Cardiology News / Recent Literature Review / Second Quarter 2017

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ESC Congress: Barcelona, 26-30/8/2017

HCS 2017, 28th Panhellenic Cardiology Congress: Athens, 19-21/10/2017

TCT Congress: Denver, Colorado, 29/10-2/11/2017

AHA Meeting: Anaheim, Ca, 11-15/11/2017

ACC.18 Congress: Orlando, FL, 10-12/3/2018

In CRT-Eligible Heart Failure Patients with no History of Ventricular Arrhythmias, Addition of ICD Conveys Survival Benefit in Patients with Ischemic Cardiomyopathy (CM) but not in Those with Nonischemic CM

According to an observational, multicenter, European cohort study of 5,307 consecutive patients with dilated or ischemic CM, no history of sustained ventricular arrhythmias, who underwent CRT implantation with (n=4,037) or without (n=1,270) a defibrillator, over 41.4 ± 29.0 months, patients with ischemic (not dilated) CM had better survival when receiving CRT-D compared with those who received CRT-P (hazard ratio-HR: 0.76; p=0.005). Compared with recipients of ICD, the excess mortality in patients who did not receive ICDs was related to sudden cardiac death in 8% among those with ischemic CM but in only 0.4% of those with dilated CM (Barra S et al, *J Am Coll Cardiol* 2017; 69:1669-1678).

SELECT-LV Study: In a Population of Failed Conventional CRT Patients, Cardiac Resynchronization With Endocardial LV Stimulation via a Novel Leadless Pacing Electrode was Technically Feasible and Efficacious

Among 35 patients indicated for CRT who had "failed" conventional CRT, implantation of an LV endocardial leadless pacing electrode and a subcutaneous pulse generator was successful in 97.1% (n=34). The most common indications for endocardial LV pacing were difficult CS anatomy (n=12), failure to respond to conventional CRT (n=10), and a high CS pacing threshold or phrenic nerve stimulation (n=5). The primary performance endpoint, biventricular pacing on the 12-lead ECG at 1 month, was achieved in 33 of 34 patients. A total of 28 patients (84.8%) had improvement in the clinical composite score at 6 months, and 21 (66%) demonstrated a positive echocardiographic CRT response (≥5% absolute increase in LV ejection fraction). There were no pericardial effusions, but serious procedure/device-related events occurred in 3 patients (8.6%) within 24 h, and 8 patients (22.9%) between 24 h and 1 month (Reddy VY et al, *J Am Coll Cardiol* 2017;69:2119-29).

Improvements in both Survival and Heart Failure Hospitalizations with CRT-D were Greatest in Patients with a QRSD ≥180 ms with or without LBBB

Analysis of 24,960 patients receiving CRT-D and matched to patients with ICD indicated that among those with LBBB, patients with a QRSD ≥180 ms had a greater survival benefit with CRT-D vs standard ICD (hazard ration -HR for death: 0.65) compared with those having a QRSD 120 to 149 ms (HR: 0.85) and 150 to 179 ms (HR: 0.87). CRT-D vs ICD was associated with an improvement in survival in those with non-LBBB and a QRSD≥180 ms (HR for death: 0.78), but not in those with non-LBBB and a QRSD 150 to 179 ms (HR for death: 1.06) (Sundaram V et al, *J Am Coll Cardiol* 2017;69: 2026–36).

PARTNER 2 Valve-in-Valve (VIV) Registry: Use of VIV TAVI for High-Risk Patients With Degenerated Aortic Bioprostheses Confers Relatively Low Rates of Mortality and Major Complications, Improved Hemodynamics and Functional and Quality of Life (QOL) Outcomes at 1 Year

VIV procedures were performed in 365 patients (age 78.9 ± 10.2 years, STS score 9.1 ± 4.7%) At 30 days, all-cause mortality was 2.7%, stroke 2.7%, major vascular complication 4.1%, conversion to surgery 0.6%, coronary occlusion 0.8%, and new pacemaker insertion 1.9%. One-year all-cause mortality was 12.4%. Mortality fell from the initial registry to the subsequent continued access registry, both at 30 days (8.2% vs 0.7%; p=0.0001) and at 1 year (19.7% vs 9.8%; p=0.006). At 1 year, mean gradient was 17.6 mmHg, and effective orifice area was 1.16 cm^2, with greater than mild paravalvular regurgitation of 1.9%. Left ventricular ejection fraction increased (50.6% to 54.2%), and mass index decreased (135.7 to 117.6 g/m^2), with reductions in both mitral (34.9% vs 12.7%) and tricuspid (31.8% vs 21.2%) moderate or severe regurgitation (all p<0.0001). QOL improved and 6-min walk test distance results increased (mean: 163.6 to 252.3 m; both p< 0.0001) (Webb JG et al, *J Am Coll Cardiol* 2017;69:2253-62).

Patients with Concomitant Moderate Aortic Stenosis (AS) and LV Systolic Dysfunction are at High Risk for Clinical Events

At 4 years, among 305 patients (mean age 73±11 years; 75% male; 72% with ischemic heart disease) with moderate AS (aortic valve area of 1-1.5 cm^2) and LV systolic dysfunction (ejection fraction <50%), with the majority being symptomatic at the time of index echocardiogram (NYHA class II: 42%; class III: 28%; and

class IV: 4%), the primary composite endpoint (all-cause death, AVR, and HF hospitalization) occurred in 61%. The main predictors for the primary endpoint were male sex (p=0.022), NYHA functional class III or IV (p< 0.001), and peak aortic jet velocity (p< 0.001). The rate of the composite of all-cause death or heart failure (HF) hospitalization was 48%, rate of all-cause death was 36%, and rate of HF hospitalization was 27%. Aortic valve replacement (AVR) occurred in 24% of patients (van Gils L J et al, *J Am Coll Cardiol* 2017;69:2383-92).

RIVER-PCI Trial: Ranolazine Significantly Lowered HbA_{1c} and Lessened the New Onset of DM in Patients With and Without DM / Ranolazine was More Effective at Reducing Angina Frequency at 6 Months (but not 12 Months) in Patients With Diabetes With HbA_{1c}≥7.5% and Incomplete Revascularization, Suggesting a Possible Synergy Between the Drug's Effect on Angina and Glucose Control

Among 2,604 patients with chronic angina and incomplete revascularization via PCI randomized to ranolazine vs placebo (961 or 36.9% having DM at baseline), ranolazine, compared with placebo, significantly decreased HbA_{1c} by 0.42±0.08% and 0.44 ± 0.08% from baseline to 6 and 12 months, respectively, in DM patients, and by 0.19 ± 0.02% and 0.20 ± 0.02% at 6 and 12 months, respectively, in non-DM patients. Compared with placebo, ranolazine significantly reduced angina frequency at 6 months among DM patients but not at 12 months. The reductions in angina frequency were greater among patients with baseline HbA_{1c} ≥7.5% (interaction p=0.07) (Fanaroff AC et al, *J Am Coll Cardiol* 2017;69: 2304-13).

Compared with Tricuspid Aortic Stenosis (AS), TAVI in Bicuspid AS was Associated with a Similar Prognosis, but a Lower Device Success Rate / Results were Improved with New Generation Devices

Among 561 patients with bicuspid AS and 4,546 patients with tricuspid AS, comparison of 546 propensity score matched pairs indicated that bicuspid AS had more frequent conversion to surgery (2% vs 0.2%; p=0.006) and a significantly lower device success rate (85.3% vs 91.4%; p=0.002). Within the group receiving early-generation devices, bicuspid AS had more frequent aortic root injury (4.5% vs 0%; p=0.015) when receiving the balloon-expanding device, and moderate-to-severe paravalvular leak (19.4% vs 10.5%; p=0.02) when receiving the self-expanding device. Among patients with new-generation devices, however, procedural results were comparable across different prostheses. The cumulative all-cause mortality rates at 2 years were comparable between bicuspid and tricuspid AS (17.2% vs 19.4%; p=0.28) (Yoon SH et al, *J Am Coll Cardiol* 2017;69:2579-89).

Among Patients Surviving Hospitalization With AMI Without Heart Failure (HF) or LV Systolic Dysfunction (LVSD) (EF<30%), β-Blocker Use did not Confer Lower All-Cause Mortality up to 1 Year

Among 179,810 survivors of hospitalization with AMI without HF or LVSD, 91,895 patients with STEMI and 87,915 with non–STEMI, 88,542 (96.4%) and 81,933 (93.2%) received β-blockers, respectively. For the entire cohort, there were 9,373 deaths (5.2%). Unadjusted 1-year mortality was lower for patients who received β-blockers compared with those who did not (4.9% vs 11.2%; p < 0.001). However, after weighting and adjustment, there was no significant difference in mortality between those with and without β-blocker use (p=NS). Findings were similar for STEMI (p=0.637) and non–STEMI (p=0.819) (Dondo TB et al, *J Am Coll Cardiol* 2017;69:2710-20). N.B.: LVEF cutoff for systolic dysfunction was 30%.

DANAMI-3–DEFER CMR Substudy: Deferred Stenting did not Reduce Infarct Size or the Occurrence of Microvascular Obstruction (MVO) and did not Improve Myocardial Salvage

Among 510 STEMI patients randomized to PCI with deferred vs immediate stent implantation, deferred stenting did not reduce final infarct size (p = 0.67). Similarly, deferred stenting was not associated with myocardial salvage index (p = 0.80) or presence of MVO (43% vs. 42%; p = 0.78). In a post hoc analysis, stent length was the only subgroup of 7 that had an effect on outcome. In patients with a stent length ≥24 mm, deferred stenting reduced the final infarct size (p = 0.006) (Lonborg J et al, *J Am Coll Cardiol* 2017;69: 2794-2804).

DAPT Study: Discontinuing Thienopyridine after 12 or 30 Months Increases Early MI risk, Mainly Unrelated to Stent Thrombosis

Among the 11 648 randomly assigned patients, the monthly cumulative incidence of MI was lower with continued thienopyridine vs placebo at 12-15 months (0.12% vs 0.37%, *P*<0.001, in all patients; 0.13% vs 0.27%, *P*=0.02, in patients not treated with paclitaxel-eluting stents), and higher at 30-33 months (0.30% vs 0.15%, *P*=0.013, in all patients; in patients without paclitaxel-eluting stents, 0.18% vs 0.17%, *P*=0.91). The majority of MIs in both time periods (74% and 76%) were not related to stent thrombosis (Stefanescu AC et al, *Circulation* 2017;135:1720-32).

Safety Analysis of Evolocumab in 6026 Patients Pooled Across Phase 2/3 Trials & 4465 Patients who Continued in Open Label Extension Trials for 1 Year Supports a Favorable Benefit-Risk Profile for Evolocumab

Overall adverse event (AE) rates were similar between evolocumab and control in the parent trials (51.1% vs

49.6%) and in year 1 of open label extension (OLE) trials (70% vs 66%), as were those for serious AEs. Elevations of serum transaminases, bilirubin, and creatine kinase were infrequent and similar between groups. Muscle-related AEs were similar between evolocumab and control. Neurocognitive AEs were infrequent and balanced during the double-blind parent studies. In the OLE trials, 27 patients (0.9%) in the evolocumab groups and 5 patients (0.3%) in the control groups reported neurocognitive AEs. No neutralizing antievolocumab antibodies were detected (Toth PP et al, *Circulation* 2017;135:1819-31).

OCEAN Japanese Multicenter Registry: In Addition to Reflecting the Degree of Frailty, the Clinical Frailty Scale (CFS) was a Useful Marker for Predicting Late Mortality in an Elderly TAVI Cohort of 1215 Patients

The semiquantitative Clinical Frailty Scale (CFS) grade showed significant correlation with body mass index (Spearman's $\rho=-0.077$, $P=0.007$), albumin ($\rho=-0.22$, $P<0.001$), gait speed ($\rho=-0.28$, $P<0.001$), and grip strength ($\rho=-0.26$, $P<0.001$). Cumulative 1-year mortality increased with increasing CFS stage (7.2%, 8.6%. 15.7%, 16.9%, 44.1%, $P<0.001$). In a Cox regression multivariate analysis, the CFS (per 1 category increase) was an independent predictive factor of increased late cumulative mortality risk (hazard ratio, 1.28; $P<0.001$) (Shimura T et al, *Circulation* 2017;135:2013-24.

Midwall Late Gadolinium Enhancement (LGE) Identifies a Group of Patients With Dilated Cardiomyopathy (DCM) and an LVEF ≥40% at Increased Risk of SCD and Low Risk of Nonsudden Death Who May Benefit from ICD Implantation

Of 399 DCM patients with LVEF ≥40% (145 women, median age 50 years, median LVEF 50%, 25.3% with LGE) followed for a median of 4.6 years, 18 of 101 (17.8%) patients with LGE reached the prespecified end point (SCD or aborted SCD), compared with 7 of 298 (2.3%) without (hazard ratio -HR, 9.2; $P<0.0001$). Nine patients (8.9%) with LGE compared with 6 (2%) without (HR, 4.9; $P=0.002$) died suddenly, whereas 10 patients (9.9%) with LGE compared with 1 patient (0.3%) without (HR, 34.8; $P<0.001$) had aborted SCD. After adjustment, LGE predicted the composite end point (HR, 9.3; $P<0.0001$), SCD (HR, 4.8; $P=0.003$), and aborted SCD (HR, 35.9; $P<0.001$) (Halliday BP et al, *Circulation* 2017;135:2106-15).

Drone Delivered AEDs Come to the Rescue in Out-Of-Hospital Cardiac Arrest

Drones can deliver an automatic external defibrillator (AED) to the scene of an out-of-hospital cardiac arrest for bystander use. This model was applied to 53 702 out-of-hospital cardiac arrests in Toronto. It was determined that 81 bases and 100 drones would be required to deliver an AED ahead of median 911 response times by 3 minutes. In the most urban region, the 90th percentile of the AED arrival time was reduced by 6 min and 43 sec relative to historical 911 response times in the region. In the most rural region, the 90th percentile was reduced by 10 min and 34 sec. A single coordinated drone network across all regions required 39.5% fewer bases and 30% fewer drones to achieve similar AED delivery times (Boutilier JJ et al, *Circulation* 2017;135:2454-65).

SURTAVI: TAVI Noninferior to Surgery in Patients With Severe Aortic Stenosis (AS) at Intermediate Surgical Risk, With a Different Pattern of Adverse Events Associated With Each Procedure

Among 1746 intermediate-risk (STS 4.5±1.6%) patients with severe symptomatic AS undergoing randomization, 1660 (age 80±6) underwent an attempted TAVI (self-expanding valve) or surgical procedure. At 24 months, the estimated incidence of the primary end point (death from any cause or disabling stroke) was 12.6% in the TAVI group and 14% in the surgery group. Surgery was associated with higher rates of acute kidney injury, AF, and transfusion requirements, whereas TAVI had higher rates of residual aortic regurgitation and need for pacemaker implantation. TAVI resulted in lower mean gradients and larger aortic-valve areas than surgery. Structural valve deterioration at 24 months did not occur in either group (Reardon MJ et al, *N Engl J Med* 2017; 376:1321-1331).

RE-CIRCUIT: In Patients Undergoing Ablation for Atrial Fibrillation (AF), Anticoagulation With Uninterrupted Dabigatran was Associated With Fewer Bleeding Complications than Uninterrupted Warfarin

Among 635 AF patients undergoing ablation, randomized to uninterrupted dabigatran (150 mg bid) or warfarin (target INR, 2.0 to 3.0) for 4-8 weeks prior and 8 weeks after ablation, the incidence of major bleeding events during and up to 8 weeks after ablation was lower with dabigatran than with warfarin (5 patients - 1.6% vs 22 patients - 6.9%; P<0.001). Dabigatran was associated with fewer periprocedural pericardial tamponades and groin hematomas than warfarin. The two treatment groups had a similar incidence of minor bleeding events. One thromboembolic event occurred in the warfarin group. (Calkins H et al, *N Engl J Med* 2017; 376:1627-1636).

iFR-SWEDEHEART: Among Patients With Stable Angina or Acute Coronary Syndrome, an iFR-Guided Revascularization Strategy was Noninferior to an FFR-Guided Revascularization Strategy

The instantaneous wave-free ratio (iFR) is an index used to assess the severity of coronary-artery stenosis.

Among 2037 participants with stable angina or an acute coronary syndrome who had an indication for physiologically guided assessment of coronary-artery stenosis, randomly assigned to undergo revascularization guided by iFR or FFR, a primary end-point event (death from any cause, nonfatal MI, or unplanned revascularization within 12 months) occurred in 68 of 1012 patients (6.7%) in the iFR group and in 61 of 1007 (6.1%) in the FFR group (P=0.007 for noninferiority; hazard ratio, 1.12; P=0.53); The rates of myocardial infarction, target-lesion revascularization, restenosis, and stent thrombosis did not differ significantly between the two groups. A significantly higher proportion of patients in the FFR group than in the iFR group reported chest discomfort during the procedure (Götberg M et al; *N Engl J Med* 2017; 376:1813-1823).

DEFINE-FLAIR: Coronary Revascularization Guided by iFR was Noninferior To Revascularization Guided by FFR / The Rate of Adverse Procedural Signs and Symptoms was Lower and the Procedural Time was Shorter With iFR Than With FFR

Among 2492 randomly assigned patients with coronary artery disease to undergo either iFR-guided or FFR-guided coronary revascularization, at 1 year, the primary end point (death, nonfatal MI, or unplanned revascularization) had occurred in 78 of 1148 patients (6.8%) in the iFR group and in 83 of 1182 patients (7%) in the FFR group (P<0.001 for noninferiority; hazard ratio, 0.95; P=0.78). The risk of each component of the primary end point and of death from cardiovascular or non-cardiovascular causes did not differ significantly between the groups. The number of patients who had adverse procedural symptoms and clinical signs was significantly lower in the iFR than in the FFR group (39 patients - 3.1% vs 385 patients -30.8%, P<0.001), and the median procedural time was significantly shorter (40.5 minutes vs 45.0 min, P=0.001) (Davies JE et al, *N Engl J Med* 2017; 376:1824-1834).

ACCELERATE: The Cholesteryl Ester Transfer Protein (CETP) Inhibitor Evacetrapib Failed to Reduce Cardiovascular Events

Among 12,092 patients with atherosclerotic disease randomly assigned to receive either evacetrapib (130 mg qd) or matching placebo, although at 3 months, a 31.1% decrease in the mean LDL cholesterol level was observed with evacetrapib vs a 6% increase with placebo, and a 133.2% increase in the mean HDL cholesterol level was seen with evacetrapib vs a 1.6% increase with placebo, the study was terminated early because of a lack of efficacy. After a median of 26 months of evacetrapib or placebo, a primary end-point event (death from cardiovascular causes, MI, stroke, coronary revascularization, or hospitalization for unstable angina) occurred in 12.9% of the patients in the evacetrapib group and in 12.8% of those in the placebo group (hazard ratio, 1.01; P=0.91) (Linkoff AM et al, *N Engl J Med* 2017;376:1933-1942).

AIDA: Bioresorbable Scaffolds Fail to Reduce the Rate of Target-Vessel Failure Compared to Metallic Stents, while they Confer a Higher Incidence of Device Thrombosis

Among 1845 patients undergoing PCI randomly assigned to receive either a bioresorbable vascular scaffold (924 patients) or a metallic stent (921 patients), over a median of 707 days, target-vessel failure occurred in 105 patients in the scaffold group and in 94 patients in the stent group (2-year cumulative event rates, 11.7% and 10.7%, respectively; hazard ratio, 1.12; P=0.43), cardiac death in 18 vs 23 patients (2-year cumulative event rates, 2.0% and 2.7%, respectively), target-vessel MI in 48 vs 30 patients (2-year cumulative event rates, 5.5% and 3.2%), and target-vessel revascularization in 76 vs 65 patients (2-year cumulative event rates, 8.7% and 7.5%). Definite or probable device thrombosis occurred in 31 patients in the scaffold group as compared with 8 patients in the stent group (2-year cumulative event rates, 3.5% vs 0.9%; hazard ratio, 3.87; P<0.001) (Wykrzykowska JJ et al, *N Engl J Med* 2017;376:2319-2328).

Rapid Rule Out of AMI: A Single hs-cTnT Concentration Below the Limit of Detection (<0.005 µg/L) in Combination With a Nonischemic ECG May Successfully Rule Out AMI in Patients Presenting to Emergency Departments (EDs) With Possible Emergency Acute Coronary Syndrome

Of 9241 patients, in 11 cohort studies, presenting to the ED with possible acute coronary syndrome, 2825 (30.6%) were classified as low risk (no new ischemia on ECG and hs-cTnT measurements <0.005 µg/L). Fourteen (0.5%) low-risk patients had AMI. Sensitivity of the risk classification for AMI ranged from 87.5% to 100% in individual studies. Pooled estimated sensitivity was 98.7%. Sensitivity for 30-day major adverse cardiac events (MACEs) ranged from 87.9% to 100%; pooled sensitivity was 98%. No low-risk patients died (Pickering JW et al, *Ann Intern Med* 2017;166:715-724).

GEMINI-ACS-1: A Dual Pathway Antithrombotic Therapy Combining Low-Dose Rivaroxaban With A P2Y12 Inhibitor for the Treatment of Patients With Acute Coronary Syndromes Had Similar Risk of Bleeding as Aspirin and a P2Y12 Inhibitor

Among 3037 patients with acute coronary syndromes randomly assigned to receive aspirin 100 mg qd (n=1518) or rivaroxaban 2.5 mg bid (n=1519) in addition to clopidogrel or ticagrelor, with 1704 patients (56%) in the ticagrelor and 1333 (44%) in the clopidogrel strata, over median 291 days, TIMI non-CABG clinically significant

bleeding was similar with rivaroxaban vs aspirin therapy (total 154 patients - 5%; 80 participants - 5% of 1519 *vs* 74 participants - 5% of 1518; HR 1·09; p=0.5840) (Ohman EN et al, *Lancet* 2017; 389(10081):1799-1908).

ONTARGET & TRANSCEND Trials: The Lowest Blood Pressure Possible is not Necessarily the Optimal Target for High-Risk Patients / Mean Achieved SBP < 120 mmHg was Associated With Increased Risk of Cardiovascular Outcomes Except for MI and Stroke

Among 30 937 patients followed up for a median of 56 months, baseline systolic blood pressure (SBP) ≥140 mmHg was associated with greater incidence of all outcomes compared with 120 mmHg to <140 mmHg. By contrast, a baseline diastolic blood pressure (DBP) <70 mmHg was associated with the highest risk for most outcomes compared with all DBP categories ≥70 mm Hg. In 4052 patients with SBP <120 mmHg, the risk of the composite cardiovascular outcome (adjusted hazard ratio-HR 1.14), cardiovascular death (1.29), and all deaths (1.28) were increased compared with those in whom SBP was 120–140 mm Hg (HR 1 for all outcomes, n=16099). No harm or benefit was observed for MI, stroke, or hospital admission for heart failure. Mean achieved SBP more accurately predicted outcomes than baseline or time-updated SBP, and was associated with the lowest risk at ~130 mmHg, and at 110–120 mmHg risk increased for the combined outcome, cardiovascular death, and all-cause death except stroke. A mean DBP <70 mmHg (n=5352) was associated with greater risk of the composite primary outcome (HR 1.31), MI (1.55), hospital admission for heart failure (1.59) and all-cause death (1.16) than a DBP 70–80 mmHg (n=14,305). A pretreatment and mean on-treatment DBP of ~75 mmHg was associated with the lowest risk (Bohm M et al, *Lancet* 2017; 389 (10085):2226-2237).

RESOLVE & SAVORY Registries: Subclinical Leaflet Thrombosis was Frequent in Bioprosthetic Aortic Valves, More Common in Transcatheter than in Surgical Valves, Best Prevented or Managed with Oral Anticoagulants, But not Dual Antiplatelet Therapy

Of the 890 (96%) with interpretable CT scans, 106 (12%) patients had subclinical leaflet thrombosis, including 5 (4%) of 138 with thrombosis of surgical valves vs 101 (13%) of 752 with thrombosis of transcatheter valves (p=0.001). The median time from aortic valve replacement to CT for the entire cohort was 83 days. Subclinical leaflet thrombosis was less frequent among patients receiving anticoagulants (8 - 4% of 224) than among those receiving dual antiplatelet therapy (31 - 15% of 208; p<0·0001); NOACs were equally as effective as warfarin (3 - 3% of 107 *vs* 5 - 4% of 117; p=0·72). Subclinical leaflet thrombosis resolved in 36 (100%) of 36 patients (warfarin 24 - 67%; NOACs 12 -33%) receiving anticoagulants, whereas it persisted in 20 (91%) of 22 patients not receiving anticoagulants (p<0·0001). A greater proportion of patients with subclinical leaflet thrombosis had aortic valve gradients of >20 mmHg and increases in aortic valve gradients of >10 mmHg (12-14% of 88) than did those with normal leaflet motion (7-1% of 632; p<0·0001). Although stroke rates were not different between those with or without reduced leaflet motion, subclinical leaflet thrombosis was associated with increased rates of TIAs and all strokes or TIAs (Chakravarty T et al, *Lancet* 2017;389:2383-92).

Important Review and Other Articles

Advanced heart failure and ventricular arrhythmias (Santangeli P et al, *J Am Coll Cardiol* 2017;69:1842-60), Antiplatelet therapy and noncardiac surgery (Banerjee S et al, *J Am Coll Cardiol* 2017;69:1861-70), Modifiable risk factors for AF (Du X et al, *J Am Coll Cardiol* 2017;69: 1968–82), Transcatheter mitral valve replacement (Regueiro A et al, *J Am Coll Cardiol* 2017;69:2175–92), Bioprosthetic valve thrombosis (Puri R et al, *J Am Coll Cardiol* 2017;69:2193-2211), Antiphospholipid syndrome (Corban MT et al, J Am Coll Cardiol 2017;69:2317-30), Ultrafiltration therapy in heart failure (Costanzo MR et al, *J Am Coll Cardiol* 2017;69:2428-45), Novel antidiabetic drugs (Sattar N et al, *J Am Coll Cardiol* 2017;69:2646-56), Left ventricular assist devices (Pinney SP et al, *J Am Coll Cardiol* 2017;69:2845-61), 2017 ACC/AHA Advanced Training Statement on Advanced Heart Failure and Transplant Cardiology (Jessup M et al, *J Am Coll Cardiol* 2017;69:2977-3001), HIV-associated atherosclerosis (Kearns A et al, *J Am Coll Cardiol* 2017;69:3084-98), Physiologic pacing (Vijayaraman P et al, *J Am Coll Cardiol* 2017;69:3099-3114), Cardiac amyloidosis (Maurer MS et al, *Circulation* 2017;135:1357-77), Leadless cardiac pacing (Tjong FVY et al, *Circulation* 2017; 135:1458-1470), AF and heart failure (Verma A et al, *Circulation* 2017;135:1547-63), Kawasaki disease (McCrindle BW et al, *Circulation* 2017;135:e927-e999), Aortic valve bioprostheses (Holmes DR et al, *Circulation* 2017;135:1749-56), Cardiovascular safety of non-steroidal anti-inflammatory agents (Antman EM, *Circulation* 2017;135:2062-72), Biomarkers in heart failure (Chow SL et al, Circulation 2017;135:e1054-e1091), Pathophysiology of Takotsubo syndrome (Pelliccia F et al, *Circulation* 2017;135:2426-2441), Recommendations for the use of mechanical circulatory support (Cook JL et al, *Circulation* 2017;135: e1145-e1158), 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease (Nishimura RA et al, *Circulation* 2017;135:e1159-e1195), Endogenous vasoactive peptides in heart failure (Packer M et al, *Lancet* 2017;389(10081):1831-1840).