Cardiology News / Recent Literature Review / Second Quarter 2019

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ESC Meeting: Paris, 31/8-4/9/2019

TCT Meeting: San Francisco, 25-28/9/2019

HCS 40th Congress: Ioannina, 17-19/10/2019

AHA Meeting: Philadelphia, PA, USA, 16-18/11/2019

ACC Meeting: Chicago, IL, USA, 28-30/3/2020

EHRA Meeting: Vienna, 29-31/3/2020

AUGUSTUS Trial: In Patients With Atrial Fibrillation (AF) and a Recent Acute Coronary Syndrome (ACS) or PCI Treated With a $P2Y_{12}$ Inhibitor, an Antithrombotic Regimen Including Apixaban, Without Aspirin, Resulted in Less Bleeding and Fewer Hospitalizations Without Significant Differences in the Incidence of Ischemic Events Than Regimens that Included a Vitamin K Antagonist (VKA), Aspirin, or Both

Among 4614 AF patients with ACS or PCI, major or clinically relevant nonmajor bleeding was noted in 10.5% of the patients receiving apixaban, as compared with 14.7% of those receiving a VKA (hazard ratio-HR, 0.69; P<0.001 for both noninferiority and superiority), and in 16.1% of the patients receiving aspirin, as compared with 9.0% of those receiving placebo (HR, 1.89; P<0.001). Patients in the apixaban group had a lower incidence of death or hospitalization than those in the VKA group (23.5% vs. 27.4%; HR, 0.83; P=0.002) and a similar incidence of ischemic events. Patients in the aspirin group had an incidence of death or hospitalization and of ischemic events that was similar to that in the placebo group (Lopes RD et al, *N Engl J Med* 2019; 380:1509-24).

COACT Trial: Among Patients Successfully Resuscitated After Out-Of-Hospital Cardiac Arrest with no Signs of STEMI, a Strategy of Immediate Angiography Was Not Found to be Better Than a Strategy of Delayed Angiography With Respect to Overall Survival at 90 Days

At 90 days, 176 of 273 patients (64.5%) in the immediate angiography group and 178 of 265 patients (67.2%) in the delayed (delayed until after neurologic recovery) angiography group were alive (odds ratio, 0.89; P=NS). The median time to target temperature was 5.4 h in the immediate angiography group and 4.7 h in the delayed angiography group. No significant differences between the groups were found in the remaining secondary end points (Lemkers JS et al, *N Engl J Med* 2019; 380:1397-1407).

ANNEXA-4: In Patients With Acute Major Bleeding Associated With Use of a Factor Xa Inhibitor, Treatment With Andexanet Markedly Reduced Anti–Factor Xa Activity, and 82% of Patients Had Excellent or Good Hemostatic Efficacy at 12 Hours

Among 352 patients (mean age 77 years, most with CV disease) who had acute major bleeding (64% intracranial and 26% gastrointestinal) within 18 h after a factor Xa inhibitor and received a bolus of andexanet, followed by a 2-hour infusion, in patients who had received apixaban, the median anti–factor Xa activity decreased from 149.7 ng/ml at baseline to 11.1 ng/ml after the andexanet bolus (92% reduction); in patients who had received rivaroxaban, the median value decreased from 211.8 ng/ml to 14.2 ng/ml (92% reduction). Excellent or good hemostasis occurred in 204 of 249 patients (82%) who could be evaluated. Within 30 days, death occurred in 49 patients (14%) and a thrombotic event in 34 (10%). Reduction in anti–factor Xa activity was not predictive of hemostatic efficacy overall but was modestly predictive in patients with intracranial hemorrhage (Connolly SJ et al, *N Engl J Med* 2019; 380:1326-35).

Among Patients Undergoing PCI With Baseline LDL-Cholesterol ≤70mg/dl, Persistent High Residual Inflammatory Risk (RIR) (*hsCRP >2mg/l*) is Frequent and is Associated With Increased Risk of MACCE

Among 3,013 patients undergoing PCI with baseline LDL ≤70 mg/dl, residual inflammatory risk (RIR), defined as hsCRP >2mg/l, was persistent low (first low then low hsCRP) in 41.7%, attenuated (first high then low hsCRP) in 13.7%, increased (first low then high hsCRP) in 11.5%, or persistent high (first high then high hsCRP) in 34.1%. Overall, there was a stepwise increase in the incidence rates of major adverse cardiac and cerebrovascular events (MACCE) (death, MI, or stroke), within 1 year of the second hsCRP measurement, transitioning from the persistent low to the attenuated, increased, and persistent high RIR (respectively, 64.4 vs 96.6 vs. 138.0 vs 152.4 per 1,000 patient-years; p< 0.001). The presence of persistent high RIR remained strongly associated with MACCE (adjusted hazard ratio: 2.10; p< 0.001) (Guedeney P et al, *J Am Coll Cardiol* 2019;73: 2401-09).

Infusion Needle Radiofrequency (RF) Ablation for Refractory Ventricular Arrhythmias: Novel, Effective but is it Safe?

An RF ablation catheter with an extendable/retractable 27-g needle capable of targeting deep arrhythmia

(intramural) substrate was used in 31 patients who failed at least one prior catheter ablation procedure for sustained ventricular tachycardia (VT; n=26) or nonsustained VA with associated LV dysfunction (n=5) (71% nonischemic heart disease). After a median of 15 needle lesions/patient, ablation abolished at least 1 inducible VT in 19 of 26 VT patients (73%), and suppressed ambient arrhythmia in 4 of 5 nonsustained arrhythmia patients. At the 6-month follow-up, 48% of patients were free of recurrent arrhythmia and another 19% were improved. Procedure-related complications included 1 pericardial effusion treated with percutaneous drainage and a LV pacing lead dislodgement with no deaths (Stevenson WG et al, *J Am Coll Cardiol* 2019;73:1413-25).

YOUNG-MI Registry: Need for More Aggressive Lipid-Lowering Therapy in Young Familial Hypercholesterolemia (FH) and Non-FH Patients Post-MI / FH is Present in Nearly 1 of 10 Patients With MI at a Young Age / Only Two-Thirds of FH Patients Were Discharged on High-Intensity Statin Therapy, and the Vast Majority Had Elevated LDL-C at 1 Year

Among 1,996 patients who experienced an MI at or below age 50 years included in the YOUNG-MI registry (median age of 45 years; 19% were women, and 54% had STEMI), probable/definite FH was present in 180 (9%) of whom 42.8% were not on statins prior to their MI. Of the 1,966 patients surviving until hospital discharge, 89.4% of FH patients and 89.9% of non-FH patients were discharged on statin therapy ($p = 0.82$). Among FH patients, 63.3% were discharged on high-intensity statin compared with 48.4% for non-FH patients ($p < 0.001$). At 1-year follow-up, the percent reduction in LDL-C among FH patients was −44.4% compared with −34.5% ($p = 0.006$) in non-FH patients. The proportion of patients with LDL-C ≥70 mg/dl was higher among FH patients (82.2%) compared with non-FH patients (64.5%; $p< 0.001$) (Singh A et al, *J Am Coll Cardiol* 2019; 73:2439-50).

Among Non-LBBB CRT-D–Eligible Patients, CRT-D Implantation Was Associated With Better Outcomes Compared With ICD Alone Specifically in Non-Specific Intraventricular Conduction Delay (IVCD) Patients With a QRS Duration of ≥150 ms

In 11,505 non-LBBB CRT-eligible patients, after multivariable adjustment, among patients with RBBB, CRT-D was not associated with better outcomes, compared with ICD alone, regardless of QRS duration. Among patients with IVCD and a QRS ≥150 ms, CRT-D was associated with decreased mortality at 3 years compared with ICD alone (HR: 0.602; p=0.0071). Among 5,954 CRT-D–implanted patients, after multivariable adjustment IVCD compared with RBBB was associated with lower mortality at 3 years in those with a QRS duration of ≥150 ms (HR: 0.757; p=0.0044) (Kawata H et al, *J Am Coll Cardiol* 2019; 73:3082-99).

MOMENTUM 3: Among Patients With Advanced Heart Failure, a Fully Magnetically Levitated Centrifugal-Flow Left Ventricular Assist Device (LVAD) Was Associated With Less Frequent Need for Pump Replacement Than an Axial-Flow Device and Fewer Strokes

Among 1028 enrolled patients, 516 in the centrifugal-flow pump group and 512 in the axial-flow pump group, 397 patients (76.9%) in the centrifugal-flow pump group, as compared with 332 (64.8%) in the axial-flow pump group, remained alive and free of disabling stroke or reoperation to replace or remove a malfunctioning device at 2 years (relative risk, 0.84; P<0.001 for superiority). Pump replacement was less common in the centrifugal-flow pump group than in the axial-flow pump group (2.3% vs. 11.3%]; relative risk, 0.21; P<0.001). The numbers of events per patient-year for stroke of any severity, major bleeding, and gastrointestinal hemorrhage were lower in the centrifugal-flow pump group than in the axial-flow pump group (Mehra MR et al, *New Engl J Med* 2019; 380:1618-1627).

RACE 7 ACWAS Trial: In Patients Presenting to the Emergency Department (ED) With Recent-Onset Atrial Fibrillation (AF), a Wait-and-See Approach was Noninferior to Early Cardioversion (CV) in Achieving a Return to Sinus Rhythm (SR) at 4 Weeks

Patients with hemodynamically stable, recent-onset (<36 h), symptomatic AF in the ED were randomly assigned to be treated with a wait-and-see approach (delayed-CV group, n=212; initial treatment with rate-control medication only and delayed CV if AF did not resolve within 48 h) or early CV (n=215). The presence of SR at 4 weeks occurred in 91% in the delayed-CV group and in 94% in the early-CV group (P=0.005 for noninferiority). In the delayed-CV group, conversion to SR within 48 h occurred spontaneously in 150 of 218 patients (69%) and after delayed CV in 61 patients (28%). In the early-CV group, conversion to SR occurred spontaneously before the initiation of CV in 36 of 219 patients (16%) and after CV in 171 patients (78%). Among the patients who completed remote monitoring during 4 weeks of follow-up, a recurrence of AF occurred in 49 of 164 patients (30%) in the delayed-CV group and in 50 of 171 (29%) in the early-CV group. Within 4 weeks after randomization, cardiovascular complications occurred in 10 patients and 8 patients, respectively (Pluymaekers NAHA et al, *N Engl J Med* 2019; 380:1499-1508).

In Patients With HER2-Positive Breast Cancer Treated With Trastuzumab, Both Lisinopril and Carvedilol Prevented Cardiotoxicity in Patients Receiving Anthracyclines

Among 468 women (age 51±10.7 years) with breast cancer receiving chemotherapy with trastuzumab stratified by anthracycline use and then randomized to lisinopril, carvedilol or placebo, cardiotoxicity was comparable in the 3 arms (32% of placebo patients, 29% on carvedilol, and 30% on lisinopril). For patients receiving anthracyclines, the event rates were higher in the placebo group (47%) than in the lisinopril (37%) and the carvedilol (31%) groups. Cardiotoxicity-free survival was longer on both carvedilol (hazard ratio-HR: 0.49; p=0.009) and lisinopril (HR: 0.53; p=0.015) than on placebo. In the whole cohort, as well as in the anthracycline arm, patients on active therapy with either angiotensin-converting enzyme inhibitor or beta-blockers experienced fewer interruptions in trastuzumab than those on placebo (Guglin M et al et al, *J Am Coll Cardiol* 2019;73:2859-68).

PARTNER 2 Registry: At 3-Year Follow-Up, TAVI for Bioprosthetic Aortic Valve Failure Was Associated With Favorable Survival, Sustained Improved Hemodynamic Status, and Excellent Functional and Quality-Of-Life Outcomes

Among 365 patients having valve-in-valve procedures (age 78.9±10.2 years; STS score 9.1±4.7%), at 3 years, all-cause mortality was 32.7%. Aortic valve re-replacement was required in 1.9%. Mean transaortic gradient was 35 mmHg at baseline, decreasing to 17.8 mmHg at 30-days and 16.6 mmHg at 3-years. Baseline effective orifice area was 0.93 cm^2, increasing to 1.13 and 1.15 cm^2 at 30 days and 3 years, respectively. Moderate to severe aortic regurgitation was reduced from 45.1% at pre-TAVI baseline to 2.5% at 3 years. Moderate or severe mitral and tricuspid regurgitation also decreased. Baseline left ventricular (LV) ejection fraction was 50.7%, increasing to 54.7% at 3 years (p< 0.0001), while LV mass index was 136.4 g/m^2, decreasing to 109.1 g/m^2 at 3 years (p< 0.0001). NYHA functional class improved, with 90.4% in class III or IV at baseline and 14.1% at 3 years (p< 0.0001), and quality of life score increased (43.1 to 73.1; p< 0.0001) (Webb JG et al, *J Am Coll Cardiol* 2019;73: 2647-55).

Delayed AV Block: An Underappreciated Complication of TAVI Among Patients Without Pre-Procedure Pacing Devices, Occurring at Rates Similar to In-Hospital, Acute Post-TAVI AV Block / RBBB is a Risk Factor

Among 150 consecutive TAVI patients without a prior pacing device, 18 (12%) developed high-degree AV block necessitating permanent pacemaker <2 days post-TAVI, 1 died pre-discharge, and 13 declined ambulatory event monitoring (AEM); 118 had 30-day AEM data. Delayed AV block occurred in 12 (10% of AEM patients, 8% of total cohort) a median of 6 days (range 3 to 24 days) post-TAVI. Delayed AV block patients were more likely to have hypertension and right bundle branch block (RBBB). Sensitivity and specificity of RBBB in predicting AV block was 27% and 94%, respectively (Ream K et al, *J Am Coll Cardiol* 2019;73:2538–47).

Meta-Analysis: Sham-Controlled Randomized Trials of Renal Denervation (RD) in Patients With Hypertension Indicate Significantly Reduced Blood Pressure (BP) Compared with Sham Control

In a meta-analysis of 977 patients from 6 trials, the reduction in 24-h ambulatory systolic BP was significantly greater for patients treated with RD than sham procedure (mean difference −3.65 mmHg, p<0.001). Compared with sham, RD was also associated with a significant decrease in daytime systolic BP, office systolic BP, 24-h ambulatory diastolic BP, daytime ambulatory diastolic BP, and office diastolic BP (p< 0.05). Compared with first-generation trials, a significantly greater reduction in daytime BP was observed with RD in second-generation trials (6.12 mmHg vs. 2.14 mmHg; p interaction=0.04); however, this interaction was not significant for 24-h ambulatory systolic BP (Sardar P et al *J Am Coll Cardiol* 2018;72:1633–42).

The 5-Year Incidence of Infective Endocarditis (IE) Following TAVI Was 5.8% and not Significantly Different Than the Incidence Following Surgical AVR

Among 2,632 patients undergoing TAVI and 3,777 patients undergoing isolated surgical AVR, over a mean of 3.6 years, 115 patients (4.4%) with TAVI and 186 patients (4.9%) with VR were admitted with IE. The median time from procedure to IE hospitalization was 352 days in TAVI and 625 days in AVR. The crude incidence rates of IE were 1.6 and 1.2 events per 100 person-years in TAVI and AVR patients, respectively. The cumulative 1-year risk of IE was 2.3% and 1.8% in TAVI and AVR patients, respectively. Correspondingly, the cumulative 5-year risk of IE was 5.8% in TAVI and 5.1% in AVR. In multivariable analysis, TAVI was not associated with a statistically significant different risk of IE compared with AVR (hazard ratio: 1.12) (Butt JH et al, *J Am Coll Cardiol* 2018;72:1646–55).

Benefits of Eating Breakfast in Promoting Cardiovascular (CV) Health

In a prospective cohort study of 6,550 adults 40-75 years of age (mean age 53.2 years; 48.0% male), 5.1% never had breakfast, 10.9% rarely had breakfast, 25% had breakfast some days, and 59% had breakfast every day. During 112,148 person-years of follow-up, 2,318 deaths occurred including 619 deaths from CV disease. After adjustment for age, sex, race/ethnicity, socioeconomic status, dietary and lifestyle factors, body mass index, and CV risk factors, participants who never had breakfast compared with those having breakfast everyday had hazard ratios of 1.87 for CV mortality and 1.19 for all-cause mortality. The authors concluded that skipping breakfast was associated with a significantly increased risk of mortality from CV disease (Rong S et al, *J Am Coll Cardiol* 2018;72:2025-32).

Lung Disease is Associated With Cardiovascular (CV) Diseases, Particularly Ischemic Heart Disease (IHD) and Heart Failure (HF), Contributing to All-Cause Mortality / However, Patients With Lung Disease are Less Likely to Get Revascularized

Among 31,646 COPD, 60,424 asthma, and 1,662 interstitial lung disease (ILD) patients compared with controls (n=158230, n=302120, and n=8310, respectively), COPD was independently associated with IHD, HF, atrial fibrillation, and peripheral vascular disease, all of which were associated with all-cause mortality (e.g., odds ratio for the association of COPD with HF: 2.18; hazard ratio for the contribution of HF to mortality in COPD: 1.65). Asthma was independently associated with IHD, and multiple CV diseases contributed to mortality (e.g., HF hazard ratio: 1.81). ILD was independently associated with IHD and HF, both of which were associated with mortality. Patients with lung disease were less likely to receive coronary revascularization. (Carter P et al, *J Am Coll Cardiol* 2018;72:2166-77).

DECISION-CTO Trial: Chronic Total Occlusion (CTO)-PCI Was Feasible With High Success Rates, but There was no Difference in Major Adverse Cardiovascular Events (MACE)

Among 834 patients randomly assigned to the CTO-PCI (n=417) or no CTO-PCI strategy (n=398; 78 or 19.6% crossed over to receive staged CTO-PCI within 3 days of randomization), the overall CTO-PCI success rate was 90.6%. Serious nonfatal complications associated with CTO-PCI occurred in 3 patients (1 stroke, 1 cardiac tamponade, and 1 patient with recurrent episodes of ventricular tachyarrhythmia induced by intracoronary thrombus). About half of the patients in each group underwent PCI for an average of 1.3 non-CTO lesions, resulting in a comparable residual SYNTAX score confined to non-CTO vessels. During a median of 4 years, there was no significant difference between the CTO-PCI and the no CTO-PCI strategies in the incidence of the primary end point (death, MI, stroke, revascularization) (22.3% vs 22.4%). Both CTO-PCI and no CTO-PCI strategy were associated with significant improvements but without between-group differences in disease-specific health status that was sustained through 3 years (Lee SW et al, *Circulation* 2019;139:1674–83).

Focal atrial tachycardia (FAT) ablation: Highly successful with conventional mapping

Conventional mapping-guided catheter ablation in 63 FAT patients (aged 42.4±17.3 years; 14 with incessant tachycardia and 12 with tachycardiomyopathy - TCM), was successful in 61 (96.8%), applied for single foci in 59 (93.7%) and two foci in 4 patients, right (n = 46) or left sided (n = 17). The earliest atrial activation time was 41.3 ± 16.2 ms. Fluoroscopy time was 27.3±18.7 min, and procedure lasted 2.6±1.7 h. Complications occurred in 2 patients (sinus pauses in 1 needing a pacemaker and a large inguinal hematoma in 1). Over 29.0±22.9 months, 4 patients (6.5%) had recurrences, of whom 3 were re-ablated. All patients with TCM showed gradual improvement to normalization over 4-6 months (Manolis AS & Lazaridis K, *J Interv Card Electrophysiol* 2019;55:35–46).

Meta-Analysis: Glucagon-Like Peptide 1 Receptor Agonists (GLP1-RA) & Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) Reduce Atherosclerotic MACE to a Similar Degree in Patients With Established Cardiovascular (CV) Disease, Whereas SGLT2i Have a More Marked Effect on Preventing Hospitalization for Heart Failure and Progression of Kidney Disease

Data from 8 trials and 77,242 patients, 42,920 (55.6%) in GLP1-RA trials, and 34,322 (44.4%) in SGLT2i trials, showed that both drug classes reduced MACE in a similar magnitude with GLP1-RA reducing the risk by 12% (hazard ratio -HR, 0.88; $p<0.001$) and SGLT2i by 11% (HR, 0.89; $p=0.001$). For both drug classes, this treatment effect was restricted to a 14% reduction in those with established atherosclerotic CV disease (HR, 0.86; $p=0.002$), whereas no effect was seen in patients without established CV disease (HR, 1.01; 95%; p interaction, 0.028). SGLT2i reduced hospitalization for heart failure by 31% (HR, 0.69; $p<0.001$), whereas GLP1-RA did not have a significant effect (HR, 0.93; $p=0.20$). Both GLP1-RA (HR, 0.82; $p<0.001$) and SGLT2i (HR, 0.62; $p<0.001$) reduced the risk of progression of kidney disease including

macroalbuminuria, but only SGLT2i reduced the risk of worsening estimated glomerular filtration rate, end-stage kidney disease, or renal death (HR, 0.55; $p<0.001$). (Zelniker TA et al, *Circulation* 2019;139:2022–31).

Health Professionals Studies: Consumption of Sugar-Sweetened Beverages (SSBs) Increases Mortality Primarily Through CVD Mortality with a Graded Association with Dose / The Association Between High Intake Levels of Artificially-Sweetened Beverages (ASBs) and Total and CVD Mortality Observed Among Women Requires Further Confirmation

After adjusting for major diet and lifestyle factors, consumption of SSBs was associated with a higher risk of total mortality; hazard ratios - HRs across categories (<1/mo, 1–4/mo, 2–6/week, 1-<2/d, and ≥2/d) were 1.00 (reference), 1.01 (0.98, 1.04), 1.06 (1.03, 1.09), 1.14 (1.09, 1.19), and 1.21 (1.13, 1.28; *P* trend <0.0001). The association was observed for CVD mortality (HR comparing extreme categories was 1.31, *P* trend <0.0001) and cancer mortality (1.16, *P* trend =0.0004). ASBs were associated with total and CVD mortality in the highest intake category only; pooled HRs across categories were 1.00 (reference), 0.96, 0.97, 0.98, and 1.04 (*P* trend = 0.01) for total mortality and 1.00 (reference), 0.93, 0.95, 1.02, and 1.13 (*P* trend = 0.02) for CVD mortality. In cohort-specific analysis, ASBs were associated with mortality in NHS (Nurses' Health Study) but not in HPFS (Health Professionals Follow-up Study) (*P* interaction, 0.01). ASBs were not associated with cancer mortality in either cohort (Malik VS et al, *Circulation* 2019;139:2113–25).

Arrhythmic Storm With Recurrent Polymorphic VT in Patients With Coronary Disease Responds To Quinidine Therapy When Other Antiarrhythmic Drugs (Including IV Amiodarone) Fail

Among 43 patients with polymorphic VT appearing within days of an otherwise uncomplicated MI or coronary revascularization procedure, the VT events were invariably triggered by extrasystoles with short (364±36 ms) coupling interval. Arrhythmic storms (4–16 events of polymorphic VT deteriorating to VF) occurred in 23 (53%) patients and remained refractory to conventional antiarrhythmic therapy, including IV amiodarone, but invariably responded to quinidine therapy. In-hospital mortality was 17% for patients with arrhythmic storm. Patients treated with quinidine survived to hospital discharge. Over 5.6±6 years, 3 (16%) of patients discharged without quinidine developed recurrent polymorphic VT. There were no recurrent arrhythmias during quinidine therapy (Viskin S et al, *Circulation* 2019;139:2304–2314).

DECLARE-TIMI 58: Dapagliflozin Reduces Risk of MACE and Cardiovascular (CV) Death/ Hospitalization for Heart Failure in Patients With Type 2 Diabetes Mellitus and Previous MI

In patients with prior MI (n=3584), dapagliflozin reduced the relative risk of MACE by 16% and the absolute risk by 2.6% (15.2% vs 17.8%; hazard ratio - HR, 0.84; *P*=0.039), whereas there was no effect in patients without prior MI (7.1% vs 7.1%), including in patients with established CV disease but no history of MI (12.6% vs 12.8%). There was a greater benefit for MACE within 2 years after the last acute event (*P* for interaction trend= 0.007). The relative risk reductions in CV death/ hospitalizetion for heart failure were similar, but the absolute risk reductions tended to be greater: 1.9% (8.6% vs 10.5%; HR, 0.81; *P*=0.046) and 0.6% (3.9% vs 4.5%; HR, 0.85; *P*=0.055) in patients with & without prior MI, respectively (Furtado RHM et al, *Circulation* 2019;139:2516–27).

DECLARE-TIMI 58: Dapagliflozin Reduced Hospitalization for Heart Failure (HHF) in Patients With and Without HFrEF and Reduced CV Death and All-Cause Mortality in Patients With HFrEF

Of 17 160 patients, 671 (3.9%) had HFrEF, 1316 (7.7%) had HF without known reduced EF, and 15 173 (88.4%) had no history of HF at baseline. Dapagliflozin reduced CV death/HHF more in patients with HFrEF (hazard ratio - HR, 0.62) than in those without HFrEF (HR, 0.88; *P* for interaction=0.046), in whom the treatment effect of dapagliflozin was similar in those with HF without known reduced EF (HR, 0.88) and those without HF (HR, 0.88). Dapagliflozin reduced HHF both in those with (HR, 0.64) and in those without HFrEF (HR, 0.76), it reduced CV death only in patients with HFrEF (HR, 0.55) (HR, 1.08; *p* for interaction=0.012). Dapagliflozin reduced all-cause mortality in patients with HFrEF (HR, 0.59) but not in those without HFrEF (HR, 0.97; *p* for interaction= 0.016) (Kato ET et al, *Circulation* 2019;139:2528–36).

EMPRISE Study / Interim Analysis: Compared With Sitagliptin, the Initiation of Empagliflozin Was Associated With a Decreased Risk of Hospitalization for Heart Failure (HHF) Among Patients With Type 2 Diabetes as Treated in Routine Care, With and Without a History of Cardiovascular (CV) Disease

Among propensity-score matched 16,443 patient pairs started on empagliflozin or sitagliptin (mean age 59 years, 54% males, ~25% with CV disease), compared with sitagliptin, the initiation of empagliflozin decreased the risk of HHF-specific by 50% (HR, 0.50), and the risk of HHF-broad by 49% (HR, 0.51), over a mean of 5.3 months. The results were consistent in patients with and without baseline CV disease, and for empagliflozin at both

the 10- and 25-mg daily doses; analyses comparing empagliflozin vs the dipeptidyl peptidase-4 inhibitor (DPP-4i) class, and comparing sodium-glucose cotransporter-2 inhibitor vs DPP-4i classes also produced consistent findings (Patorno E et al, *Circulation* 2019;139:2822-30).

Transcatheter Valve Therapy Registry: Inverse Volume-Mortality Association for Transfemoral TAVI Procedures / Higher and More Variable Mortality at 30 Days at Hospitals With a Low Procedural Volume Than at Hospitals With a High Procedural Volume

Among 96,256 transfemoral TAVI procedures, there was a significant inverse association between annualized volume of transfemoral TAVI procedures and mortality. Adjusted 30-day mortality was higher and more variable at hospitals in the lowest-volume quartile (3.19%) than at hospitals in the highest-volume quartile (2.66%) (odds ratio-OR, 1.21; P=0.02). The difference in adjusted mortality between a mean annualized volume of 27 procedures in the lowest-volume quartile and 143 procedures in the highest-volume quartile was a relative reduction of 19.45%. After the exclusion of the first 1 year of TAVI procedures at each hospital, 30-day mortality remained higher in the lowest-volume quartile than in the highest-volume quartile (3.10% vs 2.61%; OR, 1.19) (Vemulapalli S et al, *N Engl J Med* 2019; 380:2541-50).

WRAP-IT: Adjunctive Use of an Antibacterial Envelope Resulted in a Significantly Lower Incidence of Major CIED Infections Than Standard-Of-Care Infection-Prevention Strategies Alone, Without a Higher Incidence of Complications

Among 6983 patients undergoing implantation of a cardiac implantable electronic device (CIED) randomized to the envelope (n=3495) or to the control group (n=3488), over 20.7±8.5 months, infection occurred in 25 patients in the envelope group and 42 patients in the control group (12-month Kaplan–Meier estimated event rate, 0.7% and 1.2%, respectively; hazard ratio-HR, 0.60; P=0.04). The safety end point (complications) occurred in 201 patients in the envelope group and 236 patients in the control group (12-month Kaplan–Meier estimated event rate, 6% and 6.9%, respectively; HR, 0.87; P<0.001 for noninferiority). Major CIED-related infections through the entire follow-up period occurred in 32 patients in the envelope group and 51 patients in the control group (HR, 0.63). (Tarakji KG et al, *N Engl J Med* 2019; 380:1895-1905).

RE-SPECT ESUS: In Patients With a Recent Embolic Stroke of Undetermined Source, Dabigatran Was Not Superior to Aspirin in Preventing Recurrent Stroke

Among 5390 patients with an embolic stroke of undetermined source randomized to dabigatran (2695 patients) or aspirin (2695 patients), over a median of 19 months, recurrent strokes occurred in 177 patients (6.6%) in the dabigatran group (4.1% per year) and in 207 patients (7.7%) in the aspirin group (4.8% per year) (hazard ratio-HR, 0.85; P=0.10). Ischemic strokes occurred in 172 patients (4.0% per year) vs 203 patients (4.7% per year) (HR, 0.84), major bleeding in 77 patients (1.7% per year) vs 64 patients (1.4% per year) (HR, 1.19), and clinically relevant nonmajor bleeding in 70 patients (1.6% per year) vs 41 patients (0.9% per year) (Diener HC et al, *N Engl J Med* 2019; 380:1906-17).

Evolut Low Risk Trial: In Patients With Severe Aortic Stenosis (AS) at Low Surgical Risk, TAVI with a Self-Expanding Bioprosthesis Was Noninferior to Surgery With Respect to Death or Disabling Stroke at 2 Years

Among 1403 low-risk patients (mean age 74 years) with severe AS randomized to TAVI or surgery, the 2-year incidence of the primary end point (death or stroke) was 5.3% in the TAVI group and 6.7% in the surgery group. At 30 days, TAVI patients had a lower incidence of stroke (0.5% vs 1.7%), bleeding (2.4% vs 7.5%), acute kidney injury (0.9% vs 2.8%), and atrial fibrillation (7.7% vs 35.4%) and a higher incidence of moderate/severe aortic regurgitation (3.5% vs 0.5%) and pacemaker implantation (17.4% vs 6.1%). At 1 year, TAVI patients had lower aortic-valve gradients (8.6 vs 11.2 mmHg) and larger effective orifice areas (2.3 vs 2 cm^2) (Popma JJ et al, *N Engl J Med* 2019;380:1706-15).

Ultra-Short-Term Combined Treatment With I.V. Iron, s.c. Erythropoietin Alpha, Vitamin B12, and p.o. Folic Acid Reduced RBC and Total Allogeneic Blood Product Transfusions in Patients With Preoperative Anemia or Isolated Iron Deficiency Undergoing Elective Cardiac Surgery

Patients with anemia undergoing elective cardiac surgery (n=253; Hb <12 g/dL in women and Hb <13 g/dl in men) or isolated iron deficiency (n=252; ferritin <100 mcg/L, no anemia) were randomly assigned (1:1) to receive either placebo (n=501) or combination treatment (n=505) with a slow infusion of 20 mg/kg ferric carboxymaltose, 40 000 U sc erythropoietin alpha, 1 mg sc vitamin B12, and 5 mg oral folic acid or placebo on the day before surgery. The combination treatment significantly reduced RBC transfusions from a median of 1 unit in the placebo group to 0 units in the treatment group (odds ratio 0.70 for each threshold of number of RBC transfusions, p=0.036) and until postoperative day 90 (p=0.018).

Despite fewer RBC units transfused, patients in the treatment group had a higher Hb concentration, higher reticulocyte count, and a higher reticulocyte Hb content during the first 7 days (p≤0·001). Combined allogeneic transfusions were less in the treatment group (median 0 vs 1 the placebo group (during the first 7 days, p=0·038; and until postoperative day 90, p=0·019). 73 (30%) serious adverse events were reported in the treatment group vs 79 (33%) in the placebo group (Spahn DR et al, *Lancet* 2019;393:2201-12).

Coronary Stent Trialists: The Performance of New-Generation DES in the First Year After Implantation Means That BMS Should no Longer be Considered the Gold Standard for Safety / Further Development of DES Technology Should Target Improvements in Clinical Outcomes Beyond 1 Year

A meta-analysis of 20 RCTs comparing new-generation DES or BMS among 26,616 patients undergoing PCI, indicated that over a mean of 3.2 years, the risk of the primary outcome (death or MI) was reduced in DES recipients compared with BMS recipients (HR 0.84, p<0.001) owing to a reduced risk of MI (0.79, p<0.001) and a possible slight but non-significant cardiac mortality benefit (0.89, p=0.075). All-cause death was unaffected (HR with DES 0·96, p=0.358), but risk was lowered for definite stent thrombosis (0.63, p<0·001) and target-vessel revascularisation (0.55, p<0.001). A time-dependent treatment effect was seen, with DES being associated with lower risk of the primary outcome than BMS up to 1 year after placement. While the effect was maintained in the longer term, there was no further divergence from BMS after 1 year (Piccolo R et al, *Lancet* 2019; 393:2503-10).

Spontaneous Coronary Artery Dissection (SCAD) Mainly Affects Women and Presents With MI / Despite Conservative Treatment for the Majority of Patients, Survival was Good but with Significant Cardiovascular Complications Occurring Within 30 Days

Among 750 patients with non-atherosclerotic SCAD presenting acutely (age 51.8 ± 10.2 years, 88.5% women - 55% postmenopausal, 87.7% Caucasian, and 33.9% with no cardiac risk factors), emotional stress was reported in 50.3%, and physical stress in 28.9% (9.8% lifting >50 pounds). Predisposing conditions included fibromuscular dysplasia 31.1% (45.2% had no/incomplete screening), systemic inflammatory diseases 4.7%, peripartum 4.5%, and connective tissue disorders 3.6%. Most were treated conservatively (84.3%), but 14.1% underwent PCI and 0.7% coronary artery bypass surgery. In-hospital major adverse event rate was 8.8% with a higher rate (20.6% vs 8.2%; p=0.023) in peripartum SCAD patients. Overall 30-day MACE was 8.8%. Peripartum SCAD and connective tissue disease were independent predictors of 30-day MACE (Saw J et al, *Eur Heart J* 2019;40: 1188–97).

In Routine Clinical Care, AF Ablation Was Associated With a Reduction in the Primary Composite Endpoint of All-Cause Mortality, Stroke, Major Bleeding, and Cardiac Arrest

A US database identified 183,760 patients with AF treated with ablation or medical therapy. Propensity score weighting was used to balance patients treated with ablation ($N = 12,032$) or medical therapy ($N = 171,728$). Ablation was associated with a reduction in the composite endpoint of all-cause mortality, stroke, major bleeding, and cardiac arrest (hazard ratio - HR 0.75; $P < 0.001$). The majority of patients (73.8%) were potentially trial eligible; among whom the risk reduction associated with ablation was greatest (HR 0.70; $P < 0.001$). Among the 3.8% of patients who failed to meet the inclusion criterion, i.e. patients under 65 years without stroke risk factors, the event rates were low and there was no significant relationship with ablation (HR 0.67; $P = 0.35$). Among the 22.4% patients who met at least one of the trial exclusion criteria, there was a lesser but statistically significant reduction associated with ablation (HR 0.85; $P = 0.01$) (Noseworthy PA et al, *Eur Heart J* 2019;40: 1257–64).

Age is an Important Driver for Ischemic Stroke Risk in AF / Age Thresholds for Use of NOACs Were Different for AF Patients Having Different Single Risk Factors Beyond Sex Despite the Same CHA_2DS_2-Vasc Score Point (1 for Males and 2 For Females), i.e. 35 Years for Heart Failure, 50 Years for Hypertension or Diabetes, and 55 Years for Vascular Diseases

In a study cohort of 31,039 and 39,020 AF patients who did not have any or had only one risk factor comorbidity of the CHA_2DS_2-VASc score except for age and sex, the tipping point for the use of NOACs was set at a stroke risk of 0.9%/year. The overall risk of ischemic stroke using the conventional way was overestimated compared to the dynamic or ideal assessment with the incidence rate ratio of 1.24 for patients with hypertension, 1.20 for heart failure, 1.37 for diabetes mellitus, and 1.38 for vascular diseases; all *P*-values <0.01. With heart failure, the tipping point (age 35 years) of NOACs was similar, irrespective of methods used for stroke risk assessment. According to the results of ideal assessment, the age thresholds for the use of NOACs for patients with hypertension, diabetes mellitus, and vascular diseases were 50 years, 50 years, and 55 years, respectively (Chao T-F et al, *Eur Heart J* 2019;40: 1504–14).

Overall Risk of Infection was Low in Pacemaker (PM) Implantations But Considerably Higher in CRT Systems and After Reinterventions

In the Danish Pacemaker (PM) and ICD Register, including 97,750 patients, 1827 device-related infections (DRI) causing device removals were identified with an incidence during device lifetime of 1.19% for PM, 1.91% for ICD, 2.18% for CRT-P, and 3.35% for CRT-D. Incidence rates in *de novo* implantations were 2.04/1000 DY for PM, 3.84 for ICD, 4.38 for CRT-P, and 6.76 for CRT-D. Implantation of complex devices (ICD and CRT), reoperations, prior DRI, male sex, and younger age as significantly associated with higher DRI risk (Olsen T et al, *Eur Heart J* 2019; 40: 1862–9).

Proton Pump Inhibitor Therapy is Used Less Than Suggested by Guidelines in Patients Treated With DAPT Following MI and Was Generally Associated With Reduced Risk of GI Bleeding

Among 46,301 patients on DAPT after MI, only 35% of patients at higher risk of GI bleeding received recommended treatment with a PPI based on the guideline criteria. The 1-year risk of GI bleeding was 1% and 1.7% for high-risk patients. Overall PPI compared with no therapy, was associated with a risk ratio for GI bleeding of 0.62 corresponding to an absolute risk difference of 0.44%. PPI therapy was associated with a similar absolute risk difference (0.47%) for high-risk patients (Sehested TSG et al, *Eur Heart J* 2019;40: 1963-70).

Vernakalant was Effective in Converting Recent Onset AF, Did not Require Monitoring in the Cardiac Care Unit, was Well Tolerated and May Effectively Replace Ibutilide in the Routine Care of These Patients

Vernakalant, a novel antiarrhythmic agent approved for conversion of recent-onset atrial fibrillation (AF), heralded as safer agent compared to ibutilide, was used in 23 consecutive patients (13 men; age 63±12 years) with recent-onset AF of 42±64 h duration, with ventricular rate of 115±20 bpm. Vernakalant was given as a first infusion at 3 mg/kg given over 10 min, followed by a second infusion at 2 mg/kg at 15 min later if AF was not terminated. Patients received the drug in the cardiology ward with bedside-monitoring alone. Conversion of AF was achieved in 15 (65%) patients within 25±31 min. A higher (85.7%) conversion rate was observed in patients without underlying structural heart disease (p=0.035). The study included 9 (39%) patients who failed conversion with amiodarone, and 5 (55.6%) responded to vernakalant. Conversion was independent of left atrial size, arrhythmia duration, gender or type of prior drug intake. Patients tolerated the medication well with only minor side-effects in 7 (Manolis AS et al, *Hellenic J Cardiol* 2019;60:54-56)

Important Review and Other Articles

● **Ablation** of ventricular arrhythmias (Shivkumar K et al, *N Engl J Med* 2019; 380:1555-1564)

● Obstructive **sleep apnea** (Veasey SC et al, *N Engl J Med* 2019; 380:1442-1449)

● Transthyretin **amyloid** cardiomyopathy (Ruberg FL et al, *J Am Coll Cardiol* 2019;73:2872-91)

● **Atrial functional mitral regurgitation** (Deferm S et al, *J Am Coll Cardiol* 2019;73:2465-76)

● **Depression** in patients with cardiovascular disease (Jha MK et al, *J Am Coll Cardiol* 2019;73:1827-45)

● **Type 2 MI** (Sandoval Y et al, *J Am Coll Cardiol* 2019;73:1846-60)

● **Renal denervation** update (Kiuchi MG et al, *J Am Coll Cardiol* 2019;73:3006-17)

● **Right ventricle** (Sanz J et al, *J Am Coll Cardiol* 2019;73: 1463-82)

● Intestinal **microbiota** in CV health and disease (Tang WHW et al, *J Am Coll Cardiol* 2019;73:2089-105)

● **Arrhythmia-induced cardiomyopathy** (Huizar JF et al, *J Am Coll Cardiol* 2019;73:2328-44)

● **Cardiorenal syndrome** / AHA Scientific statement (Rangaswami J et al *Circulation* 2019;139:e840–78)

● **Sudden death in HFpEF** (Manolis AS et al, *Heart Fail Rev* 2019 May 30. doi: 10.1007/s10741-019-09804-2)

● **CV effects of alcohol** (Manolis TA et al, *Alcohol* 2019 May;76:117-129)

● **MINOCA**, AHA Scientific Statement (Tamis-Holland J et al, *Circulation* 2019;139:e891–e908)

● Aortic stenosis and **small aortic annulus** (Freitas-Ferraz AB et al, Circulation. 2019;139:2685–2702)

● **American Guidelines on Cholesterol** (Grundy SM et al, *Circulation* 2019;139:e1082–e1143)

● **Thyroid and CVD** (Cappola AR et al, *Circulation* 2019;139:2892–2909)

● **Subclinical thyroid dysfunction** and CV consequences (Manolis AA et al, *Trends Cardiovasc Med* 2019 Mar 5. pii: S1050-1738(19)30029-5. doi: 10.1016/j.tcm.2019.02.011)

● The rise and fall of **aspirin** in the primary prevention of CV disease (Raber I et al, *Lancet* 2019; 393: 2155–67*)*

● HFpEF, AF and senile **amyloidosis** (van den Berg MP et al, *Eur Heart J* 2019;40)

● Management of **left main** disease (Fajadet J et al, *Eur Heart J* 2019;40: 1454–66)