

CARDIOLOGY CORNER

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HRS Meeting: Boston, 13-16/5/2015

EuroPCR: Paris, 19-22/5/2015

EHRA Europace-CardioStim: Milan, 21-24/6/2015

ESC Congress: London, 29/8-2/9/2015

TCT Meeting 2015: San Francisco, 11-15/10/2015

HCS Congress: Thessaloniki, 29-31/10/2015

AHA Scientific Sessions: Orlando, 7-11/11/2015

Low-Level Transcutaneous Electrical Vagus Nerve Stimulation (LLTS) Suppresses Atrial Fibrillation

Patients with paroxysmal atrial fibrillation (AF) were randomized to 1 hour of 20 Hz LLTS (n=20) or sham control (n=20) by attaching a flat metal clip onto the tragus in the right ear. AF was induced by burst atrial pacing at baseline and after 1 hour of LLTS or sham treatment. Blood samples from the coronary sinus and the femoral vein were collected at those time points and analyzed for inflammatory cytokines, including tumor necrosis factor alpha and C-reactive protein. Pacing-induced AF duration decreased significantly by 6.3 ± 1.9 min compared with baseline in the LLTS but not in the control group ($p=0.002$). AF cycle length increased significantly from baseline by 28.8 ± 6.5 ms in the LLTS but not in the control group ($p=0.0002$). Femoral vein but not coronary sinus tumor necrosis factor (TNF)-alpha and C-reactive protein levels decreased significantly only in the LLTS group. The authors concluded that LLTS suppresses AF and decreases inflammatory cytokines in patients with paroxysmal AF, supporting a role of neuromodulation to treat AF (Stavrakis S et al, *J Am Coll Cardiol* 2015;65:867-875).

Among Patients with Early Repolarization Syndrome, Programmed Stimulation Does not Predict Future Arrhythmic Events

In a multicenter study, 81 patients, aged 36 ± 13 years, with early repolarization (ER) syndrome and aborted sud-

den death due to ventricular fibrillation (VF) underwent an electrophysiology study (EPS). VF was inducible in only 18 of 81 (22%) patients. During follow-up of 7.0 ± 4.9 years, 6 of 18 (33%) patients with inducible VF, and 21 of 63 (33%) noninducible patients experienced VF recurrences ($p=NS$). VF storm occurred in 3 inducible and 4 noninducible patients. VF inducibility was not associated with maximum J-wave amplitude or J-wave distribution (inferior, odds ratio -OR: 0.96; lateral, OR: 1.57; inferior and lateral, OR: 0.83; all $p=NS$), which have previously been shown to predict outcome in patients with an ER pattern. The authors concluded that EPS did not enhance risk stratification in ER syndrome (Mahida S et al, *J Am Coll Cardiol* 2015;65:151-159).

ICD Therapy is an Effective Strategy in Patients With Brugada Syndrome, Treating Potentially Lethal Arrhythmias in 17% of Patients but also in 13% of Asymptomatic Patients, Albeit at Increased Risk for Complications in 16% / Risk Stratification by Means of EPS Might Identify Asymptomatic Patients at Risk

Among 176 consecutive Brugada syndrome patients, spontaneous sustained ventricular arrhythmias (VAs) occurred in 30 patients (17%) at follow-up of 7 ± 4.8 years. Eight patients (4.5%) died. Appropriate ICD shocks occurred in 28 (15.9%), inappropriate shocks in 33 patients (18.7%), and electrical storm in 4 (2.3%). Device-related complications occurred in 28 patients (15.9%). In multivariate analysis, aborted sudden cardiac death and VA inducibility on electrophysiology studies (EPS) were independent predictors of appropriate shock occurrence. The authors concluded that ICD therapy was an effective strategy in Brugada syndrome, treating potentially lethal arrhythmias in 17% of patients during long-term follow-up, but also in 13% of asymptomatic patients. Risk stratification by EPS may identify asymptomatic patients at risk for arrhythmic events. ICDs are frequently associated with device-related complications (Conte G et al, *J Am Coll Cardiol* 2015;65:879-888).

Swedish Registries: Benefit of Anticoagulation Unlikely in Patients With Atrial Fibrillation (AF) and a CHA₂DS₂-VASc Score of 1

According to a retrospective study of 140,420 patients with AF, among those with a CHA₂DS₂-VASc score of 1, the annual event rates varied between 0.5% and 0.9%; women were truly low risk, with an annual ischemic stroke rate of only 0.1% to 0.2%. For men, the ischemic stroke rate was between 0.5% and 0.7%. When the endpoint included diagnoses of TIA, pulmonary embolism, arterial embolism, and stroke not specified as ischemic or hemorrhagic, the annual event rate for men was 1.3%. The authors concluded that the risk of ischemic stroke in patients with AF and a CHA₂DS₂-VASc score of 1 seems to be lower than previously reported (Friberg L et al, *J Am Coll Cardiol* 2015;65:225–32).

Taiwanese Study: Anticoagulation Should be Considered for AF Patients With 1 Additional Stroke Risk Factor Given their High Risk of Ischemic Stroke

A retrospective study investigated the risk of ischemic stroke in patients with a single additional stroke risk factor, i.e., CHA₂DS₂-VASc score=1 (males) or 2 (females). Among 12,935 male AF patients with a CHA₂DS₂-VASc score of 1, 1,858 patients (14.4%) had an ischemic stroke during follow-up (5.2±4.3 years), with an annual stroke rate of 2.75%. Ischemic stroke risk ranged from 1.96%/year for men with vascular disease to 3.5%/year for those 65 to 74 years of age. For 7,900 females with AF and a CHA₂DS₂-VASc score of 2, 14.9% experienced ischemic stroke for an annual stroke rate of 2.55%. Ischemic stroke risk increased from 1.91%/year for women with hypertension to 3.34%/year for those 65 to 74 years of age. The authors concluded that among risk factors, age 65 to 74 years is associated with the highest stroke rate. Oral anticoagulation should be considered for AF patients with 1 additional stroke risk factor given their high risk of ischemic stroke (Chao T et al, *J Am Coll Cardiol* 2015;65:635–642).

ITALIC Trial: Bleeding and Thrombotic Event Rates Not Different Between 6- & 24-Month DAPT After PCI with 2nd-Generation DES/6-Month DAPT Non-inferior to 24-Month DAPT in Good Aspirin Responders

Of 2,031 enrolled patients undergoing implantation of everolimus-eluting stents with confirmed nonresistance to aspirin, 941 patients were randomized to 24-month and 953 to 6-month dual antiplatelet therapy (DAPT). The primary endpoint (death, myocardial infarction, urgent target vessel revascularization, stroke, and major bleeding at 12 months post-stenting) was no different (24-month: 1.5% vs 6-month: 1.6%; p=NS). 6-month was noninferior to 24-month DAPT. There were no significant differences in stent thrombosis or

bleeding complications. In the 792 (44%) high-risk patients with ACS, primary and secondary endpoints did not significantly differ (hazard ratio: 1.7; p=NS). The authors concluded that rates of bleeding and thrombotic events were not significantly different according to 6- vs 24-month DAPT after PCI with new-generation DES in good aspirin responders (Gilard M et al, *J Am Coll Cardiol* 2015;65:777–786).

Meta-Analysis: Short-Term (≤6 Months) Dual Antiplatelet Therapy (DAPT) After Implantation of Drug-Eluting Stents Produced Similar Rates of Major Adverse Cardiac Events (MACE) But Significantly Less Bleeding Than Longer-Term (≥1 Year) DAPT

Metaanalysis of 4 randomized trials including 8,180 patients indicated that at 1-year, short-term (≤6 months) DAPT was associated with similar rates of MACE (hazard ratio - HR: 1.11; p=NS), but significantly lower rates of bleeding (HR: 0.66; p=0.03) versus prolonged DAPT (1 year). Comparable results were apparent between DAPT discontinuation and 1-year follow-up (for MACE: HR: 1.20; p=NS) (for bleeding: HR: 0.44; p=0.03). There were no significant differences in 1-year rates of MACE among 3-month vs 1-year DAPT, 6-month vs 1-year DAPT, or 3-month vs 6-month DAPT. The authors concluded that compared with prolonged DAPT, short-term DAPT is associated with similar rates of MACE but lower rates of bleeding after DES placement (Palmerini T et al, *J Am Coll Cardiol* 2015;65:1092-1102).

Occupational Health Hazards of Working in the Interventional Laboratory: More Work-Related Musculoskeletal Pain but No Cancer

Among 1,543 Mayo Clinic employees (aged 43±11.3 years, 33% male) working in interventional cardiology or radiology laboratories responding (57%) to a survey, 1,042 (67.5%) were involved with procedures utilizing radiation. They reported experiencing work-related pain more often than the control group before (54.7% vs 44.7%; p<0.001) and after adjustment for confounding factors (odds ratio: 1.67; p<0.001). Musculoskeletal pain varied significantly by job description, with the highest incidence reported by technicians (62%) and nurses (60%) followed by physicians (44%) and trainees (19%; p<0.001). There was no difference in cancer prevalence between groups (9% vs 9%) (Orme NM et al, *J Am Coll Cardiol* 2015;65:820-826).

Circulating Levels of Amyloid Beta are Predictive of Cardiovascular Mortality in Patients With Established Coronary Heart Disease (CHD)

Amyloid beta peptide, a major protein constituent of neuritic plaques in Alzheimer disease, with a central role in vascular inflammation pathophysiology, was measured (amyloid beta 40 form: Abeta40) in blood samples collected from

1,464 patients with CHD. Abeta40 independently predicted cardiovascular (CV) death and major adverse cardiac events (MACE) in patients with CHD ($p < 0.05$ for all). Cohort-based analysis revealed that Abeta40 levels were significantly and independently associated with arterial stiffness progression, incident subclinical atherosclerosis and CHD. The authors concluded that measuring blood levels of Abeta40 identified patients at high risk for CV death. (Stamatelopoulos K et al, *J Am Coll Cardiol* 2015;65:904-916).

CvLPRIT: In Patients Undergoing Primary-PCI for STEMI, Complete Revascularization During Index Admission Confers Significantly Fewer MACE at 12 Months Than When Only the IRA is Treated

In CvLPRIT (Complete versus Lesion-only Primary PCI trial), 296 patients with STEMI undergoing primary PCI (P-PCI) in 7 UK centers were randomized to either in-hospital complete revascularization (either at the time of P-PCI or before hospital discharge) ($n=150$) or infarct-related artery (IRA)-only revascularization ($n=146$). The primary endpoint (all-cause death, recurrent myocardial infarction -MI, heart failure, and ischemia-driven revascularization within 12 months), but not death or MI, was reduced with complete compared with IRA-only revascularization (10% vs 21.2%; hazard ratio: 0.45; $p=0.009$). A trend toward benefit was seen early after complete revascularization ($p=0.055$ at 30 days). The authors concluded that in patients presenting for P-PCI with multivessel disease, index admission complete revascularization significantly lowered the rate of the composite primary endpoint at 12 months compared with treating only the IRA (Gershlick AH et al, *J Am Coll Cardiol* 2015;65:963-972). N.B. The 2 randomized trials, PRAMI & CvLPRIT, reporting reduced MACE for PCI on non-infarct-related stenotic coronary arteries, have led to withdrawal of class III practice guideline recommendations not to treat significant non-infarct-related stenoses in patients with STEMI and multivessel disease undergoing primary angioplasty.

PARADIGM-HF: Angiotensin Receptor Neprilysin Inhibition Compared With Enalapril Reduces the Risk of Clinical Progression in Surviving Patients With Heart Failure

Therapy with angiotensin-neprilysin inhibitor LCZ696 (400 mg daily) compared with enalapril (20 mg daily) in 8399 patients with heart failure and reduced ejection fraction led to fewer patients needing intensification of anticongestive treatment (520 vs 604; hazard ratio-HR, 0.84; $P=0.003$) or visiting the emergency room for worsening heart failure (HR, 0.66; $P=0.001$). The LCZ696 group had 23% fewer hospitalizations for worsening heart failure ($P < 0.001$) (evident within the first 30 days) and were less likely to require intensive care (18%

rate reduction, $P=0.005$), to receive inotropic agents (31% risk reduction, $P < 0.001$), and to have implantation of a heart failure device or cardiac transplantation (22% risk reduction, $P=0.07$). LCZ696 led to an early and sustained reduction in biomarkers of myocardial wall stress and injury (N-terminal pro-B-type natriuretic peptide and troponin) vs enalapril. The authors concluded that angiotensin-neprilysin inhibition prevents clinical progression of surviving patients with heart failure more effectively than angiotensin-converting enzyme inhibition (Packer M et al, *Circulation* 2015;131:54-61).

ORBIT-AF: Bridging Anticoagulation is Associated With Higher Risk of Bleeding and Adverse Events

The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) recorded temporary interruptions of oral anticoagulation for a procedure. Of 7372 patients treated with oral anticoagulation, 2803 overall interruption events occurred in 2200 patients (30%) at a median of 2 years. Bridging was used in 24% ($n=665$), mostly with low-molecular weight heparin (73%, $n=487$) and unfractionated heparin (15%, $n=97$). Bridged patients were more likely to have had prior cerebrovascular events (22% vs 15%; $P=0.0003$) and mechanical valves (9.6% vs 2.4%; $P < 0.0001$); however, there was no difference in CHA2DS2-VASc scores (scores ≥ 2 in 94% vs 95%; $P=0.5$). Bleeding events were more common in bridged than non-bridged patients (5% vs 1.3%; odds ratio-OR, 3.84; $P < 0.0001$). The incidence of myocardial infarction, stroke or systemic embolism, major bleeding, hospitalization, or death within 30 days was also significantly higher in patients receiving bridging (13% vs 6.3%; OR, 1.94; $P=0.0001$) (Steinberg PA et al, *Circulation* 2015;131:488-494).

Meta-Analysis for Myocardial Infarction (MI) With Nonobstructive Coronary Arteries (MINOCA): 6% Prevalence / More Likely in Younger and Female Patients and with Lower All-Cause Mortality at 12 Months (4.7% vs 6.7%) Compared With MI With Obstructive Coronary Artery Disease

According with a meta-analysis of 28 publications, the prevalence of MINOCA was 6% with a median patient age of 55 years and 40% women. However, in comparison with those with MI associated with obstructive coronary artery disease, patients with MINOCA were more likely to be younger and female but less likely to have hyperlipidemia. All-cause mortality at 12 months was lower in MINOCA compared with MI associated with obstructive coronary artery disease (4.7% vs 6.7%). Typical MI on cardiac magnetic resonance imaging is found in only 24% of patients, myocarditis in 33% and no significant abnormality in 26%. Coronary artery spasm was inducible in 27% of MINOCA patients, and thrombophilia disorders were detected in 14% (Pasupathy S et al, *Circulation* 2015;131:861-870).

Dabigatran and Rivaroxaban Confer Great Risk in Dialysis Patients

Dabigatran and rivaroxaban are eliminated through the kidneys, hence their use in dialysis patients is discouraged because these drugs can accumulate and cause inadvertent bleeding. Nevertheless, a steady increase of dabigatran and rivaroxaban use has been recorded among 29,977 hemodialysis patients with atrial fibrillation in the USA, where 5.9% of anticoagulated dialysis patients are started on these new anticoagulants, with consequent higher risk of hospitalization or death from bleeding when compared with warfarin (rate ratio 1.48 for dabigatran, $P=0.0001$) and 1.38 for rivaroxaban, $P=0.04$). The risk of hemorrhagic death was even larger with dabigatran (rate ratio, 1.78; $P=0.006$) and rivaroxaban (rate ratio, 1.71; $P=0.07$) relative to warfarin. Differences in stroke and arterial embolism could not be detected in this study as there were too few events. The authors concluded that more dialysis patients are being started on dabigatran and rivaroxaban, even when their use is contraindicated and there are no studies to support that the benefits outweigh the risks of these drugs in end-stage renal disease (Chan KE et al, *Circulation* 2015;131:972-979).

TRA 2°P - TIMI 50 Trial: Vorapaxar in Patients With Diabetes Mellitus and Previous Myocardial Infarction Reduces CV Risk but Increases Bleeding

In patients with diabetes (DM) and prior MI ($n=3623$), barring those with prior TIA or stroke (whereby the drug is contraindicated), vorapaxar significantly reduced the primary end point (cardiovascular-CV death, MI, or stroke) (11.4% vs 14.3%; hazard ratio-HR, 0.73; $P=0.002$) with a number needed to treat to avoid 1 major CV event of 29. The incidence of bleeding was increased with vorapaxar (4.4% vs 2.6%; HR, 1.60). However, net clinical outcome (efficacy and safety) was improved with vorapaxar (HR, 0.79). The authors concluded that in patients with previous MI and DM, vorapaxar added to standard therapy significantly reduced the risk of major CV events, albeit at a cost of increased bleeding (Cavender MA et al, *Circulation* 2015;131:1047-1053).

Reduced Cardiovascular and Mortality Risks in Elderly Medicare Patients with Atrial Fibrillation (AF) Treated With Dabigatran Compared to Warfarin, but Increased Major Gastrointestinal Bleeding Risk

Among 134414 Medicare patients with 37587 person-years of follow-up, the hazard ratios comparing dabigatran with warfarin were 0.80 for ischemic stroke; 0.34 for intracranial hemorrhage; 1.28 for major gastrointestinal (GI) bleeding; 0.92 for acute MI; and 0.86 for death. In the subgroup of dabigatran 75 mg bid, there was no difference in risk compared with warfarin for any outcome except reduced intracranial hemorrhage.

The authors concluded that dabigatran was associated with reduced risk of ischemic stroke, intracranial hemorrhage, and death and increased risk of major GI hemorrhage compared with warfarin in elderly patients with nonvalvular AF. These associations were most pronounced in patients treated with dabigatran 150 mg bid, whereas the lower dose of 75 mg bid was similar to warfarin except for a lower risk of intracranial hemorrhage (Graham DJ et al, *Circulation* 2015;131:157-164).

Icatibant, a Selective Bradykinin B₂ Receptor Antagonist, is Effective in ACE-Inhibitor-Induced Angioedema

All 27 patients with ACE-inhibitor-induced angioedema of the upper aerodigestive tract had complete resolution of edema with therapy. The median time to resolution was 8 hours for those randomly assigned to 30 mg of subcutaneous icatibant, a selective bradykinin B₂ receptor antagonist, as compared with 27.1 hours in those assigned to current off-label standard therapy (IV 500 mg prednisolone plus 2 mg clemastine) ($P=0.002$), with 3 patients in the standard therapy group requiring rescue intervention with icatibant and prednisolone; 1 patient required tracheotomy. More patients in the icatibant than in the standard-therapy group had complete resolution of edema within 4 hours (5 of 13 vs 0 of 14, $P=0.02$). The median time to the onset of symptom relief was shorter with icatibant than with standard therapy (2 vs 11.7 hours, $P=0.03$). The authors concluded that among patients with ACE-inhibitor-induced angioedema, the time to complete resolution of edema was shorter with icatibant than with combination therapy with a glucocorticoid and an antihistamine (Bas M et al, *N Engl J Med* 2015;372:418-425).

Good Efficacy of a Device that Narrows the Coronary Sinus in Refractory Angina

A total of 104 patients with refractory (CCS class III or IV) angina and myocardial ischemia, who were not candidates for revascularization, were randomized to implantation of a balloon-expandable, stainless steel, hourglass-shaped, coronary-sinus reducing device (creating a focal narrowing and increasing pressure in the coronary sinus, thus redistributing blood into ischemic myocardium) (treatment group, $n=52$) or to a sham procedure (control group, $n=52$). More (35% vs 15%) patients in the treatment compared to the control group had an improvement of at least two CCS angina classes at 6 months ($P=0.02$), or improvement of at least one CCS angina class (71% vs 42%; $P=0.003$). Quality of life was significantly improved in the treatment vs control group ($P=0.03$), with no significant between-group differences in improvement in exercise time or in the mean change in the wall-motion index by dobutamine echocardiography. At 6 months, 1 patient in the treatment group had a myocardial infarction (MI); in the control group, 1 patient died and 3 had an MI. The authors

concluded that implantation of the coronary-sinus reducing device was associated with significant improvement in symptoms and quality of life in patients with refractory angina who were not candidates for revascularization (Verheye S et al, *N Engl J Med* 2015;372:519-527).

BEST Trial: Bypass Surgery (CABG) Superior to Second Generation (Everolimus-Eluting) Stents in Multivessel Coronary Artery Disease (CAD)

A total of 880 patients with multivessel CAD were randomized to PCI with everolimus-eluting stents (n=438) or to CABG (n=442). At 2 years, the primary end point (death, MI, or target-vessel revascularization) occurred in 11% vs 7.9% in the 2 groups, respectively (P=0.32 for noninferiority). At longer-term follow-up (median, 4.6 years), the primary end-point had occurred in 15.3% vs 10.6% (hazard ratio, 1.47; P=0.04). Rates of any repeat revascularization and spontaneous MI were significantly higher after PCI than after CABG. The authors concluded that among patients with multivessel CAD, the rate of major adverse cardiovascular events was higher among those who underwent PCI with use of everolimus-eluting stents than among those having CABG (Park S-J et al, *N Engl J Med* 2015;372:1204-1212).

Clinical-Practice Registry Study Comparing Second Generation Stenting with Bypass Surgery: Similar Risk of Death but Higher Risk of MI and Repeat Procedures and Lower Risk of Stroke with PCI

At a mean follow-up of 2.9 years of 18,446 patients, 9223 patients undergoing PCI with everolimus-eluting stents and 9223 having CABG, PCI vs CABG had similar risk of death (3.1% vs 2.9% per year; hazard ratio-HR, 1.04; P=0.50), higher risks of MI (1.9% vs 1.1% per year; HR, 1.51; P<0.001, only for those with incomplete revascularization) and repeat revascularization (7.2% vs 3.1% per year; HR, 2.35; P<0.001), and a lower risk of stroke (0.7% vs 1.0% per year; HR, 0.62; P<0.001). The authors concluded that the risk of death with PCI was similar to that associated with CABG. PCI was associated with a higher risk of MI (among patients with incomplete revascularization) and repeat revascularization but a lower risk of stroke (Bangalore S et al, *N Engl J Med* 2015;372:1213-1222).

In-stent Restenosis Detected by Angiographic Surveillance in 10 004 patients is Predictive of 4-Year Mortality Even in Asymptomatic Patients

Among 10 004 stented patients undergoing routine control angiography after 6-8 months, restenosis was detected in 2643 (26.4%) patients. Of 702 deaths occurring during follow-up, 218 occurred among patients with restenosis and 484 deaths in

patients without restenosis (hazard ratio- HR: 1.19; P=0.03). Restenosis was an independent predictor of 4-year mortality; HR: 1.23; P=0.02). Other independent correlates of 4-year mortality were age (for each 10-year increase, HR: 2.34; P<0.001), diabetes mellitus (HR: 1.68; P<0.001), current smoking habit (HR: 1.39; P=0.01), and left ventricular ejection fraction (for each 5% decrease, HR: 1.39; P<0.001). The authors concluded that the presence of restenosis at follow-up angiography after coronary stenting was predictive of 4-year mortality, even in patients that were asymptomatic. The evidence of restenosis provided prognostic information complementary to that provided by other clinical characteristics (age, gender, diabetes mellitus, smoking, previous by-pass surgery, ejection fraction). These findings suggest that newer-generation drug-eluting stents may have a meaningful impact on long-term mortality through the reduction in restenosis after coronary stenting (Cassese S et al, *Eur Heart J* 2015;36:94-99).

Network Meta-Analysis: Effectiveness of PFO Closure Depends on the Device Used / PFO Closure With Amplatzer Occluder Appears Superior to Medical Therapy in Preventing Strokes in Patients with Cryptogenic Embolism

A network meta-analysis of 4 randomized trials (2963 patients with 9309 patient-years) including 3 devices (Amplatzer, STARFlex, and HELEX) indicated that patients allocated to PFO closure with Amplatzer were less likely to experience a stroke than patients allocated to medical therapy (rate ratio -RR 0.39), while no significant differences were found for the other devices. No significant differences were found for transient ischemic attack and death. The risk of new-onset atrial fibrillation was more pronounced for STARFlex (RR 7.67), than Amplatzer (RR 2.14) and HELEX (RR 1.33), when compared with medical therapy. The authors concluded that network meta-analysis provided evidence in favour of percutaneous closure of PFO with one of the examined devices (Amplatzer) in patients with a history of cryptogenic stroke or embolism and a PFO (Storteky S et al, *Eur Heart J* 2015;36:120-128).

ANSWER Study: AAI-DDD Changeover Mode to Minimize Ventricular Pacing (SafeR) Compared to DDD Mode did not Reduce Heart Failure (HF) Hospitalization or Atrial Fibrillation (AF)

A total of 650 patients (52% sinus node disease, 48% AV block) were randomized to SafeR (n=314) or DDD (n=318) mode. The SafeR mode showed a significant decrease in ventricular pacing (VP) compared with DDD (11.5 vs 93.6%, P<0.0001 at 3 years). Deaths and syncope did not differ in the two groups. No significant difference was found in the time to event of the co-primary composite of hospitalization for HF, AF, or cardioversion, nor in the individual components. How-

ever, SafeR showed a 51% risk reduction (RR) in experiencing cardiac death or HF hospitalization (hazard ratio-HR=0.49; $P=0.02$) and 30% RR in experiencing cardiovascular hospitalizations (HR=0.70; $P=0.05$). The authors concluded that SafeR vs DDD safely and significantly reduced VP with no effect on hospitalization for HF, AF, or cardioversion, but admitted that the favourable effect of SafeR-mediated VP prevention on HF outcomes warrants further investigation, as the combined clinical secondary outcome of cardiac death or HF hospitalization differed in favour of the SafeR group, with an observed borderline significant reduction in cardiovascular hospitalizations and shorter duration of hospital stay for these hospitalizations (Stockburger M et al, *Eur Heart J* 2015;36:151-157).

Ibaraki Study: Presence of Atrial Premature Beats (APBs) in 12-Lead ECGs is Associated with Increased Risk of Cardiovascular (CV) Death and New-Onset Atrial Fibrillation (AF) in the General Population

Among 63,197 individuals (mean age, 58.8 ± 9.9 years; 67.6% women) who participated in annual community-based health checkups, during a 14-year mean follow-up, in subjects with APBs, compared with those without APBs, the hazard ratio (HRs) of stroke death was 1.24 for men and 1.63 for women, of CV death 1.22 for men and 1.48 for women, and of all-cause death 1.08 for men and 1.21 for women. The presence of APBs at baseline was also a significant predictor of AF onset (HR 4.87 for men and 3.87 for women). The authors concluded that the presence of APBs in 12-lead ECGs was a strong predictor of AF development, and associated with increased risk of CV death in the general population (Murakoshi N et al, *Eur Heart J* 2015;36:170-178).

Analysis of 6563 Aspirin-Treated Patients in ACTIVE-A and AVERROES: Patients with Permanent AF are at a Higher Risk of Stroke Compared with Patients with Non-Permanent AF / in Deciding whether to Offer Anticoagulation to Low-Risk Patients, it May be Useful to Consider the Pattern of AF Occurrence

Among 6563 aspirin-treated patients with AF from the ACTIVE-A/AVERROES databases (mean age: 69 ± 9.9 for paroxysmal, 68.6 ± 10.2 for persistent, and 71.9 ± 9.8 years for permanent AF ($P < 0.001$), the CHA₂DS₂-VASc score was similar in patients with paroxysmal and persistent AF (3.1 ± 1.4), but higher in permanent AF (3.6 ± 1.5 , $P < 0.001$). Annual stroke rates were 2.1% for paroxysmal, 3% for persistent, and 4.2% for permanent AF, with hazard ratio of 1.83 ($P < 0.001$) for permanent vs paroxysmal and 1.44 ($P = 0.02$) for persistent vs paroxysmal. Age ≥ 75 years, gender, history of stroke or TIA, and AF pattern were independent predictors of stroke, with AF

pattern being the second strongest predictor after prior stroke or TIA. The authors concluded that among non-anticoagulated AF patients, pattern of AF was a strong independent predictor of stroke risk and may be helpful to assess risk/benefit for anticoagulant therapy in lower risk patients (Vanassche T et al, *Eur Heart J* 2015;36:281-288).

ROCKET-AF Trial: Higher Risk of Death and Stroke in Persistent vs Paroxysmal Atrial Fibrillation (AF)

Of 14,062 patients in the ROCKET-AF trial, 11,548 (82%) had persistent and 2,514 (18%) had paroxysmal AF. Patients with persistent AF were marginally older (73 vs 72, $P = 0.03$), less likely female (39 vs 45%, $P < 0.0001$), and more likely to have prior use of vitamin K antagonists (64 vs 56%, $P < 0.0001$) compared with patients with paroxysmal AF. In patients randomized to warfarin, time in therapeutic range was similar (58 vs 57%, $P = \text{NS}$). Patients with persistent AF had higher rates of stroke or systemic embolism (2.18 vs 1.73 events per 100-patient-years, $P = 0.048$) and all-cause mortality (4.78 vs 3.52, $P = 0.006$). Rates of major bleeding were similar (3.55 vs 3.31, $P = \text{NS}$). Rates of stroke or systemic embolism in both types of AF did not differ by treatment assignment (rivaroxaban vs warfarin). The authors concluded that patients with persistent AF have a higher risk of stroke and death compared with paroxysmal AF (Steinberg BA et al, *Eur Heart J* 2015;36:288-296).

The Swedish Atrial Fibrillation (AF) Cohort Study: Stroke Benefit from Anticoagulation, but Higher Risk of Bleeding in Patients with AF and Renal Failure

In a retrospective non-randomized study of Swedish health registers comprising 307,351 patients with AF, ischemic stroke occurred more often among 13,435 with prior diagnosis of renal failure (annual rate, 3.9% vs no renal failure, 2.9%), but this was related to concomitant comorbidities (hazard ratio -HR 1.02). Adding renal failure to the established risk stratification (CHA₂DS₂ and CHA₂DS₂-VASc) did not improve predictive value. Renal failure was an independent risk factor for intracranial bleeding (HR: 1.27). Most patients with renal failure benefited from warfarin treatment, despite their high bleeding risk. The incidence of the combined endpoint ischemic or hemorrhagic stroke or death was lower among those who used warfarin (HR: 0.76). The authors concluded that patients with AF and renal failure will probably benefit most from having same treatment as is recommended for other patients with AF, by careful considerations of net benefit, optimal management of other risk factors for stroke and bleeding, and rigorous control of INR. Adding additional points for renal failure to the CHA₂DS₂-VASc score did not improve predictive value (Friberg L et al, *Eur Heart J* 2015;36:297-306).

Denmark Cohort Study: Thromboembolic Risk Beyond 3 Months after Radiofrequency Ablation (RFA) of AF is Relatively Low

During a median follow-up of 3.4 years of 4050 patients (median age 59.5, 26.5% females) undergoing first-time RFA, 71 (1.8%) thromboembolism cases were identified, where incidence rates with and without oral anticoagulation (OAC) were 0.56 and 0.64, respectively. Discontinuation of OAC remained insignificant (hazard ratio-HR 1.42) in multivariable analysis. Beyond 3 months after RFA, 87 (2.1%) serious bleedings occurred (incidence rates with and without OAC 0.99 and 0.44, respectively). OAC therapy was significantly associated with serious bleeding risk (HR 2.05). In an age- and gender-matched cohort of 15,848 non-ablated AF patients receiving rhythm-control therapy, thromboembolic rates with and without OAC were 1.34 and 2.14, respectively. The authors concluded that thromboembolic risk beyond 3 months after RFA was relatively low compared with a matched non-ablated AF cohort. With cautious interpretation due to low number of events, serious bleeding risk associated with OAC seems to outweigh the benefits of thromboembolic risk reduction. The CHA₂DS₂-VASc score may not be an appropriate tool for thromboembolic risk stratification in this population (Karasoy D et al, *Eur Heart J* 2015;36:307-315).

MADIT-CRT Trial: in Patients with LBBB, Biventricular (BIV) Pacing >90% Confers Benefit of Cardiac Resynchronization Therapy-Defibrillator (CRT-D) in Heart Failure (HF)/Death when Compared with Implantable Cardioverter Defibrillator (ICD)

The threshold of BIV pacing percentage needed for CRT-D to be superior to ICD on the end-point of heart failure (HF) or death was estimated in 1219 left bundle branch block (LBBB) patients in the MADIT-CRT trial (NYHA class I/II HF patients in sinus rhythm). In multivariable analyses, no difference was seen in the risk of HF/death between ICD and CRT-D patients with BIV pacing $\leq 90\%$ (HR=0.78, $P=NS$), and with increasing BIV pacing the risk of HF/death was decreased (CRT-D BIV 91–96% vs ICD: HR=0.63, $P=0.024$; and CRT-D BIV $\geq 97\%$ vs ICD: HR=0.32, $P<0.001$). The risk of death alone was reduced by 52% in CRT-D patients with BIV $\geq 97\%$ (HR=0.48, $P<0.016$), when compared with ICD patients. Within the CRT-D group, for every 1% increase in BIV pacing, the risk of HF/death and death alone significantly decreased by 6 and 10%, respectively. The authors concluded that in patients with LBBB, BIV pacing $>90\%$ was associated with a benefit of CRT-D in HF/death when compared with ICD patients. Also, BIV pacing $\geq 97\%$ was associated with an even further reduction in HF/death, a significant 52% reduction in death alone, and increased reverse remodelling. Physicians should be aware of patients with suboptimal BIV pacing to

implement preventive and optimizing measures to improve outcome and prognosis in these patients (Ruwald A et al, *Eur Heart J* 2015;36:440-448).

Systemic Review & Meta-analysis: Thrombolysis is Associated with a Significant Reduction of Mortality in Patients with Pulmonary Embolism (PE), but this Reduction is not Statistically Significant after Exclusion of Studies with High-Risk PE, While it is Associated with an Increase in Fatal, Intracranial, or Major Hemorrhage

According to meta-analysis of 15 randomized trials comparing thrombolytic therapy plus anticoagulation with anticoagulation alone in 2057 patients with acute pulmonary embolism (PE), thrombolytic therapy was associated with a significant reduction of overall mortality (OR; 0.59). This reduction was not statistically significant after exclusion of studies including high-risk PE (OR; 0.64). Thrombolytic therapy was associated with a significant reduction in the combined endpoint of death or treatment escalation (OR: 0.34), PE-related mortality (OR: 0.29) and PE recurrence (OR: 0.50). Major hemorrhage (OR; 2.91) and fatal or intracranial bleeding (OR: 3.18) were significantly more frequent among patients receiving thrombolysis. The authors concluded that thrombolytic therapy reduces total mortality, PE recurrence, and PE-related mortality in patients with acute PE, albeit at increased risk of major and fatal or intracranial hemorrhage. The decrease in overall mortality is, however, not significant in hemodynamically stable patients with acute PE (Marti C et al, *Eur Heart J* 2015;36:605-614).

CONFIRM-HF: Beneficial Effects of Long-term Intravenous (IV) Iron Therapy in Patients with Symptomatic Heart Failure and Iron Deficiency

A total of 304 heart failure (HF) patients with left ventricular ejection fraction $\leq 45\%$, elevated natriuretic peptides, and iron deficiency (ferritin <100 ng/mL or 100–300 ng/mL if transferrin saturation $<20\%$), were randomized 1:1 to IV iron, as ferric carboxymaltose (FCM, $n=152$) or placebo (saline, $n=152$) for 52 weeks. Treatment with FCM significantly prolonged 6-min-walk-test (6MWT) distance at Week 24 (difference FCM vs placebo: 33 ± 11 m, $P=0.002$). The treatment effect of FCM was consistent in all subgroups and was sustained to Week 52 (difference FCM vs placebo: 36 ± 11 m, $P<0.001$). Throughout the study, an improvement in NYHA class, patient global assessment, quality of life (QoL), and fatigue score in patients treated with FCM was detected with statistical significance observed from Week 24 onwards. Treatment with FCM was associated with a significant reduction in the risk of hospitalizations for worsening HF (hazard ratio: 0.39, $P=0.009$). The number of deaths (FCM: 12, placebo: 14 deaths) and the incidence of adverse events were comparable between groups. The authors concluded that treatment of

symptomatic, iron-deficient HF patients with FCM over a 1-year period resulted in sustainable improvement in functional capacity, symptoms, and QoL and may be associated with risk reduction of hospitalization for worsening HF (Ponikowski P et al, *Eur Heart J* 2015;36:657-668).

ABSORB II Trial: Stents with Bioresorbable Scaffold Had 1-year Clinical Outcome Similar to Metallic Stents

A total of 501 patients undergoing percutaneous coronary intervention were randomly assigned (2:1 ratio) to the bioresorbable scaffold stent group (everolimus-eluting bioresorbable scaffold) (335 patients, 364 lesions) or the metallic stent group (everolimus-eluting metallic stent) (166 patients, 182 lesions). Acute lumen gain was lower for the bioresorbable scaffold. At 1 year, cumulative rates of first new or worsening angina were lower (22%) in the bioresorbable scaffold group (vs 30% in the metallic stent group; $p=0.04$), whereas performance during maximum exercise and angina status were similar. Three patients in the bioresorbable scaffold group had stent thromboses, compared with no patients in the metallic stent group. There were 5% major cardiac adverse events in the bioresorbable scaffold group compared with 3% events in the metallic stent group, with the most common events being myocardial infarction and need for target-lesion revascularisation. The authors concluded that everolimus-eluting bioresorbable scaffold showed similar 1-year clinical outcomes to the everolimus-eluting metallic stent (Serruys PW et al, *Lancet* 2015;385:43-54).

RUTHERFORD-2: In Patients with Heterozygous Familial Hypercholesterolemia, PCSK9 Inhibition With Evolocumab was Well Tolerated and Yielded Rapid 60% Reductions in LDL Cholesterol Compared with Placebo

A total of 331 patients with heterozygous familial hypercholesterolemia were randomly assigned to 4 treatment groups: evolocumab 140 mg every 2 weeks ($n=111$), evolocumab 420 mg monthly ($n=110$), placebo every 2 weeks ($n=55$), or placebo monthly ($n=55$). Compared with placebo, evolocumab at both dosing schedules led to a significant reduction in mean LDL cholesterol at week 12 (every-2-weeks dose: 59.2% reduction, monthly dose: 61.3% reduction; both $p<0.0001$) and at the mean of weeks 10 and 12 (60.2% reduction and 65.6% reduction; both $p<0.0001$). Evolocumab was well tolerated, with rates of adverse events similar to placebo. The most common adverse events occurring more frequently in the evolocumab-treated patients were nasopharyngitis (9% vs 5%) and muscle-related adverse events (5% vs 1%). The authors concluded that in patients with heterozygous familial hypercholesterolemia, evolocumab administered either 140 mg every 2 weeks or 420 mg monthly was well tolerated and yielded rapid 60% reduc-

tions in LDL cholesterol compared with placebo (Raal FJ et al, *Lancet* 2015;385:331-340).

TESLA Part B Trial: Inhibition of PCSK9 with Evolocumab in Patients with Homozygous Familial Hypercholesterolemia on Lipid-Lowering Therapy and not on Apheresis, Significantly Reduced LDL Cholesterol Compared with Placebo

Patients ($N=49$), aged ≥ 12 years, with homozygous familial hypercholesterolemia, on stable lipid-regulating therapy for at least 4 weeks, and not receiving lipoprotein apheresis, were randomly assigned (2:1 ratio) to receive subcutaneous evolocumab 420 mg ($n=33$) or placebo ($n=16$) every 4 weeks for 12 weeks. Compared with placebo, evolocumab significantly reduced LDL cholesterol at 12 weeks by 30.9% ($p<0.0001$). Adverse events occurred in 10 (63%) of 16 patients in the placebo group and 12 (36%) of 33 in the evolocumab group. No serious clinical or laboratory adverse events occurred, and no anti-evolocumab antibody development was detected during the study. The authors concluded that in patients with homozygous familial hypercholesterolemia, evolocumab was well tolerated and significantly reduced LDL cholesterol compared with placebo (Raal FJ et al, *Lancet* 2015;385:341-350).

International Carotid Stenting Study (ICSS) Trial: Long-term Outcomes Similar After Stenting or Endarterectomy for Treatment of Symptomatic Carotid Stenosis

A total of 1710 patients with symptomatic carotid stenosis were randomly assigned to open treatment with stenting ($n=855$) or endarterectomy ($n=858$) and followed up for a median of 4.2 years. The number of fatal or disabling strokes (52 vs 49) and cumulative 5-year risk did not differ between the stenting and endarterectomy groups (6.4% vs 6.5%; hazard ratio -HR 1.06, $p=NS$). Any stroke was more frequent in the stenting group than in the endarterectomy group (119 vs 72 events ($p=0.04$), but were mainly non-disabling strokes. The authors concluded that long-term functional outcome and risk of fatal or disabling stroke are similar for stenting and endarterectomy for symptomatic carotid stenosis (Bonati LH et al, *Lancet* 2015;385:529-538).

SIMPLE Study: Routine Defibrillation Testing (DFT) at the Time of ICD Implantation is Well Tolerated, but does not Improve Shock Efficacy or Reduce Arrhythmic Death

A total of 1253 patients having an implantable cardioverter defibrillator (ICD) implantation were randomly assigned to defibrillation testing (DFT) and 1247 to no-testing, and followed up for a mean of 3.1 years. The primary outcome of arrhythmic death or failed appropriate shock occurred in fewer patients (7% per year) in the no-testing group than patients who did

receive it (8% per year; HR 0.86). The first safety composite outcome occurred in 5.6% of patients with no-testing and in 6.5% of patients with DFT ($p=NS$). The second, pre-specified safety composite outcome, which included only events most likely to be directly caused by testing, occurred in 3.2% of patients with no-testing and in 4.5% with DFT, $p=0.08$. Heart failure needing intravenous treatment with inotropes or diuretics was the most common adverse event (2% in both groups). The authors concluded that routine DFT at the time of ICD implantation is generally well tolerated, but does not improve shock efficacy or reduce arrhythmic death (Healey J et al, *Lancet* 2015;385:785-791).

Systematic Review and Meta-analysis: Extended Duration Dual Antiplatelet Therapy is not Associated with a Difference in Risk of Total, Cardiovascular (CV), or non-CV Mortality

Including the Dual Antiplatelet Therapy (DAPT) Study, which showed that continuation of dual antiplatelet therapy beyond 12 months after coronary stenting was associated with an unexpected increase in non-CV death, 14 trials were identified that randomly assigned 69,644 participants to different durations of dual antiplatelet therapy. Compared with aspirin alone or short duration dual antiplatelet therapy (≤ 6 months), continued treatment was not associated with a difference in all-cause mortality (hazard ratio -HR 1.04; $p=NS$). Similarly, CV (HR 1.01) and non-CV mortality (HR 1.04; $p=NS$) were no different with extended duration versus short duration dual antiplatelet therapy or aspirin alone. The authors concluded that extended duration dual antiplatelet therapy was not associated with a difference in the risk of all-cause, CV, or non-CV death compared with aspirin alone or short duration dual antiplatelet therapy (Elmariah S et al, *Lancet* 2015;385:792-798).

Cardiac Screening of Low-Risk Adults with Functional Stress Testing: No Evidence that it Improves Patient Outcomes, while it Confers Increased Costs and Potential Harms

Literature review indicates that cardiac screening in adults with resting or stress electrocardiography, stress echocardiography, or myocardial perfusion imaging has not been shown to improve patient outcomes. Contrariwise, it may be associated with potential harms due to false-positive results as it can lead to subsequent, potentially unnecessary tests and procedures. It is particularly inefficient in adults at low risk for coronary artery disease due to low prevalence and predictive values of testing in this population and low likelihood that positive findings will affect treatment decisions. It is preferable that clinicians focus on strategies that reduce cardiovascular risk by modifying and managing risk factors, such as smoking, diabetes, hypertension, hyperlipidemia, and obesity, while encouraging exercise and healthy diet. The authors conclude that clinicians should not

screen for cardiac disease in asymptomatic, low-risk adults with resting or stress electrocardiography, stress echocardiography, or stress myocardial perfusion imaging (Chou R et al, *Ann Intern Med* 2015;162:438-447).

Population-Based Case-Control Study: Association of Amiodarone Use and Risk of Acute Pancreatitis

According to a Taiwanese case-control study involving 4986 subjects (aged 20–84) with a first episode of acute pancreatitis and 19,944 matched subjects without acute pancreatitis, current use of amiodarone was positively associated with acute pancreatitis (odds ratio 5.21). There was no significant association between recent or past amiodarone use and acute pancreatitis. The authors concluded that patients with current use of amiodarone are at an increased risk of acute pancreatitis (Lai S et al, *Heart Rhythm* 2015;12:163-166).

Permanent His-Bundle Pacing is Feasible in Routine Clinical Practice

With use of the Select Secure (model 3830) pacing lead via a guiding catheter, His bundle pacing (HBP) was attempted in 94 consecutive patients, while 98 patients underwent right ventricular pacing (RVP). HBP was successful in 75 patients (80%) with similar fluoroscopy time, albeit higher pacing threshold compared with the RVP group (1.35 ± 0.9 V vs 0.6 ± 0.5 V at 0.5 ms; $P < 0.001$) that remained stable over a 2-year follow-up period. In patients with $>40\%$ ventricular pacing ($>60\%$ of patients), heart failure hospitalization was significantly reduced in the HBP group (2% vs 15%; $P=0.02$), with no difference in mortality (13% vs 18%; $P=NS$). The authors concluded that permanent HBP without a mapping catheter was successfully achieved in 80% of patients, displaying higher pacing threshold, but achieving better clinical outcomes (Sharma PS et al, *Heart Rhythm* 2015;12:305-312).

Implantable Devices (Defibrillators-ICDs/Pacemakers-PPMs) Exacerbate Tricuspid Regurgitation (TR) which Confers Higher Mortality Risk

Among 1,596 patients (aged 60 ± 10 years, 61% men) who had cardiac devices implanted (62% ICDs or CRT-D; 38% PPMs), the prevalence of grade 3 or 4+ TR increased from 27% to 31% by 1 month and to 35% at 4 years. Device type (ICD vs PPM) and the number of leads placed did not have an effect on post-procedural TR. Right ventricular systolic pressure did not change over time. One-year and 5-year survival was 93% and 73%, respectively. Post-procedural TR was an independent risk factor for late death ($P < 0.05$). The authors concluded that cardiac device implantation was associated with a small but significant increase in the prevalence of moderate and severe TR, both acutely and chronically after implantation, similar for both ICD and PPM placement, not related to the number of leads implanted. Postimplantation TR was

associated with a higher risk of mortality (Al-Bawardy R et al, *Pacing Clin Electrophysiol* 2015;38:259-266).

Systematic Review and Meta-Analysis: Blood Pressure Lowering Improves Survival in Type 2 Diabetes

Analysis of 40 randomized controlled trials (100,354 participants) of blood pressure (BP) lowering in diabetics indicated that each 10-mm Hg lower systolic BP was associated with a significantly lower risk of mortality (relative risk -RR, 0.87); absolute risk reduction (ARR) in events per 1000 patient-years (3.16), cardiovascular events (RR, 0.89; ARR, 3.90), coronary artery disease (RR, 0.88; ARR, 1.81), stroke (RR, 0.73; ARR, 4.06), albuminuria (RR, 0.83; ARR, 9.33), and retinopathy (RR, 0.87; ARR, 2.23). The associations between BP-lowering treatments and outcomes were not significantly different, irrespective of drug class, except for stroke and heart failure. The authors concluded that among patients with type 2 diabetes, BP lowering was associated with improved clinical outcomes with lower RRs observed among those with baseline BP of ≥ 140 mm Hg (Emdin CA et al, *JAMA* 2015;313:603-615).

Reperfusion Success is Influenced by Thrombus Burden, which May be Improved by Mesh-Covered Stents in Acute Myocardial Infarction

Among 433 patients with ST elevation myocardial infarction (STEMI) randomized to the mesh-covered MGuard stent vs a control bare-metal or drug-eluting stent, angiographically visible thrombus was identified in 383 patients (88.5%). Lesions with large thrombus were treated more frequently with manual aspiration (80.8% vs 65.8%, $p=0.0009$) and longer and larger stents. Percutaneous coronary intervention (PCI) of lesions with large thrombus burden had more thrombotic complications (30.6% vs 15.9%, $p=0.0007$) and reduced angiographic success (80.3% vs 91.1%, $p=0.003$). In lesions with large thrombus, the MGuard stent was more effective than control stents in achieving TIMI-3 flow (87.9% vs 74.5%, $p=0.02$) and tended to result in less slow flow or no reflow (8.8% vs 17.6%, $p=0.07$). The authors concluded that reperfusion success is reduced after primary PCI in lesions with large thrombus burden, an outcome that may be improved by the MGuard stent (Costa RA et al, *Am J Cardiol* 2015;115:161-166).

Obstructive Sleep Apnea (OSA) is a Predictor of Stroke in Patients With Atrial Fibrillation (AF)

Of 5,138 patients screened for obstructive sleep apnea

(OSA), 402 (7.7%) had AF and 332 (6.4%) constituted the study population, whereby the occurrence of first-time stroke was 22.9%. Ischemic stroke was more common in patients with OSA (25.4% vs 8.2%, $p=0.006$; odds ratio 3.65). Subgroup analysis showed significantly higher rates of stroke in patients with CHADS₂ scores of 0 and CHA₂DS₂-VASc scores of 0 and 1 and co-morbid OSA. The authors concluded that OSA in patients with AF is an independent predictor of stroke (Yaranov DM et al, *Am J Cardiol* 2015;115:461-465).

Important Review and Other Articles

Central sleep apnea in heart failure (Costanzo MR et al, *J Am Coll Cardiol* 2015;65:72-84), Remote ischemic preconditioning (Heusch G et al, *J Am Coll Cardiol* 2015; 65:177-195), Substrate modification for AF ablation (Kottkamp H et al, *J Am Coll Cardiol* 2015;65:196-206), Device-detected AF (Chen-Scarabelli C et al, *J Am Coll Cardiol* 2015;65:281-294), Hyponatremia in acute heart failure (Verbrugge FH et al, *J Am Coll Cardiol* 2015;65: 480-492), Sudden death in the older athlete (Chugh SS & Weiss JB, *J Am Coll Cardiol* 2015;65:493-502), Revascularization in severe LV dysfunction (Velazquez EJ & Bonow RO, *J Am Coll Cardiol* 2015;65:281-294), The myth of the "vulnerable plaque" (Arbab-Zadeh A & Fuster V, *J Am Coll Cardiol* 2015;65:846-855), Peripheral artery disease (Patel MR et al, *J Am Coll Cardiol* 2015;65:931-941), Angiotensin receptor antagonism-nepriylsin inhibitor therapy in heart failure (Braunwald E, *J Am Coll Cardiol* 2015;65:1029-1041), Dietary sodium (Farquhar WB et al, *J Am Coll Cardiol* 2015;65:1042-1050), Secondary (functional) mitral regurgitation (Asgar AW et al, *J Am Coll Cardiol* 2015;65:1231-1248), Porcelain aorta (Abramowitz Y et al, *Circulation* 2015;131:827-836), AHA statement on secondary prevention after coronary bypass (Kulik A et al, *Circulation* 2015;131:927-964), Left atrial appendage occlusion (Whitlock RP et al, *Circulation* 2015;131:756-761), Disorders of plasma sodium (Sterns RH, *N Eng J Med* 2015; 372:55-65), Carotid artery stenting (Cremonesi A et al, *Eur Heart J* 2015;36:13-21), Air pollution and cardiovascular disease (Newby DE et al, *Eur Heart J* 2015;36:83-93), Myocardial infarction with no obstructive coronary atherosclerosis (Niccoli G et al, *Eur Heart J* 2015; 36:475-481), Ularitide for treatment of acute heart failure (Anker SD et al, *Eur Heart J* 2015;36:715-723), Cryptogenic stroke and silent atrial fibrillation (Glotzer TV & Ziegler PD, *Heart Rhythm* 2015;12:234-241), Early repolarization syndrome (Mahida S et al, *Heart Rhythm* 2015;12:242-249).