Cardiology News / Recent Literature Review / Third Quarter 2020

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TCT/ Virtual Event: 14-18/10/2020

HCS/Panhellenic (41st) Congress of Cardiology: Athens, 22-24/10/2020

AHA Meeting 2020: cancelled

ACC Meeting: Atlanta, 20-22/3/2021

EHRA Meeting: Barcelona, 28-30/3/2021

COMPASS Trial: Rivaroxaban 2.5 mg bid Plus ASA vs ASA Alone Resulted in Fewer Events (Stroke and Cardiovascular Mortality), Particularly in High-Risk Subgroups and Those With Multiple Risk Characteristics With Less Frequent Severe Bleedings and Less Clinical Impact

Rivaroxaban 2.5 mg bid plus aspirin 100 mg reduced the risk of cardiovascular (CV) events as compared with ASA monotherapy in the COMPASS trial but increased the risk of major bleedings. The current prespecified analysis was performed to assess the net clinical benefit (NCB) of adding rivaroxaban 2.5 mg bid to ASA monotherapy in patients with chronic vascular disease in the COMPASS study cohort with a specific focus on high-risk subgroups. A lower number of NCB adverse outcomes was observed with rivaroxaban 2.5 mg bid plus ASA vs ASA alone (hazard ratio, 0.80, *P*=0.0005), which became increasingly favorable with longer treatment duration. In selected high-risk subgroups, a larger absolute risk reduction for experiencing a NCB event was observed (Steffel J et al, *Circulation* 2020; 142:40-48)**.**

COVID-19: The Prevalence of DVT is High, Associated With Adverse Outcomes in Hospitalized Patients With COVID-19 / Prophylaxis for DVT May be Protective in Patients With a Padua Protection Score ≥4 After Admission

Of the 143 patients hospitalized with COVID-19 (age 63±14 years, 51.7% men), 66 patients developed lower extremity DVT (46.1%). Compared with patients who did not have DVT, patients with DVT were older and had a lower oxygenation index, a higher rate of cardiac injury, and worse prognosis, including an increased rate of deaths (34.8% vs 9 11.7%; *P*=0.001) and a decreased proportion of patients discharged (48.5% vs 77.9%; *P*<0.001). In the subgroup of patients with a Padua prediction score ≥4 and whose ultrasound scans were performed >72 h after admission, DVT was present in 34% patients in the subgroup receiving thromboprophylaxis vs 66% patients in the nonprophylaxis group (*P*=0.010) (Zhang L et al, *Circulation* 2020; 142:114–128).

Meta-Analysis: Prasugrel and Ticagrelor Reduced Ischemic Events and Increased Bleeding Compared With Clopidogrel in Patients with ACS / A Significant Mortality Reduction Was Observed With Ticagrelor Only /There was no Efficacy and Safety Difference Between Prasugrel and Ticagrelor

According to a network meta-analysis of 12 RCTs including 52 816 patients with acute coronary syndrome (ACS), in comparison with clopidogrel, ticagrelor significantly reduced cardiovascular mortality (hazard ratio-HR, 0.82) and all-cause mortality (HR, 0.83), with no significant mortality reduction with prasugrel (HR, 0.90 and HR, 0.92, respectively). In comparison with each other, there were no significant differences in mortality. In comparison with clopidogrel, prasugrel reduced myocardial infarction (HR, 0.81), whereas ticagrelor showed no risk reduction (HR, 0.97). Differences between prasugrel and ticagrelor were not significant. Stent thrombosis risk was significantly reduced by both ticagrelor and prasugrel versus clopidogrel (28%–50% range of reduction). In comparison with clopidogrel, both prasugrel (HR, 1.26) and ticagrelor (HR, 1.27) significantly increased major bleeding. There were no significant differences between prasugrel and ticagrelor for all outcomes explored (Navarese EP et al, *Circulation.* 2020;142:150–160).

Sudden Cardiac Death (SCD) Risk Prediction in Pediatric Hypertrophic Cardiomyopathy (HCM): A Validated SCD Risk Prediction Model With >70% Prediction Accuracy Incorporating Risk Factors That Are Unique to Pediatric HCM

In 572 pediatric patients with HCM, the 5-year cumulative proportion of SCD events was 9.1% (14 SCD, 25 resuscitated sudden cardiac arrests, and 14 aborted SCD). Risk predictors included age at diagnosis, documented nonsustained VT, unexplained syncope, septal diameter *z*-score, LV posterior wall diameter *z* score, left atrial diameter *z* score, peak LV outflow tract gradient, and presence of a pathogenic variant. Unlike in adults, LV outflow tract gradient had an inverse association, and family history of SCD had no association with SCD. Clinical and clinical/genetic models were developed to predict 5-year freedom from SCD. Both models adequately discriminated between patients with and without SCD events, and demonstrated good agreement between predicted and observed events in the primary and

validation cohorts (Miron A et al, *Circulation* 2020;142:217–229).

Spectrum of Cardiac Manifestations in COVID-19: LV Systolic Function is Preserved in The Majority of Patients, But LV Diastolic Function and RV Function are Impaired / Patients with Elevated Troponin and Poorer Clinical Status Have Worse RV Function / In Patients With Clinical Worsening at Follow-Up, Acute RV Dysfunction, With Or Without Deep Vein Thrombosis, is More Common, with Acute LV Systolic Dysfunction Noted In ≈20%

Among 100 COVID-19 patients undergoing echocardiographic evaluation within 24h of admission, 32% had a normal echocardiogram at baseline. The most common cardiac pathology was RV dilatation and dysfunction (39%), followed by LV diastolic dysfunction (16%) and LV systolic dysfunction (10%). Patients with elevated troponin (20%) or worse clinical condition did not demonstrate any significant difference in LV systolic function compared with patients with normal troponin or better clinical condition, but they had worse RV function. Clinical deterioration occurred in 20% of patients. In these patients, the most common echocardiographic abnormality at follow-up was RV function deterioration (12 patients), followed by LV systolic and diastolic deterioration (in 5 patients). DVT was diagnosed in 5 of 12 patients with RV failure (Szekely Y et al, *Circulation* 2020;142:342–53).

Impact of TAVI Durability on Life Expectancy in Low-Risk Patients With Severe Aortic Stenosis: According to a Simulation Model, the Durability of TAVI Valves Must be 70% Shorter Than That of Surgical Valves to Result in Reduced Life Expectancy / In Younger Patients, This Threshold for TAVI Valve Durability Was Much Higher / Thus, Durability Concerns in Younger Low-Risk Patients Must be Weighed Against Other Patient Factors Such as Life Expectancy

According to a simulation model comparing TAVI vs surgical aortic valve replacement (AVR) durability in patients with aortic stenosis at low surgical risk with a mean age of 73.4±5.9 years, the standardized difference in life expectancy was <0.10 between TAVI and AVR until transcatheter valve prosthesis failure time was 70% shorter than that of surgical prostheses. At a transcatheter valve failure time <30% compared with surgical valves, AVR was the preferred option. In younger patients, life expectancy was reduced when TAVI durability was 30%, 40%, and 50% shorter than that of surgical valves in 40-, 50-, and 60-year-old patients, respectively (Tam DY et al, *Circulation* 2020;142:354–64).

Acute Heart Failure in COVID-19-Associated Multisystem Inflammatory Syndrome in Children / Recovery of LV Function May Follow Treatment with Immunoglobulin

According to a series of 35 febrile pediatric patients with prominent GI symptoms and acute heart failure potentially associated with SARS-CoV-2 infection and the multisystem inflammatory syndrome in children, with 31 (88%) tested positive for SARS-CoV-2 infection (median age 10 years, 28% comorbidities including asthma and overweight, LVEF <30% in one-third; 80% requiring inotropic support with 28% treated with extracorporeal membrane oxygenation-ECMO; inflammation markers suggestive of cytokine storm: interleukin-6 median, 135 pg/mL, and macrophage activation: D-dimer median, 5284 ng/mL; mean BNP elevated at 5743 pg/mL), all patients received intravenous immunoglobulin, with adjunctive steroid therapy used in one-third. LV function was restored in the 25 of 35 of those discharged from the intensive care unit. No patient died, and all patients treated with ACMO were successfully weaned (Belhadjer G et al, *Circulation* 2020;142:429–436).

Meta-Analysis: Discontinuation of Aspirin With Continued $P2Y_{12}$ Inhibitor Monotherapy Reduces Risk of Bleeding When Stopped 1-3 Months After PCI with no Increased Risk of MACE

A meta-analysis of 5 RCTs including 32,145 patients: 14,095 (43.8%) with stable coronary artery disease and 18,046 (56.1%) with acute coronary syndrome (ACS), receiving clopidogrel (16.5%) and prasugrel or ticagrelor (83.5%), discontinuation of aspirin therapy 1-3 months after PCI significantly reduced risk of major bleeding by 40% compared with dual antiplatelet therapy (1.97% vs 3.13%; hazard ratio -HR, 0.60), with no increase in the risk of MACE (2.73% vs 3.11%; HR, 0.88), myocardial infarction (1.08% vs 1.27%; HR, 0.85), or death (1.25% vs 1.47%; HR, 0.85). Findings were consistent among patients who underwent PCI for an ACS, in whom discontinuation of aspirin after 1-3 months reduced bleeding by 50% (1.78% vs 3.58%; HR, 0.50) and did not increase the risk of MACE (2.51% vs 2.98%; HR, 0.85) (O'Donoghue ML et al, *Circulation* 2020;142:538–54).

DECLARE-TIMI 58: Patients With vs Without Peripheral Artery Disease (PAD) are at a Higher Risk of CV Death, HF Hospitalization (HHF), and Kidney Outcomes, with Consistent Benefits for CV Death/HHF and Progression of Kidney Disease With Dapagliflozin / Patients With PAD Had a Higher Risk of Limb Events

Among 17,160 patients with type 2 diabetes, including 1025 (6%) with PAD randomized to dapagliflozin, those

with vs those without PAD without tended to have higher risk of CV death, MI, or stroke (adjusted hazard ratio-aHR, 1.23, *P*=0.094) and higher adjusted risk of CV death/HHF (aHR, 1.60, *P*=0.0010) and progression of kidney disease (aHR, 1.51, *P*=0.0058), and limb adverse events (aHR, 8.37, *P*<0.001). The relative risk reductions with dapagliflozin for CV death/HHF (HR, 0.86, PAD; HR, 0.82, no-PAD; *P*-interaction=0.79) and progression of kidney disease (HR, 0.78, PAD; HR, 0.76, no-PAD; *P*-interaction=0.84) were consistent regardless of PAD. There were 560 patients with ≥1 limb ischemic event, 454 patients with ≥1 peripheral revascularization, and 236 patients with ≥1 amputation, with a total of 407 amputations reported. Overall, there were no significant differences in any limb outcome with dapagliflozin vs placebo including limb ischemic adverse events (HR, 1.07) and amputation (HR, 1.09), with no significant interactions by a history of PAD vs not (Bonaca MP et al, *Circulation* 2020;142:734–747).

Meta-Analysis: In Patients With Stable Ischemic Heart Disease, Routine Revascularization Was not Associated With Improved Survival But was Associated With a Lower Risk of Nonprocedural MI and Unstable Angina With Greater Freedom From Angina at the Expense of Higher Rates of Procedural MI

Meta-analysis of 14 RCTs of 14 877 patients followed up for a mean of 4.5 years showed that revascularization compared with medical therapy alone was not associated with a reduced risk of death (relative risk -RR, 0.99). Revascularization was associated with a reduced nonprocedural MI (RR, 0.76) but also with increased procedural MI (RR, 2.48) with no difference in overall MI (RR, 0.93). A significant reduction in unstable angina (RR, 0.64) and increase in freedom from angina (RR, 1.10) was also observed with revascularization. There were no treatment-related differences in the risk of heart failure or stroke (Bangalore S et al, *Circulation* 2020;142:841–857).

Exposure to Air Pollution and Particle Radioactivity: Intermediate (21-Day) $PM_{2.5}$ Exposure Was Associated With Higher Odds of a Ventricular Arrhythmia (VA) Event Onset Among Patients With Known Cardiac Disease and Indication for ICD Independently of Particle Radioactivity

A total of 1,050 VAs were recorded among 91 patients (123 sustained VA among 25 patients). In the single-pollutant model of $PM_{2.5}$, each interquartile range increase in daily $PM_{2.5}$ levels for a 21-day moving average was associated with 39% higher odds of a VA event. In the single-pollutant model of particle radioactivity, each interquartile range increase in particle radioactivity for a 2-day moving average was associated with 13% higher odds of a VA event. In the 2-pollutant model, for the same averaging window of 21 days, each interquartile range increase in daily $PM_{2.5}$ was associated with 48% higher odds of a VA event, and each interquartile range increase of particle radioactivity with 10% lower odds of a VA event. With higher levels of particle radioactivity, the effect of $PM_{2.5}$ on VAs was reduced (Peralta AA et al, *Circulation*. 2020;142:858–67).

Sudden Cardiac Death (SCD): Markers of Lipids, Subclinical Myocardial Injury, Myocardial Strain, and Vascular Inflammation Show Significant Independent Associations With SCD Risk in Apparently Low-Risk Populations

According to a nested case-control study within 6 prospective cohort studies using 565 SCD cases matched to 1090 controls indicated that over a median follow-up of 11.3 years, the mutually adjusted odds ratios for the top compared with the bottom quartile were 1.90 for total to HDL cholesterol ratio, 2.59 for high-sensitivity cardiac troponin I, 1.65 for NT-proBNP, and 1.65 for high-sensitivity CRP (Everett BM et al, *Circulation* 2020;142: 1148-58).

PARAGON-HF Trial: In Patients With Heart Failure With Preserved Ejection Fraction (HFpEF), Sacubitril/ Valsartan Reduced the Risk of Renal Events, and Slowed Decline in EGFR, in Comparison With Valsartan

Among assigned 4822 patients with HFpEF assigned to sacubitril/valsartan (n=2419) or valsartan (n=2403), at randomization, eGFR was 63±19 $mL \cdot min^{-1} \cdot 1.73\ m^{-}2$. At study closure, the composite renal outcome (time to first occurrence of either: ≥50% reduction in eGFR, end-stage renal disease, or death from renal causes)) occurred in 33 patients (1.4%) vs 64 patients (2.7%) (hazard ratio-HR, 0.50; *P*=0.001). The treatment effect on the composite renal end point did not differ according to the baseline eGFR (<60 vs ≥60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ (*P*-interaction=0.92). The decline in eGFR was less for sacubitril/ valsartan than for valsartan (–2.0 vs –2.7 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ per year) (Mc Causland FR et al, *Circulation* 2020;142:1236–45).

Smartphone Activation of Citizen Responders Facilitates Defibrillation in Out-of-Hospital Cardiac Arrest (OHCA)

Citizen responders were alerted in 819 suspected OHCAs, of which 438 (53.5%) were confirmed cardiac arrests. At least 1 citizen responder arrived before Emergency Medical Services (EMS) in 42% (n=184) of all included OHCAs. When citizen responders arrived before

EMS, the odds for bystander CPR increased (odds ratio-OR: 1.76; p=0.027) and the odds for bystander defibrillation more than tripled (OR: 3.73; p<0.001) compared with OHCAs in which citizen responders arrived after EMS (Andelius L et al, *J Am Coll Cardiol* 2020;76:43-53).

ISAR-TEST-5: At 10 Years, There Were no Differences in Outcomes Between Patients Treated With Polymer-Free vs Durable Polymer DES / Incidence of Stent Thrombosis was Low and Comparable / High Overall Adverse Clinical Event Rates Were Observed During Extended Follow-Up

Among 3,002 patients (median age 67.8 years) randomized to polymer-free sirolimus- and probucol-eluting stents (n=2,002) or durable polymer zotarolimus-eluting stents (n=1,000), at 10 years, 63.9% of patients were alive. The rates of composite of cardiac death, target vessel–related MI, or target lesion revascularization (device-oriented composite endpoint-DOCE]) and patient-oriented composite endpoint (POCE) (all-cause death, any MI, or any revascularization; individual components of the composite endpoints; and definite or probable stent thrombosis) were high in both groups with no difference in the incidence between polymer-free sirolimus- and probucol-eluting stents and durable polymer zotarolimus-eluting stents (DOCE: 43.8% vs. 43.0%, POCE: 66.2% vs. 67.7%; hazard ratio-HR: 0.94; p=NS). The rates of the individual components of the composite endpoints were comparable in both groups. The incidence of stent thrombosis over 10 years was low and comparable in both groups (1.6% vs. 1.9%; HR: 0.85; p=NS) (Kufner S et al, *J Am Coll Cardiol* 2020;76:146-58).

PATCH: Hydroxychloroquine (HCQ) Significantly Reduces Recurrence of Congenital Heart Block (CHB) Below the Historical Rate by >50%, Suggesting that HCQ Should be Prescribed for Secondary Prevention of Fetal Cardiac Disease in Anti-SSA/Ro-Exposed Pregnancies

Among 54 anti-SSA/Ro–positive mothers with a previous pregnancy complicated by CHB (n=19 Stage 1; n=35 Stage 2) receiving 400 mg daily of HCQ prior to completion of gestational week 10, maintained through pregnancy, by intention-to-treat (ITT) analysis, 4 of 54 evaluable pregnancies resulted in a primary outcome (7.4%). Because 9 mothers took potentially confounding medications (glucocorticoids and/or IV immunoglobulin) after enrollment but prior to a primary outcome, to evaluate HCQ alone, 9 additional mothers were recruited. In the per-protocol analysis restricted to pregnancies exposed to HCQ alone, 4 of 54 (7.4%) fetuses developed a primary outcome as in the ITT. Secondary outcomes included mild endocardial fibroelastosis (n=1) and cutaneous neonatal lupus (n=4) (Izmirly P et al, *J Am Coll Cardiol* 2020;76:292-302).

RASTAVI: In a High-Risk Population of Older Patients With Cardiovascular Disease, Randomization to Ramipril Had no Impact on Incidence or Severity of COVID-19

Among 102 patients (50 in the ramipril and 52 in the control group; mean age 82 years, 57% male) with median time of ramipril treatment of 6 months, 11 patients (10.8%) were diagnosed with COVID-19 (6 in control group and 5 receiving ramipril; hazard ratio: 1.150). The risk of COVID-19 was increased in older patients (p=0.019) and those with atrial fibrillation (p=0.066), lower hematocrit (p=0.084), and more comorbidities according to (p=0.065). Admission and oxygen supply was required in 5% of patients (2 in the ramipril group and 3 in the control group) and 4 of them died (2 in each) (Amat-Santos IJ et al, *J Am Coll Cardiol* 2020;76:268-76).

Myocardial Injury is Prevalent Among Patients Hospitalized With COVID-1, Albeit with Low Troponin Concentrations / Patients With CVD Are More Likely to Have Myocardial Injury Than Patients Without CVD / Troponin Elevation Among Patients Hospitalized With COVID-19 is Associated With Higher Risk of Mortality

Among 2,736 hospitalized patients with COVID-19 with high cardiac troponin (cTn) I (median age 66.4 years, 59.6% men), cardiovascular disease (CVD), including coronary artery disease, AF, and heart failure, was more prevalent in patients with higher cTn concentrations, as were hypertension and diabetes. A total of 506 (18.5%) patients died during hospitalization. In all, 985 (36%) patients had elevated cTn. Even small amounts of myocardial injury were significantly associated with death (adjusted hazard ratio-aHR: 1.75; p<0.001) while greater amounts (e.g., troponin I >0.09 ng/dl) were significantly associated with higher risk (aHR: 3.03; p<0.001) (Lala A et al, *J Am Coll Cardiol* 2020;76:533-46).

Arrhythmic Mitral Valve Prolapse (MVP) (AMVP): In Patients With MVP, Ventricular Arrhythmia (VA) on Holter Was Frequent But Rarely Severe / AMVP Was Independently Associated With Mitral Annulus Disjunction (MAD), Marked Leaflet Redundancy, and Repolarization Abnormalities / Long-Term Severe Arrhythmia Was Independently Associated With Excess Mortality and Reduced Event-Free Survival, Particularly Under Medical Management

Among 595 patients (age 65 ± 16 years; 278 women) with MVP, VA was frequent (43% with at least VA ≥5%), most often moderate (VT, 120-179 bpm) in 27%, and rarely severe (VT≥180 bpm) in 9%. Presence of VA was

associated with male sex, bileaflet prolapse, marked leaflet redundancy, MAD, a larger LA and LV end-systolic diameter, and T-wave inversion/ST-segment depression (all p≤ 0.001). Severe VA was independently associated with presence of MAD, leaflet redundancy, and T-wave inversion/ST-segment depression (all p<0.0001) but not with mitral regurgitation severity or ejection fraction. Overall mortality after arrhythmia diagnosis (8 years; 13 ± 2%) was strongly associated with arrhythmia severity (8 years; 10 ± 2% for no/trivial, 15 ± 3% for mild and/or moderate, and 24 ± 7% for severe arrhythmia; p=0.02). Excess mortality was substantial for severe arrhythmia (hazard ratio-HR: 2.70; p=0.01 vs. no/trivial arrhythmia), even after it was comprehensively adjusted, including for MVP characteristics (adjusted HR-aHR: 2.94; p=0.006) and by time-dependent analysis (aHR: 3.25; p=0.002). Severe arrhythmia was also associated with higher rates of mortality, defibrillator implantation, VT ablation (aHR: 4.68; p<0.0001), particularly under medical management (aHR: 5.80; p<0.0001), and weakly post-mitral surgery (aHR: 3.69; p=0.06) (Essayagh B et al, *J Am Coll Cardiol* 2020;76:637-49).

Patients With Sarcoidosis Have a Higher Associated Risk of Heart Failure (HF) and Other Adverse Cardiac Outcomes Compared With Matched Controls

Among 11,834 patients of 12,042 diagnosed with sarcoidosis, and matched with 47,336 controls (median age: 42.8 years, 54.3% men; median follow-up 8.2 years) absolute 10-year risks of outcomes were as follows: HF: 3.18% for sarcoidosis patients and 1.72% for controls; the composite of ICD implantation, ventricular arrhythmias, and cardiac arrest: 0.96% vs 0.45%; the composite of pacemaker implantation, atrioventricular block, and sinoatrial dysfunction: 0.94% vs 0.51%; atrial fibrillation or flutter: 3.44% vs 2.66%; and all-cause mortality: 10.88% vs 7.43% (Yafasova A et al, *j Am Coll Cardiol* 2020;76:767-77).

PersAFOne: The Unique Safety Profile of Pulsed Field Ablation (PFA) Potentiates Efficient, Safe, and Durable PVI and Left Atrial Posterior Wall (LAPW) Ablation, Extending the Potential Role of PFA Beyond Paroxysmal to Persistent Forms of AF

PFA is a nonthermal ablative mechanism that preferentially ablates myocardial tissue. The PFA generator delivers a pulsed electrical waveform over multiple channels. In 25 patients with persistent AF, acute PVI (96 of 96 pulmonary veins-PVs; mean ablation time: 22 min) and LAPW ablation (24 of 24 patients; median ablation time: 10 min) were 100% acutely successful with the multispline PFA catheter alone. Using the focal PFA catheter, acute cavotricuspid isthmus block was achieved in 13 of 13 patients (median: 9 min). The median total procedure time was 125 min. Post-procedure esophagogastroduodenoscopy and repeat cardiac computed tomography revealed no mucosal lesions or PV narrowing, respectively. Invasive remapping demonstrated durable isolation (defined by entrance block) in 82 of 85 PVs (96%) and 21 of 21 LAPWs (100%) treated with the pentaspline catheter. In 3 patients, there was localized scar regression of the LAPW ablation, albeit without conduction breakthrough (Reddy VY et al, *J Am Coll Cardiol* 2020;76:1068-80).

STEMI and COVID-19 Infection: Higher Thrombus Burden and Poorer Outcomes

Among 115 patients with STEMI undergoing primary PCI, those presenting with concurrent COVID-19 infection (n=39) had higher levels of troponin T and lower lymphocyte count, but elevated D-dimer and C-reactive protein. There were higher rates of multivessel thrombosis, stent thrombosis, higher modified thrombus grade post first device with consequently higher use of glycoprotein IIb/IIIa inhibitors and thrombus aspiration. Myocardial blush grade and LV function were lower in patients with COVID-19 with STEMI. Higher doses of heparin to achieve therapeutic activated clotting times were needed. These patients had a longer in-patient admission and higher rates of ICU admission (Choudry FA et al, *J Am Coll Cardiol* 2020;76:1168-76)

Multisystem Inflammatory Syndrome in Children (MIS-C) Associated With SARS-Cov-2 Led to Serious and Life-Threatening Illness in Previously Healthy Children and Adolescents

Among 186 patients with MIS-C (median age 8.3 years, 62% male, 73% previously healthy) 131 (70%) were positive for SARS-CoV-2, and 164 (88%) were hospitalized. Organ-system involvement included the GI system in 171 (92%), cardiovascular in 149 (80%), hematologic in 142 (76%), mucocutaneous in 137 (74%), and respiratory in 131 (70%). The median duration of hospitalization was 7 days; 148 patients (80%) received intensive care, 37 (20%) mechanical ventilation, 90 (48%) vasoactive support, and 4 (2%) died. Coronary-artery aneurysms were documented in 15 patients (8%), and Kawasaki's disease–like features in 74 (40%). Most patients (92%) had elevations in at least four biomarkers indicating inflammation. The use of immunomodulating therapies was common: IV immune globulin was used in 77%, glucocorticoids in 49%, and interleukin (IL)-6 or IL-1Ra inhibitors in 20% (Feldstein LR et al, *N Engl J Med* 2020; 383:334-346).

PRAETORIAN: In Patients With an Indication for an ICD But No Indication for Pacing, the Subcutaneous (SC) ICD Was Noninferior to the Transvenous (TV) ICD Regarding Device-Related Complications and Inappropriate Shocks

Among 849 patients (426 in SC ICD group and 423 in TV ICD group), at a median of 49.1 months, a primary end-point event (composite of device-related complications and inappropriate shock) occurred in 68 patients in the SC ICD group and in 68 patients in the TV ICD group (48-month Kaplan–Meier estimated cumulative incidence, 15.1% and 15.7%, respectively; hazard ratio-HR, 0.99; P=0.01 for noninferiority; P=0.95 for superiority). Device-related complications occurred in 31 vs 44 patients (HR, 0.69); inappropriate shocks in 41 vs 29 patients (HR, 1.43). Death occurred in 83 vs 68 (HR, 1.23); appropriate shocks occurred in 83 vs 57 patients (HR, 1.52) (Knops RE et al, *N Engl J Med* 2020; 383:526-36).

Analysis of 3 RCTs in HFrEF: Anticipated Treatment Effects of Early Comprehensive Disease-Modifying Pharmacological Therapy are Substantial and Support the Combination of an ARNI, β-Blocker, MRA, and SGLT2 Inhibitor as a New Therapeutic Standard

Analysis of 3 pivotal trials, EMPHASIS-HF (n=2737), PARADIGM-HF (n=8399), and DAPA-HF (n=4744), showed that the hazard ratio (HR) for the aggregate treatment effects of comprehensive disease-modifying vs conventional therapy on the primary endpoint of CV death or hospital admission for heart failure (HF) was 0.38. HRs were also favorable for CV death alone (0.50), hospital admission for heart failure alone (0.32), and all-cause mortality (0.53). Treatment with comprehensive disease-modifying pharmacological therapy was estimated to afford 2.7 additional years (for an 80-year-old) to 8.3 additional years (for a 55-year-old) free from CV death or first hospital admission for HF and 1.4 additional years (for an 80-year-old) to 6.3 additional years (for a 55-year-old) of survival compared with conventional therapy (Vaduganathan M et al, *Lancet* 2020;396:121-8).

Hospital Admissions in England for Acute Coronary Syndrome (ACS): Compared With the Weekly Average in 2019, there was a Substantial Reduction in Numbers of Patients With ACS Admitted to Hospital by the End of March, 2020, Partly Reversed by End of May, 2020, Likely Having Resulted in Increases in Out-Of-Hospital Deaths and Long-Term Complications of MI and Missed Opportunities for Secondary Prevention of Coronary Heart Disease

Hospital admissions for ACS declined from mid-February, 2020, falling from a 2019 baseline rate of 3017 to 1813 admissions per week by the end of March, 2020, a reduction of 40%. This decline was partly reversed during April and May, 2020, such that by the last week of May, 2020, there were 2522 admissions, representing a 16% reduction from baseline. During the period of declining admissions, there were reductions in the numbers of admissions for all types of ACS, (STEMI and NSTEMI), but relative and absolute reductions were larger for NSTEMI, with 1267 admissions per week in 2019 and 733 per week by the end of March, 2020, a percent reduction of 42%. In parallel, reductions were recorded in the number of PCI procedures for patients with both STEMI (438 PCI procedures per week in 2019 *vs* 346 by the end of March, 2020; percent reduction 21%) and NSTEMI (383 PCI procedures per week in 2019 *vs* 240 by the end of March, 2020; percent reduction 37%). The median length of stay among patients with ACS fell from 4 days in 2019 to 3 days by the end of March, 2020 (Mafham MM et al, *Lancet* 2020; 396:381-389).

Patients With Severe Sepsis-Induced Cardiogenic Shock Treated With Venoarterial (VA)-ECMO Had a Large and Significant Improvement in Survival Compared With Controls not Receiving ECMO

Comparing outcomes of 82 patients (aged ≥18 years) with septic shock who received VA-ECMO with 130 controls (not receiving ECMO), at baseline patients treated with VA-ECMO had more severe myocardial dysfunction (mean cardiac index 1.5 L/min per m^2 *vs* 2.2 L/min per m^2, LVEF 17% *vs* 27%), more severe hemodynamic impairment, and more severe organ failure ($p<0.0001$ for each comparison). Survival at 90 days for patients treated with VA-ECMO was higher than for controls (60% *vs* 25%, risk ratio-RR for mortality 0.54; $p<0{\cdot}0001$). After propensity score weighting, ECMO remained associated with improved survival (51% *vs* 14%, adjusted RR for mortality 0.57; p=0.0029). Lactate and catecholamine clearance were also significantly enhanced in patients treated with ECMO. Among the 49 survivors treated with ECMO, 32 who had been treated at the largest center reported satisfactory health-related quality of life at 1-year follow-up (Brechot N et al, *Lancet* 2020;396:545-52).

SENIOR-NSTEMI: The Survival Advantage of Invasive vs Non-Invasive Management Appears to Extend to Patients With NSTEMI Who are Aged ≥80 Years

Of the 1976 patients with NSTEMI, 101 died within 3 days of their peak troponin concentration and 375 were excluded because of extreme propensity scores. The remaining 1500 patients had a median age of 86 years of whom 56% received non-invasive management. During a

median of 3 years, 613 (41%) patients died. The adjusted cumulative 5-year mortality was 36% in the invasive management group and 55% in the non-invasive management group (adjusted hazard ratio-aHR 0.68). Invasive management was associated with lower incidence of hospital admissions for heart failure (aHR 0.67) (Kaura A et al, *Lancet* 2020; 396:623-634).

EXPLORER-HCM: Treatment With Mavacamten Improved Exercise Capacity, LVOT Obstruction, NYHA Class, and Health Status in Patients With Obstructive Hypertrophic Cardiomyopathy (HCM)

Among 429 adults with HCM, of whom 251 (59%) were randomly assigned to mavacamten (selective allosteric inhibitor of cardiac myosin ATPase) (49%) or placebo (51%), 45 (37%) of 123 patients on mavacamten vs 22 (17%) of 128 on placebo met the primary endpoint (≥1.5 mL/kg/min increase in peak oxygen consumption (pVO_2) and at least one NYHA class reduction or a ≥3 mL/kg/min pVO_2 increase without NYHA class worsening) (difference +19·4%; p=0.0005). Patients on mavacamten had greater reductions than those on placebo in post-exercise LVOT gradient (−36 mmHg; p<0.0001), greater increase in pVO_2 (+1.4 mL/kg/min; p=0.0006), and improved symptom scores (p<0.0001). 34% more patients in the mavacamten group improved by at least one NYHA class (p<0.0001). Safety and tolerability were similar to placebo. Treatment-emergent adverse events were generally mild. One patient had sudden death in the placebo group (Olivotto I et al, *Lancet* 2020;396:759-69).

Meta-analysis: The Effects of Empagliflozin and Dapagliflozin on Hospitalizations for Heart Failure Were Consistent in the 2 Independent Trials and Suggest that these Agents Also Improve Renal Outcomes and Reduce All-Cause and Cardiovascular Death in Patients With HFrEF

Meta-analysis of DAPA-HF (dapagliflozin) and EMPEROR-Reduced (empagliflozin) RCTs indicated that among 8474 patients, the estimated treatment effect was a 13% reduction in all-cause death (pooled HR 0.87; p=0.018) and 14% reduction in CV death (HR 0.86; p=0.027). SGLT2 inhibition conferred a 26% relative reduction in the combined risk of CV death or first hospitalization for HF (HR 0.74; p<0.0001), and a 25% decrease in the composite of recurrent hospitalizations for HF or CV death (HR 0.75; p<0.0001). The risk of the composite renal endpoint was also reduced (HR 0.62; p=0.013). The pooled treatment effects showed consistent benefits for subgroups based on age, sex, diabetes, treatment with an ARNI and baseline eGFR, but suggested treatment-by-subgroup interactions for subgroups based on NYHA class and race (Zannad F et al, *Lancet* 2020; 396:819-29).

Valve-in-Valve TAVI (VIV-TAVI) Confers an Advantage Over Repeat Surgical Aortic Valve Replacement (Re-SAVR) in Terms of 30-Day Mortality, Morbidity, and Bleeding Complications in High-Risk Patients With Degenerated Bioprosthetic Aortic Valves

In patients with degenerated bioprosthetic aortic valves who underwent either VIV-TAVI ($n = 3443$) or isolated re-SAVR ($n = 3372$), VIV-TAVR patients conferred lower 30-day mortality (2.7% vs. 5.0%), 30-day morbidity (66.4% vs. 79%), and rates of major bleeding (35.8% vs. 50%). On multivariable analysis, re-SAVR was a significant risk factor for both 30-day mortality (adjusted odds ratio-aOR 0.48) and 30-day morbidity (aOR 0.54). After matching ($n = 2181$ matched pairs), VIV-TAVI was associated with lower odds of 30-day mortality (OR 0.41), 30-day morbidity (OR 0.53), major bleeding (OR 0.66), shorter length of stay (median savings of 2 days) and higher odds of routine home discharges (OR 2.11) (Hirji SA et al, *Eur Heart J* 2020;41: 2747–2755).

New-Onset Persistent Left Bundle Branch Block (NOP-LBBB) and Implantation of Permanent Pacemaker (PPM) After TAVI Confer Increased Risk of All-Cause Death and Heart Failure Hospitalization at 1-Year / Periprocedural NOP-LBBB Also Increased Risk of Cardiac Death and PPM at 1 Year

Meta-analysis of 30 studies, including 7792 patients (12 studies) and 42,927 patients (21 studies) for the evaluation of the impact of NOP-LBBB and PPM after TAVI indicated that NOP-LBBB was associated with an increased risk of all-cause death (risk ratio-RR 1.32; $P < 0.001$), cardiac death (RR 1.46; $P < 0.001$), heart failure hospitalization (RR 1.35; $P = 0.02$), and PPM (RR 1.89; $P < 0.001$) at 1-year follow-up. Periprocedural PPM after TAVI was associated with a higher risk of all-cause death (RR 1.17; $P < 0.001$) and heart failure hospitalization (RR 1.18; $P = 0.02$). PPM implantation was not associated with an increased risk of cardiac death (RR 0.84; $P = 0.13$) (Faroux L et al, *Eur Heart J* 2020; 41: 2771–2781).

Catheter Ablation Improves Survival Rate, Reduces Re-Hospitalization, Increases Maintenance of Sinus Rhythm, Contributes to Preserve Cardiac Function, and Improves Quality of Life for AF Patients Complicated With Heart Failure (HF)

Pooled analysis of 11 studies involving 3598 patients showed that, as compared with rate control, antiarrhythmic drug (AAD) rhythm control was associated with similar all-cause mortality (odds ratio-OR: 0.96, $P = $ NS), higher

rate of re-hospitalization (OR: 1.25, $P = 0.01$), and similar rate of stroke and thromboembolic events (OR: 0.91, $P = 0.76$). Catheter ablation was associated with lower all-cause mortality (OR: 0.51, $P = 0.0003$), reduced re-hospitalization rate (OR: 0.44, $P = 0.003$), similar rate of stroke events (OR: 0.59, $P = 0.27$), greater improvement in LVEF (weighted mean difference: 6.8%, $P = 0.0004$), lower arrhythmia recurrence (29.6% vs. 80.1%, OR: 0.04, $P < 0.00001$), and greater improvement in quality of life ($P = 0.007$) (Chen S et al, *Eur Heart J* 2020;41: 2863–73).

Increase in Out-of-Hospital Cardiac Arrest (OHCA) in 2020 is Correlated to the COVID-19 Pandemic, Coupled With a Reduction in Short-Term Outcome

The cumulative incidence of COVID-19 from 21/2/2020 to 20/4/2020 in an Italian territory was 956 COVID-19/100,000 inhabitants and cumulative incidence of OHCA was 21 cases/100,000 inhabitants, with a 52% increase as compared with 2019 (490 OHCAs in 2020 vs 321 in 2019). A correlation was found between difference in cumulative incidence of OHCA between 2020 and 2019 per 100,000 inhabitants and the COVID-19 cumulative incidence per 100,000 inhabitants both for the overall territory (ρ 0.87, $P<0.001$) and for each province ($P < 0.001$) (Baldi E et al, *Eur Heart J* 2020;41: 3045–3054).

Intensive Systolic Blood Pressure (SBP) Lowering: Current Literature Supports Intensive BP Lowering in Patients With Hypertension for Improving CV Outcomes, But Data are Less Clear for Patients With Diabetes or CV Disease

Per 8 systematic reviews of RCTs examining either a standardized SBP target of −10 mm Hg (1 SR) or BP lowering below a target threshold, there is benefit of a 10–mmHg reduction in SBP for CV outcomes among patients with hypertension in the general population, chronic kidney disease, and heart failure. Evidence on reducing SBP for CV outcomes in patients with a history of CV disease (moderate strength) or diabetes (high strength) to a lower SBP target was mixed. Low-strength evidence supported intensive lowering to a 10–mm Hg reduction in SBP for CV outcomes in patients with a history of stroke. Safety results were mixed or inconclusive (D'Ansi K et al, *Ann Intern Med* 2020; Sep 1. doi: 10.7326/M20-203)

Important Review and Other Articles

● **Medical Marijuana, Recreational Cannabis, and Cardiovascular Health: AHA Statement (**Page II RL et al, *Circulation* 2020;142:e131–e152)

● **Heart Regeneration** by endogenous stem cells and cardiomyocyte proliferation (He L et al, *Circulation* 2020; 142:275-91)

● **Cardiorespiratory fitness** in youth (Raghuveer G et al *Circulation* 2020;142: e101–e118)

● **Glucagon-Like Peptide 1 Receptor Agonists and Heart Failure** (Khan MS et al, *Circulation* 2020:142:1205–1218)

● **Tachyarrhythmias in Pheochromocytoma** *(*Nazari MA et al, *J Am Coll Cardiol 2020;76:451-64)*

● **Heart failure with recovered LVEF** (Wilcox JE et al, *J Am Coll Cardiol* 2020;76: 719–34)

● **Spontaneous coronary artery dissection** (Hayes SN et al, *J Am Coll Cardiol* 2020;76:961–84)

● **Renin-Angiotensin-System Blocker Facilitation vs Countering COVID-19 Infection** (Manolis AS et al, *J Cardiovasc Pharmacol* 2020. doi: 10.1097/FJC.0000000000000894*)*

● ACC Consensus: Management of **bleeding in patients on oral anticoagulants** (Tomaselli GF et al, *J Am Coll Cardiol* 2020; 76:594-622)

● **Cardiorenal syndrome** (Jentzer JC et al, *J Am Coll Cardiol* 2020; 76:1084-101)

● **Pulmonary Hypertension in HFpEF and HFrEF** (Guazzi M et al, *J Am Coll Cardiol* 2020; 76:1102-11)

● **CT coronary angiography** (Abdelrahman KM et al, *J Am Coll Cardiol* 2020; 76: 1226-43)

● Telehealth and arrhythmia monitoring during the pandemic (Varma N et al, *J Am Coll Cardiol* 2020; 76: 1363-74)

● **MI management during the COVID-19 pandemic: SCAI/ACC/ACEP** Position Statement (Mahmud E et al, *J Am Coll Cardiol* 2020;76:1375-84)

● Acute **ischemic stroke** (Powers WJ, *N Engl J Med* 2020; 383:252-260)

● **Coffee, caffeine and health** (van Dam RM et al, *N Eng J Med* 2020; 383:369-378)

● **Endocarditis** (Chambers HF et al, *N Eng J Med* 2020; 383:567-576)

● **Atherosclerotic plaque healing** (Vergallo R et al, *N Engl J Med* 2020; 383:846-857)

● **Cardiogenic shock** (Combes A et al, *Lancet* 2020;396:199-312)

● **Vulnerable plaques** (Tomaniak M et al, *Eur Heart J* 2020; 41:2997–3004)

● **ACS-NNOCA and sudden cardiac death** (Kosmas N et al, *Europace* 2020;22:1303-1310)

● **COVID-19** Infection: Viral **Macro- and Micro-Vascular Coagulopathy and Thromboembolism** (Manolis AS et al, *J Cardiovasc Pharmacol Ther* 2020 Sep 14; doi: 10.1177/1074248420958973)

● **Mitochondrial dysfunction in cardiovascular disease** (Manolis AS et al, *Med Res Rev* 2020 Sep 21. doi: 10.1002/med.21732)