Cardiology News / Recent Literature Review / Last Quarter 2020

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26th Annual International **AF** Virtual **Symposium**, 29-31/1/2021

EHRA online **Congress**, 23-25/4/2021

ACC Meeting: Atlanta, 15-17/5/2021

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TCT Meeting, San Francisco, 22-26/10/2021

Active Myocardial Inflammation is a Powerful Predictor of Recurrent Ventricular Tachycardia (VT) Following Catheter Ablation: VT Ablation Should be Avoided During Active Myocarditis (AM), But is Often of Benefit for Recurrent VT After the Acute Phase of Myocarditis

Among 125 consecutive patients (age 51±14 years, 91% men, LVEF 52%±9%) with myocarditis diagnosed by endomyocardial biopsy (59%) and/or cardiac magnetic resonance (90%), undergoing VT ablation, with all patients showing low-voltage areas (LVA) at electro-anatomical map (97% epicardial or endoepicardial), VT recurrences were documented in 25 patients (20%) by 12 months, and in 43 (34%) by last follow-up (median 63 months). At multivariable analysis, active myocarditis (AM) stage was the only predictor of VT recurrences by 12 months (hazard ratio: 9.5; $p < 0.001$), whereas both AM stage and wide border zone were associated with arrhythmia recurrences anytime during follow-up. No VT episodes were found after redo ablation was performed in 23 patients with previous (non-active) myocarditis (Peretto G et al, *J Am Coll Cardiol* 2020;76:1644–1656).

Left Ventricular (LV) Non-Compaction (LVNC): Vigorous Recreational Physical Activity (VPA) May be a Possible Determinant of LV Hypertrabeculation in Asymptomatic Individuals

In PESA (Progression of Early Subclinical Atherosclerosis) study participants (n = 4,184 subjects free of cardiovascular disease), LVNC phenotype prevalence according to the Petersen criterion was significantly higher among participants in the highest VPA quintile (Q5 = 30.5%) than in participants with no VPA (14.2%). The Jacquier and Grothoff criteria were also more frequently fulfilled in participants in the highest VPA quintile (Jacquier Q5 = 27.4% vs no VPA = 12.8% and Grothoff Q5 = 15.8% vs no VPA = 7.1%). The prevalence of the systolic Stacey LVNC criterion was low (3.6%) and did not differ significantly between no VPA and Q5 (de la Chica JA et al, *J Am Coll Cardiol* 2020;76: 1723–1733).

Interleukin-1β (IL-1β) Measured on Admission is Associated with Risk of Premature Death in Patients With Myocardial Infarction

IL-1β concentration measured at admission in 1,398 patients with ST-segment elevation MI (STEMI) was associated with all-cause mortality at 90 days (adjusted hazard ratio - adjHR: 1.47 per 1 SD increase; $p < 0.002$). The relation was nonlinear, and the highest tertile of IL-1β was associated with higher mortality rates at 90 days (adjHR: 2.78; $p = 0.0002$) and at 1 year (adjHR: 1.93; $p = 0.005$), regardless of the hs-CRP concentration. Significant relationships were equally observed when considering cardiovascular mortality and MACEs at 90 days (adjHR: 2.42; $p = 0.002$, and adjHR: 2.29; $p = 0.004$, respectively) and at 1 year (adjHR: 2.32; $p = 0.002$, and adjHR: 2.35; $p = 0.001$, respectively) (Silvain J et al, *J Am Coll Cardiol* 2020;76:1763–1773).

Anticoagulation Confers Lower Mortality and Intubation Among Hospitalized COVID-19 Patients

Among 4,389 patients (median age 65 years, 44% women), compared with no anticoagulation (n = 1,530; 34.9%), therapeutic (n = 900; 20.5%) and prophylactic anticoagulation (n = 1,959; 44.6%) were associated with lower in-hospital mortality (adjusted hazard ratio -aHR: 0.53; and aHR: 0.50, respectively), and intubation (aHR: 0.69 and aHR: 0.72, respectively). When initiated ≤48 h from admission, there was no statistically significant difference between therapeutic (n=766) versus prophylactic anticoagulation (n = 1,860) (aHR: 0.86; 95% CI: 0.73 to 1.02; $p = 0.08$). Overall, 89 patients (2%) had major bleeding adjudicated by clinician review, with 27 of 900 (3.0%) on therapeutic, 33 of 1,959 (1.7%) on prophylactic, and 29 of 1,530 (1.9%) on no anticoagulation. Of 26 autopsies, 11 (42%) had thromboembolic disease not clinically suspected and 3 of 11 (27%) were on therapeutic anticoagulation (Nadkarni GN et al, *J Am Coll Cardiol* 2020;76:1815–1826)

PARTNER 2A Trial & Registry: Compared with Surgical Aortic Valve Replacement (SAVR), the Second-Generation, But not the Third-Generation, SAPIEN XT Balloon-Expandable Valve Has a Higher 5-Year Rate of Structural Valve Deterioration (SVD)

Compared with SAVR, the SAPIEN-XT TAVI cohort had a significantly higher 5-year exposure adjusted incidence rates (per 100 patient-years) of SVD

(1.61±0.24% vs 0.63±0.16%), SVD-related bioprosthetic valve failure (BVF) (0.58±0.14% vs 0.12±0.07%), and all-cause BVF (0.81±0.16% vs 0.27±0.10%) ($p \leq 0.01$ for all). The 5-year rates of SVD (0.68±0.18% vs 0.60±0.17%; p=0.71), SVD-related BVF (0.29±0.12% vs 0.14±0.08%; p=0.25), and all-cause BVF (0.60±0.15% vs 0.32±0.11%; p=0.32) in SAPIEN 3 TAVI were not significantly different to a propensity score matched SAVR cohort (Pibarot P et al, *J Am Coll Cardiol* 2020;76: 1830–1843).

Outcomes of Surgical Explantation of a TAVI Prosthesis: Although the Overall Incidence is Low (0.2%: 0.28% in the Early and 0.14% in the Newer TAVI Era), Short-Term Mortality is High (13% at 1 Month and 23% at 1 Year)

Among patients undergoing TAVI (2012-2017), the incidence of surgical explantation was 0.2% (227 of 132,633 patients); 0.28% and 0.14% in the early and newer TAVI era, respectively. The median time to surgical explant was 212 days, whereas 8.8% and 70.9% underwent surgical explantation within 30 days and 1 year, respectively. The primary indication for reintervention was bioprosthetic failure (79.3%). Compared with the no-explant cohort, the explant cohort was younger (mean age 73.7 years vs. 81.7 years), with a lower prevalence of heart failure (55.9% vs 65.8%) but more likely a lower-risk profile cohort (15% vs 2.4%; all $p<0.05$). The 30-day and 1-year mortality rates were 13.2% and 22.9%, respectively, and did not vary by either time to surgical explant or TAVI era, or between patients with vs without endocarditis (all $p>0.05$). The time-dependent Cox regression analysis demonstrated a higher mortality in those with surgical explantation (hazard ratio: 4.03 vs. no-explant group). Indication, time-to-surgical-explant, and year of surgical explantation were not associated with worse post-explantation survival (all $p>0.05$) (Hirji SA et al, *J Am Coll Cardiol* 2020;76:1848-59)

Unlike Classic Kawasaki Disease (KD), Coronary Arteries May be Spared in Early Multisystem Inflammatory Syndrome in Children (MIS-C); However, Myocardial Injury is Common / At Short Follow-Up, there is Recovery of Systolic Function But Persistence of Diastolic Dysfunction and No Coronary Aneurysms

Of 28 MIS-C, 20 healthy control subjects and 20 classic Kawasaki disease (KD) patients, only 1 case in the MIS-C group (4%) manifested coronary artery dilatation (z score = 3.15) in the acute phase, showing resolution during early follow-up. Left ventricular (LV) systolic and diastolic function measured by deformation parameters were worse in patients with MIS-C compared with KD. Moreover, MIS-C patients with myocardial injury were more affected than those without myocardial injury with respect to all functional parameters as assessed by strain echo. The preserved LV ejection fraction (EF) group in MIS-C showed diastolic dysfunction. During the subacute period (interval 5.2 ± 3 days), LVEF returned to normal (median from 54% to 64%; $p<0.001$) but diastolic dysfunction persisted (Matsubara D et al, *J Am Coll Cardiol* 2020;76:1947–1961)

3 Large U.S. Prospective Cohort Studies Indicate that Dietary Patterns With Higher Inflammatory Potential are Significantly Associated With a Higher Incidence of Cardiovascular Disease (CVD) and Stroke

Using a food-based empirical dietary inflammatory pattern (EDIP) score, dietary patterns associated with lower inflammation (e.g., the Mediterranean diet / green leafy vegetables, yellow vegetables, whole grains, coffee, tea, and wine, rich in anti-inflammatory compounds, e.g., vitamins, carotenoids, flavonoids, and fiber) were compared with proinflammatory dietary patterns (e.g. refined grains, processed, red, and organ meat) in 74,578 women from the Nurses' Health Study (NHS) (1984–2016), 91,656 women from the NHSII (1991–2015), and 43,911 men from the Health Professionals Follow-up Study (1986–2016) who were free of CVD and cancer at baseline. During 5,291,518 person-years, 15,837 incident CVD cases were documented, including 9,794 coronary heart disease (CHD) cases and 6,174 strokes. In pooled analyses of the 3 cohorts, a higher dietary inflammatory potential, as indicated by higher EDIP scores, was associated with an increased risk of CVD (hazard ratio-HR comparing the highest to lowest quintiles: 1.38; p for trend <0.001), CHD (HR: 1.46; $p<0.001$), and stroke (HR: 1.28; $p<0.001$). These associations were consistent across cohorts and between sexes, and they remained significant after further adjustment for other dietary quality indices. In a subset of participants (n=33,719), a higher EDIP was associated with a higher circulating profile of proinflammatory biomarkers, lower levels of adiponectin, and an unfavorable lipid profile ($p<0.001$) (Li J et al, *J Am Coll Cardiol* 2020;76:2181-93)

CAPIAS: Vulnerable (Complicated) Carotid Artery Plaques (CAPs) Without Significant Stenosis as a Cause of Cryptogenic Stroke (CS)

Among 234 patients, 196 had either CS (n=104), cardioembolic or small vessel stroke (CES/SVS) (n=79), or large artery stroke (LAS) (n=19) and complete carotid MRI data. Prevalence of complicated CAP in patients with CS was higher ipsilateral (31%) compared with contra-lateral to the infarct (12%; p=0.0005). The prevalence of

ipsilateral complicated CAP was significantly higher in CS (31%) compared with CES/SVS (15%; p=0.02) and lower in CS compared with LAS (68%; p=0.003). Lipid-rich and/or necrotic cores in ipsilateral CAP were significantly larger in CS compared with CES/SVS (p<0.05) (Kopczak A et al, *J Am Coll Cardiol* 2020;76:2212–22)

History of Heart Failure (HF) Confers Higher Risk of Mechanical Ventilation and Mortality Among Patients Hospitalized for COVID-19, Regardless of LVEF

A retrospective analysis of 6,439 patients admitted for COVID-19 (mean age 63.5 years, 45% women) showed that compared with patients without HF, those with previous HF experienced longer length of stay (8 vs 6 days; p<0.001), increased risk of mechanical ventilation (22.8% vs 11.9%; adjusted odds ratio-OR: 3.64; p<0.001), and mortality (40% vs 24.9%; OR: 1.88; p=0.002). Outcomes among patients with HF were similar, regardless of LVEF or renin-angiotensin-aldosterone inhibitor use (Alvarez-Garcia J et al, *J Am Coll Cardiol* 2020;76:2334-48)

ISAR-REACT 5 Trial (Post-Hoc Analysis): In Patients With Non-ST Elevation Acute Coronary Syndromes (NSTE-ACS), Prasugrel Was Superior to Ticagrelor in Reducing the Combined 1-Year Risk of Death, MI, and Stroke Without Increasing the Risk of Bleeding

Among 1,179 patients with NSTE-ACS assigned to ticagrelor and 1,186 assigned to prasugrel, the primary endpoint (death, MI, or stroke) was reached in 8.7% in the ticagrelor and in 6.3% in the prasugrel group (hazard ratio-HR: 1.41). The HR for all-cause death was 1.43 and that for MI 1.43. The safety endpoint (BARC class 3-5) occurred in 49 (5.2%) vs 41 (4.7%) patients (HR: 1.09). Landmark analysis revealed persistence of efficacy advantage with prasugrel after the first month (Valina C et al, *J Am Coll Cardiol* 2020;76: 2436-46).

DUBIUS: In Patients With NSTE-ACS With Planned Invasive Treatment, Both a Downstream Strategy With Prasugrel or Ticagrelor or a Ticagrelor-Based Pre-Treatment Strategy Showed Low and Similar Rates of 30-Day Major Ischemic and Bleeding Events

Among 1,449 patients randomized to downstream or upstream oral $P2Y_{12}$ inhibitor administration, the rate of the primary endpoint, a composite of death due to vascular causes; nonfatal MI or nonfatal stroke; and BARC type 3, 4, and 5 bleeding through day 30, did not differ between the downstream and upstream groups (percent absolute risk reduction: –0.46). These results were confirmed among patients undergoing PCI (72% of population) and regardless of the timing of coronary angiography (within or after 24 h from enrollment) (Tarantini G et al, *J Am Coll Cardiol* 2020;76:2450-59).

Percutaneous Mitral Valve Edge-To-Edge Repair With the Mitraclip Device Showed a 15% Incidence of Acute Kidney Injury (AKI) Post-Procedurally Despite the Lack of Significant Contrast Use / Post-Procedural AKI Negatively Affected Survival and Renal Function at Follow-Up, With Worse Outcomes Especially if Mitral Repair Was Suboptimal

Among 721 patients undergoing MitraClip (aged 72 ± 11 years; 28% women), AKI occurred in 106 patients (14.7%). Baseline hemoglobin (<11 g/dl) (odds ratio-OR: 1.97; p=0.003), urgent procedure (OR: 3.44; p=0.003), and absence of device success (OR: 3.37; p<0.001) were predictors of AKI. Patients with AKI had worse outcomes compared to those without AKI, including a higher proportion of in-hospital bleeding events (3.8% vs 0.8%; p=0.011), 2-year all-cause mortality (40.5% vs 18.7%; p<0.001), and major adverse cardiac events (63.6% vs 23.5%; p<0.001). Combination of AKI with significant residual MR after the procedure conferred even worst outcomes (2-year all-cause mortality 50% vs 19.6%; p=0.001, and major adverse cardiac events 70% vs 18.9%; p<0.001) (Armijo G et al, *J Am Coll Cardiol* 2020;76: 2463-73).

More Severe Brain Injuries in Bicuspid Aortic Valve (BAV) Patients Due to Greater Number of Lesions, But Also Larger Lesion Size in the Early Phase After TAVI

Among 204 consecutive severe aortic stenosis patients undergoing TAVI, 83 (40.7%) were BAV patients, and the other 121 patients were tricuspid aortic valve (TAV) patients. Median ages (76 vs 79 years; p=0.004) and STS scores (4.87 vs 6.38; p=0.044) of the BAV and TAV patients were significantly different, while the overt stroke rates (2.4% vs 1.7%; p=0.704) were comparable. BAV patients were associated with higher number of new lesions (4 vs 2; p=0.008), total lesion volume (290 vs 140 mm^3; p=0.008), and the volume per lesion (70.0 mm^3 vs 57.5 mm^3; p=0.037) in diffusion-weighted MRI (DW-MRI). Moreover, the proportion of patients with lesions >1 cm^3 (28.6% vs 10.9%; p=0.005) was higher in BAV patients than in TAV patients (Fan J et al, *J Am Coll Cardiol* 2020;76:2579-90).

DISRUPT CAD III: Coronary Intravascular Lithotripsy (IVL) Safely and Effectively Facilitated Stent Implantation in Severely Calcified Lesions

Among 431 patients undergoing IVL, the primary safety endpoint of the 30-day freedom from major adverse cardiovascular events was 92.2%; the lower bound of the 95% confidence interval was 89.9%, which exceeded the pre-specified performance goal (PG) of 84.4% (p< 0.0001). The primary effectiveness endpoint of procedural

success was 92.4%; the lower bound of the 95% confidence interval was 90.2%, which exceeded the PG of 83.4% (p<0.0001). Mean calcified segment length was 47.9±18.8 mm, calcium angle was 292.5±76.5°, and calcium thickness was 0.96±0.25 mm at the site of maximum calcification. OCT demonstrated multiplane and longitudinal calcium fractures after IVL in 67.4% of lesions. Minimum stent area was 6.5±2.1 mm^2 and was similar regardless of demonstrable fractures on OCT (Hill JD et al, *J Am Coll Cardiol* 2020;76:2635-46).

Empagliflozin May Have a Favorable Effect on Reducing Cardiac Filling Pressure After 12 Weeks of Treatment in Patients With Stable HFrEF

Among 70 patients with HFrEF (mean age 57 years, mean LVEF 26%, 12 (17%) with diabetes) randomized to empagliflozin 10 mg or matching placebo qd on guideline-driven heart failure therapy for 12 weeks, there was no significant treatment effect on peak pulmonary wedge pressure (PWP)/cardiac index (CI) (−0.13 mm Hg/l/min/m^2; p=0.86). Considering hemodynamics over the full range of exercise loads, PWP was significantly reduced (−2.40 mm Hg; p=0.003), but not CI (−0.09 l/min/m^2; p = 0.448) by empagliflozin. This was consistent among patients with and without type 2 diabetes (Omar M et al, *J Am Coll Cardiol* 2020;76:2740-51).

Echocardiography-Guided Risk Stratification for Long QT Syndrome: Electromechanical Window (EMW) Negativity (Difference Between the Interval from QRS Onset to Aortic Valve Closure Midline, as Derived for Continuous-Wave Doppler, and the ECG-Derived QT Interval for the Same Beat) Outperformed Heart Rate–Corrected QT Interval as a Predictor of Symptomatic Status

In a cohort of 651 patients with LQTS (age 26±17 years; 60% females; 158 symptomatic; 51% LQTS type 1; 33% LQTS type 2; 11% LQTS type 3; 5% multiple mutations) and 50 healthy controls, a negative EMW was found among nearly all patients with LQTS compared to controls, with more profound EMW negativity in patients with symptomatic LQTS compared to those with asymptomatic LQTS (−52±38 ms vs −18±29 ms; p<0.0001). Logistic regression identified EMW, QTc, female sex, and LQTS genotype as univariate predictors of symptomatic status. After multivariate analysis, EMW remained an independent predictor of symptomatic status (odds ratio for each 10-ms decrease in EMW: 1.37; p< 0.0001). EMW outperformed QTc in predicting symptomatic patients (area under the curve: 0.78 vs 0.70; p=0.01). After training and implementation, EMW correlation from echo sonographers showed excellent reliability (intraclass correlation coefficient: 0.93) (Sugrue A et al, *J Am Coll Cardiol* 2020;76:2834–2843).

Swedish Registries: The Incidence of Out-Of-Hospital Cardiac Arrest (OHCA) Within 90 Days after MI was <0.3% / 5 Clinical Parameters in Addition to LVEF Predicted OHCA and Non-OHCA Death Better Than LVEF Alone

Among 121,379 cases, OHCA occurred in 349 (0.29%) and non-OHCA death in 2,194 (1.8%). A total of 6 variables (male sex, diabetes, eGFR <30 ml/min/1.73 m^2, Killip class ≥II, new-onset atrial fibrillation/flutter, and impaired LVEF categorized as 40-49%, 30-39%, and <30%) were identified as independent predictors, were assigned points, and were grouped into 3 categories, where the incidence of OHCA ranged from 0.12% to 2.0% and non-OHCA death from 0.76% to 11.7%. Stratified by LVEF <40% alone, the incidence of OHCA was 0.20% and 0.76% and for non-OHCA death 1.1% and 4.9% (Faxen J et al, *J Am Coll Cardiol* 2020;76:2926-36).

RAPCO Trials on Best Second Conduit: The 10-year Patency Rate of the Radial Artery (RA) is Significantly Higher than that of the Free RIMA and Better than that of the Saphenous Vein (SV)

In the RA vs RIMA comparison, the estimated 10-year patency was 89% for RA vs 80% for free RIMA (hazard ratio-HR for graft failure, 0.45). 10-year patient survival estimate was 90.9% in the RA arm vs 83.7% in the RIMA arm (HR for mortality, 0.53). In the RA vs SV comparison, the estimated 10-year patency was 85% for the RA vs 71% for the SV (HR for graft failure, 0.40), and 10-year patient survival estimate was 72.6% for the RA group vs 65.2% for the SV group (HR for mortality, 0.76) (Buxton BF et al, *Circulation* 2020;142:1330-38)

Meta-Analysis: In Comparison With 1-Year Dual Antiplatelet Therapy (DAPT), Short-Term DAPT Followed by P2Y12 Inhibitor Monotherapy Reduces Major Bleeding After PCI With Drug-Eluting Stents, Whereas Extended-Term DAPT Reduces MI at the Expense of More Bleeding Events

Meta-analysis of 24 randomized, controlled trials comprising 79,073 patients, showed that at a median follow-up of 18 months, extended-term DAPT was associated with a reduced risk of MI in comparison with 12-month DAPT (absolute risk difference, –3.8 incident cases per 1000 person-years; relative risk, 0.68), midterm DAPT (absolute risk difference, –4.6 incident cases per 1000 person-years; relative risk, 0.61), and short-term DAPT followed by aspirin monotherapy (absolute risk difference, –6.1 incident cases per 1000 person-years; relative risk, 0.55), or P2Y12 inhibitor monotherapy

(absolute risk difference, –3.7 incident cases per 1000 person-years; relative risk, 0.69). Conversely, extended-term DAPT conferred a higher risk of major bleeding than all other DAPT groups. In comparison with 12-month DAPT, no significant differences in the risks of ischemic end points or major bleeding were observed with midterm or short-term DAPT followed by aspirin monotherapy, with the exception that short-term DAPT followed by P2Y12 inhibitor monotherapy was associated with a reduced risk of major bleeding. There were no significant differences in mortality between the different DAPT strategies. In ACS, extended-term in comparison with 12-month DAPT was associated with a reduced risk of MI without a significant increase in the risk of major bleeding (Khan SU et al, *Circulation* 2020;142:1425–143).

DAI-T4F Nationwide French Registry: Patients with Tetralogy of Fallot (ToF) and an ICD Experience High Rates of Appropriate Therapies, Including Those Implanted in Primary Prevention, Albeit with Considerable Long-Term ICD-Related Complications

Among 165 ToF patients (aged 42.2±13.3 years, 70.1% males, 104 or 63% in secondary prevention), over a median of 6.8 years, 78 (47.3%) patients received at least 1 appropriate ICD therapy. The annual incidence of the primary outcome (appropriate ICD therapy) was 10.5% (7.1% and 12.5% in primary and secondary prevention, respectively; *P*=0.03). Overall, 71 (43%) patients presented with at least 1 ICD complication, including inappropriate shocks in 42 (25.5%) and lead dysfunction in 36 (21.8%) patients. Among 61 (37%) patients in primary prevention, the annual rate of appropriate ICD therapies was 4.1%, 5.3%, 9.5%, and 13.3% in patients with, respectively, 0, 1, 2, or ≥3 guidelines-recommended risk factors. QRS fragmentation was the only independent predictor of appropriate ICD therapies (hazard ratio, 3.47), and its integration in a model with current criteria increased the 5-year time-dependent area under the curve from 0.68 to 0.81 (*P*=0.006). Patients with congestive heart failure or reduced LVEF had a higher risk of nonarrhythmic death or heart transplantation (hazard ratio, 11.01) (Waldmann V et al, *Circulation* 2020;142:1612-22).

SWEDEHEART Registry: Ticagrelor in Elderly Patients With MI Was Associated With Higher Risk of Bleeding and Death Compared With Clopidogrel

Among 14,005 patients ≥80 years who were discharged alive with aspirin combined with either clopidogrel (60.2%) or ticagrelor (39.8%) after a MI, the incidence of the primary ischemic outcome (hazard ratio-HR, 0.97) was similar for ticagrelor- and clopidogrel-treated patients. Ticagrelor was associated with a 17% and 48% higher risk of death (HR, 1.17) and bleeding (HR, 1.48), but a lower risk of MI (HR, 0.80) and stroke (HR, 0.72). In <80-year-old patients, the incidence of the primary ischemic outcome was 17% (HR, 0.83) lower with ticagrelor. Ticagrelor was associated with 15% (HR, 0.85) lower risk of death, 32% higher risk of bleeding (HR, 1.32), but lower risk of MI (HR, 0.82) and stroke (HR, 0.82) (Szummer K et al, *Circulation* 2020;142:1700-08).

ISAR REACT-5 Trial: In Patients With STEMI Undergoing Primary PCI, there was no Significant Difference in Death/MI/Stroke Between Prasugrel and Ticagrelor / However, Ticagrelor Was Associated With a Significant Increase in the Risk for Recurrent MI

Among 1653 patients with STEMI randomized to ticagrelor or prasugrel, the primary end point (death, MI, or stroke at 1 year) occurred in 83 patients (10.1%) in the ticagrelor and in 64 patients (7.9%) in the prasugrel group (hazard ratio-HR, 1.31; *P*=0.10). One-year incidence of all-cause death (4.9% vs 4.7%; *P*=0.83), stroke (1.3% vs 1%; *P*=0.46), and definite stent thrombosis (1.8% vs 1%; *P*=0.15) did not differ significantly in patients assigned to ticagrelor or prasugrel. One-year incidence of MI (5.3% vs 2.8%; HR, 1.95; *P*=0.010) was higher with ticagrelor than with prasugrel. BARC type 3 to 5 bleeding occurred in 46 patients (6.1%) in the ticagrelor group and in 39 patients (5.1%) in the prasugrel group (HR, 1.22; *P*=0.36) (Aytekin A et al, *Circulation* 2020;142:2329-37).

Left Ventricular (LV) Unloading Using Impella Confers Lower Mortality in Patients With Cardiogenic Shock (CS) Treated With Venoarterial Extracorporeal Membrane Oxygenation (VA-ECMO), Albeit with More Complications

LV unloading with Impella was used in 337 of the 686 patients (49%) with CS. After matching, 255 patients with LV unloading were compared with 255 patients without LV unloading. In the matched cohort, LV unloading was associated with lower 30-day mortality (hazard ratio-HR, 0.79; *P*=0.03) without differences in various subgroups. Complications occurred more often in patients with LV unloading: severe bleeding in 98 (38.4%) vs 45 (17.9%), access site–related ischemia in 55 (21.6%) vs 31 (12.3%), abdominal compartment in 23 (9.4%) vs 9 (3.7%), and renal replacement therapy in 148 (58.5%) vs 99 (39.1%) (Schrage B et al, *Circulation* 2020;142:2095–2106).

VERTIS CV Trial: In Patients With Diabetes, Ertugliflozin Reduced Risk for First and Total Hospitalization for Heart Failure (HHF) and Total HHF/CV Death

Among 8246 patients randomized to ertugliflozin (n=5499) or placebo (n=2747), 1958 (23.7%) had a history of heart failure (HF) and 5006 (60.7%) had pretrial ejection

fraction (EF) available, including n=959 with EF ≤45%. Ertugliflozin did not reduce first HHF/CV death (hazard ratio-HR, 0.88). Overall, ertugliflozin reduced risk for first HHF (HR, 0.70; *P*=0.006). Previous HF did not modify this effect (HF: HR, 0.63; no HF: HR, 0.79; *P* interaction=0.40). In patients with HF, the risk reduction for first HHF was similar for those with reduced EF ≤45% vs preserved EF >45% or unknown. However, in the overall population, the risk reduction tended to be greater for those with EF ≤45% (HR, 0.48) vs EF >45% (HR, 0.86). Effect on risk for first HHF was consistent across most subgroups, but greater benefit was observed in 3 groups: baseline estimated glomerular filtration rate <60 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$, albuminuria, and diuretic use (each *P* interaction <0.05). Ertugliflozin reduced total events of HHF (rate ratio-RR, 0.70) and total HHF/CV death (RR, 0.83) (Cosentino F et al, *Circulation* 2020;142:2205-15).

SCOPE 2: Transfemoral TAVI With the Self-Expanding ACURATE Neo was Inferior to the Self-Expanding Corevalve Evolut in All-Cause Death or Stroke at 1 Year / It Conferred Lower Incidence of New Permanent Pacemaker Implantation / It was also Associated with More Moderate-Severe Aortic Regurgitation and Cardiac Death at 30 Days and 1 Year

Among 796 patients (age 83.2±4.3 years; STS score 4.6±2.9%), randomized to the ACURATE neo (n=398) or the CoreValve Evolut bioprostheses (n=398) (with clinical follow-up information available for 778 or 98% patients), within 1 year, the primary end point (all-cause death or stroke at 1 year) occurred in 15.8% in the ACURATE neo group and in 13.9% of patients in the CoreValve Evolut group (*P*=0.0549 for noninferiority). The 30-day rates of new permanent pacemaker implantation were 10.5% vs 18% (*P*=0.0027). No significant differences were observed in the components of the primary end point. Cardiac death at 30 days (2.8% vs 0.8%; *P*=0.03) and 1 year (8.4% vs 3.9%; *P*=0.01), and moderate or severe aortic regurgitation at 30 days (10% vs 3%; *P*=0.002) were significantly increased in the ACURATE neo group (Tamburino C et al, *Circulation* 2020;142:2431-42).

HOST-REDUCE-POLYTECH-ACS: In East Asian Patients With Acute Coronary Syndrome Receiving PCI, a Prasugrel-Based Dose De-Escalation Strategy from 1 Month After PCI Reduced the Risk of Net Clinical Outcomes up to 1 Year, Mainly Driven by a Reduction in Bleeding Without an Increase in Ischemia

Among 2338 patients randomized to the de-escalation group (n=1170) or the conventional group (n=1168), the primary endpoint occurred in 82 patients (Kaplan-Meier estimate 7.2%) in the de-escalation group and 116 patients (10.1%) in the conventional group (hazard ratio-HR 0.70, $p_{equivalence}$=0.012). There was no increase in ischemic risk in the de-escalation group compared with the conventional group (0.76; p=0.40), and the risk of bleeding events was significantly decreased (0.48; p=0.0007) (Kim HS et al, *Lancet* 2020; 396:1079-89).

BASKET-SMALL 2: There is Maintained Efficacy and Safety of Drug-Coated Balloon (DCB) vs Drug Eluting Stents (DES) in the Treatment of De-Novo Coronary Small Vessel Disease up to 3 Years

Among 758 patients randomized to DCB (n=382) or DES (n=376), the rate of major adverse cardiac events (MACE) was 15% in both the DCB and DES groups (hazard ratio-HR 0.99; p=0.95). The two groups were also very similar concerning the single components of MACE: cardiac death (5% *vs* 4%, HR 1.29; p=0.49), non-fatal MI (both 6%, HR 0.82; p=0.52), and target vessel revascularization (TVR) (both 9%, HR 0.95; p=0.83). Rates of all-cause death were similar in DCB vs DES patients (both 8%, HR 1.05; p=0.87). Rates of probable or definite stent thrombosis (1% *vs* 2%; HR 0.33; p=0.18) and major bleeding (2% *vs* 4%, HR 0.43; p=0.088) were numerically, but not significantly, lower in DCB vs DES (Jeger RV et al, *Lancet* 2020;396:1504-10).

Meta-Analysis: In Patients Aged ≥75 Years, Lipid Lowering Was as Effective in Reducing Cardiovascular Events as it was in Younger Patients

Among 244,090 patients from 29 trials, 21,492 (8.8%) were aged ≥75 years, of whom 11,750 (54.7%) were from statin trials, 6209 (28·9%) from ezetimibe trials, and 3533 (16·4%) from PCSK9 inhibitor trials. Over a median of 2.2-6.0 years, LDL cholesterol lowering significantly reduced the risk of major vascular events (n=3519) in older patients by 26% per 1 mmol/L reduction in LDL cholesterol (RR 0.74; p=0.0019), with no significant difference with the risk reduction in patients <75 years. Among older patients, RRs were not different for statin (0.82) and non-statin treatment (0.67). The benefit of LDL cholesterol lowering in older patients was observed for each component of the composite, including CV death (0.85), MI (0.80), stroke (0.73), and revascularization (0.80) (Gencer B et al, *Lancet* 2020; 396:1637-43).

ALPHEUS Study: Ticagrelor was not Superior to Clopidogrel in Reducing Periprocedural Myocardial Necrosis After Elective PCI and did not Increase Major Bleeding, But Did Increase Minor Bleeding at 30 Days / These Results Support the Use of Clopidogrel as the Standard of Care for Elective PCI

Among patients randomized to ticagrelor (n=956) or clopidogrel (n=954), at 48 h, the primary outcome (PCI-

related type 4 (a or b) MI or major myocardial injury) occurred in 334 (35%) of 941 patients in the ticagrelor group and 341 (36%) of 942 patients in the clopidogrel group (odds ratio-OR 0.97; p=0.75). The primary safety outcome did not differ, but minor bleeding events were more frequent with ticagrelor than clopidogrel at 30 days (105 [11%] of 941 patients in the ticagrelor group *vs* 71 [8%] of 942 patients in the clopidogrel group; OR 1.54; p=0.0070) (Silvain J et al, *Lancet* 2020;396:1737-44).

EAST-AFNET 4: Early Rhythm-Control Therapy was Associated With a Lower Risk of Adverse CV Outcomes Than Usual Care Among Patients With Atrial Fibrillation (AF) and CV Condition

Among 2789 patients with early AF (median time since diagnosis, 36 days) randomized to early rhythm control or usual care, over a median of 5.1, a first-primary-outcome event (death from CV causes, stroke, or hospitalization with worsening of HF or ACS) occurred in 249 of the patients assigned to early rhythm control (3.9 per 100 person-years) and in 316 patients assigned to usual care (5.0 per 100 person-years) (hazard ratio-HR, 0.79; P=0.005). The mean (±SD) number of nights spent in the hospital did not differ significantly between the groups (5.8±21.9 and 5.1±15.5 days per year, respectively; P=0.23). The percentage of patients with a primary safety outcome event (death, stroke, or serious adverse events) did not differ significantly between the groups (serious adverse events related to rhythm-control therapy: 4.9% vs 1.4%) (Kirchhof P et al, *N Engl J Med* 2020;383:1305-16).

EMPEROR-Reduced Trial: **Empagliflozin Reduced Risk of Cardiovascular (CV) Death or Hospitalization for Heart Failure (HHF) in Patients with HFrEF, Regardless of the Presence or Absence of Diabetes**

During a median of 16 months, a primary outcome event (CV death or HHF) occurred in 361 of 1863 patients (19.4%) in the empagliflozin group and in 462 of 1867 patients (24.7%) in the placebo group (hazard ratio -HR, 0.75; P<0.001). The effect of empagliflozin on the primary outcome was consistent in patients regardless of the presence or absence of diabetes. The total number of HHF was lower in the empagliflozin group (HR, 0.70; P<0.001). The annual rate of decline in the estimated glomerular filtration rate was slower in the empagliflozin group (P<0.001), and empagliflozin-treated patients had a lower risk of serious renal outcomes. Uncomplicated genital tract infection was reported more frequently with empagliflozin (Packer M et al, *N Engl J Med* 2020; 383:1413-24).

Among Patients Undergoing TAVI, Bleeding and Bleeding or Thromboembolic Events at 1 Year Were Significantly Less Frequent With Aspirin Than With Aspirin Plus Clopidogrel Administered for 3 Months

Among 331 patients assigned to aspirin and 334 to aspirin plus clopidogrel, a bleeding event occurred in 50 patients (15.1%) with aspirin and in 89 (26.6%) with aspirin plus clopidogrel (risk ratio-RR, 0.57; P=0.001). Non–procedure-related bleeding occurred in 50 patients (15.1%) vs 83 patients (24.9%) (RR, 0.61; P=0.005). A secondary composite 1 event (CV death, non–procedure-related bleeding, stroke, or MI) occurred in 76 patients (23.0%) vs 104 (31.1%) (P<0.001 for non-inferiority; RR, 0.74; for superiority, P=0.04). A secondary composite 2 event (CV death, stroke, or MI at 1 year) occurred in 32 patients (9.7%) vs 33 patients (9.9%), respectively (P=0.004 for non-inferiority; RR, 0.98; P=0.93 for superiority). A total of 44 patients (13.3%) and 32 (9.6%), respectively, received oral anticoagulation during the trial (Brouwer J L et al, *N Engl J Med* 2020; 383:1447-1457).

ELDERCARE-AF: In Very Elderly (≥80) Patients with AF, a 15-mg Daily Dose of Edoxaban was Superior to Placebo in Preventing Stroke or Systemic Embolism and did not Increase Major Bleeding

Among 984 patients assigned to 15 mg of edoxaban (492 patients) or placebo (492 patients), the annualized rate of stroke or systemic embolism was 2.3% vs 6.7% (hazard ratio-HR, 0.34; P<0.001), and the annualized rate of major bleeding was 3.3% vs 1.8% (HR, 1.87; P=0.09). There were substantially more events of GI bleeding in the edoxaban group. There was no substantial between-group difference in death from any cause (9.9% vs 10.2%; HR, 0.97) (Okumura K et al, *N Engl J Med* 2020; 383:1735-45)

ELEVATE Registry: Heartmate 3 (HM3) Left Ventricular Assist Device Conferred Good Long-Term Survival, Sustained Improvement of Functional Capacity, and Low Rates of Adverse Events (Including Pump Thrombosis)

Among 540 patients, implanted with HM3 (age 55.6 ±11.7 years; 89% males, 48% ischemic cardiomyopathy; 70% in INTERMACS Profile 1–3, 12.7% on temporary mechanical circulatory support), survival was 83% after 2 years; strokes were observed in 10.2%, GI bleedings in 9.7%, pump thrombosis in 1.5%, and outflow graft twists in 3.5%. HM3 implantation resulted in a significant and sustained improvement of functional capacity and quality of life (Zimpfer D et al, *Eur Heart J* 2020;41:3801-09).

Less Dementia After Catheter Ablation for Atrial Fibrillation (AF)

Among adults with AF treated with ablation (n=9119) or medical therapy (n=17,978) over a median of 52 months, ablated patients showed lower incidence and risk of dementia (8.1 vs 5.6 per 1000 person-years; hazard ratio-HR 0.73). The associations between ablation and dementia risk were consistently observed after additionally censoring for incident stroke (HR 0.76) and more pronounced in cases of ablation success whereas no significant differences observed in cases of ablation failure (Kim D et al, *Eur Heart J* 2020;41:4483-93).

Loss of Preexcitation During Noninvasive Testing Does Not Exclude High-Risk Accessory Pathways (APs)

Of 1589 patients ≤21 years with WPW, 244 (15%) had nonpersistent and 1345 (85%) had persistent preexcitation, with no differences in sex (58% vs 60% male; *P*=NS) or age (13.3±3.6 years vs 13.1±3.9 years; *P*=NS) between groups. Although effective refractory period (344±76 ms vs 312±61 ms; *P*<0.001) and shortest preexcited paced cycle length (394±123 ms vs 317±82 ms; *P*<0.001) were longer in nonpersistent vs persistent preexcitation, there was no difference in shortest preexcited R-R interval (SPERRI) at EPS (331±71 ms vs 316±73 ms; *P*=NS). Nonpersistent preexcitation was associated with fewer high-risk APs (13% vs 23%; *P*<0.001) than persistent preexcitation. Of 61 patients with sudden cardiac arrest (SCA) or rapidly conducting AF (RC-AF), 6 (10%) had nonpersistent preexcitation (3 SCA, 3 RC-AF) (Escudero CA et al, *Heart Rhythm* 2020;17:1729-37)

Important Review and Other Articles

● **2020 AHA Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care (***Circulation,* Oct 20, 2020- Vol.142, Issue 16, Suppl 2)

Preeclampsia (Ives CW et al, *J Am Coll Cardiol* 2020;76: 1690–1702)

● **Type A Aortic Dissection** (Zhu Y et al, *J Am Coll Cardiol* 2020;76:1703–1713)

● **Cardiac and pulmonary sarcoidosis** (Trivieri MG et al, *J Am Coll Cardiol* 2020; 76: 1878–1901)

● **COVID-19 and the cardiovascular system** (Giustino G et al, *J Am Coll Cardiol* 2020;76:2011–2023)

● **Cardiovascular implications and complications of COVID-19** (Manolis AS et al, *Curr Opin Cardiol* 2020 Dec 30; doi: 10.1097/HCO.0000000000000838.)

● **Pregnancy-associated venous thromboembolism** (Nichols KM et al, *J Am Coll Cardiol* 2020;76:2128–2141)

● **Antithrombotic management of venous thromboembolism** (Renner E & Barnes GD, *J Am Coll Cardiol* 2020;76:2142-54)

● **Role of Renin-Angiotensin-System Blocking in COVID-19** (Manolis AS et al, *J Cardiovasc Pharmacol* 2020;76:397-406*)*

● **Chronic thromboembolic pulmonary hypertension** (Papamatheakis DG et al, *J Am Coll Cardiol* 2020;76:2155–69)

● Evaluation and Management of Patients with **Stable Angina** (Ferraro R et al, *J Am Coll Cardiol* 2020;76:2252-66)

● **2020 ACC Expert Consensus Decision Pathway on Management of Conduction Disturbances in Patients Undergoing TAVI** (Lilly SM et al, *J Am Coll Cardiol* 2020;76: 2391–2411)

● **2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy** (Ommen SR et al, *J Am Coll Cardiol* 2020;76:e159–e240 / *Circulation* 2020;142:e558–e631)

● **Cardiac xenotransplantation** (Pierson III RN et al, *Circulation* 2020;142:1389–1398)

● **AHA Statement on Drug-Induced Arrhythmias** (Tisdale JE et al, *Circulation* 2020;142:e214–e233)

● **AHA Guidance to Reduce the Cardiovascular Burden of Ambient Air Pollutants** (Kaufman JD, *Circulation.* 2020;142: e432–e447)

● **Prevention of Complications in the CCU** (Fordyce CB, *Circulation* 2020;142:e379–e406)

● **Stroke prevention in AF** (Katsanos AH et al, *Circulation* 2020;142:2371–2388**)**

● **Spontaneous coronary artery dissection** (Kim ESH, *N Eng J Med* 2020; 383:2358-2370)

● **COVID-19 infection and cardiac arrhythmias** (Manolis AS et al, *Trends Cardiovasc Med* 2020;30:451-460)

● **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* 2021;26:12-24*)*

● **Mitochondrial dysfunction in CV disease** (Manolis AS et al, *Med Res Rev* 2021;41:275-313)

● An EAPCI Expert Consensus Document on Ischemia with Non-Obstructive Coronary Arteries (**INOCA**) (Kunadian V et al, *Eur Heart J*; 41:3504–3520)

● Management of **non-culprit coronary plaques** in patients with ACS (Montone RA et al, *Eur Heart J*;41:3579–86)

● European Position Statement: **Recommendations for participation in competitive sport in adolescent and adult athletes with Congenital Heart Disease** (Budts W et al, *Eur Heart J* 2020;41**:**4191–4199)