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# CARDIOLOGY NEWS

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## Cardiology News /Recent Literature Review / First Quarter 2014

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**Athens Cardiology Update 2014**: Athens (Crown Plaza Hotel), 10-12/4/2014

**HRS** Meeting: San Francisco, 7-10/5/2014

**EuroPCR**: Paris, 20-23/5/2014

**CardioStim**: Nice, 18-21/6/2014

**ESC** Congress: Barcelona, 30/8-3/9/14

**TCT:** Washington, 12-17/9/14

**HCS** Annual Meeting: Athens, 23-25/10/2014

**AHA:** Chicago, 15-19/11/14

### Cutting Inappropriate ICD Shocks: Long Arrhythmia-Detection Time Strategy Confirmed

Programming implantable cardioverter defibrillators (ICDs) to delay the time they take to treat ventricular arrhythmias cuts mortality by 23% and inappropriate shocks by more than one-half in a meta-analysis encompassing ~4900 patients. The included studies were prospective and multicenter and covered both primary and secondary prevention and patients with either ischemic or nonischemic cardiomyopathy. The risk of syncope did not rise significantly with longer detection times, despite traditional concerns that lots of patients would not tolerate prolonged arrhythmia exposure before their ICD is allowed to deliver therapy, either shocks or antitachycardia pacing (ATP). Instead, the extra time frequently gave devices a better chance to exclude non–life-threatening arrhythmias like atrial fibrillation and to let otherwise self-terminating ventricular arrhythmias play out on their own. Current nominal settings used by some ICD manufacturers are likely to be too aggressive, with arrhythmia detection times that in some cases may be as short as 1-3s. These results highlight the importance of setting longer default ICD detection times. The analysis included 4896 patients from the MADIT-RIT, ADVANCE 3, and PROVIDE randomized trials and the RELEVANT non-randomized study. Overall, 264 patients received appropriate shocks and 253 experienced inappropriate shocks at follow-up (12 - 17 months). The relative risk (RR) of death from any cause was 0.77 (p=0.02) in the prolonged-detection-time groups compared with controls; the risks of inappropriate shocks and appropriate and inappropriate ATP also fell significantly. Why there were fewer deaths with longer detection times is unclear but it may derive from less exposure to potential hazards of shocks and ATP; inappropriate shocks may up mortality, and ATP poses a small risk of inducing ventricular fibrillation; or it may be due to some other factor, e.g. avoidance of treatment for multiple ICD therapies (e.g., prescription of antiarrhythmic drugs) (Scott PA et al, ***Heart Rhythm*** 2014; DOI:10.1016/j.hrthm.2014.02.009. Epub 2014 Feb 12).

### MRI Aids in Atrial Fibrillation Ablation Success

The Delayed Enhancement-MRI Determinant of Successful Catheter Ablation of Atrial Fibrillation (DECAAF) study, which shows that magnetic resonance imaging (MRI) can be used to detect the degree of atrial fibrosis and predict ablation success, is now published. Atrial tissue fibrosis in the left atrium contributes to the progression of atrial fibrillation (AF); the more fibrosis there is, the more likely the arrhythmia will persist following ablation. Briefly, atrial fibrosis estimated by delayed-enhancement MRI in 260 AF patients, including 65% with paroxysmal AF, was a significant predictor of recurrence. Each 1% increase in fibrosis was associated with a 6% increased risk of recurrence. The extent of atrial disease was the only predictor of outcomes. When you look at MRI, you can predict the chance of patient having a recurrence, independent of the operator, experienced centers, and type of lesions. This is another major finding, that encircling the pulmonary veins with lesions as seen on the MRI was not

important in terms of treatment success. At one year, 88% of patients with stage 1 fibrosis were free of AF. For those with stage 2, 3, or 4 fibrosis, respectively, 69%, 55%, and 45% were free of recurrence at one year. At 475 days, 86%, 64%, 51%, and 35% of those with stage 1, 2, 3, and 4 fibrosis were free of AF, respectively (Marrouche et al, ***JAMA*** 2014;311:498-506).

**Distinguishing Ventricular Arrhythmia Originating from the Right Coronary Cusp, Peripulmonic Valve Area, and the Right Ventricular Outflow Tract: Utility of Lead I**

Outflow tract ventricular arrhythmias (OTVA) can be complicated to target for ablation when originating from either the periaortic or pulmonary valve (PV) region. Both sites may present with a small R wave in lead V1. However, the utility of lead I in distinguishing these arrhythmia locations is unknown. Thirty-six consecutive patients (mean age 41 ± 14 years) underwent catheter ablation for OTVA. OTVA origin was determined from intracardiac electrogram tracings and electro-anatomic maps. Observers blinded to results measured QRS waveform amplitude and duration from standard 12-lead ECG tracings. Measurements with highest diagnostic performance were modeled into an algorithm. Sites of successful ablation were anterior right ventricular outflow tract (RVOT; n = 6), posterior RVOT (n = 4), PV (n = 18), and right coronary cusp (RCC; n = 8). Highest performing surface ECG discriminators were from lead I to V1 vectors: RCC, lead I R wave ≥1.5 mV, and V1 R wave ≥2.0 mV (sensitivity 87%, specificity 93%); PV, V1 R wave >0 mV, and lead I R/(R+S) ≤0.75 (sensitivity 78%, specificity 72%); anterior RVOT, V1 R wave = 0 mV, and lead I R/(R+S) <0.4 (sensitivity 67%, specificity 97%); posterior RVOT, V1 R wave >0 mV, and lead I R/(R+S) >0.75 (sensitivity 75%, specificity 84%). Sequential algorithmic application of these criteria resulted in an overall accuracy of 72% in predicting site of OTVA origin. A relatively large R wave in lead I is seen with RCC origin but not PV origin (Ebrille et al, ***J Cardiovasc Electrophysiol,*** Epub Jan 8, 2014).

**Bacteremia Appears to Increase 30-Day Risk of Myocardial Infarction or Stroke**

Patients who had bacteremia mainly urinary tract infections, pneumonia, or sepsis when admitted to hospital were much more likely to have a myocardial infarction (MI) or stroke within 30 days, compared with healthy controls or patients hospitalized for other reasons. This study corroborates that acute infection may trigger cardiovascular events. It is the first study to demonstrate that many different bacterial infections may affect MI and stroke risk. The research suggests that bacteremia should be considered a risk factor for MI and stroke, but only for a short period of time after onset of infection, and it hints that infection with *Staphylococcus aureus* may confer a particularly high risk. Patients admitted with signs of acute infection and bacteremia/sepsis should be monitored closely for complications, and treated early with fluid therapy, oxygen, and antibiotics. Moreover, it seems prudent to increase vaccination efforts (e.g., influenza and pneumococcal vaccination), particularly in patients who already have established cardiovascular disease, since infection may trigger new cardiovascular events. Future studies are needed to clarify whether specific cardiovascular therapies (e.g., antithrombotic or anti-inflammatory drugs) may reduce the risk of cardiovascular complications in patients with bacteremia, An estimated one million Americans have an acute MI or stroke each year, and it would be useful to understand how acute infections might trigger these events, but most previous studies lacked laboratory confirmation of infection. Using population-based databases, they identified 4389 patients (mean age 73 years) in Northern Denmark who had positive blood cultures when admitted to hospital (1992-2010). The pathogens were *E. coli, S. pneumoniae, S aureus,* other bacteria, and fungi. Most patients had urinary tract infections or pneumonia, while others had central nervous system infections, endocarditis, and other infections. Based on age, gender, and date of admission, each patient was matched with ~5 patients hospitalized for other reasons and ~10 individuals in the general population. Researchers identified all incident MI and stroke events that occurred within 0-30 days, 31-180 days, and 181-365 days after the day of hospitalization. Patients with community-acquired bacteremia had a greatly increased risk of MI or stroke within 30 days. At 31-180 days, these patients had a modestly higher risk of MI or stroke compared with healthy controls, but not compared with other hospitalized patients. No differences in cardiovascular risk were seen after >6 months. Increased efforts should be made to improve suboptimal vaccination rates among patients with cardiovascular disease. Further studies would be required to assess whether antiplatelet, beta-blocker, or statin therapies might result in lower cardiovascular complications and possibly better outcomes after acute infection (Dalager-Pedersen et al, ***Circulation*** 2014; doi: 10.1161/CIRCULATIONAHA.113.006699. Epub 2014 Feb 12).

**In-hospital Switching of Oral P2Y12 Inhibitor**

In the context of the GReek AntiPlatelet REgistry (GRAPE), Alexopoulos et al assessed the prevalence, predictive factors and short-term outcome of in-hospital P2Y12 inhibitor switching in 1794 ACS patients undergoing PCI. Switching occurred in 636 (35.5%) patients of which in the form of clopidogrel to a novel agent, novel agent to clopidogrel and between prasugrel and ticagrelor in 574 (90.4%), 34 (5.3%) and 27 (4.3%) patients, respectively. Presentation to non PCI-capable hospital, bivalirudin use, age ≥75 years (inverse predictor), and regional trends emerged as predictive factors of switching to a novel agent. In-hospital switching in initially

clopidogrel treated patients was not accompanied by differences in the rate of major adverse cardiac events (MACE) or bleeding events compared with patients who started antiplatelet treatment with a novel agent since their admission. Reports with prasugrel use are in the same line of evidence. In contrast, in-hospital switching in initially clopidogrel treated patients was accompanied by a higher risk of BARC type 1, type 2 and any type bleeding and less ischemic events, when compared to patients receiving clopidogrel only. Of note, the observed difference in BARC any type bleeding was driven by BARC type 1 bleeding events. Both findings are in agreement with the described higher anti-ischemic and bleeding potential of prasugrel and ticagrelor compared to clopidogrel. Having 3 oral P2Y12 inhibitors to select for clinical use in addition to aspirin in patients with acute coronary syndromes (ACS) undergoing PCI, in-hospital switching represents a common clinical practice. Clinical factors and regional practice differences seem to affect the choice of this strategy, while in-hospital switching to a novel P2Y12 inhibitor may be associated with an increased risk of bleeding up to one month post treatment initiation (Alexopoulos et al, ***Am Heart J*** 2014;167:68-76).

**Monitor Detects AF in Cryptogenic Stroke**

An implanted cardiac monitor was much more effective at picking up atrial fibrillation (AF) than standard monitoring in patients with cryptogenic stroke in the CRYSTAL-AF trial. Because AF is one of the most important risk factors for stroke and the risk can be reduced greatly with anticoagulation therapy, such monitoring could bring about a significant reduction in recurrent stroke rates. Approximately 30% of strokes are labeled as cryptogenic, meaning no known cause. But patients with stroke of unknown etiology should not settle for this diagnosis after just 1 round of tests. Many will have AF, and finding it can prevent them from having a recurrent stroke. This idea of needing to pick up undiagnosed AF is not restricted to this 1 device, but we would say long-term cardiac monitoring is definitely coming into play, but how exactly we are going to do this is still very much open to question. We have to consider costs and logistics. If we did not have an effective treatment for AF, then this study would not be relevant, but we do have an effective treatment. Anticoagulation is the single most effective stroke prevention there is, having been shown to prevent about 70% of strokes, so the potential for benefit is huge. This is a very interesting device. There are many patients who have had a stroke, and we do a full workup and still cannot figure out why. This device picks up AF, which is a treatable cause of stroke; also, it could make a big difference. The CRYSTAL-AF trial included 441 patients who had had an unexplained stroke. All received at least 24 hours of standard cardiac monitoring within 90 days of the stroke, and half were then tracked with an insertable monitor (Reveal XT, Medtronic), which can provide data continuously for up to 3 years. The device, which is about the size of a USB stick, is inserted under the skin with a minimally invasive 15- to 30-min outpatient procedure under local anesthetic. Results showed a far greater detection of AF in the group receiving the monitor vs the control group. Among patients in the study who were found to have AF, oral anticoagulants were prescribed for 97% of cases. There were numerically fewer strokes in the device arm, but this study was not powered to show a reduction in stroke. The benefits of the insertable device far outweigh risks, noting that 2.4% of the devices had to be removed in the study because of complications, and the patients had no long-term problems. Results showed that in the control group, there were 121 ECGs, 32 24-hour Holter recordings, and 1 event recorder, but all these picked up only 4 cases of AF in 1 year in 220 patients, while 29 new cases were found in the device group. This shows how inadequate current methods of detecting AF are (International Stroke Conference - ISC 2014. Abstract LB11. Presented February 14, 2014).

**Aldosterone-Antagonist did not Reduce Mortality and Morbidity in Heart Failure (HF) Patients with Preserved Ejection Fraction.**

A randomized clinical trial in patients with HF with preserved ejection fraction (HFPEF) has its researchers and some experts hopeful that there may finally be a drug for the disorder that can improve clinical outcomes. The study was negative, all agree: patients who took the aldosterone inhibitor **spironolactone** failed to show benefit for the clinical composite primary end point. But they did have significantly fewer heart-failure hospitalizations, a part of the primary end point, over the average follow-up of 3.3 years in the trial, called Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist **(TOPCAT)**. Overall, all-cause hospitalizations and all-cause mortality did not seem to be meaningfully impacted by this drug. And we have to acknowledge that, minus the careful [creatinine and serum potassium] monitoring that occurred in the clinical trial, the prevalence of worsening renal function and hyperkalemia would likely be more common in clinical practice. When physicians use a mineralocorticoid antagonist in patients with HFPEF, they agree on the importance of good safety monitoring, especially for renal function, and look carefully for any other reason that would further corroborate the decision to give any aldosterone antagonist, like hypertension, for example. TOPCAT randomized 3445 heart-failure patients at least aged 50 with an LVEF >45% at 270 sites in 6 countries to receive the aldosterone antagonist or placebo. Spironolactone was titrated up to 30 to 45 mg/day. There were no significant differences in adverse events, except, more hyperkalemia with spironolactone and more hypokalemia on placebo; there were no hyperkalemia-related deaths (Shah et al, ***Circ Heart Fail*** 2014;7:104-115).

**Cardiac Resynchronization Therapy (CRT) in Mild Heart Failure Patients**

Patients with mild – heart failure symptoms, left ventricular dysfunction and left bundle branch block (LBBB), early intervention with CRT-D was associated with a significant long term survival benefit. The MADIT-CRT trial showed that at 7 years of follow up, the cumulative rate of death from any cause among patients with LBBB was 18% among patients randomly assigned to CRT-D, as compared with 29% among those randomly assigned to defibrillator (D) therapy alone. The survival difference corresponded to 9 patients who would need to be treated with CRT-D to save one life within 7 years. The long-term survival benefit of CRT-D in patients with LBBB did not differ significantly according to sex, cause of cardiomyopathy (ischemic or nonischemic), or QRS duration. In contrast, CRT-D was not associated with any clinical benefit and possibly with harm in patients without LBBB. The lack of survival benefit associated with CRT-D in patients without LBBB was consistent among those with a longer (≥150 ms) or a shorter QRS duration (<150 ms), and among patients with QRS morphologic findings showing RBBB or intra-ventricular conduction delay. The final study sample included the 1818 patients from MADIT-CRT for whom baseline ECG data were available (Goldenberg et al, ***N Engl J Med,*** Epub 2014 Mar 30).

**Is there a Place for Evolocumab in the Age of Statins?**

LAPLACE-2 is a study evaluating the investigational drug evolocumab. Evolocumab is a monoclonal antibody in the new PCSK9 inhibitor class. The purpose of the LAPLACE-2 study was to look at the efficacy and safety of adding evolocumab to moderate- or high-intensity statin therapy and to compare it with ezetimibe. This was a large, phase 3 trial with more than 1800 participants who were randomly assigned to receive atorvastatin 80 mg or rosuvastatin 40 mg for high-intensity statin therapy or to atorvastatin 10 mg, rosuvastatin 5 mg, or simvastatin 40 mg for moderate-intensity statin therapy. The primary finding was that the dose of statin did not matter. There was an additional 65% reduction in low-density lipoprotein cholesterol (LDL-C) when evolocumab was added to moderate- or high-intensity statin therapy, and that was in comparison with a 20%-25% reduction in LDL-C when ezetimibe was added to moderate- or high-intensity statin therapy. The other thing that was very interesting about the LAPLACE-2 study is that it reported, for the first time, achieved LDL-C levels. Those who received a moderate-intensity statin started out with a little bit lower LDL-C level than the high-intensity group, but at the end of the day, both groups achieved a fairly similar LDL-C level: 35-40 mg/dL in the high-intensity group compared with 35-45 mg/dL in the moderate-intensity group. We are achieving, for the first time, very low LDL-C levels. It is exciting to contemplate the added efficacy in terms of reducing heart attack and stroke from achieving very dramatic additional LDL reductions. LAPLACE-2 was only a 12-week study and it did not address that question, but it is basically the model for the design of the ongoing FOURIER trial which is testing whether evolocumab will further reduce heart attack and stroke events in optimally statin-treated patients. That trial will be completed circa 2018. In the meantime, we all hope that these PCSK9 inhibitors will be available to treat our patients who need additional LDL lowering -- such as people with genetic hypercholesterolemia whose LDL-C levels are still very high on a high-intensity statin, or people who are statin-intolerant and are either not able to tolerate a statin at all or can only tolerate a suboptimal statin dose. It would be very nice to have something to add to further lower their LDL-C levels in the meantime (ACC 2014 Scientific Sessions; Washington, DC; March 29-31, 2014. Session 402-10).

**Radiofrequency Ablation vs Antiarrhythmic Drugs**

The Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Therapy of Atrial Fibrillation (RAAFT 2) trial showed that radiofrequency catheter ablation with pulmonary vein isolation could be successfully performed as first-line therapy in patients with atrial fibrillation (AF). Most important, when the results are analyzed with other data, the study reinforces the conclusion that AF ablation for most patients is not a curative procedure. This trial and others make it clear that symptomatic and asymptomatic recurrences of AF are not uncommon following AF ablation and that the efficacy of this procedure, even in optimal candidates, is modest: 54.5% of patients with persistent or paroxysmal AF treated with first-line ablation therapy experienced a documented atrial tachyarrhythmia lasting more than 30 sec over the 24-month follow-up period. In comparison, 72.1% of patients treated with antiarrhythmic medication experienced an atrial tachyarrhythmia. This translated into a 44% lower risk of symptomatic or asymptomatic AF, atrial flutter, or atrial tachycardia over the 2-year period. Recurrent arrhythmias were documented by electrocardiogram, Holter, transtelephonic monitor, or rhythm strip. Regarding secondary end points in the 127-patient trial conducted at 16 centers in Europe and North America, 59% of patients treated with antiarrhythmic medication had a recurrence of symptomatic AF, atrial flutter, or atrial tachycardia at 2 years compared with 47% of patients treated with first-line catheter ablation therapy. There were no deaths or stroke in the ablation arm, but 4 cases of cardiac tamponade were documented. Quality of life was improved with both treatments. The RAAFT-2 trial results show that ablation is not without its risks. The overall complication rate in the trial was 9%, and the rate of cardiac tamponade was 6%. These rates are higher than those reported in a recent worldwide survey of AF-ablation procedures. RAAFT-2 reinforces the recommendations of the 2012 HRS/EHRA consensus statement and the 2012 ESC updated AF guidelines. Catheter ablation is class 1 recommendation (A level of evidence) in

patients with paroxysmal AF who have failed at least one antiarrhythmic drug. It is only a class 2 recommendation (B level of evidence) for paroxysmal AF patients who have not yet failed drug therapy. In clinical practice, it is uncommon to find a patient who is eager to undergo catheter ablation without at least one trial of an antiarrhythmic medication. This is especially true after a thorough discussion of the risks of the procedure, the fact that 30%-50% of patients require a repeat procedure, and consideration that the techniques and tools used for catheter ablation continue to improve. The one subgroup of patients that might benefit from immediate ablation of AF comprises those with paroxysmal AF and significant sinus-node dysfunction. The data suggest the procedure can help control AF and eliminate the need for a pacemaker in this patient subgroup (Morillo et al, ***JAMA*** 2014; 311:692-699 & ***JAMA*** 2014;311: 679-680).

**Heparin versus Bivalirudin in STEMI**

One trial at the American College of Cardiology 2014 Scientific Sessions took heat like no other: the How Effective Are Antithrombotic Therapies in Primary PCI (HEAT-PPCI) trial. The single-center randomized trial of unfractionated heparin vs bivalirudin (Angiomax, the Medicines Company) (with bailout GPIIb/IIIa inhibitors) in ST elevation myocardial infarction (STEMI) patients surprised by showing a significantly lower rate of major adverse cardiac events (MACE) in the heparin-treated patients at 28 days and no differences in bleeding complications. The trial recruited 1829 patients over a 22-month period at a single UK hospital with 14 interventional cardiologists participating in the study. In the heparin group, patients received a bolus dose of 70 units/kg preprocedure, while bivalirudin was given as a bolus of 0.75 mg/kg, followed by infusion of 1.75 mg/kg per hour for the duration of the procedure. At four weeks, the primary efficacy end point (MACE, defined as all-cause mortality, cerebrovascular accident, reinfarction, or unplanned target lesion revascularization [TLR]) had occurred in 8.7% of bivalirudin-treated patients and in 5.7% of heparin-treated patients, an absolute increased risk of 3%. Definite or probable stent thrombosis was 3.4% in the bivalirudin group and 0.9% in the heparin group. Minor bleeds, as well as major/minor bleeds, were no different between groups. Bailout glycoprotein-GP IIb/IIIa-inhibitor use was similar in both groups, at 13.5% in the bivalirudin group and 15.5% in the heparin-treated patients. In the HORIZONS trial, bivalirudin alone was compared with heparin plus routine GPIIb/IIIa-inhibitor use. EuroMAX, the only large randomized trial that studied bivalirudin vs heparin (low-molecular-weight or unfractionated) with bailout GPIIb/IIIa-inhibitor use in both arms, also showed an increase in stent thrombosis in the bivalirudin group, although bleeding risk was lower. In REPLACE 2, bleeding was lower with bivalirudin, but the comparator arm was heparin plus GPIIb/IIIa inhibitors. In ACUITY, bleeding rates were lower for the bivalirudin-monotherapy group but were equivalent in the other two trial arms where routine GPIIb/IIIa inhibitors were used on top of either heparin/enoxaparin or bivalirudin (Shahzad A. Presented at the American College of Cardiology/i2 Annual Scientific Session. March 31, 2014. Washington, DC).

**Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis vs Surgical Aortic Valve Replacement**

A total of 795 patients with severe aortic stenosis and an increased risk of death during surgery, underwent randomization at 45 centers in the United States. In the as-treated analysis, the rate of death from any cause at 1 year was significantly lower in the TAVR (self-expanding transcatheter aortic-valve bioprosthesis) than in the surgical group (14.2% vs. 19.1%). In the TAVR group there were more vascular complications, the same strokes and fewer bleedings and renal dysfunctions compared with the surgical group. In a hierarchical testing procedure, TAVR was noninferior with respect to echocardiographic indexes of valve stenosis, functional status, and quality of life. Exploratory analyses suggested a reduction in the rate of major adverse cardiovascular and cerebrovascular events and no increase in the risk of stroke. In the TAVR group more than 20% of the patients required implantation of a permanent pacemaker vs 10% of the surgical group. In addition, more patients had paravalvular leak at 1 year (6.1% vs 0.5%). CoreValve has already indication in the USA in patients who are not candidates for operation and will ask to have indication for patients with severe aortic stenosis and an increased risk of death during surgery (Adams et al, ***N Engl J Med*** 2014; doi: 10.1056/NEJMoa1400590. Epub 2014 Mar 29).

**Renal Denervation**

SYMPLICITY HTN-3 trial was the first randomized control trial of renal denervation, where patients with therapy-resistant hypertension were randomized in a 2-to-1 fashion to renal denervation (active treatment) or to a sham procedure. Patients were blinded to whether they received renal denervation or only renal arteriography. Office systolic blood pressure tended to be lower in the renal denervation group, but this was far away from reaching statistical significance, and the 24-hour blood pressure lowering was not significant between both groups. There was no significant difference between both groups 6 months after treatment. (Bhatt et al, ***N Engl J Med*** 2014; doi: 10.1056/NEJMoa1402670. Epub 2014 Mar 29).

**Beta-Blockers vs ACE Inhibitors in Dialysis Patients**

Dr Agarwal recently published in the *Nephrology, Dialysis, and Transplant* journal that beta-blockers are better than angiotensin converting enzyme (ACE) inhibitors in patients on dialysis. This study looked at people with left ventricular hypertrophy and compared lisinopril vs atenolol, with cardiovas-

cular mortality, myocardial infarction, and stroke as endpoints. Atenolol was really working well in these individuals. The primary endpoint was regression of left ventricular hypertrophy or change in left ventricular mass index from baseline to 12 months. The trial was terminated early due to a strong signal favoring atenolol in terms of cardiovascular event rate and all-cause hospitalizations. Many patients in the lisinopril group were hospitalized, and they were hospitalized more frequently. The same was true for cardiovascular event rates. More patients in the lisinopril group had myocardial infarctions, strokes, heart failure hospitalizations, and cardiovascular-related death. Everything looked better for atenolol. There is a whole literature promulgated by the cardiologists about the fact that beta-blockers really do not do a good job on left ventricular mass regression, whereas ACE inhibitors, angiotensin receptor blockers, and even calcium channel blockers (CCBs) are better; but in the COSMOS trial, where the investigators actually randomly assigned people to ACE inhibition or beta blockade using carvedilol, the key factor was blood pressure control. It did not matter what drug you used; if the blood pressure was controlled, you actually saw left ventricular mass regression. Many people do not appreciate that beta-blockers reduce blood pressure by renin inhibition, not by their effects on the sympathetic system. They do affect the sympathetic system, but that is not the mechanism through which they reduce blood pressure. The advantage in dialysis patients is that the renin angiotensin system is almost nonexistent in most of those patients because the kidneys are pretty much not functioning. The sympathetic nervous system is playing a role, however. The ACE inhibitors are essentially worthless for blood pressure control in dialysis patients because their target is not really functional, whereas the beta-blockers are better at lowering blood pressure. Not only that, but many of these people on dialysis are prone to atrial fibrillation and other arrhythmias, and the beta-blockers have a role in controlling atrial fibrillation (Agarwal et al, ***Nephrol Dial Transplant*** 2014;29:672-681).

### Cryoballoon Ablation vs Radiofrequency Ablation of Atrial Fibrillation

Junxia Xu et al sought to undertake a meta-analysis with special emphasis on comparing the efficacy and safety between cryoballoon and radiofrequency ablations by synthesizing published clinical trials. Articles were identified by searching the MEDLINE and EMBASE databases before September 2013, by reviewing the bibliographies of eligible reports, and by consulting with experts in this field. Pulmonary vein isolation (PVI) via catheter ablation has become the recommended choice of treatment for patients with drug-refractory paroxysmal or persistent atrial fibrillation (AF). Conventionally radiofrequency current is the preferred source of energy for ablation procedures, whereas its application has been limited by disrupting tissues due to excess heating or generation of inhomogeneous lesions. An alternative energy source, cryothermal energy, has recently been developed to overcome this limitation. The most noteworthy of this study was that there was greater improvement in fluoroscopic time and total procedure duration in patients referred for cryoballoon ablation than those for radiofrequency ablation in PVI of AF. Moreover, success rate of PVI, the percentages of recurrence of AF and major complications were comparable between the two procedures. To our knowledge, this is so far the first comprehensive meta-analysis comparing cryoballoon ablation with radiofrequency ablation in terms of the efficacy and safety for electrical isolation of pulmonary veins. There were respectively 469 and 635 patients referred for cryoballoon and radiofrequency ablation procedures in PVI for the treatment of AF. Distributions of age, AF duration, left ventricular ejection fraction, previous percutaneous ablation, coronary artery disease, hypertension and diabetes were comparable between patients referred for cryoballoon and radiofrequency ablations ($P>0.05$). There were more males for radiofrequency ablation (79.2%) than cryoballoon ablation (72.0%) ($P = 0.0284$). Left atrium diameter was slightly elevated for radiofrequency ablation (42.96% vs 41.89% for cryoballoon ablation, $P = 0.0212$). By contrast, there were more patients with paroxysmal AF referred for cryoballoon ablation (87.36%) than radiofrequency ablation (71.91%) ($P = 0.0076$). Pooling the results of all qualified trials observed that cryoballoon ablation significantly reduced fluoroscopic time and total procedure time by a weighted mean of 14.13 ($P = 0.014$) minutes and 29.65 ($P = 0.006$) minutes compared with radiofrequency ablation, respectively (Xu et al, ***PLoS One*** 2014;9:e90323).

### Increased Risk for Cardiovascular Disease Early and Late After a Diagnosis of Giant-Cell Arteritis According to a Cohort Study

Involvement of large arteries is well-documented in giant-cell (or temporal) arteritis (GCA). An observational cohort study evaluated the risks for incident myocardial infarction (MI), cerebrovascular accident (CVA), and peripheral vascular disease (PVD) in 3408 patients with GCA in comparison with 17,027 age- and gender-matched control individuals without baseline cardiovascular disease (MI, CVA, or PVD). Data were taken from electronic medical records. Among the 3408 patients with GCA (73% female; mean age, 73 years), the incidence rates of MI, CVA, and PVD were 10.0, 8.0, and 4.2 events per 1000 person-years, respectively, vs 4.9, 6.3, and 2.0 events per 1000 person-years, respectively, among controls. The hazard ratios-HRs were 1.70 for the combined outcome, 2.06 for MI, 1.28 for CVA, and 2.13 for PVD. The HRs were higher in the first month after GCA diagnosis (combined HR, 4.92; HR for MI, 11.89; HR for CVA, 3.93; HR for PVD, 3.86). A major limitation was the missing information on temporal artery biopsies The authors concluded that giant-cell arteritis

is associated with increased risks for MI, CVA, and PVD (Tomasson G, et al, ***Ann Intern Med*** 2014;160:73-80).

### ADJUST-PE Study: Age-Adjusted D-Dimer Cutoff Levels Better Rules Out Pulmonary Embolism (PE)

Among 3346 patients presenting to the emergency department with clinically suspected PE, the prevalence of PE was 19%. Patients with a D-dimer value between the conventional cutoff of 500 μg/L and their age-adjusted cutoff, defined as age X 10 in patients >50 years, did not undergo computed tomography pulmonary angiography and were left untreated. Among the 2898 patients with nonhigh or unlikely probability, 817 patients (28.2%) had a D-dimer level <500 μg/L and 337 patients (11.6%) had a D-dimer between 500 μg/L and their age-adjusted cutoff. The 3-month failure rate in patients with a D-dimer level >500 μg/L but below the age-adjusted cutoff was 1 of 331 patients (0.3%). Among the 766 patients >75 years, of whom 673 had a nonhigh clinical probability, using the age-adjusted instead of the 500 μg/L cutoff increased the proportion of patients in whom PE could be excluded on the basis of D-dimer from 43 of 673 patients (6.4%) to 200 of 673 patients (29.7%), without any additional false-negative findings. The authors concluded that compared with a fixed D-dimer cutoff of 500 μg/L, the combination of pretest clinical probability assessment with age-adjusted D-dimer cutoff was associated with a larger number of patients in whom PE could be considered excluded with a low likelihood of subsequent clinical thromboembolism (Righini M, et al, ***JAMA*** 2014;311:1117-1124).

### Catheter Ablation is Superior to Drugs for Maintaining Sinus Rhythm in Patients with Persistent AF

Patients (n=146; aged 55± 9 years) with persistent AF were randomly assigned to catheter ablation (CA) or antiarrhythmic drugs (AD). After a 3-month blanking period, 69 of 98 patients (70.4%) in the CA group and 21 of 48 patients (43.7%) in the AD group were free of arrhythmia (>24h) recurrence (P=0.002); an absolute risk difference of 26.6% in favour of CA. The proportion of patients free of any recurrence (>30 s) was higher in the CA than in the AD group (60.2 vs. 29.2%; P <0.001) and cardioversion was less frequent (34.7 vs 50%; P = 0.018). The authors concluded that catheter ablation is superior to medical therapy for the maintenance of sinus rhythm in patients with persistent AF at 12-month follow-up (Mont L, et al, ***Eur Heart J*** 2014;35:501-507).

### Important Review and Other Articles

TASER devices causing cardiac arrest (Zipes DP, *Circulation* 2014;129:101-111), Assessment of aortic stenosis (Saikrishnan N et al, *Circulation* 2014;129:244-253), Thrombophilia (Cohoon KP & Heit JA, *Circulation* 2014;129:254-257), Heart disease & stroke statistics 2014 (Go AS et al, *Circulation. 2014;129:399-410*), Risk stratification for sudden cardiac death (Goldberger JJ et al, *Circulation* 2014;129:516-526), Nonsteroidal anti-inflammatory drugs and the heart (Patrono C & Baigent C, *Circulation* 2014;129: 907-916), Fibromuscular dysplasia (Olin JW et al, *Circulation* 2014;129:1048-1078), Lomitapide & Mipomersen (Rader DJ & Kastelein JJP (*Circulation* 2014;129:1022-1032), Endovascular therapy for stroke (Sun C et al, *Circulation* 2014;129: 1152-1160), Chronic hypertension in pregnancy (Seely EW & Ecker J, *Circulation* 2014;129: 1254-1261), Depression as a risk factor in acute coronary syndrome (Lichtman JH et al, *Circulation* 2014;129: 1350-1369), Atrial autonomic innervation (Linz D et al, *J Am Coll Cardiol* 2014;63:215-224), Left atri al appendage occlusion (Holmes DR et al, *J Am Coll Cardiol* 2014;63:291-298), Left atrial size & function (Hoit BD, *J Am Coll Cardiol* 2014;63:493-505), Performance measures for PCI (Nallamothu BK et al, *J Am Coll Cardiol* 2014;63:722-745), Frailty assessment (Afilalo J et al, *J Am Coll Cardiol* 2014;63:747-762), Transcatheter therapies for mitral regurgitation (O'Gara PT et al, *J Am Coll Cardiol* 2014;63:840-852), AF in cancer (Farmakis D et al, *J Am Coll Cardiol* 2014;63:945-953), Cardiac MRI (*J Am Coll Cardiol* 2014;63:1031-1045 & 1046-1047), Biomarkers and ACS (Mueller C, *Eur Heart J, 2*014;35:552-556).

## Cardiology News / Recent Literature Review / Second Quarter 2014

*Antonis S. Manolis, MD, Konstantinos Vlachos, MD, Hector Anninos, MD, Evagelismos Hospital, Athens, Greece*

**ESC** Congress: Barcelona, 30/8-3/9/14
**TCT**: Washington, 12-17/9/14
**HCS** Annual Meeting: Athens, 23-25/10/2014
**AHA**: Chicago, 15-19/11/14
**20th Annual Boston AF Symposium**: Orlando, 8-10/1/15
**HCS Working Groups Seminar**: Ioannina, 2/2015
**ACC**: San Diego, 14-16/3/15
**HRS**: Boston, 13-16/5/15
**EuroPCR**: Paris, 19-22/5/15
**Europace**: Milan, 21-24/6/15
**ESC**: London, 29/8-2/9/15

### Short QT Syndrome is Highly Lethal

A total of 62 out of 73 short QT syndrome (SQTS) patients (84% male; mean age, 26 ± 15 years; corrected QT interval, 329 ± 22 ms) were followed for 60 ± 41 months. Cardiac arrest (CA) was the most frequent presenting symptom (40% of probands). There was an age dependency in the susceptibility to arrhythmias, with a peak in the occurrence of CA in the first year of life (4%) and a second peak (1.3%) between 20 and 40 years of age; the probability of a first occurrence of CA by 40 years of age was 41%. Despite the male predominance, female patients had a similar risk profile. Familial disease was present in 44% of kindreds, but the yield of genetic screening was low (14%). A history of CA was the only predictor of recurrences at follow-up ($p < 0.0000001$). Arrhythmias occurred mainly at rest. The authors concluded that SQTS is highly lethal with CA often as the first manifestation of the disease with a peak incidence in the first year of life; survivors of CA have a high CA recurrence rate; implantation of a defibrillator is strongly recommended (Mazzanti A et al, ***J Am Coll Cardiol*** 2014;63:1300-1308).

### Inferior Vena Cava (IVC) Filters in Patients With Acute Symptomatic Venous Thromboembolism (VTE) and a Significant Bleeding Risk Lower Pulmonary Embolism Mortality but Increase Risk of Recurrence

In a prospective cohort study of patients with acute VTE identified from the RIETE (Computerized Registry of Patients With Venous Thromboembolism), the investigators assessed the association between IVC filter insertion due to significant bleeding risk and the 30-day outcomes [all-cause mortality, pulmonary embolism (PE)-related mortality, and VTE rates]. Of 40,142 patients who had acute symptomatic VTE, 371 received an IVC filter. A total of 344 patients treated with a filter were matched with 344 patients treated without a filter. There was a non-significant trend toward lower risk of all-cause death for filter insertion (6.6% vs 10.2%; $p = 0.12$). The risk adjusted PE-related mortality rate was lower for filter insertion than no insertion (1.7% vs 4.9%; $p = 0.03$). Risk-adjusted recurrent VTE rates were higher for filter insertion than for no insertion (6.1% vs 0.6%; $p < 0.001$). The authors concluded that in patients presenting with VTE and a significant bleeding risk, IVC filter insertion compared with anticoagulant therapy was associated with a lower risk of PE-related death and a higher risk of recurrent VTE (Muriel et al, ***J Am Coll Cardiol*** 2014;63:1675–1683).

### Three-Year Follow-up of CONFIRM trial: FIRM-Guided Ablation is More Effective than Conventional Ablation Alone at Preventing AF Recurrences

Source (focal impulse and rotor modulation [FIRM]) ablation (n=27) was compared with conventional ablation (pulmonary vein isolation-PVI) (n=65) of atrial fibrillation (AF). FIRM mapping revealed a median of 2 rotors or focal sources in 97.7% of patients during AF. At 3 years, patients receiving FIRM-guided ablation, compared to FIRM blinded therapy, maintained higher freedom from AF after 1.2±0.4 procedures (median 1) (77.8% vs 38.5%, $p = 0.001$) and a single procedure ($p < 0.001$) and higher freedom from all atrial arrhythmias ($p = 0.003$). The authors concluded that FIRM-guided ablation is more durable than conventional trigger-based ablation in preventing 3-year AF recurrence (Narayan et al, ***J Am Coll Cardiol*** 2014;63:1761–1768).

### Successful Catheter Ablation of Atrial Fibrillation (AF) May Last a Decade in the Majority of Patients

A prospectively identified group of 445 patients who demonstrated freedom from AF for at least 1 year postablation (single procedure in 87.9%) was followed for 66.0 ± 34.0 months. At 40.7±27.0 months postablation, 97 (21.8%) patients experienced at least 1 episode of recurrent AF. The majority of events were symptomatic. There was a steady attrition rate reaching 16.3% at 5 years and 29.8% at 10 years. In 29 patients (29.5%) recurrences were self-limited; the remainder required either medical therapy or repeat ablation. By multivariate analysis, persistent AF (hazard ratio-HR 3.08; $P < 0.0001$) and hypertension (HR 1.08; $P = 0.009$) were independent risk factors for the recurrence of AF; presence of both factors led to recurrence in 37.6% at 5 years and 68.8% at 10 years. The authors concluded that at 10 years after a successful ablation of AF, most patients continue to demonstrate freedom from AF. Hypertension and prior persistent AF predict recurrences (Steinberg et al, ***Heart Rhythm*** 2014;11:771-776).

**EMBRACE: 30-Day Event –Triggered Recorder Better Detects Atrial Fibrillation in Patients with Cryptogenic Stroke**

A total of 572 patients ≥55 years of age, without known atrial fibrillation (AF), who had had a cryptogenic ischemic stroke or transient ischemic attack (TIA) within the previous 6 months were randomly assigned to undergo ambulatory ECG monitoring with either a 30-day event-triggered recorder or a conventional 24-hour monitor. AF lasting ≥30 s was detected in 16.1% in the event recorder group vs 3.2% in the control group (P<0.001; number needed to screen, 8). AF lasting ≥2.5 min was present in 9.9% in the longer monitored group vs 2.5% in the control group (P<0.001). By 90 days, oral anticoagulant therapy had been prescribed for more patients in the event monitor group than in the control group (18.6% vs 11.1%; P=0.01). The authors concluded that among patients with a recent cryptogenic stroke or TIA ≥55 years of age, paroxysmal AF was common. Noninvasive ambulatory ECG monitoring for 30 days significantly improved the detection of AF by a factor of >5 and nearly doubled the rate of anticoagulant treatment (Gladstone et al, ***N Engl J Med*** 2014; 370:2467-2477).

**CRYSTAL AF: Insertable Loop Monitor Better Detects Atrial Fibrillation (AF) in Patients With Cryptogenic Stroke**

A total of 441 patients (≥40 years old) with cryptogenic stroke were randomized to an insertable cardiac monitor (ICM) or conventional follow-up to assess detection of AF. By 6 months, AF was detected in 8.9% of patients in the ICM group (19 patients) vs 1.4% of patients in the control group (3 patients) (hazard ratio, 6.4; P<0.001). By 12 months, AF was detected in 12.4% of patients in the ICM group (29 patients) vs 2.0% of patients in the control group (4 patients) (hazard ratio, 7.3; P<0.001). The authors concluded that ECG monitoring with an ICM was superior to conventional follow-up for detecting AF after cryptogenic stroke (Sanna et al, ***N Engl J Med*** 2014; 370:2478-2486).

**Pharmacologic Rate- and Rhythm-Control Therapies are Comparable, but Ablation is Better in Patients With Atrial Fibrillation**

A total of 200 articles (162 studies) involving 28 836 patients were reviewed comparing rate- and rhythm-control strategies. Strength of evidence (SOE) was moderate supporting comparable efficacy with regard to all-cause mortality (odds ratio-OR, 1.34), cardiac mortality (OR, 0.96), and stroke (OR, 0.99) in older patients with mild AF symptoms. For rhythm-control therapies in reducing AF recurrence, SOE was high favoring pulmonary vein isolation vs antiarrhythmic drugs (OR, 5.87) and the surgical maze procedure done during other cardiac surgery vs other cardiac surgery alone (OR, 7.94).

The authors concluded that pharmacologic rate- and rhythm-control strategies have comparable efficacy in older patients with mild AF symptoms. Pulmonary vein isolation is better than antiarrhythmic medications at reducing recurrences of AF in younger patients with paroxysmal AF and mild structural heart disease (Al-Khatib et al, ***Ann Intern Med*** 2014;160:760-773).

**Colchicine May Reduce One-Year Postablation AF Recurrence**

Among patients with paroxysmal atrial fibrillation (AF) who had a single ablation, those who then received a short course of colchicine were less likely to have AF recurrence and more likely to have higher quality of life a year later, researchers report. The mid-term results from the current study were impressive. Only 6 patients needed to be treated to avoid one AF recurrence. The generic drug colchicine – used for a long time, is approved for gout and familial Mediterranean fever, and has been studied for resistant pericarditis – "seems to be a rather simple and powerful approach to reducing subsequent effects" in people with paroxysmal AF. The study showed that colchicine "is a durable, long-lasting, preventive measure associated with isolated pulmonary vein ablation". What's really incredible is that it's a really cheap addition to a very expensive procedure. According to current consensus, the first 3 months after ablation is considered a "blanking" period – that is, any AF or atrial flutter during this time is considered "early recurrence" and is not considered as part of "AF recurrence." The researchers hypothesized that colchicine might help reduce inflammation after ablation and thus decrease AF recurrence. In fact, an earlier study did demonstrate "proof of principle". There was a significant reduction in the incidence of early AF recurrence and smaller increases in the proinflammatory biomarkers C-reactive protein (CRP) and interleukin-6 (IL-6) in patients who had received colchicine compared with those who received placebo after ablation for AF. The primary outcome in the current study was efficacy at 12 months after the blanking period. The secondary outcome was change in scores for physical and psychological health in the World Health Organization Quality of Life scale at 3 and 12 months compared with baseline. The researchers analyzed data from 206 patients with paroxysmal AF who were seen in 3 centers in Europe and randomized to undergo pulmonary vein isolation followed by 0.5-mg colchicine bid for 3 months or placebo. The patients were younger than 80 (with a mean age of 62.2), and 70% were men. They had no severe liver or kidney disease, since about 80% of the drug is metabolized in the liver and about 20% is excreted in the urine. Each patient had an average of 13.8 Holter recordings. After a median of 15 months, 32 of 103 patients (31.1%) in the colchicine group vs 51 of 103 patients (49.5%) in the control group had AF recurrence (p=0.01), a 37% reduction in relative risk. These significant differences were seen even when the blanking period

was not excluded. Most recurrences occurred within the first 6 months after ablation. CRP and IL-6 levels were strongly associated with subsequent recurrences. Diarrhea and nausea were the most frequently reported adverse events. Diarrhea was reported in 10 of 103 patients (9.7%) in the treatment group vs 2 of 103 patients (1.9%) in the control group. However, only 5 cases in the colchicine group and one case in the control group lasted more than one week. Nausea was reported by 6 patients taking colchicine (5.8%) vs 3 patients taking placebo (2.9%). Physical- and psychological-health quality-of-life scores increased in both groups, but the improvement was greater in the patients who had received colchicine. On the whole, colchicine has a potent anti-inflammatory effect, and, even more important, it is probably the only medication with anti-inflammatory action that can be used safely for a relatively long period of time in patients with cardiovascular disease, given the well-known and feared cardiovascular adverse effects of other anti-inflammatory classes, including corticosteroids and nonsteroidal anti-inflammatory drugs. Before this use of colchicine becomes part of clinical practice, funding is needed to conduct further studies to determine the optimal dose and length of treatment and to conduct a large-scale clinical trial that could lead to regulatory approval (Deftereos et al, ***Heart Rhythm*** 2014;11:620-628).

### Athlete-Specific ECG Criteria Proposed for Sports Screening

The current study, presented at the Heart Rhythm Society-HRS 2014 Scientific Sessions, suggests that the history and physical may not be that good for picking up abnormalities that could put these athletes at risk of sudden death. We need to be looking at further screening methods such as an ECG to determine what best way to prevent sudden death in these young people. In the current study, 4812 teenaged athletes were screened at US high schools from October 2010 through June 2013. All completed a questionnaire with personal and family history screening questions like those recommended by the AHA and underwent 12-lead ECG, with additional echocardiography for anyone with an abnormality in the other tests. The ESC criteria for interpreting ECGs of athletes were used for the first two-thirds of the cohort and the Seattle criteria for the latter one-third. Women made up 46% of the group; 65% were white, 10% Asian, and 6% were African American. The screening process identified "significant abnormalities requiring further evaluation" in 23 of the subjects, or about 0.5% of the cohort; they included 9 cases of Wolff-Parkinson-White syndrome, 4 anomalous coronary arteries, 3 dilated aortic roots or aneurysms, 3 long-QT syndromes, 2 of hypertrophic cardiomyopathies, one with ventricular arrhythmia, and one with short-QT syndrome. An abnormal history or physical pointed to the diagnoses in 61% of cases and an abnormal ECG in 70%. The rate of false-positive diagnoses was 50% for the initial history and physical (which improved to 32% after physician review), 4% for the ECG, and 35% for the postreview history and physical considered with the ECG. Abnormalities pointing to possibly increased sudden-death risk in the Seattle criteria include:

- T-wave inversion (defined as >1 mm in depth in ≥2 leads V2-V6, II and aVF, or I and aVL).
- Long QT interval (corrected QT-QTc >470 ms in men, >480 ms in women).
- Short QT interval (QTc <320 ms).
- ST-segment depression (>0.5 mm in ≥2 leads).
- Pathologic Q waves (>3 mm in depth or >40 ms in duration in ≥2 leads, excluding III and aVR).
- Left atrial enlargement (P-wave duration >120 ms in leads I or II with negative portion of the P wave >1 mm in depth and >40 ms in duration in lead V1).
- Right ventricular hypertrophy ($R\text{-}V_1 + S\text{-}V_5$ >10.5 mm plus right axis deviation >120°).
- Compete LBBB or any QRS >140 ms.
- Mobitz type II 2° AV block or complete heart block.
- Ventricular preexcitation (PR interval <120 ms with a delta wave and QRS >120 ms).
- Profound sinus bradycardia defined as <30 beats per minute or sinus pauses >3 s.
- Atrial tachyarrhythmias (supraventricular tachycardia or atrial fibrillation or flutter).
- PVCs (>2 per 10-sec tracing), ventricular arrhythmias (couplets, nonsustained VT).
- Type 1 Brugada pattern.

(HRS 2014 Scientific Sessions; Abstract PO01-194).

### COMPARE Trial: Performing Catheter Ablation for AF Without Warfarin Discontinuation Reduces Occurrence of Stroke and/or Minor Bleeding When Compared to Bridging With Heparin

The "COMPARE" Randomized Trial is the first randomized study showing that performing catheter ablation of AF without warfarin discontinuation reduces the occurrence of peri-procedural stroke and minor bleeding complications when compared to bridging with low molecular weight heparin (LMWH). "COMPARE" was a prospective, randomized, parallel-group, multicenter study assessing the role of continuous warfarin therapy in preventing periprocedural thromboembolic (TE) events after radiofrequency catheter ablation. Inclusion criteria were: age 18 or above, INR in the range of 2.0-3.0 in the last 3-4 weeks prior to ablation and CHADS2 score >1 or CHADS score=1. A total of 1584 patients were randomly assigned (1:1 ratio) to anticoagulation strategy of either discontinued warfarin (group I) or continuous warfarin (group II). Periprocedural symptomatic TE events occurred in 39 (4.9%) patients in group I [29 (3.7%) stroke and 10 (1.3%) TIA] and only in 2 (0.25%) patients (both stroke) in group II

(p <0.001). Compared to group I, patients in group II had significantly lower risk for periprocedural TE; the unadjusted relative risk was 0.051, with a relative risk reduction of 95% in favor of the uninterrupted warfarin. Eighty-five percent of all the TE events (35/41) occurred in the long standing-persistent (LSP) AF population. In the off warfarin population (group I), one TIA and one stroke were reported in PAF, 2 TIAs and 2 strokes in persistent AF patients while 7 TIAs and 26 strokes were reported in LSP AF patients. In group II patients, both events occurred in LSP AF patients. Both patients had subtherapeutic INR the day of the procedure (1.6 and 1.7 respectively). Both patients had a TEE that did not show thrombus and did not receive LMWH. Significant reduction in TE risk in the "on" warfarin group, as compared to the "off" warfarin, was consistently observed across 6 major subgroups- female gender, age >75 years, diabetes, coronary artery disease, and prior history of cerebrovascular accident (CVA) and or /TIA, and CHADS2 score. No statistical differences between groups were found for major bleeding. Although not statistically different, group II (on warfarin) had a relative risk reduction for major bleedings of 50% when compared to group I (off warfarin). Of great clinical interest is the fact that in case of tamponade no major differences in the patients' management were found between groups with the exception of more fluid aspirated and more protamine utilized in group II. In group II, besides protamine to reverse the effect of i.v. heparin, fresh frozen plasma was necessary to reverse the effect of warfarin. Minor bleeding complications were significantly higher in the off warfarin group. Of note is the fact that all procedures were performed under intracardiac echo (ICE) guidance. The use of ICE could help reducing bleeding complication, in addition to facilitate transseptal access, confirm ablation catheter contact and improve anatomical orientation (Di Biase et al, ***Circulation*** 2014;129:2638-2644).

## Predicting Coronary Plaque Rupture

The "napkin-ring sign", a feature seen on coronary computed-tomography angiography (CCTA) can help identify coronary plaques at risk of rupture. In Nature Reviews Cardiology, Dr Pαl Maurovich-Horvat and colleagues argue that there is a role for CCTA that goes beyond ruling out coronary stenosis. Some of the CCTA plaque features are more important than others to identify high-risk plaques and to predict adverse cardiovascular events. Low CT attenuation, positive remodeling, and the napkin-ring sign indicate a 5- to 20-fold increase in the risk of suffering acute coronary syndrome (ACS). To further improve the prognostic value of CCTA to identify high-risk plaques, however, it is necessary to combine different quantitative and qualitative plaque characteristics – for example, plaque volume and napkin-ring sign – with functional information, such as fractional flow reserve (FFR) or endothelial shear stress, or preventive therapies based on patient-specific information. Large plaque burden with high-risk features might warrant intensified statin therapy. Combining functional and morphological features could lead to a vulnerable plaque score that could help predict the likelihood of plaque rupture and sudden luminal thrombosis (Maurovich-Horvat et al, ***Nat Rev Cardiol*** 2014; DOI:10.1038/nrcardio.2014.60. Epub 2014 Apr 22).

## Prophylactic Implantable Cardioverter-Defibrillators (ICDs) Confer Improved Survival in Patients With Left Ventricular Ejection Fraction (LVEF) Between 30% and 35%

A retrospective cohort study of Medicare beneficiaries in the National Cardiovascular Data Registry ICD registry compared 3120 patients with an LVEF between 30% and 35% (816 in matched cohorts) who received an ICD during a heart failure hospitalization with similar patients with no ICD. The analysis was repeated for 4578 patients (2176 in matched cohorts) with an LVEF <30%. There were no significant differences in the baseline characteristics of the matched groups (n = 408 for both groups). Among patients with an LVEF between 30% and 35%, there were 248 deaths in the ICD Registry group, within a median follow-up of 4.4 years and 249 deaths in the control group, within a median follow-up of 2.9 years. The risk of all-cause mortality in patients with an LVEF between 30% and 35% and an ICD was significantly lower than that in matched patients without an ICD (3-year mortality rates: 51.4% vs 55.0%; hazard ratio-HR, 0.83; $P = 0.04$). Presence of an ICD also was associated with better survival in patients with an LVEF <30% (3-year mortality rates: 45% vs 57.6%; HR, 0.72; $P < 0.001$) ($P$ = NS for interaction). The authors concluded that among Medicare beneficiaries hospitalized for heart failure and with an LVEF between 30% and 35% and <30%, survival at 3 years was better in patients who received a prophylactic ICD than in comparable patients with no ICD (Al-Khatib et al, ***JAMA*** 2014;311:2209-2215).

## CRT-D Better than ICD in Older than 65 Years Old Patients

7090 propensity-matched patients older than 65 years with reduced left ventricular ejection fraction (<0.35) and prolonged QRS duration on electrocardiography (≥120 ms) were treated with CRT-D or ICD implantation. At the 3-year follow-up period, compared with ICD therapy, CRT-D was associated with lower risks for mortality (cumulative incidence, 25.7% vs 29.8%; adjusted hazard ratio-HR, 0.82), all-cause readmission (cumulative incidence, 68.6% vs 72.8%; adjusted HR, 0.86 ), cardiovascular readmission (cumulative incidence, 45.0% vs 52.4%; adjusted HR, 0.80), and heart failure readmission (cumulative incidence, 24.3% vs 29.4%, HR O.78). It was also associated with greater risks for device-related infection (cumulative incidence, 1.9% vs 1.0%). The lower risks for heart failure readmission associated with CRT-D compared with

ICD therapy were most pronounced among patients with left bundle branch block or a QRS duration at least 150 ms and in women. In older patients with reduced left ventricular ejection fraction and prolonged QRS duration, CRT-D was associated with lower risks for death and readmission than ICD therapy alone (Masoudi et al, ***Ann Intern Med*** 2014;160:603-611).

### Safe and Effective Transcathter Aortic Valve Implantation (TAVI) Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Very High Risk for Surgery

A prospective, multicenter, nonrandomized study evaluated the safety and efficacy of self-expanding TAVI in patients (n=489) with symptomatic severe aortic stenosis with prohibitive risks for surgery at 41 US sites. All-cause mortality or major stroke occurred in 26% vs expected 43% at 12 months (p <0.0001). Individual 30-day and 1-year events included all-cause mortality (8.4% and 24.3%, respectively) and major stroke (2.3% and 4.3%, respectively). Procedural events at 30 days: life-threatening bleeding (12.7%), major vascular complications (8.2%), and need for permanent pacemaker placement (21.6%). Moderate or severe paravalvular aortic regurgitation was lower 12 months after self-expanding TAVI (4.2%) than at discharge (10.7%; p = 0.004). The authors concluded that TAVI with a self-expanding bioprosthesis was safe and effective in patients with symptomatic severe aortic stenosis with a prohibitive risk for surgery (Popma et al, ***J Am Coll Cardiol*** 2014;63:1972–1981).

### Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis Superior to Surgery in Patients at Increased Surgical Risk

This study compared transcatheter aortic-valve implantation (TAVI), using a self-expanding aortic-valve bioprosthesis, with surgical aortic-valve replacement in 795 patients with severe aortic stenosis and an increased risk of death during surgery. In the as-treated analysis, the rate of death from any cause at 1 year was significantly lower in the TAVI group than in the surgical group (14.2% vs 19.1%) (P <0.001 for noninferiority; P = 0.04 for superiority). The results were similar in the intention-to-treat analysis. The authors concluded that in patients with severe aortic stenosis who are at increased surgical risk, TAVI compared to surgery was associated with a significantly higher rate of survival at 1 year (Adams et al, ***N Engl J Med*** 2014; 370:1790-1798).

### CHOICE Trial: Balloon-Expandable Superior to Self-Expandable Valves in Patients Undergoing TAVI

A total of 241 patients undergoing transcatheter aortic valve implantation (TAVI) were randomly assigned to receive a balloon-expandable valve (Edwards Sapien XT) (n=121) or a self-expandable valve (Medtronic CoreValve) (n=120). Device success was 95.9% in the balloon-expandable valve group and 77.5% in the self-expandable valve group (relative risk -RR, 1.24, $P < .001$), due to a significantly lower frequency of residual more-than-mild aortic regurgitation (4.1% vs 18.3%; RR, 0.23; $P < .001$) and a less frequent need for implanting more than 1 valve (0.8% vs 5.8%, $P = 0.03$) in the balloon-expandable valve group. Cardiovascular mortality at 30 days was comparable (4.1% vs 4.3%, RR, 0.97; $P$ = NS), as well as bleeding and vascular complications. Need for a permanent pacemaker was less frequent in the balloon-expandable valve group (17.3% vs 37.6%, $P = 0.001$). The authors concluded that among patients with high-risk aortic stenosis undergoing TAVI, the use of a balloon-expandable valve resulted in a greater rate of device success than use of a self-expandable valve (Abdel-Wahab et al, ***JAMA*** 2014;311:1503-1514).

### ARISTOTLE Trial: Major Bleeding in Patients With Atrial Fibrillation is Less in Patients Receiving Apixaban than Warfarin

The on-treatment safety population in the ARISTOTLE trial included 18,140 patients. The rate of major hemorrhage among patients in the apixaban group was 2.13% per year compared with 3.09% in the warfarin group (hazard ratio -HR 0.69; p< 0.001). The most frequent sites of major hemorrhage were gastrointestinal (31%; n= 248), intracranial (22%; n= 171), and soft tissue (10%; n= 75). Compared with warfarin, apixaban-related major extracranial bleeding led to reduced hospitalization, medical or surgical intervention, transfusion, or change in antithrombotic therapy. Fatal major hemorrhage within 30 days occurred half as often wiith apixaban than warfarin (HR 0.50; p< 0.001). Older age, prior hemorrhage, prior stroke or transient ischemic attack, diabetes, lower creatinine clearance, decreased hematocrit, aspirin therapy, and nonsteroidal anti-inflammatory drugs were independently associated with an increased risk. The authors conclude that apixaban, compared with warfarin, was associated with fewer intracranial hemorrhages, less adverse consequences following extracranial hemorrhage, and a 50% reduction in fatal hemorrhage at 30 days (Hylek et al, ***J Am Coll Cardiol*** 2014;63:2141-2147).

### MENDEL-2: Anti-PCSK9 Inhibitor Most Effective for Hypercholesterolemia

This study comprised 614 patients (18-80 years old) with fasting low-density lipoprotein cholesterol (LDL-C) >100 and <190 mg/dl and Framingham risk scores >10%, randomized (1:1:1:1:2:2) to oral placebo and subcutaneous (SC) placebo biweekly; oral placebo and SC placebo monthly; ezetimibe and SC placebo biweekly; ezetimibe and SC placebo monthly; oral placebo and evolocumab 140 mg biweekly; or oral placebo and evolocumab 420 mg monthly. Evolocumab, a human monoclonal antibody against proprotein convertase subtilisin/kexin type 9 (PCSK9), significantly reduced LDL-C from baseline,

on average, by 55% to 57% more than placebo and 38% to 40% more than ezetimibe (p <0.001 for all). Therapy-related adverse events (AEs), muscle-related AEs, and laboratory abnormalities were comparable across treatment groups. The authors concluded that evolocumab significantly reduced LDL-C compared with placebo or ezetimibe and was well tolerated in patients with hypercholesterolemia (Koren et al, ***J Am Coll Cardiol*** 2014;63:2531–2540).

**GAUSS-2: Evolocumab is Promising for High-Risk Statin-Intolerant Hypercholesterolemic Patients**

GAUSS-2 (Goal Achievement after Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects) trial was a 12-week, double-blind study comprising 307 patients, aged 62±10 years with LDL-C 193±59 mg/dl, (2:2:1:1) randomized to evolocumab 140 mg every 2 weeks (Q2W) or evolocumab 420 mg once monthly (QM) both with daily oral placebo or subcutaneous placebo Q2W or QM both with daily oral ezetimibe 10 mg. Evolocumab reduced LDL-C from baseline by 53-56%, differences of 37-39% vs ezetimibe (p <0.001). Muscle adverse events occurred in 12% with evolocumab vs 23% with ezetimibe. Treatment-related adverse events and laboratory abnormalities were comparable among treatment groups. The authors concluded that evolocumab is a promising therapy for high-risk patients with high cholesterol who are statin intolerant (Stroes et al, ***J Am Coll Cardiol*** 2014;63:2541–2548).

**DESCARTES: A Successful 52-Week Placebo-Controlled Trial of Evolocumab in Hyperlipidemia**

A total of 901 patients with hyperlipidemia were started on diet alone or diet plus atorvastatin at a dose of 10 mg daily, atorvastatin at 80 mg daily, or atorvastatin at 80 mg daily plus ezetimibe at 10 mg daily, for a run-in period of 4 to 12 weeks. Patients with an LDL cholesterol (LDL-C) level of ≥75 mg/dl were then randomly assigned in a 2:1 ratio to receive either evolocumab (420 mg) or placebo every 4 weeks. Evolocumab reduced LDL-C by 57.0±2.1% (P<0.001). Evolocumab treatment also significantly reduced levels of apolipoprotein B, non–high-density lipoprotein cholesterol, lipoprotein(a), and triglycerides. The most common adverse events were nasopharyngitis, upper respiratory tract infection, influenza, and back pain. The authors concluded that at 52 weeks, evolocumab added to diet alone, to low-dose atorvastatin, or to high-dose atorvastatin with or without ezetimibe significantly reduced LDL-C levels in patients with a range of cardiovascular risks (Blom et al, ***N Engl J Med*** 2014; 370:1809-1819).

**LEADLESS Trial: Implantation of Permanent Leadless Cardiac Pacemakers is Feasible and Safe**

This study tested the safety and performance of a novel, self-contained leadless cardiac pacemaker in 33 patients (aged 77±8 years), mostly (67%) for complete AV block in the setting of permanent atrial fibrillation (AF). The implant success rate was 97% (n=32); 5 patients (15%) required >1 devices. One patient died after developing cardiac tamponade and stroke. The overall complication-free rate was 94% (31/33). After 3 months of follow-up, the measures of pacing performance (sensing, impedance, and pacing threshold) either improved or remained stable. The authors concluded that a single-chamber leadless cardiac pacemaker is safe and feasible, representing a paradigm shift in cardiac pacing (Reddy et al, ***Circulation*** 2014**;** 129: 1466-1471).

**French Registry (FAST-MI Trial): In a Real-World Setting, in Patients With STEMI, a Pharmaco-invasive strategy (Thrombolysis With Subsequent PCI) is a Valid Alternative to Primary PCI, with Equivalent 5-Year Survival**

Although primary percutaneous coronary intervention (pPCI) is the preferred reperfusion method for ST-segment-elevation myocardial infarction (STEMI), it remains difficult to implement. Five-year mortality was assessed in 1492 patients with STEMI of whom 447 (30%) received fibrinolysis (66% prehospital; 97% with subsequent angiography, 84% with subsequent PCI), 583 (39%) had pPCI, and 462 (31%) received no reperfusion. Five-year survival was 88% for fibrinolysis, 83% for pPCI, and 59% for no reperfusion, with hazard ratios of 0.73 for fibrinolysis vs pPCI, 0.57 for prehospital fibrinolysis vs pPCI, and 0.63 for fibrinolysis vs pPCI. In propensity score-matched populations, survival rates were not significantly different for fibrinolysis and pPCI, both in the whole population (88% lysis, 85% pPCI) and in the population seen early (87% fibrinolysis, 85% pPCI beyond 90 minutes from call). The authors concluded that in a real-world setting, on a nationwide scale, a pharmaco-invasive strategy is a valid alternative to pPCI, with an equivalent 5-year survival to that of thrombolysis (Danchin et al, ***Circulation*** 2014;129:1629-1636).

**SORT OUT III study: Superiority of Sirolimus-Eluting Stent at 1 year over Zotarolimus-Eluting Stent is Lost at 5 Years**

A total of 2332 patients were randomly assigned to the zotarolimus-eluting Endeavor Sprint stent (ZES) (Medtronic, Santa Rosa, CA, USA) (n=1162) or the sirolimus-eluting Cypher Select Plus stent (SES) (Cordis, Johnson & Johnson, Warren, NJ, USA) (n=1170). At 5-year follow-up, rates of major adverse cardiac events were similar in patients treated with both types of stents (ZES 17% *vs* SES 15.6%; odds ratio-OR 1.10; p=NS). This finding contrasted with results for rates of major adverse cardiac events at 1-year follow up (zotarolimus 8% *vs* sirolimus 3.9%; OR 2.13; p<0·0001) compared with those at follow-up between 1 and 5 years (9% *vs* 11.6%; OR 0.78; p=0.071). At 1-year follow-up, definite

stent thrombosis was more frequent after implantation of the ZES (1.1%) than the SES (0.3%; OR 3.34; p=0.036), whereas the opposite finding was recorded for between 1 and 5 years' follow-up (ZES 0.1% *vs* SES 1.8%, OR 0.05; p=0.003). 30% target lesion revascularisations in the ZES group occurred between 1 and 5 years' follow-up, whereas 77% of those in the SES group occurred during this follow-up period. The authors concluded that the superiority of SES compared with ZES at 1-year follow-up was lost after 5 years (Maeng et al, ***Lancet*** 2014;383(9934):2047–2056).

### PEITHO: Fibrinolysis Prevented Hemodynamic Compromise but Increased Risk of Major Hemorrhage and Stroke in Intermediate Risk Patients for Pulmonary Embolism

Tenecteplase plus heparin was compared with placebo plus heparin in normotensive patients with intermediate-risk pulmonary embolism. Of 1006 patients who underwent randomization, 1005 were included in the intention-to-treat analysis. Death or hemodynamic compromise occurred in 13 of 506 patients (2.6%) in the tenecteplase group and 28 of 499 (5.6%) in the placebo group (odds ratio, 0.44; P=0.02). Between randomization and day 7, a total of 6 patients (1.2%) in the tenecteplase group and 9 (1.8%) in the placebo group died (P=0.42). Extracranial bleeding occurred in 32 patients (6.3%) in the tenecteplase group and 6 patients (1.2%) in the placebo group (P<0.001). Stroke occurred in 12 patients (2.4%) in the tenecteplase group and was hemorrhagic in 10 patients; 1 patient (0.2%) in the placebo group had a stroke, which was hemorrhagic (P=0.003). At 1 month, death rate was 2.4%) in the tenecteplase group and 3.2% in the placebo group (P=0.42). The authors concluded that in patients with intermediate-risk pulmonary embolism, fibrinolysis prevented hemodynamic decompensation but increased risk of major hemorrhage and stroke (Meyer et al, ***N Engl J Med*** 2014; 370:1402-1411).

### RELAX-AHF Trial: Serelaxin is Effective in Acute Heart Failure Patients with Preserved Left Ventricular Ejection Fraction

RELAX-AHF randomized 1161 acute heart failure (AHF) patients to 48-h serelaxin (30 mg/kg/day) or placebo within 16 h from arrival; drug effects were compared between preserved (≥50%) (HFpEF) and reduced (<50%, HFrEF) ejection fraction heart failure. HFpEF was present in 26% of patients. Serelaxin induced a similar dyspnea relief in HFpEF vs HFrEF patients No differences were encountered in the effect of serelaxin on short- or long-term outcome between HFpEF and HFrEF patients regarding cardiovascular death or hospitalization for heart/renal failure at 2 months, cardiovascular death and all-cause death at 3 months. Similar safety and changes in biomarkers were found in both groups. The authors concluded that in AHF patients with HFpEF compared with those with HFrEF, serelaxin was well tolerated and effective in relieving dyspnea and had a similar effect on short- and long-term outcome, including survival benefit (Filippatos et al, ***Eur Heart J*** 2014; 35: 1041–1050).

### TOPCAT: Spironolactone for Heart Failure with Preserved Ejection Fraction

A total of 3445 patients with symptomatic heart failure and a left ventricular ejection fraction of ≥45% were assigned to receive either spironolactone (15 to 45 mg daily) or placebo. At a mean follow-up of 3.3 years, the primary outcome (composite of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for the management of heart failure) occurred in 18.6% of patients in the spironolactone group and 20.4% 351 of patients in the placebo group (hazard ratio, 0.89; P=0.14). Hospitalization for heart failure had a significantly lower incidence in the spironolactone group (12% vs 14%; hazard ratio, 0.83; P=0.04). Neither total deaths nor hospitalizations for any reason were significantly reduced by spironolactone. Treatment with spironolactone was associated with increased serum creatinine levels and a doubling of the rate of hyperkalemia (18.7%, vs 9.1%) but reduced hypokalemia. With frequent monitoring, there were no significant differences in the incidence of serious adverse events, a serum creatinine level of 3 mg/dl (265 μmol/L) or higher, or dialysis. The authors concluded that in patients with heart failure and a preserved ejection fraction, treatment with spironolactone did not significantly reduce the incidence of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for heart failure (Pitt et al, ***N Engl J Med*** 2014; 370:1383-1392).

### Effective Combination Therapy With Statin and Another Agent vs Intensified Statin Monotherapy for Patients Intolerant of or Unresponsive to Statins

According to a review of 36 trials, for patients intolerant of or unresponsive to statins, low-intensity statin plus bile acid sequestrant decreased LDL cholesterol level 0-14% more than mid-intensity monotherapy among high-risk hyperlipidemic patients. Mid-intensity statin plus ezetimibe decreased LDL cholesterol level 5-15% and 3-21% more than high-intensity monotherapy among patients with atherosclerotic heart disease and diabetes, respectively. Evidence was insufficient to evaluate LDL cholesterol for fibrates, niacin, and ω-3 fatty acids, or to assess long-term clinical outcomes, adherence, and harms for all regimens. The authors concluded that clinicians could consider using lower-intensity statin combined with bile acid sequestrant or ezetimibe among high-risk patients intolerant of or unresponsive to statins; however, this strategy should be used with caution given the lack of evidence on long-term clinical benefits or harms (Gudzune et al, ***Ann Intern Med*** 2014;160:468-476).

**CORP-2: Colchicine is Effective and Safe for Treatment of Multiple Recurrences of Pericarditis**

Adult patients with multiple recurrences of pericarditis (≥2) were randomly assigned (1:1) to placebo (n=120) or colchicine (n=120) (0.5 mg bid for 6 months for those weighing >70 kg or 0.5 mg qd for weight ≤70 kg) in addition to conventional anti-inflammatory treatment with aspirin, ibuprofen, or indomethacin. The proportion of patients who had recurrent pericarditis was 21.6% in the colchicine group and 42.5% in the placebo group (relative risk 0.49; p=0·0009; number needed to treat 5). Adverse effects and discontinuation of study drug occurred in similar percentages in each group. The most common adverse events were gastrointestinal intolerance (9 patients in each group) and hepatotoxicity (3 vs 1). No serious adverse events were reported. The authors concluded that colchicine added to conventional anti-inflammatory treatment significantly reduced the rate of subsequent recurrences of pericarditis in patients with multiple recurrences (Imazio et al, ***Lancet*** 2014;383(9936):2232 – 2237).

**Important Review and Other Articles**

Obesity & cardiovascular disease (Lavie et al, *J Am Coll Cardiol* 2014;63:1345-1354), Subcutaneous defibrillator (Aziz et al, *J Am Coll Cardiol* 2014;63:1473-1479), Coronary artery calcification (Madhavan et al, *J Am Coll Cardiol* 2014;63:1703-1714), Lone AF (Wyse et al, *J Am Coll Cardiol* 2014;63:1715-1723), Severe hypercholesterolemia (Sniderman et al, *J Am Coll Cardiol* 2014;63:1935-1947), Percutaneous mitral valve repair (Feldman & Young, *J Am Coll Cardiol* 2014;63:2057-2068), Micro-RNAs in cardiovascular disease (Condorelli et al, *J Am Coll Cardiol* 2014;63:2177-2187), 2014 AHA/ACC Guideline for the management of patients with valvular heart disease (Nishimura et al, *J Am Coll Cardiol* 2014;63:2438-2488 63 & e57-e185; *Circulation* 2014;129: 2440-2492), In-stent restenosis (Alfonso et al, *J Am Coll Cardiol* 2014;63:2659-2673), Mitral regurgitation & TAVI (Nombela-Franco et al, *J Am Coll Cardiol* 2014;63:2643-2658), 2013 ACC/AHA Guidelines for treating hypercholesterolemia (Stone et al, *J Am Coll Cardiol* 2014; 63:2889–934), Bicuspid aortic valve (Michelena et al, *Circulation* 2014;129:2691-2704), heart failure with preserved ejection fraction (Komajda & Lam, *Eur Heart J* 2014; 35: 1022-1032), Complications after cardiac implantable electronic device implantations Kirkfeldt et al, *Eur Heart J* 2014; 35: 1186-1194), Risk of proarrhythmia by psychotropic medications (Fanoe et al, *Eur Heart J* 2014; 35: 1306-1315), Depression and cardiovascular disease (Hare et al, *Eur Heart J* 2014;35:1365-1372), HIV infection and cardiovascular disease (Hemkens & Bucher, *Eur Heart J* 2014;35: 1373-1381), Aortic dilatation in bicuspid aortic valve (Verma & Siu, *N Engl J Med* 2014; 370:1920-1929), Cardiovascular remodelling (Heusch et al, *Lancet* 2014; 383 (9932): 1933 – 1943).