LDL cholesterol target group (<70 and 90-110 mg/dl), the mean LDL of 135 mg/dl at baseline dropped to 65 mg/dl in the lower-target group and to 96 mg/dl in the higher-target group. The trial was stopped for administrative reasons after 277 of an anticipated 385 end-point events had occurred. The composite primary end point (major CV events: ischemic stroke, MI, new symptoms leading to urgent coronary or carotid revascularization, or CV death) occurred in 121 patients (8.5%) in the lower-target group and in 156 (10.9%) in the higher-target group (adjusted hazard ratio, 0.78; P=0.04). The incidence of intracranial hemorrhage and newly diagnosed diabetes did not differ significantly between the two groups (Amarenco P et al, *N Engl J Med* 2020;382:9-19).

Abstinence from Alcohol Reduced Arrhythmia Recurrences in Regular Drinkers With Atrial Fibrillation (AF)

Among 140 patients (85% men; age, 62±9 years), with 70 randomized to the abstinence group and 70 to the control group, after a 2-week blanking period, AF recurred in 37 of 70 patients (53%) in the abstinence group and in 51 of 70 patients (73%) in the control group. The abstinence group had a longer period before AF recurrence than the control group (hazard ratio, 0.55; P=0.005). The AF burden over 6 months was significantly lower in the abstinence group (median percentage of time in AF, 0.5% vs. 1.2%; P=0.01). (Voskoboinik A et al, *N Engl J Med* 2020; 382:20-28).

GALILEO: In Patients Without an Established Indication for Oral Anticoagulation After Successful TAVI, Rivaroxaban (10 mg qd) Was Associated With a Higher Risk of Death or Thromboembolic Complications and a Higher Risk of Bleeding Than an Antiplatelet-Based Strategy.

Among 1644 patients randomized to rivaroxaban (10 mg/d) & aspirin (75-100 mg/d) for the first 3 months (rivaroxaban group) or aspirin (75-100 mg/d) with clopidogrel at a dose of 75 mg daily for the first 3 months (antiplatelet group), after a median of 17 months, death or a first thromboembolic event (intention-to-treat analysis) had occurred in 105 vs patients (hazard ratio-HR with rivaroxaban, 1.35; P=0.04). Major, disabling, or life-threatening bleeding (intention-to-treat analysis) had occurred in 46 and 31 patients, respectively (HR, 1.50; P=0.08). A total of 64 deaths occurred in the rivaroxaban group and 38 in the antiplatelet group (HR, 1.69) (Dangas GD et al, *N Engl J Med* 2020; 382:120-129).

PARTNER 2: Among Patients With Aortic Stenosis With Intermediate Surgical Risk, There Was No Significant Difference in the Incidence of Death or Disabling Stroke at 5 Years After TAVI as Compared With Surgical Aortic-Valve Replacement

Among 2032 intermediate-risk patients with severe, symptomatic aortic stenosis randomly assigned to either TAVI or surgical replacement, at 5 years, there was no significant difference in the incidence of death from any cause or disabling stroke between the 2 groups (47.9% and 43.4%, respectively; hazard ratio-HR, 1.09; P=0.21). Results were similar for the transfemoral-access cohort (44.5% and 42%, respectively; HR, 1.02), but the incidence of death or disabling stroke was higher after TAVI than after surgery in the transthoracic-access cohort

(59.3% vs 48.3%; HR, 1.32). At 5 years, more patients in the TAVI group had at least mild paravalvular aortic regurgitation (33.3% vs 6.3%). Repeat hospitalizations were more frequent after TAVI (33.3% vs 25.2%), as were aortic-valve reinterventions (3.2% vs 0.8%). Improvement in health status at 5 years was similar for TAVI and surgery (Makkar RR et al, *N Engl J Med* 2020; 382:799-809).

ONYX ONE: Among Patients at High Bleeding Risk Who Received 1 Month of Dual Antiplatelet Therapy After PCI, Use of Polymer-Based Zotarolimus-Eluting Stents Was Noninferior to Use of Polymer-Free Drug-Coated Stents With Regard to Safety and Effectiveness

A total of 1996 patients at high bleeding risk were randomly assigned in a 1:1 ratio to receive zotarolimus-eluting stents (1003 patients) or polymer-free drug-coated stents (993 patients). At 1 year, the primary outcome (a safety composite of CV death, MI, or stent thrombosis) was observed in 169 of 988 patients (17.1%) in the zotarolimus-eluting stent group and in 164 of 969 (P=0.01 for noninferiority). The principal secondary outcome (target-lesion failure, an effectiveness composite of death from cardiac causes, target-vessel MI, or clinically indicated target-lesion revascularization) was observed in 174 patients (17.6%) in the zotarolimus-eluting stent group and in 169 (17.4%) in the polymer-free drug-coated stent group (P=0.007 for noninferiority) (Windecker S et al, *N Engl J Med* 2020; 382:1208-1218).

High-Sensitivity Cardiac Troponin (hs-cTn): In Symptomatic Patients With CAD, Very Low hs-cTnI, Including Concentrations <2.5 ng/L, Do Not Generally Allow Users to Safely Exclude Inducible Ischemia

Of 1896 consecutive patients with coronary artery disease (CAD) referred with symptoms, 865 (46%) had inducible myocardial ischemia. The hs-cTnI cutoff of 2.5 ng/L provided a negative predictive value (NPV) of 70% and a sensitivity of 90% for exclusion of inducible myocardial ischemia. No hs-cTnI cutoff reached both performance characteristics predefined as targets. Similarly, using the alternative assays for hs-cTnI or hs-cTnT, no cutoff achieved the target performance: hs-cTnT concentrations <5 ng/L yielded an NPV of 66%, and hs-cTnI concentrations <2 ng/L yielded an NPV of 68% (Walter J et al, *Ann Intern Med* 2020;171: 175-85).

EMPA-REG Outcome Trial: Hypoglycemia Increases Risk of HF Hospitalization (HFH) and MI / Hypoglycemia Risk was not Increased with Empagliflozin and Incident Hypoglycemia did not Attenuate its Cardio-Protective Effects

Among 7020 patients with diabetes type 2 (T2D) treated with empagliflozin 10 or 25 mg, or placebo and followed for a median of 3.1 years, hypoglycemia ≤70 mg/dl occurred in 28% in each group and <54 mg/dl in 19%. In the placebo group, hypoglycemia was associated with an increased risk of HFH for both types of hypoglycemia (hazard ratio-HR 1.91 and 1.72 respectively). Hypoglycemia ≤70 mg/dl was associated with an increased risk of MI (HR 1.56). Empagliflozin improved CV outcomes, regardless of occurrence of hypoglycemia (*P*-for interactions >0.05) (Fitchett D et al, *Eur Heart J* 2020; 41:209-17-20).

A Healthy Sleep Pattern is Associated with Reduced Risks of Cardiovascular Disease (CVD), Coronary Artery Disease (CAD), and Stroke

A total of 385,292 participants initially free of CVD from UK Biobank were studied. A healthy sleep score was used according to 5 sleep factors and defined the low-risk groups as: early chronotype, sleep 7–8 h/d, never/rarely insomnia, no snoring, and no frequent excessive daytime sleepiness; with the overall sleep patterns defined as 'healthy sleep pattern' (healthy sleep score ≥4), 'intermediate sleep pattern' (2≤healthy sleep score ≤3), and 'poor sleep pattern' (healthy sleep score ≤1). During a median of 8.5 years, compared to those with a sleep score of 0–1, participants with a score of 5 had a 35%, 34%, and 34% reduced risk of CVD, CAD, and stroke, respectively. About 10% of CV events in this cohort could be attributed to poor sleep pattern. Participants with poor sleep pattern and high genetic risk showed the highest risk of CAD and stroke (Fan M et al, *Eur Heart J* 2020; 41:1182-89).

NOBLE Trial: PCI for Left Main Had an Inferior Outcome at 5 Years Compared With CABG / Mortality Was Similar But PCI Had Higher Rates of Non-Procedural MI and Repeat Revascularization

Among 1201 enrolled patients, allocated to PCI (n=598) or CABG (n=603), at a median of 4·9 years, Kaplan-Meier 5-year estimates of MACCE were 28% (165 events) for PCI and 19% (110 events) for CABG (HR 1.58); the HR exceeded the limit for non-inferiority of PCI compared to CABG. CABG was found to be superior to PCI for the primary composite endpoint (p=0.0002). All-cause mortality was 9% after PCI vs 9% after CABG; non-procedural MI was 8% after PCI vs 3% after CABG (HR 2.99; p=0.0002); and repeat revascularization was 17% after PCI vs 10% after CABG (HR 1.73; p=0.0009) (Holm NR et al, *Lancet* 2020; 395:191-199).

RAFF2: Immediate Rhythm Control for Patients in the Emergency Department With Acute Atrial Fibrillation (AF) Leads to Excellent Outcomes

Two protocols for conversion (CV) of acute AF were used; Protocol 1 with attempted pharmacological CV with

IV procainamide (15 mg/kg over 30 min) followed by electrical CV if necessary (up to 3 shocks, each of ≥200 J), and placebo infusion followed by electrical CV; for patients having electrical CV, Protocol 2 was used, a comparison of anteroposterior vs anterolateral pad positions. 396 patients were enrolled. In the drug–shock group (n=204), CV to sinus rhythm occurred in 196 (96%) patients and in the shock-only group (n=192), CV occurred in 176 (92%) patients (p=0.07). The proportion of patients discharged home was 97% (n=198) vs 95% (n=183; p=0·60). 106 (52%) patients in the drug–shock group converted after drug infusion only. No patients had serious adverse events in follow-up. The different pad positions in Protocol 2 (n=244) had similar CVs to sinus rhythm (94% *vs* 92%; p=0.68) (Stiell IG et al, *Lancet* 2020;395:339-49).

ERADICATE-AF: Among Patients With Paroxysmal Atrial Fibrillation (AF) and Hypertension, Renal Denervation Added to Catheter Ablation (Without a Sham-Control), Compared With Catheter Ablation Alone, Significantly Increased the Likelihood of Freedom from AF at 1 Year

Of the 302 randomized patients (median age, 60 years; 60% men), 283 (93.7%) completed the trial. Freedom from AF, flutter, or tachycardia at 1 year was observed in 56.5% of those undergoing pulmonary vein isolation (PVI) alone and 72.1% of those undergoing PVI plus renal denervation (hazard ratio-HR, 0.57; $P = 0.006$). Of 5 prespecified secondary end points, 4 are reported and 3 differed between groups. Mean systolic blood pressure from baseline to 1 year decreased from 151 mm Hg to 147 mm Hg in the isolation-only group and from 150 mm Hg to 135 mm Hg in the renal denervation group ($P < 0.001$). Procedural complications occurred in 7 patients (4.7%) in the isolation-only group and 7 (4.5%) of the renal denervation group (Steinberg JS et al, JAMA 2020; 323:248-255).

SAFARI-STEMI: Adequately Trained Operators Achieve Similar Results When Using Either Radial Access or Femoral Access for Primary Percutaneous Coronary Intervention (PCI)

Among 2292 patients with STEMI undergoing primary PCI, 883 were randomized to radial access and 901 to femoral access. The trial was stopped early following a futility analysis. A vascular closure device was used in 789 patients (68.3%) in the femoral group. The primary outcome, 30-day all-cause mortality, occurred in 17 patients (1.5%) assigned to radial access and in 15 patients (1.3%) assigned to femoral access. There were no significant differences between patients assigned to radial and femoral access in the rates of reinfarction (1.8% vs 1.6%), stroke (1% vs 0.4%), and bleeding (1.4% vs 2%) (Le May M et al, *JAMA Cardiol* 2020;5:126-134).

COVID-19: The Potential Risk Factors of Older Age, High SOFA (Sequential Organ Failure Assessment) Score, and D-Dimer >1 µg/ml Could Help Identify Patients With Poor Prognosis at an Early Stage

Of 191 patients with COVID-19 infection, 137 were discharged and 54 died in hospital. 91 (48%) patients had a comorbidity, with hypertension being the most common (30%), followed by diabetes (19%) and coronary heart disease (8%). Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.10, per year increase; p=0·0043), higher SOFA score (5.65; p<0.0001), and d-dimer >1 µg/mL (18.42; p=0.0033) on admission. Median duration of viral shedding was 20 days in survivors, but COVID-19 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days (Zhou F et al, *Lancet* 2020; 395:1054-62).

COVID-19: Myocardial Injury is Significantly Associated With Fatal Outcome of COVID-19, While the Prognosis of Patients With Underlying CVD But Without Myocardial Injury is Relatively Favorable

Among 187 patients (mean age 58.5 years) with confirmed COVID-19, 66 (35.3%) had underlying CVD including hypertension, CAD, and cardiomyopathy, and 52 (27.8%) exhibited myocardial injury as indicated by elevated cardiac troponin T (cTnT) levels. The mortality during hospitalization was 7.6% for patients without underlying CVD and normal cTnT levels, 13.3% for those with underlying CVD and normal cTnT levels, 37.5% for those without underlying CVD but elevated cTnT levels, and 69.4% for those with underlying CVD and elevated cTnT. Plasma cTnT levels demonstrated a high and significantly positive linear correlation with plasma high-sensitivity CRP levels and NT-proBNP levels. During hospitalization, patients with elevated cTnT levels had more frequent malignant arrhythmias, and the use of glucocorticoid therapy (71% vs 51%) and mechanical ventilation (59.6% vs 10.4%) were higher compared with patients with normal cTnT levels. The mortality rates of patients with and without use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers was 36.8% and 25.6% (Guo T et al, *JAMA Cardiol* 2020, Mar 27. doi:10.1001/jamacardio.2020.1017).

COVID-19: Cardiac Injury is a Common Condition Among Hospitalized Patients With COVID-19 Associated With Higher Risk of In-Hospital Mortality

Among 416 hospitalized patients with COVID-19 (median age 64 years, 50.7% female) who presented with

fever (80%), cough (34.6%), and shortness of breath (28%), 82 patients (19.7%) had cardiac injury, and compared with patients without cardiac injury, they were older (median age, 74 vs 60 years; P <0 .001); had more comorbidities (e.g., hypertension in 60% vs 23%; P < .001); and higher leukocyte counts, CRP, procalcitonin, creatinine kinase–myocardial band, high-sensitivity troponin I, NT-proBNP, aspartate aminotransferase, and creatinine; and worse radiographic findings. More patients with cardiac injury required noninvasive or invasive mechanical ventilation than those without cardiac injury. Complications were more common in patients with cardiac injury than those without cardiac injury and included acute respiratory distress syndrome (58.5% vs 14.7%; P <0 .001), acute kidney injury (8.5% vs 0.3%; P < 0.001), electrolyte disturbances (15.9% vs 5.1%; P = 0.003), hypoproteinemia (13.4% vs 4.8%; P = 0.01), and coagulation disorders (7.3% vs 1.8%; P =0 .02). Patients with cardiac injury had higher mortality than those without cardiac injury (51.2% vs 4.5%; P <0.001) (Shi S et al, *JAMA Cardiol* 2020 Mar 25. doi:10.1001/jamacardio.2020.0950).

Heart Failure (HF) Patients Have Elevated Methylmalonic Acid (MMA) Levels, Independently of Age, Gender, HF Category or Comorbidities, Possibly Indicating Subclinical Vitamin-B12 Deficiency or a Biomarker of Oxidative Stress

Among 105 consecutive patients admitted with acute decompensated HF, 43.8% had elevated MMA levels, but only 10.5% had overt vitamin B12 deficiency, defined as cobalamin serum levels below 189 pg/ml. Mean MMA level was higher in HF patients vs controls (n=51) (33.0±9.6 vs 19.3±6.3 ng/ml; p<0.001). This difference remained significant when adjusted for age, sex, vitamin B12 and folate serum levels and kidney function (B =14.7 (9.6-19.7); p<0.001). MMA levels were higher in patients with acutely decompensated chronic HF compared with newly diagnosed acute HF (34.7±10.5 vs 30.7±7.8 ng/ml; p=0.036). Correlation analysis revealed significantly negative correlation between MMA and B12 levels only in patients without comorbidities (Polytarchou et al, *Hellenic J Cardiol* 2019 Nov 15; doi: 10.1016/j.hjc.2019.10.010)

Important Review and Other Articles

● 2019 **ESC/EAS** Guidelines for the management of **dyslipidemias** (Mach F et al, *Eur Heart J*, 2020;41:111–188)

● **2019 ESC Guidelines on diabetes**, pre-diabetes, and cardiovascular diseases (Cosentino F et al, *Eur Heart J*, 2020; 41:255–323)

● **2019 ESC Guidelines for management of SVT** (Brugada J et al, *Eur Heart J* 2020; 41:655-720)

● **AHA:** Heart Disease and Stroke Statistics—2020 Update (Virani SS et al, *Circulation* 2020;141:e139–e596)

● **AHA** Statement on Sudden Cardiac Arrest Survivorship (*Circulation* 2020;140: e654–e685)

● Exercise-related acute cardiovascular events (Franklin BA et al, *Circulation* 2020;141:e705–e736)

● Management of pericarditis (Chiabrando JG et al, *J Am Coll Cardiol* 2020; 75: 76-92)

● Peripartum cardiomyopathy (Davis MB et al, *J Am Coll Cardiol* 2020; 75: 207-21)

● Atrial failure (Bisbal F et al, *J Am Coll Cardiol* 2020;75:222-32)

● Marijuana use in cardiac patients (DeFilippis EM et al, *J Am Coll Cardiol* 2020; 75:320-32)

● Embolic stroke of undetermined source (Ntaios G, *J Am Coll Cardiol* 2020;75:333-40)

● Cardiorenal effects of sodium-glucose cotransporter 2 (SGLT2) inhibitors (Zelniker TA et al, *J Am Coll Cardiol* 2020;75:422-47)

● Salt reduction to prevent hypertension and CVD (He FJ et al, *J Am Coll Cardiol* 2020;75:632-47)

● Carotid stenting in asymptomatic stenosis (Beckman JA et al, *J Am Coll Cardiol* 2020;75:648-56)

● Drug-coated balloon (Yerasi C et al, *J Am Coll Cardiol* 2020;75:1061-73)

● Risk stratification in non-ischemic CM (Marrow BA et al, *J Am Coll Cardiol* 2020;75:1196-207)

● Inflammation in heart failure (Murphy SP et al, *J Am Coll Cardiol* 2020;75:1324-40)

● Dietary cholesterol and CV risk (Carson JAS et al, *Circulation* 2020;141:e39–e53)

● Regulatory RNAs in heart failure (da Costa Gomes CP et al, *Circulation* 2020;141:313-328)

● Fulminant myocarditis (Kociol RD et al, *Circulation* 2020; 141:e69–e92)

● Screening for AF (Jones NR, et al, *Eur Heart J* 2020;41: 1075–85)

● Antithrombotic therapy in TAVI patients (Saito Y et al, *JAMA Cardiol* 2020; 5:92-101)

● Proton pump inhibitors and cardiovascular adverse effects (Manolis AA et al, *Eur J Intern Med*. 2020;72:15-26.)