

Cardiology News / Recent Literature Review / Third Quarter 2015

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

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

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

Boston AF Symposium: Orlando, 14-16/1/2016

ACC 65th Annual Session: Chicago, 2-4/4/2016

HRS 37th Annual Meeting: San Francisco, 4-7/5/16

CardioStim/Europace: Nice, 8-11/6/2016

Euro PCR: Paris, 17-20/5/2016

ESC Meeting: Rome, 27-31/8/2016

Sustained Chronic Obesity Results in Chronic Stretch, Diffuse Interstitial Fibrosis, Conduction Abnormalities, and Increased Vulnerability to AF

In an animal study, 10 chronically obese sheep, compared with 10 age-matched controls, demonstrated greater total body fat, left atrial (LA) volume, LA pressure, and pulmonary artery pressures, reduced atrial conduction velocity with increased conduction heterogeneity, increased fractionated electrograms, decreased posterior LA voltage, and increased voltage heterogeneity (all $p < 0.001$), with no change in the effective refractory period (ERP) or ERP heterogeneity. Obesity was associated with more episodes ($p = 0.02$), prolongation ($p = 0.01$), and greater cumulative duration ($p = 0.02$) of atrial fibrillation (AF). Epicardial fat infiltrated the posterior LA in the obese group ($p < 0.001$), consistent with reduced endocardial voltage in this region. Atrial fibrosis ($p = 0.03$) and atrial transforming growth factor (TGF)- $\beta 1$ protein ($p = 0.002$) were increased in the obese group. The authors concluded that obesity results in global biatrial endocardial remodeling, and increased propensity for AF (Mahajan R et al, *J Am Coll Cardiol* 2015;66:1-11).

An Increased Percentage of PVCs on 24-h Holter Monitor Confers a Decrease in LVEF, Increased Incident CHF, and Increased Mortality: PVCs might be an Important Cause of Occult or “Idiopathic” Cardiomyopathy and an Important Determinant of Incident CHF Among Those with Other Established CHF Risk Factors Among 1,139 Cardiovascular Health Study (CHS) participants, with a normal LVEF and no history of CHF, randomly assigned to 24-h Holter monitoring, those in the upper quartile vs the lowest quartile of PVC frequency had a 3-fold greater odds of a 5-year decrease in LVEF (odds ratio - OR: 3.10; $p = 0.005$),

a 48% increased risk of incident CHF (HR: 1.48; $p = 0.02$), and a 31% increased risk of death (HR: 1.31; $p = 0.01$) during a median follow-up of > 13 years. The specificity for the 15-year risk of CHF exceeded 90% when PVCs included at least 0.7% of ventricular beats. The population-level risk for incident CHF attributed to PVCs was 8.1%. The authors concluded that in a population-based sample, a higher frequency of PVCs was associated with a decrease in LVEF, an increase in incident CHF, and increased mortality (Dukes JW et al, *J Am Coll Cardiol* 2015;66:101-109).

Excessive Atrial Ectopy and Short Atrial Runs Confer an Increased Risk of Stroke Beyond Atrial Fibrillation (AF): Undiscovered Incident AF, Thrombogenic Atrial Disease or an Increased Vascular Risk Profile?

15-year data from the Copenhagen Holter Study (678 patients, ages 55-75 years, with no prior history of cardiovascular disease, stroke, or AF) showed that 99 (15%) individuals had excessive supraventricular ectopic activity (ESVEA), i.e. ≥ 30 premature atrial contractions (PACs)/h daily or any runs of ≥ 20 PACs. ESVEA was associated with ischemic stroke when censoring subjects at time of AF (hazard ratio -HR: 1.96) or when modeling AF as a time-varying exposure (HR: 2.0). Among subjects with ESVEA who developed a stroke, $\sim 14\%$ had diagnosed AF before their stroke. The incidence of stroke in subjects with ESVEA and a CHA₂DS₂-VASc score ≥ 2 was 2.4% per year, comparable to the risk observed in AF. The authors concluded that ESVEA may confer an increased risk of ischemic stroke beyond manifest AF. Stroke was more often the first clinical presentation, rather than AF (Larsen BS et al, *J Am Coll Cardiol* 2015;66:232-241).

Trends in Acute Aortic Dissection (AAD) Over 17 Years: Patients with Type A AAD have been More Often Managed Surgically with Decreasing Mortality / Endovascular Repair is Increasingly Used at Referral Centers for Patients with Complicated Type B Dissection

Over 17-years, Registry data from 4,428 patients (AAD type: A, $n = 2,952$; B, $n = 1,476$) indicated no change in the presenting complaints of severe or worst-ever pain for type A (93%) and type B AAD (94%), nor in the incidence of chest pain (83% & 71%, respectively). Use of computed tomography (CT) for diagnosis of type A increased from 46% to 73% ($p < 0.001$), and surgical management from 79% to 90% ($p < 0.001$). Endovascular management of type B increased from 7% to 31% ($p < 0.001$). Type A in-hospital mortality decreased significantly (31% to 22%; $p < 0.001$), as surgical mortality (25% to 18%; $p = 0.003$). There was no significant trend in in-hospital mortality in type B (12% & 14%) (Pape LA et al, *J Am Coll Cardiol* 2015;66:350-358).

Consensus & New Definition of Early Repolarization Jp (the Peak of an End-QRS Notch and/or the Onset of an End-QRS Slur as a Measure) should be ≥ 0.1 mV, while ST Elevation is not a Required Criterion

According to a consensus paper, *early repolarization* is present if all of the following criteria are met: 1) An **end-QRS notch or slur** on the downslope of a prominent R-wave. The notch and the onset of a slur should lie entirely above the baseline. 2) $J_p \geq 0.1$ mV in 2 or more contiguous ECG leads, excluding leads V_1 to V_3 . 3) QRS duration < 120 ms. ST-segment elevation in the absence of a slur or notch should not be reported as early repolarization. QRS duration should be measured using those leads that do not exhibit a notch or slur. Leads V_1 to V_3 have been excluded from the new definition of early repolarization to avoid confusion with the Brugada pattern, which is regarded by some as a form of early repolarization. Finally, they suggest that an upward-sloping ST-segment, followed by an upright T-wave in the presence of end-QRS notching or slurring, is benign, whereas early repolarization with a **horizontal or downward-sloping ST-segment** is potentially more serious. The authors conclude that in view of the relatively high prevalence of the early repolarization pattern without ST-segment elevation in apparently healthy subjects, *in the absence of syncope or a strong family history of juvenile SCD, the finding of early repolarization does not merit further investigation, irrespective of ST-segment slope* (Macfarlane PW et al, *J Am Coll Cardiol* 2015;66:470-477).

RITA-3 Trial: The Advantage of Reduced Mortality of a Routine Invasive vs a Selective Invasive Strategy in Non-ST-Segment Elevation Acute Coronary Syndrome Seen at 5 Years Attenuated at 10 Years

RITA-3 trial comparing outcomes of a routine early invasive strategy to those of a selective invasive strategy (for recurrent ischemia only) in patients with non-ST-segment elevation acute coronary syndrome (NSTEMACS) showed a 24% reduction of all-cause mortality of the routine invasive strategy at a median of 5 years. At 10-years, among 1,810 patients with NSTEMACS, there were no differences in mortality between the 2 groups. Risk of death varied markedly from 14.4 % in the low-risk group to 56.2% in the high-risk group. This mortality trend did not depend on the assigned treatment strategy (Henderson RA et al, *J Am Coll Cardiol* 2015;66:511-520).

PROSE-ICD: Among Patients Undergoing Primary Prevention ICD Implantation, 40% Showed an Improved LVEF During Follow-Up, and in 25%, LVEF Improved to $> 35\%$

Among 538 patients having an ICD for primary prevention of sudden cardiac death, over a mean follow-up of 4.9 years, LVEF decreased in 13%, improved in 40%,

and was unchanged in 47% of the patients. Comparing patients with an improved LVEF with those with an unchanged LVEF, the hazard ratios were 0.33 for mortality and 0.29 for appropriate shock. During follow-up, 25% of patients showed an improvement in LVEF to $> 35\%$ and their risk of appropriate shock decreased but was not eliminated (not enough to warrant deferring ICD generator replacement) (Zhang Y et al, *J Am Coll Cardiol* 2015;66:524-531).

ACTION Registry-GWTG: $\sim 1/4$ of Older Patients With AF who Undergo Coronary Stenting after Acute MI in the US are Discharged on DAPT plus an Anticoagulant (Triple Therapy) and Have Similar Rates of MACE but Significantly Greater Risk of Bleeding, Including Intracerebral Hemorrhage

Among 4,959 patients ≥ 65 years of age with acute MI and AF who underwent coronary stenting, 27.6% ($n = 1,370$) were discharged on triple therapy (dual antiplatelet therapy - DAPT plus warfarin). Relative to DAPT, patients on triple therapy had a similar risk of MACE (hazard ratio - HR: 0.99) but significantly greater risk of bleeding requiring hospitalization (HR: 1.61) and greater risk of intracranial hemorrhage (HR: 2.04) (Hess CN et al, *J Am Coll Cardiol* 2015;66:616-627).

Like Hyponatremia, Hypochloremia in Patients Hospitalized for Acute Decompensated Heart Failure (ADHF) is Independently Associated With Long-Term Mortality

Among 1,318 consecutive patients with chronic heart failure admitted for ADHF and also in an independent ADHF cohort ($n = 876$), admission serum chloride levels were independently and inversely associated with long-term mortality (hazard ratio - HR per unit change: 0.94; $p < 0.001$), and in multivariable analysis remained independently associated with mortality (HR: 0.93; $p < 0.001$) in contrast to admission sodium levels, which were no longer significant ($p > 0.05$) (Grodin JL et al, *J Am Coll Cardiol* 2015;66:659-666).

APPRAISE-2 Trial: in Patients with Acute Coronary Syndrome (ACS), no Benefit and Greater Bleeding with Apixaban Given Concomitantly with Aspirin or with the Combination of Aspirin plus Clopidogrel

A total of 7,364 high-risk ACS patients treated with aspirin ($n = 1,202$ or 16.3%) or aspirin plus clopidogrel ($n = 5,814$ or 79%) were randomized to apixaban 5 mg twice daily or placebo. No differential effect of apixaban vs placebo was observed for the composite endpoint (cardiovascular death, MI, and ischemic stroke) in patients taking aspirin (12.21 vs 13.21 per 100 patient-years; hazard ratio - HR: 0.91) or aspirin plus clopidogrel (13.22 vs 14.24; HR: 0.95). Compared with placebo, apixaban

increased major bleeding in patients taking aspirin (1.48 vs 0.25; HR: 6.62) and in patients taking aspirin plus clopidogrel (2.58 vs 1.02; HR: 2.44). Similar results were obtained and in patients treated with and without PCI. The authors concluded that post-ACS treatment with apixaban vs placebo showed no efficacy, but it increased bleeding regardless of concomitant therapy with aspirin alone or aspirin plus clopidogrel (Hess CN et al, *J Am Coll Cardiol* 2015;66:777-787).

IPAC Study: Most Women Presenting With Peripartum Cardiomyopathy (PPCM) Recover Myocardial Function Completely With Conventional Heart Failure Therapy During the First Year Post-Partum / Women With More Severe LV Dysfunction or Dilation at Presentation Have Less Chance of Full Recovery

100 women with PPCM were followed through 1 year post-partum. Among them 30% were black, 65% white, 5% other; mean age 30 ± 6 years; 88% were receiving beta-blockers and 81% angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. The LVEF at study entry was 0.35 ± 0.10 , 0.51 ± 0.11 at 6 months, and 0.53 ± 0.10 at 12 months. By 1 year, 13% had experienced major events or had persistent severe cardiomyopathy with an LVEF <0.35 , and 72% achieved an LVEF ≥ 0.50 . An initial LVEF <0.30 , an LVEDD ≥ 6 cm, black race, and presentation after 6 weeks post-partum were associated with a lower LVEF at 12 months. No subjects with both a baseline LVEF <0.30 and an LVEDD ≥ 6 cm recovered by 1 year, whereas 91% with both a baseline LVEF ≥ 0.30 and an LVEDD <6 cm recovered ($p < 0.00001$) (McNamara DM et al, *J Am Coll Cardiol* 2015;66:905-914).

CARDIO-FIT Study: Increased Cardiorespiratory Fitness is Synergistic With Weight Loss as Part of the Management Strategy for Rhythm Control in Overweight and Obese Patients With AF

Of 308 patients with atrial fibrillation (AF) and a body mass index ≥ 27 kg/m² offered risk factor management and participation in a tailored exercise program, 95 patients had low, 134 adequate, and 79 high cardio-respiratory fitness at baseline. Over 49 ± 19 months, total arrhythmia-free survival rates was 17% in the low, 76% in the adequate, and 84% in the high cardiorespiratory fitness groups ($p < 0.001$). On multivariable analysis, the low cardiorespiratory fitness (hazard ratio - HR: 5.94; $p < 0.001$) and no weight loss group (HR: 3.64) remained an independent predictor of AF recurrence. Arrhythmia-free survival with and without rhythm control strategies was greatest in patients with high cardiorespiratory fitness ($p < 0.001$). AF burden and symptom severity decreased significantly in the group with cardiorespiratory fitness gain ≥ 2 METs as compared to <2 METs group ($p < 0.001$). The authors concluded that cardiorespiratory fitness

predicts arrhythmia recurrence in obese individuals with symptomatic AF. Improvement in cardiorespiratory fitness augments the beneficial effects of weight loss (Pathak RK et al, *J Am Coll Cardiol* 2015;66:985-996).

PREVEND Study: Despite Considerable Progress in Management of Cardiovascular Disease, the Incidence of AF has not Decreased, and is Associated With Adverse Cardiovascular Outcomes, Including Heart Failure and Stroke / Obesity Has Emerged as an Additional Risk Factor for AF

Among 8,265 Dutch participants over 9.7 ± 2.3 years of follow-up, 265 participants developed AF (overall AF incidence of 3.3 per 1,000 person-years). Advancing age, male gender, antihypertensive drug use, higher body mass index, previous myocardial infarction, and previous stroke were associated with AF. AF was associated with cardiovascular events (hazard ratio - HR: 2.24; $p = 0.035$), heart failure with either reduced or preserved ejection fraction (HR: 4.52; $p < 0.001$), and all-cause mortality (HR: 3.02; $p < 0.001$) (Vermond RA et al, *J Am Coll Cardiol* 2015;66:1000-1007).

Successful Initial Experience of Transapical Mitral Valve Replacement (TMVR) With a Novel Transcatheter Mitral Valve

The first 3 patients (mean age 71 ± 9 years, 2 men; EF 25-30%) who had successful TMVR (Edwards FORTIS device) via a transapical approach in Canada, had improvement in functional status, in exercise capacity, and in quality of life. At 6-month follow-up, all 3 patients remain alive, without hospital readmission for heart failure and with NYHA functional class \leq II (Altisent OA et al, *J Am Coll Cardiol* 2015;66:1011-1019)

Percutaneous Pericardiocentesis With Continuous Drainage for 3-5 Days is a Safe and Effective Strategy for Pericardial Effusion (PE) Management in Patients With Cancer, Even in Presence of Thrombocytopenia

Of 1,645 cancer patients referred for pericardial effusion (PE), 212 (13%) underwent pericardiocentesis, which was 99% successful with no procedural deaths. Four patients had major procedure-related bleeding independently of platelet count. Patients with catheter drainage for 3-5 days had the lowest recurrence rate (10%). Median overall survival was 143 days; older age (i.e., >65 years), lung cancer, platelet count $<20,000/\mu$ l, and malignant pericardial fluid were independently associated with poor prognosis. Patients with lung cancer, but not those with breast cancer, with proven malignant effusions had a significantly shorter median 1-year survival compared with those with nonmalignant effusions (16% vs 49%, respectively; $p = 0.01$) (El Haddad D et al, *J Am Coll Cardiol* 2015;66:1119-1128).

The Age Threshold (65 Years) Used in the CHA2DS2-Vasc System for Initiating Oral Anticoagulants (OACs) May Be Lower (50 Years), at Least in Taiwanese Atrial Fibrillation (AF) Patients

Among 186,570 non-anticoagulated AF Taiwanese patients, the annual risk of ischemic stroke for males <65 years (CHA2DS2-VASc score 0; n=9,416) was 1.15% and females (score 1; n=6,390) 1.12%, and continuously increased from younger to older age groups, with an increment in stroke risk evident for patients >50 years of age. At a cutoff of 50 years, patients (both males and females) could be further stratified into 2 subgroups with different stroke risks (>50 years: 1.78%/year; vs <50 years: 0.53%/year). The authors concluded that for Taiwanese patients 50-64 years of age, the annual stroke risk was 1.78%, which may exceed the threshold for OAC use for stroke prevention, while this was only 0.53% for AF patients <50 years of age, a truly low-risk obviating the need for OACs (Chao T-F et al, *J Am Coll Cardiol* 2015;66:1339-1347).

CHANCE Trial: The Early (90-Day) Benefit of Clopidogrel and Aspirin in Decreasing Stroke Risk is Maintained at 1 Year

The CHANCE trial showed that treatment with clopidogrel and aspirin decreases the 90-day risk of stroke without increasing bleeding risk among 5170 patients randomly assigned within 24 hours after onset of minor stroke or high-risk transient ischemic attack to clopidogrel-aspirin therapy or to aspirin-alone. At 1-year, stroke occurred in 275 (10.6%) patients in the clopidogrel-aspirin group, in comparison with 362 (14%) patients in the aspirin group (hazard ratio, 0.78; $P=0.006$). Moderate or severe bleeding occurred in 7 (0.3%) patients in the clopidogrel-aspirin group and in 9 (0.4%) patients in the aspirin group ($P=NS$) (Wang Y et al, *Circulation* 2015;132:40-46).

Review & Meta-Analysis: Direct Oral Anticoagulants (DOACs) Have Equal Efficacy to Vitamin K Antagonists (VKA) in Managing Thrombotic Risks in the Elderly With Atrial Fibrillation (AF), but Different Bleeding Patterns

Review and meta-analysis of 11 randomized trials of direct oral anticoagulants (DOACs) (dabigatran, apixaban, rivaroxaban, and edoxaban) reporting data for the elderly (≥ 75 years) for efficacy and bleeding outcomes in comparison with VKA during treatment for acute venous thromboembolism or stroke prevention in AF, indicated similar or superior to VKA efficacy in managing thrombotic risks for each DOAC. A nonsignificantly higher risk of major bleeding than with VKA was observed with dabigatran 150 mg (odds ratio-OR, 1.18) but not with the 110-mg dose. There were significantly higher gastrointestinal bleeding risks with dabigatran 150 mg (OR

1.78) and dabigatran 110 mg (OR 1.40) and lower intracranial bleeding risks than VKA for dabigatran 150 mg (OR 0.43) and dabigatran 110 mg (OR 0.36). A significantly lower major bleeding risk in comparison with VKA was observed for apixaban (OR 0.63), edoxaban 60 mg (OR 0.81), and 30 mg (OR 0.46), whereas rivaroxaban showed similar risks (Sharma M et al, *Circulation* 2015;132:194-204).

Danish Cohort Study: Restarting Anticoagulant Treatment After Intracranial Hemorrhage in Patients With Atrial Fibrillation (AF) Confers Lower Risk of Recurrent Stroke & Mortality Than not Restarting

Among 1752 patients with AF on oral anticoagulant treatment with incident intracranial hemorrhage, at 1 year of follow-up, the rate of ischemic stroke/systemic embolism and all-cause mortality (per 100 person-years) for patients treated with oral anticoagulants was 13.6 (hazard ratio 0.55), in comparison with 27.3 for nontreated patients and 25.7 for patients receiving antiplatelet therapy. The rate of recurrent intracranial hemorrhage for patients treated with oral anticoagulants was 8, in comparison with 8.6 for nontreated patients and 5.3 for patients receiving antiplatelet therapy. The authors concluded that oral anticoagulant treatment was associated with a significant reduction in ischemic stroke/all-cause mortality rates, supporting oral anticoagulant treatment reintroduction after intracranial hemorrhage as feasible (Nielsen PB et al, *Circulation* 2015;132:517-525).

Fibrosis of the Papillary Muscles and Inferobasal Left Ventricular Wall May be the Arrhythmic Substrate of Mitral Valve Prolapse (MVP)

Cardiac pathology of 43 (7%) MVP patients out of 650 young (≤ 40 years) adults with sudden cardiac death (SCD) (26 females; age 19–40 years, median 32 years) showed bileaflet involvement in 70%, left ventricular fibrosis at the level of papillary muscles in all, and inferobasal wall in 88%. Among 12 cases with available ECG, 10 (83%) had inverted T waves on inferior leads, and all had right bundle-branch block (RBBB) ventricular arrhythmias (VAs). Living patients with MVP with (n=30) and without (control subjects; n=14) complex VAs underwent contrast-enhanced cardiac magnetic resonance. Patients with either RBBB type or polymorphic complex VAs (22 females; age range, 28–43 years; median, 41 years), showed a bileaflet involvement in 70% of cases. Left ventricular late enhancement was identified by contrast-enhanced cardiac magnetic resonance in 93% of patients vs 14% of control subjects ($P<0.001$). The authors concluded that fibrosis of the papillary muscles and inferobasal left ventricular wall is the structural substrate for VAs origin, and that contrast-enhanced cardiac magnetic resonance may help to identify

this concealed substrate (Basso C et al, *Circulation* 2015;132:556-566).

Extracranial Systemic Embolic Events (SEEs) Constitute 11.5% of Clinically Recognized Thromboembolic Events in Patients with AF and are Associated with High Morbidity and Mortality

A total of 221 extracranial systemic embolic events (SEEs) in 219 patients were reported among 37,973 patients in 4 randomized clinical trials of anticoagulation in AF over 91,746 patient-years of follow-up. The SEE incidence was 0.24 of 100 and stroke incidence was 1.92 of 100 patient-years. In comparison with patients with stroke, those with SEE were more often female (56% vs 47%; $P=0.01$) and had comparable mean age (73.1 ± 8.5 vs 73.5 ± 8.8 years; $P=NS$) and mean CHADS₂ scores (2.4 ± 1.3 vs 2.5 ± 1.2 ; $P=0.33$). SEEs more frequently involved the lower extremity (58%) than visceral-mesenteric (31%) or upper extremity (10%). Management comprised clinic assessment alone in 5%, hospitalization in 30%, endovascular or surgical intervention in 60%, and amputation in 5%. Within 30 days, 54% of patients recovered fully, 20% survived with deficits, and 25% died. Visceral-mesenteric SEE had higher mortality than lower- or upper-extremity SEE. The relative risk of death was 4.33 after SEE vs 6.79 after stroke (Bekwelem W et al, *Circulation* 2015;132:796-803).

REACH Registry: Severe 4-Year Impact of Diabetes Mellitus on Hospitalization for Heart Failure, Cardiovascular (CV) Events, and Death

Of the 45,227 patients in the REACH registry having 4-year follow-up, 43.6% ($n=19,699$) had diabetes (DM) at baseline. Overall risk and hazard ratio (HR) of CV death, nonfatal MI, or nonfatal stroke were greater in patients with DM (16.5% vs 13.1%; hazard ratio-HR, 1.27). There was also an increase in both CV death (8.9% vs 6%; HR, 1.38) and overall death (14.3% vs 9.9%; HR, 1.40). DM was associated with a 33% greater risk of hospitalization for heart failure (9.4% vs 5.9%; odds ratio - OR, 1.33). In diabetics, heart failure at baseline was independently associated with CV death (HR, 2.45; $P<0.001$) and hospitalization for heart failure (OR, 4.72; $P<0.001$) (Cavender MA et al, *Circulation* 2015;132:923-931).

Danish Registry: A Family History of Premature Cardiomyopathy Death is Associated With an Increase in Risk of Cardiomyopathy, Supporting Need for Screening of Relatives of Cardiomyopathy Patients

In a cohort of 3.9 million persons born from 1950 to 2008, 3890 cardiomyopathies were identified in 89 million person-years of follow-up. Premature cardiomyopathy deaths in first- and second-degree relatives were associated with 29- and 6-fold increases in the rate of

cardiomyopathy, respectively. If the first-degree relative died aged <35 years, the rate of cardiomyopathy increased 100-fold; given ≥ 2 premature deaths in first-degree relatives, the rate increased >400 -fold, while a family history of premature death from other cardiac or noncardiac conditions increased the rate of cardiomyopathy only 3-fold (Ranthe MF et al, *Circulation* 2015;132:1013-1019).

Endovascular Repair, Compared With Open Repair, of Abdominal Aortic Aneurysm (AAA) Confers an Early Survival Advantage but this Gradually Decreases Over Time, while the Rate of Late Rupture is Higher After Endovascular than After Open Repair

Among 39,966 matched pairs of patients with AAA who had undergone either open or endovascular repair, the overall perioperative mortality was 1.6% with endovascular vs 5.2% with open repair ($P<0.001$). Over time, perioperative mortality decreased by 0.8% among patients with endovascular repair ($P=0.001$) and by 0.6% in patients who underwent open repair ($P=0.01$). The rate of conversion from endovascular to open repair decreased from 2.2% in 2001 to 0.3% in 2008 ($P<0.001$). Survival was higher after endovascular vs open repair at the first 3 years of follow-up, but similar afterwards. At 8 years, interventions for the aneurysm or its complications were more common after endovascular repair, whereas interventions for complications related to laparotomy were more common after open repair. Aneurysm rupture occurred in 5.4% of patients after endovascular repair vs 1.4% of patients after open repair ($P<0.001$) (Schermerhorn ML et al, *N Engl J Med* 2015; 373:328-338).

Idarucizumab for Dabigatran Reversal

A total of 90 patients received 5 g of IV idarucizumab because of serious bleeding from dabigatran (group A, $n=51$) or because they required an urgent procedure (group B, $n=39$), and among 68 patients with an elevated dilute thrombin time and 81 with an elevated ecarin clotting time at baseline, the median maximum percentage reversal was 100%. Idarucizumab normalized the test results in 88-98% of patients within minutes. Concentrations of unbound dabigatran remained <20 ng/ml at 24 hours in 79% of patients. Among 35 patients in group A being assessed, hemostasis was restored at a median of 11.4 hours. Among 36 patients in group B who underwent a procedure, normal intraoperative hemostasis was reported in 33, and abnormal hemostasis in 3 patients. One thrombotic event occurred within 3 days after idarucizumab in a patient in whom anticoagulants had not been reinitiated. The authors concluded that idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes (Pollack CV et al, *N Engl J Med* 2015; 373:511-520).

BARI 2D Study: Abnormal Cardiac Troponin T is an Independent Predictor of Death from Cardiovascular Causes, MI, or Stroke in Diabetic Patients with Stable Ischemic Heart Disease, but does not Predict Benefit from Prompt Coronary Revascularization

Of the 2285 diabetic patients with stable ischemic heart disease, 2277 (99.6%) had detectable (≥ 3 ng per liter) high-sensitivity troponin T and 897 (39.3%) had abnormal troponin T (≥ 14 ng per liter) at baseline. The 5-year rate of the composite end point (death from cardiovascular causes, MI, or stroke) was 27.1% among patients with abnormal troponin T at baseline, as compared with 12.9% among those with normal baseline troponin T. The hazard ratio (HR) for the composite end point among patients with abnormal troponin T was 1.85 ($P < 0.001$). Among patients with abnormal troponin T, random assignment to prompt revascularization, as compared with medical therapy alone, did not result in a significant reduction in the rate of the composite end point (HR, 0.96) (Everett BM et al, *N Engl J Med* 2015; 373:610-620).

BRIDGE Trial: for Patients With AF who Require Temporary Interruption of Warfarin for an Elective Operation or Invasive Procedure, a Strategy with no Bridging was Noninferior to Perioperative Bridging with Low-Molecular-Weight Heparin for Prevention of Arterial Thromboembolism and also Decreased the Risk of Major Bleeding

After perioperative interruption of warfarin, 1884 patients were randomly assigned to receive bridging anticoagulation with low-molecular-weight heparin (100 IU/kg of dalteparin) ($n=934$) or matching placebo ($n=950$) administered subcutaneously twice daily, from 3 days before the procedure until 24 hours before the procedure and then for 5-10 days after the procedure. Warfarin was stopped 5 days before the procedure and was resumed within 24 hours later. The incidence of arterial thromboembolism at 30 days was 0.4% in the no-bridging group and 0.3% in the bridging group ($P=0.01$ for noninferiority). The incidence of major bleeding was 1.3% in the no-bridging group and 3.2% in the bridging group (relative risk, 0.41; $P=0.005$ for superiority) (Douketis JD et al, *N Engl J Med* 2015; 373:823-833).

Takotsubo Registry: Takotsubo Cardiomyopathy Represents an Acute Heart Failure Syndrome With Substantial Morbidity and Mortality and Has a Higher Prevalence of Neurologic or Psychiatric Disorders than an Acute Coronary Syndrome

Of 1750 patients with takotsubo cardiomyopathy, 89.8% were women (mean age, 66.8 years). Emotional triggers were present in 27.7% and physical triggers in 36%, while 28.5% of patients had no evident trigger. In

patients with takotsubo, as compared with an acute coronary syndrome, rates of neurologic or psychiatric disorders were higher (55.8% vs 25.7%) and the mean left ventricular ejection fraction was much lower ($40.7 \pm 11.2\%$ vs $51.5 \pm 12.3\%$) ($P < 0.001$). Rates of severe in-hospital complications including shock and death were similar in the two groups. Physical triggers, acute neurologic or psychiatric diseases, high troponin levels, and a low ejection fraction on admission were independent predictors for in-hospital complications. During long-term follow-up, the rate of major adverse cardiac and cerebrovascular events was 9.9% per patient-year, and the rate of death was 5.6% per patient-year (Templin C et al, *N Engl J Med* 2015; 373:929-938).

MATRIX Trial: in Patients With an Acute Coronary Syndrome, Rates of Major Adverse Cardiovascular Events Were not Significantly Lower with Bivalirudin than with Unfractionated Heparin, nor was the Composite of Urgent Target-Vessel Revascularization, Stent Thrombosis, or Adverse Clinical Events with a Post-PCI Bivalirudin Infusion

A total of 7213 patients with an acute coronary syndrome for whom PCI was anticipated were randomized to either bivalirudin or unfractionated heparin; patients in the bivalirudin group were then randomly assigned to receive or not a post-PCI bivalirudin infusion. The rate of major adverse cardiovascular events (death, MI, or stroke) was not significantly lower with bivalirudin (10.3%) than with heparin (10.9%) (relative risk, 0.94; $P=NS$), nor was the rate of net adverse clinical events (major bleeding or a major adverse cardiovascular event) (11.2% and 12.4%, respectively; relative risk, 0.89; $P=NS$). Post-PCI bivalirudin infusion, as compared with no infusion, did not significantly decrease the rate of urgent target-vessel revascularization, definite stent thrombosis, or net adverse clinical events (11% and 11.9%, respectively; relative risk, 0.91; $P=NS$) (Valgimigli M et al, *N Engl J Med* 2015; 373:997-1009).

CIRCUS Trial: Cyclosporin did not Attenuate Reperfusion Injury / In Patients With Anterior STEMI Referred for Primary PCI, Cyclosporine did not Result in Better Clinical Outcomes and did not Prevent Adverse Left Ventricular Remodeling at 1 Year

A total of 970 patients with an acute anterior ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) within 12 hours after symptom onset, having complete occlusion of the culprit coronary artery, were randomized to a bolus injection of cyclosporine (2.5 mg/kg) ($n=395$) or matching placebo ($n=396$) before coronary recanalization. The rate of the primary outcome, i.e. composite of death from any cause, worsening of heart failure during the

initial hospitalization, rehospitalization for heart failure, or adverse left ventricular remodeling (increase of $\geq 15\%$ in the left ventricular end-diastolic volume) at 1 year, was 59% in the cyclosporine group and 58.1% in the control group (odds ratio, 1.04; $P=NS$). Cyclosporine did not reduce the incidence of the separate clinical components of the primary outcome or other events, including recurrent infarction, unstable angina, and stroke. Safety profile was similar in the two groups (Cung T-T et al, *N Engl J Med* 2015; 373:1021-1031).

LEADLESS II Study: Satisfactory Performance of the Leadless Pacemaker

An active-fixation leadless cardiac pacemaker was successfully implanted in 504 (95.8%) of 526 patients who required permanent single-chamber ventricular pacing. The intention-to-treat primary efficacy end point (both an acceptable pacing threshold, i.e. ≤ 2.0 V at 0.4 ms, and an acceptable sensing amplitude, i.e. R wave ≥ 5 mV) through 6 months was met in 270 of the 300 patients in the primary cohort (90%, $P=0.007$), and the primary safety end point (freedom from device-related serious adverse events through 6 months) was met in 280 of the 300 patients (93.3%; $P<0.001$). At 6 months, device-related serious adverse events were observed in 6.7% of the patients; events included device dislodgement with percutaneous retrieval (in 1.7%), cardiac perforation (in 1.3%), and pacing-threshold elevation requiring percutaneous retrieval and device replacement (in 1.3%) (Reddy VY et al, *N Engl J Med* 2015; 373:1125-1135).

3SITES Study: Complications of Central Venous Catheterization / Subclavian-Vein Catheterization was Associated with a Lower Risk of Bloodstream Infection and Symptomatic Thrombosis and a Higher Risk of Pneumothorax than Jugular-Vein or Femoral-Vein Catheterization

A total of 3471 catheters were inserted in 3027 ICU patients. There were 8, 20, and 22 primary outcome events (catheter-related bloodstream infection and symptomatic deep-vein thrombosis) in the subclavian, jugular, and femoral groups, respectively (1.5, 3.6, and 4.6 per 1000 catheter-days; $P=0.02$). In pairwise comparisons, the risk of the primary outcome was significantly higher in the femoral group than in the subclavian group (hazard ratio - HR, 3.5; $P=0.003$) and in the jugular group than in the subclavian group (HR, 2.1; $P=0.04$), whereas the risk in the femoral group was similar to that in the jugular group (HR, 1.3; $P=0.30$). Pneumothorax requiring chest-tube insertion occurred in association with 13 (1.5%) of the subclavian-vein insertions and 4 (0.5%) of the jugular-vein insertions (Parienti J-J et al, *N Engl J Med* 2015; 373:1220-1229).

The Extent of Coronary Artery Calcification (CAC) Accurately Predicts 15-Year Mortality in a Large Cohort of Asymptomatic Patients

Among 9715 asymptomatic patients, the coronary artery calcification (CAC) score, over median follow-up of 14.6 years, was highly predictive of all-cause mortality ($P<0.001$). Overall 15-year mortality rates ranged from 3% to 28% for CAC scores from 0 to ≥ 1000 ($P<0.001$). The relative hazard for all-cause mortality ranged from 1.68 for a CAC score of 1-10 ($P<0.001$) to 6.26 for a score of ≥ 1000 ($P<0.001$) (Shaw LJ et al, *Ann Intern Med* 2015;163:14-21).

Meta-Analysis: PCSK9 Monoclonal Antibody Therapy Seems to be a Safe and Effective Strategy for Patients with Dyslipidemia

Meta-analysis of 24 randomized trials comprising 10,159 patients indicated that, compared with no antibody, treatment with PCSK9 antibodies led to marked reductions in LDL cholesterol levels (mean difference, -47.49% ; $P<0.001$) and other atherogenic lipid fractions, and it reduced all-cause mortality (odds ratio - OR, 0.45; $P=0.015$) and cardiovascular mortality (OR, 0.50; $P=0.084$). The rate of MI was significantly reduced with PCSK9 antibodies (OR, 0.49; $P=0.030$), and increases in the serum creatine kinase level were reduced (OR, 0.72; $P=0.026$). Serious adverse events did not increase with PCSK9 antibodies (Navarese ER et al, *Ann Intern Med* 2015;163:40-51).

Meta-Analysis: Extended Dual-Antiplatelet Therapy (DAPT) is Associated with Approximately 8 Fewer Myocardial Infarctions per 1000 Treated Patients per Year but 6 More Major Bleeding Events than Shorter-Duration DAPT

Analysis of 9 trials comprising 28,808 patients indicated that longer-duration DAPT decreased risk for myocardial infarction (risk ratio - RR, 0.73) and increased mortality (RR, 1.19). There was evidence of increased risk for major bleeding with DAPT (RR, 1.63) (Spencer FA et al, *Ann Intern Med* 2015;163:118-126).

In Patients with Mild Heart Failure (NYHA Class II), LVEF $\leq 30\%$, QRS ≥ 120 ms, CRT-D Appears to be Cost-Effective Compared to ICD Alone when a Reduction in Mortality is Expected

Use of cardiac resynchronization therapy-defibrillator (CRT-D) in patients aged ≥ 65 years with a left ventricular ejection fraction (LVEF) of $\leq 30\%$, QRS duration of ≥ 120 ms, and NYHA class I or II symptoms, increased life expectancy (9.8 years vs 8.8 years), QALYs (8.6 vs 7.6 years), and costs (\$286,500 vs \$228,600), yielding a cost per QALY gained of \$61,700. The cost-effectiveness of CRT-D was most dependent on the degree of mortality

reduction, device cost, battery life and patient's age (Woo CY et al, *Ann Intern Med* 2015;163:417-426).

North American Study of Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC): Competitive Sport was Associated with a Two-Fold Increased Risk of Ventricular Tachyarrhythmia (VTA)/Death and Earlier Presentation of Symptoms, When Compared With Inactive Patients, and to Patients who Participated in Recreational Sport

Among probands diagnosed with ARVC ($n = 108$), category of sports participation, i.e. competitive ($n = 41$), recreational ($n = 48$), and inactive ($n = 19$) determined prognosis. Competitive sport was associated with a significantly higher risk of VTA/death when compared with both recreational sport (hazard ratio - HR = 1.99, $P = 0.007$) and inactive patients (HR = 2.05, $P = 0.030$). No increased risk of VTA/death was associated with recreational sport when compared with patients who were inactive (HR = 1.03, $P = 0.930$). Symptoms developed at an earlier age in patients who participated in competitive sport (30 ± 12 years), when compared with patients who participated in recreational sport (38 ± 17 years) ($P = 0.015$) and inactive patients (41 ± 11 years) ($P = 0.002$) (Ruwald A-C et al, *Eur Heart J* 2015; 36: 1735-1743).

Rotterdam Study: Chronic Obstructive Pulmonary Disease (COPD) is Associated with an Increased Risk for Sudden Cardiac Death (SCD) / The Risk Especially Increases in Persons with Frequent Exacerbations 5 Years After the Diagnosis of COPD

Among 13,471 subjects aged ≥ 45 years with up to 24 years of follow-up, 1615 having a diagnosis of COPD, there were 551 cases of SCD. COPD was associated with an increased risk of SCD (hazard ratio - HR, 1.34). The risk particularly increased in the period 5.48 years after the diagnosis of COPD (HR 2.12) and increased further to a $>$ three-fold higher risk in COPD subjects with frequent exacerbations during this period (HR 3.58) (Lahousse L et al, *Eur Heart J* 2015;36:1754-1761).

VENTURE-AF: in Patients Undergoing Catheter Ablation (CA) for Atrial Fibrillation (AF), the Use of Uninterrupted Oral Rivaroxaban was Feasible and Event Rates Were Similar to those for Uninterrupted Vitamin K Antagonist (VKA) Therapy

A total of 248 non-valvular AF patients (mean age 59.5 years, 71% male, 74% paroxysmal AF, CHA₂DS₂-VASc score of 1.6) were randomized to uninterrupted rivaroxaban (20 mg qd) or to an uninterrupted VKA prior to CA and for 4 weeks afterwards. The average total heparin dose used intra-procedurally was slightly higher and mean ACT level attained slightly lower in rivaroxaban and VKA arms, respectively. The incidence of major

bleeding was low (0.4%; 1 major bleeding event). Thromboembolic events were also low (0.8%; 1 ischemic stroke and 1 vascular death). All events occurred in the VKA arm and all after CA (Cappato R et al, *Eur Heart J* 2015;36:1805-1811).

Review & Meta-Analysis: Digoxin is Associated with Increased Mortality in Patients Treated for Atrial Fibrillation (AF) or for Heart Failure (HF) / Negative Effects of Digoxin are Particularly Seen in the AF Population and Somewhat Less Unfavourable Effects in the HF Population

Meta-analysis of 19 reports (9 with AF patients, 7 with HF patients, and 3 with both) comprising 326,426 patients, indicated that digoxin use was associated with an increased relative risk of all-cause mortality (hazard ratio - HR 1.21, $P < 0.01$). Compared with subjects not receiving the drug, digoxin was associated with a 29% increased mortality risk (HR 1.29) in the subgroup of publications comprising 235,047 AF patients. Among 91,379 heart failure patients, digoxin-associated mortality risk increased by 14% (HR 1.14). The authors concluded that digoxin use is associated with an increased mortality risk, particularly among patients suffering from AF (Vamos M et al, *Eur Heart J* 2015; 36: 1831-1838).

PARADIGM-HF trial: Mode of Death / Treatment With Valsartan/Sacubitril or LCZ696 (Entresto), an Angiotensin Receptor-Neprilysin Inhibitor (ARNi), Compared With Enalapril in Chronic Heart Failure Patients Reduced Cardiovascular (CV) Death Primarily by Reducing Both Death Due to Worsening Heart Failure and Sudden Cardiac Death (SCD)

Over a median of 27 months, among 8399 patients with chronic heart failure, NYHA class II–IV, and left ventricular ejection fraction $\leq 40\%$, the majority of deaths were cardiovascular (CV) (80.9%), and the risk of CV death was significantly reduced by treatment with ARNi (hazard ratio - HR 0.80, $P < 0.001$). Among CV deaths, both SCD (HR 0.80, $P = 0.008$) and death due to worsening heart failure (HR 0.79, $P = 0.034$) were reduced by treatment with ARNi compared with enalapril. Deaths attributed to other CV causes, including MI and stroke, were infrequent and distributed evenly between treatment groups, as were non-CV deaths (Desai AS et al, *Eur Heart J* 2015; 36: 1990-1997).

Dutch Registry: Secundum Atrial Septal Defect (ASD) is Associated with Reduced Survival in Adult Men

In a total of 2207 adult patients (mean age 44.8 years, 33% male), 102 deaths occurred during a cumulative follow-up of 13,584 patient-years. Median survival was 79.7 years for men and 85.6 years for women with ASD. Compared with the age- and gender-matched general

population, survival was lower for male, but not for female patients ($P = 0.015$ and 0.766 , respectively). Men had a higher risk of conduction disturbances (odds ratio - OR = 1.63) supraventricular dysrhythmias (OR = 1.41), cerebrovascular thromboembolic events (OR = 1.53), and heart failure (OR = 1.91) (Kuijpers JM et al, *Eur Heart J* 2015; 36: 2079-2086).

EMPHASIS-HF Trial: Post Hoc Analysis Indicates that Eplerenone is Safe, Improves Survival, and May Prevent Re-Admission When Initiated Soon After a Hospitalization for HF or Acute Coronary Syndromes in Patients With Systolic HF and Mild Symptoms

Post hoc analysis in 2338 patients (NYHA class II / left ventricular ejection fraction $\leq 35\%$) randomized to eplerenone within 180 days of a cardiovascular hospitalization (CVH) indicated that most of the CVHs at a median of 42 days were for heart failure (HF) ($N = 1496$, 64%), acute coronary syndromes ($N = 390$, 16.7%), and arrhythmias ($N = 197$, 7.2%). The relative rate reductions in CV death/CVH, and all-cause mortality were similar whether treatment was initiated <42 or $42+$ days after qualifying CVH. Absolute rate reductions were -5.61 events per 100 patient \times years in the <42 days group and -3.58 in the $42+$ days group. The adverse effects of eplerenone were also unaffected by the time from the qualifying CVH (Girerd N et al, *Eur Heart J* 2015; 36: 2310-2317).

PADIS-PE Trial: Among Patients With Pulmonary Embolism Receiving 6 Months of Anticoagulant, Extended Treatment to 18 Months Reduced the Composite Outcome of Recurrent Venous Thrombosis and Major Bleeding Compared With Placebo, But the Benefit was Lost after Stopping Anticoagulation

Among 371 adult patients who had experienced a first episode of symptomatic pulmonary embolism and had been treated initially for 6 months with a vitamin K antagonist, in those randomized to extended therapy or not, the primary outcome (recurrent venous thromboembolism or major bleeding at 18 months) occurred in 6 of 184 patients (3.3%) in the warfarin group and in 25 of 187 (13.5%) in the placebo group (hazard ratio - HR, 0.22 ; $P = 0.001$). Recurrent venous thromboembolism occurred in 3 patients in the warfarin group and 25 patients in the placebo group (HR, 0.15); major bleeding in 4 patients in the warfarin group and in 1 patient in the placebo group (HR, 3.96). Over 42 months, the composite outcome occurred in 33 patients (20.8%) in the warfarin group and in 42 (24.0%) in the placebo group (HR, 0.75). Rates of recurrent venous thromboembolism, major bleeding, and unrelated death did not differ between groups (Couturaud F et al, *JAMA* 2015;314:31-40).

AMETHYST-DN Trial: in Patients with Hyperkalemia and Diabetic Kidney Disease, Patiromer, a Potassium-Binding Polymer, in Doses of 4.2-16.8 g bid Resulted in Significant Decreases in Serum Potassium Level After 4 Weeks of Treatment, Lasting Through 52 Weeks

In 306 outpatients with type 2 diabetes (glomerular filtration rate, 15 to <60 mL/min/ 1.73 m² and serum potassium >5.0 mEq/L), all receiving RAAS inhibitors, randomized to patiromer, the least squares mean reduction from baseline in serum potassium level at week 4 or time of first dose titration in patients with *mild* hyperkalemia was 0.35 mEq/L for the 4.2 g bid starting-dose group, 0.51 mEq/L for the 8.4 g bid starting-dose group, and 0.55 mEq/L for the 12.6 g bid starting-dose group. In those with *moderate* hyperkalemia, the reduction was 0.87 mEq/L for the 8.4 g bid starting-dose group, 0.97 mEq/L for the 12.6 g bid starting-dose group, and 0.92 mEq/L for the 16.8 g bid starting-dose group ($P < 0.001$). From week 4 through week 52, significant mean decreases in serum potassium levels were observed at each monthly point in patients with mild and moderate hyperkalemia. Adverse events comprised hypomagnesemia (7.2%), constipation (6.3%), and hypokalemia (<3.5 mEq/L) (5.6%) (Bakris GL et al, *JAMA* 2015;314:151-161).

Association Between Inadequate Blood Pressure Control and Increased Risk of Recurrent Intracerebral Hemorrhage (ICH)

Among 1145 of 2197 consecutive patients with ICH surviving at least 90 days and followed up for a median of 36.8 months, there were 102 recurrent ICH events among 505 survivors of lobar ICH and 44 recurrent ICH events among 640 survivors of nonlobar ICH. During follow-up adequate BP control was achieved on at least 1 measurement by 625 patients (54.6%) and consistently by 495 patients (43.2%). The event rate for lobar ICH was 84 per 1000 person-years among patients with inadequate BP control compared with 49 per 1000 person-years among patients with adequate BP control. For nonlobar ICH the event rate was 52 per 1000 person-years with inadequate BP control compared with 27 per 1000 person-years for patients with adequate BP control. Inadequate BP control was associated with higher risk of recurrence of both lobar ICH (hazard ratio - HR, 3.53) and nonlobar ICH (HR, 4.23). Systolic BP during follow-up was associated with increased risk of both lobar ICH recurrence (HR, 1.33 per 10-mm Hg increase) and nonlobar ICH recurrence (HR, 1.54). Diastolic BP was associated with increased risk of nonlobar ICH recurrence (HR, 1.21 per 10-mm Hg increase) but not with lobar ICH recurrence (HR, 1.36) (Biffi A et al, *JAMA* 2015;314:904-912).

Meta-Analysis for Treatment of In-Stent Restenosis (ISR)/ Two strategies should be considered: PCI with

Everolimus Eluting Stents Because of the Better Angiographic and Clinical Results than with the Other Treatment Strategies, and Drug-Coated Balloons Because of their Ability to Provide Favourable Results Without Adding a New Stent Layer

Meta-analysis of 27 trials comprising 5923 patients with in-stent restenosis indicated that PCI with everolimus-eluting stents was the most effective treatment for percent diameter stenosis, with a difference of -9% vs drug-coated balloons (DCB), -9.4% vs sirolimus-eluting stents, -10.2% vs paclitaxel-eluting stents, -19.2% vs vascular brachytherapy, -23.4% vs bare metal stents, -24.2% vs balloon angioplasty, and -31.8% vs rotablation. DCB were ranked as the second most effective treatment, but without significant differences from sirolimus-eluting (-0.2%) or paclitaxel-eluting (-1.2%) stents (Siontis GC et al, *Lancet* 2015;386 (9994):655-664).

DANAMI-3—PRIMULTI Trial: in Patients with STEMI and Multivessel Disease, Complete Revascularization Guided by FFR Measurements During the Index Admission Reduces the Risk of Future Events by Reducing Repeat Revascularizations

After successful percutaneous coronary intervention (PCI) of the infarct-related artery, patients with STEMI (n=627) were randomly allocated either no further invasive treatment (n=313) or complete fractional flow reserve (FFR)-guided revascularization (n=314) before discharge. Over a median of 27 months, events comprising the primary endpoint (all-cause mortality, non-fatal reinfarction, and ischemia-driven revascularization of lesions in non-infarct-related arteries) were recorded in 68 (22%) patients who had PCI of the infarct-related artery only and in 40 (13%) patients who had complete revascularization (hazard ratio 0.56; p=0.004) (Engström T et al, *Lancet* 2015; 386(9994):665-671).

ADVICE Study: Adenosine Testing to Identify and Target Dormant Pulmonary Vein Conduction During Catheter Ablation of Atrial Fibrillation is a Safe and Effective Strategy to Improve Arrhythmia-Free Survival in Patients With Paroxysmal Atrial Fibrillation

Adenosine unmasked dormant pulmonary vein conduction in 284 (53%) of 534 patients. 102 (69.4%) of 147 patients with additional adenosine-guided ablation were free from recurrence compared with 58 (42.3%) of 137 patients with no further ablation, corresponding to an absolute risk reduction of 27.1% (p<0.0001) and a hazard ratio of 0.44 (p<0.0001). Of 115 patients without dormant pulmonary vein conduction, 64 (55.7%) remained free from recurrences (p=0.0191). Serious adverse events were similar in each group. One death (massive stroke) was

deemed probably related to ablation in a patient included in the registry (Macle L et al, *Lancet* 2015; 386(9994): 672-679).

Important Review and Other Articles

Non-compaction of the left ventricle (Hussein A et al, *J Am Coll Cardiol* 2015;66:578-585), Duration of dual antiplatelet therapy (Montalescot G et al, *J Am Coll Cardiol* 2015;66:832-847), orthostatic hypotension (Ricci F et al, *J Am Coll Cardiol* 2015;66:848-860), Cardiac fibrosis in atrial fibrillation (Dzeshka MS et al, *J Am Coll Cardiol* 2015;66:943-959), Cardiovascular toxicities associated with kinase inhibitors employed in cancer therapies (Li W et al, *J Am Coll Cardiol* 2015;66:1160-1178), Leadless pacemakers (Miller MA et al, *J Am Coll Cardiol* 2015;66:1179-1189), Bridging anticoagulation (Rechenmacher SJ & Fang JC, *J Am Coll Cardiol* 2015;66:1392-1403), 2015 ACC/HRS/SCAI left atrial appendage occlusion device societal overview (Masoudi FA et al, *J Am Coll Cardiol* 2015;66:1497-1513), Atrial myopathy underlying atrial fibrillation (Goldberger JJ et al, *Circulation*. 2015;132:278-291), International Task Force Consensus Statement on Treatment of Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (Corrado D et al, *Circulation* 2015;132:441-453), AHA/ADA Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus (Fox CS et al, *Circulation* 2015;132:691-718), Drug therapy for heart valve diseases (Bore JS & Sharma A, *Circulation* 2015;132:1038-1045), Heparin-induced thrombocytopenia (Greinacher A, *N Engl J Med* 2015; 373:252-261), Ischemic limb gangrene with pulses (Warkentin TE, *N Engl J Med* 2015; 373:642-655), Guide for monitoring patients receiving direct oral anticoagulants for stroke prevention in atrial Fibrillation (Gladstone DJ et al, *Ann Intern Med* 2015;163:382-385), Diabetic cardiomyopathy (Seferović PM & Paulus WJ, *Eur Heart J* 2015; 36: 1718-1727), Electromagnetic interference in cardiac implants (Napp A et al, *Eur Heart J* 2015; 36: 1798-1804), Recommendations on pre-hospital and early hospital management of acute heart failure (Mebazaa A et al, *Eur Heart J* 2015; 36: 1958-1966), Impact of antidiabetic agents on cardiovascular disease (Ferrannini E et al, *Eur Heart J* 2015; 36: 2288-2296), Atrial flutter (Bun S-S et al, *Eur Heart J* 2015; 36: 2356-2363), PCSK9 inhibitors (Shimada YJ et al, *Eur Heart J* 2015; 36: 2415-2424), Treatment of atrial fibrillation (Prystowsky EN et al, *JAMA* 2015; 314:278-288), Diabetes advances in diagnosis and treatment (Natham DM, *JAMA* 2015; 314:1052-1062), Hypertension (Poulter NR et al, *Lancet* 2015; 386(9995): 801-812), Non-compaction cardiomyopathy (Towbin JA et al, *Lancet* 2015; 386(9995):813-825).