Cardiology News /Recent Literature Review / Last Quarter 2012

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HCS Working Group Seminars will take place in Thessaloniki, 14-16/2/2013

ACC Meeting is slated for San Francisco, 9-11/3/13

HRS Meeting will take place in Denver, 8-11/5/13

EuroPCR to be held in Paris, 21-24/5/13

EuroPace will be held in Athens, 23-26/6/13

ESC Congress will be held in Amsterdam, 31/8-4/9/13

TCT Meeting: San Francisco, 28/10-1/11/13

AHA 2013: Dallas, 16-20/11/13

Metoprolol is not Effective in Long QT Syndromes Types 1 and 2 Compared to Propranolol and Nadolol

The effect of beta blockers was assessed in 382 LQT1/ LQT2 patients (56% female, 27% symptomatic, mean heart rate 76 bpm, mean QTc 472 ms) started on propranolol (n=134), metoprolol (n=147), and nadolol (n=101) at a median age of 14 years. The QTc shortening with propranolol was significantly greater than with other beta-blockers in all patients and in the subset with QTc >480 ms. None of the asymptomatic patients had arrhythmia events. Among symptomatic patients (n=101), 15 had syncope. The QTc shortening was significantly less pronounced among patients with syncope. There was a greater risk of syncope for symptomatic patients initiated on metoprolol compared to users of the other 2 beta-blockers combined, after adjustment for genotype (odds ratio: 3.95, p=0.025). Kaplan-Meier analysis showed a significantly lower event-free survival for symptomatic patients receiving metoprolol compared to propranolol/nadolol. The authors concluded that propranolol and nadolol are significantly more effective than metoprolol in preventing arrhythmic events in symptomatic patients. Also, propranolol was superior to both nadolol and metoprolol in terms of shortening the QTc, particularly in high-risk patients with markedly prolonged QTc. Patients with syncope had significantly less QTc shortening than the event-free patients (Chockalingam P et al, ***J Am Coll Cardiol*** 2012;60:2092–2099).

Still Limitations in Subcutaneous ICD

A total of 118 patients (75% males, mean age 50 years) received the entirely subcutaneous implantable cardioverter defibrillator (S-ICD) system. After 18 months of follow-up, 8 patients experienced 45 successful appropriate shocks (98% first shock conversion efficacy). No sudden deaths occurred. Inappropriate shocks occurred in 15 patients (13%), mainly due to T-wave oversensing, mostly solved by a software upgrade and changing the sensing vector of the S-ICD. Complications were noted in 16 patients (14%), more frequently in the first 15 implantations per center. The authors concluded that S-ICD is effective in terminating ventricular arrhythmias, but it has still limitations due to its subcutaneous position. Inappropriate therapy is an important issue in the S-ICD. However, both inappropriate shocks and device-related complications seemed to be related to a learning curve of both the device and the physician (Nordkamp et al, ***J Am Coll Cardiol*** 2012;60:1933–1939).

Chest Compression Only CPR: More Effective Than Conventional CPR

In Japan, over 5 years (2005-2009), among 1376 bystander-witnessed out-of-hospital cardiac arrests in individuals who received CPR and shocks with public-access automatic external defibrillators (AEDs) by bystanders, 506 (36.8%) received chest compression–only CPR and 870 (63.2%) received conventional CPR. The chest compression–only CPR group (40.7%, 206 of 506) had a significantly higher rate of 1-month survival with favorable neurological outcome than the conventional group (32.9%, 286 of 870; adjusted odds ratio, 1.33). The authors concluded that compression-only CPR is more effective than conventional CPR for patients in whom out-of-hospital cardiac arrest is witnessed and shocked with public-access defibrillation **(**Iwami T et al, ***Circulation*** 2012;126:2844-2851)

Hypothermia in Out-of-Hospital Cardiac Arrest: Better Outcome with Lower Cooling Level (32^{o} C)

Patients (n=36; 26 shockable rhythm, 10 asystole) with a witnessed out-of-hospital cardiac arrest were cooled to a target temperature of either 32°C (n=18) or 34°C (n=18) for 24 hours followed by 12-24 hours of controlled rewarming. Survival free from severe dependence was accomplished in 8/18 patients in the 32°C group (44.4%) compared with 2 of 18 in the 34°C group (11.1%) (*P*=0.12). All patients whose initial rhythm was asystole died before 6 months in both groups. Of those with initial shockable rhythm assigned to 32°C, 8/13 (61.5%) were alive free from severe dependence at 6 months compared with 2 of 13 (15.4%) assigned to 34°C (log-rank *P*=0.029). Complication rate was similar in both groups except for the incidence of seizures, which was lower (1 vs 11; *P*=0.0002) in patients assigned to

32°C compared with 34°C; but there was a trend toward a higher incidence of bradycardia (7 versus 2; *P*=0.054) in patients assigned to 32°C. Although potassium levels decreased to a greater extent in patients assigned to 32°C, the incidence of hypokalemia was similar in both groups. The authors concluded that a lower cooling level may be associated with a better outcome in patients surviving out-of-hospital cardiac arrest secondary to a shockable rhythm **(**Lopez-de-Sa E et al, ***Circulation*** 2012;126: 2826-2833)

Atrial Fibrillation: Rhythm Control is Superior, With Lower Rates of Stroke

In Quebec during the period 1999 to 2007, among 16325 patients ≥65 years with atrial fibrillation (AF) who filled a prescription for thyrhm control and 41193 patients who had rate control therapy, at a mean follow-up of 2.8 years (max 8.2 years), fewer patients on rhythm control therapy than on rate control therapy had a CHADS2 score of ≥2 (58.1% vs 67.0%, *P*<0.001). Treatment with antithrombotics was comparable in the 2 groups (76.8% vs 77.8%). Incidence of stroke/TIA was lower in patients treated with rhythm control (1.74 vs 2.49, per 100 person-years, *P*<0.001). This association was more pronounced in the moderate- and high-risk groups. In multivariable analysis, rhythm control therapy was associated with a lower risk of stroke/TIA (hazard ratio, 0.80). Lower stroke/TIA rate was confirmed in a propensity score–matched cohort. The authors concluded that compared with rate control therapy, rhythm control was associated with lower rates of stroke/TIA among patients with AF, more so in those with moderate and high risk of stroke **(**Tsadok MA et al, ***Circulation*** 2012;126:2680-2687)

Novel Oral Anticoagulants: a Metaanalysis Finds Them More Efficacious

A meta-analysis of 12 phase II an III randomized, controlled trials comparing novel oral anticoagulants (NOACs) (3 with dabigatran, 4 with rivaroxaban, 2 with apixaban, and 3 with edoxaban) with vitamin K antagonists in 54875 patients with atrial fibrillation indicated that NOACs significantly reduced total mortality (5.61% vs 6.02%; RR, 0.89), cardiovascular mortality (3.45% vs 3.65%; RR, 0.89), and stroke/ systemic embolism (2.40% vs 3.13%; RR, 0.77). There was a trend toward reduced major bleeding (RR, 0.86) with a significant reduction of intracranial hemorrhage (RR, 0.46). No difference in myocardial infarction was observed. The authors concluded that NOACs are associated with an overall clinical benefit compared with vitamin K antagonists **(**Dentali F et al, ***Circulation*** 2012;126:2381-2391)

Colchicine Reduces Early AF Recurrences After Ablation

Patients with paroxysmal atrial fibrillation (AF) undergoing radiofrequency ablation were randomized to a 3-month course of colchicine 0.5 mg twice daily or placebo. Over 3 months, AF recurred in 27 (33.5%) of 80 patients receiving placebo and in 13 (16%) of 81 patients receiving colchicine (odds ratio: 0.38). Diarrhea was reported in 7 patients in the colchicine group (8.6%) and 1 in the placebo group (1.3%, p = 0.03). Higher reductions in CRP and interleukin (IL)-6 levels were observed in the colchicine group. The authors concluded that colchicine is an effective and safe treatment for prevention of early AF recurrences after pulmonary vein isolation and is associated with a significant decrease in inflammatory mediators (Deftereos S et al, ***J Am Coll Cardiol*** 2012;60: 1790–1796)

ARISTOTLE Trial: Apixaban Reduces Stroke, Death, and Major Bleeding Regardless of Renal Function

Among patients with atrial fibrillation (AF) in the ARISTOTLE trial treated with apixaban, a novel oral anticoagulant with partial renal excretion, there were 7518 patients (42%) with an estimated GFR (eGFR) of >80 mL/min, 7587 (42%) between >50 and 80 mL/min, and 3017 (15%) with an eGFR of ≤50 mL/min. Cardiovascular and bleeding events were more in patients with impaired renal function (≤80 mL/min). Apixaban was more effective than warfarin in preventing stroke or systemic embolism and reducing mortality irrespective of renal function. These results were consistent, regardless of methods for GFR estimation. Apixaban was associated with less major bleeding events across all ranges of eGFRs. The authors concluded that in patients with AF, renal impairment was associated with increased risk of cardiovascular events and bleeding. When compared with warfarin, apixaban reduced stroke, death, and major bleeding, regardless of renal function. Patients with impaired renal function seemed to have the greatest reduction in major bleeding with apixaban (Hohnloser SH et al, ***Eur Heart J*** 2012; 33: 2821–2830)

MASTER Trial: Superior Rates of Epicardial Coronary Flow and Complete ST Segment Resolution with the MGuard Micronet Mesh–Covered Stent Compared with Conventional Metal Stents

A total of 433 patients with STEMI presenting within 12 h and undergoing PCI were randomized to the MGuard (a novel thin-strut metal stent with a polyethylene terephthalate micronet) (n=217) or commercially available bare metal or drug-eluting stents

(n=216). The primary endpoint of post-procedure complete ST-segment resolution was significantly improved in patients randomized to the MGuard stent compared with control patients (57.8% vs 44.7%; p = 0.008). The MGuard stent compared with control stents also resulted in superior rates of TIMI 3 flow (91.7% vs. 82.9%, p = 0.006) with comparable rates of myocardial blush grade 2 or 3 (83.9% vs. 84.7%, p = 0.81). Mortality (0% vs. 1.9%, p = 0.06) and major adverse cardiac events (1.8% vs. 2.3%, p=NS) at 30 days were not significantly different between patients randomized to the MGuard stent and control stent. The authors concluded that among patients with STEMI undergoing emergent PCI, the MGuard micronet mesh–covered stent compared with conventional metal stents resulted in superior rates of epicardial coronary flow and complete STsegment resolution (Stone GW et al, ***J Am Coll Cardiol*** 2012;60:1975–1984).

SIMPLICITY HTN-2: Benefit of Renal Denervation Persists at 1 Year

Catheter-based renal denervation produced significant blood pressure lowering in resistant hypertension (HTN) at 1 year (n=47) with a mean fall in office systolic blood pressure of -28.1 mm Hg (P<0.001) similar to the 6-month fall (-31.7 mm Hg; P=0.16). The mean systolic blood pressure of the crossover group 6 months after the procedure was also significantly lowered (from 190.0±19.6 to 166.3±24.7 mm Hg; change, -23.7±27.5; P<0.001). Complications: 1 renal artery dissection corrected by stenting, and 1 hypotensive episode. The authors concluded that the effect of renal denervation is sustained at 1 year and that patients who crossed over to renal denervation with the Symplicity system had a significant drop in blood pressure similar to that observed in patients receiving immediate denervation **(**Esler MD et al, ***Circulation*** 2012;126:2976-2982.)

Novel Hypocholesterolemic Drug Appears Promising in Phase 1 Studies

AMG 145 is a human monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9: a down-regulator of surface expression of the LDL receptor that leads to increased LDL cholesterol). AMG 145 prevents PCSK9/LDL receptor interaction, restoring LDL-receptor recycling. The drug was administered subcutaneously either once weekly (QW) or every 2 weeks (Q2W) or every 4 weeks in healthy (phase 1a) and hypercholesterolemic adults (phase 1b) receiving statins. In the trials (AMG 145 n = 85, placebo n = 28), AMG 145 reduced LDL cholesterol up to 64% (p < 0.0001) vs placebo after 1 dose ≥21 mg and up to 81% (p < 0.001) with repeated doses ≥35 mg QW. No serious adverse events occurred. The authors concluded that in phase 1 studies, AMG 145 significantly reduced serum LDL cholesterol in healthy and hypercholesterolemic statin-treated subjects, with an overall side-effect profile similar to placebo (Dias CS et al, ***J Am Coll Cardiol*** 2012;60: 1888–1898).

Ablation Results are Poor in Long-Standing Persistent AF, Unless Arrhythmia Duration is < 2 Years

A single ablation procedure was successful in maintaining sinus rhythm (SR) for a mean duration of 56 months only in 41 of 202 (20.3%) patients with long-standing atrial fibrillation (AF). Multiple procedures increased the success rate to 45% (91 of 202 patients including 24 patients receiving antiarrhythmic drugs). In 105 patients, pulmonary vein isolation (PVI) was the sole ablative therapy, 49 (46.7%) of those patients remained in SR during follow-up. Patients with a total AF duration of <2 years had a higher ablation success rate than the other patients with longer AF duration (76.5% vs. 42.2%; p = 0.033). The authors concluded that over 5 years, single ablation procedure had a poor (20%) success rate in patients with long-standing AF; multiple ablation procedures increased success to 45%. For patients with a total AF duration of <2 years, the outcomes were more favorable (Tilz RR et al, ***J Am Coll Cardiol*** 2012;60: 1921–1929).

PRAGUE 12 Study: No Improved Clinical Outcomes at 1 Year after Surgical Ablation of Atrial Fibrillation

A total of 224 patients with AF scheduled for valve and/or coronary surgery were randomized into 2 groups: group A (left atrial surgical ablation, n = 117) vs. group B (no ablation, n = 107). Sinus rhythm (SR) was found at Holter-ECG after 1 year in 60.2% of group A patients vs. 35.5% in group B (P = 0.002). The combined safety end-point (death/myocardial infarction/stroke/renal failure) at 30 days occurred in 10.3% (group A) vs. 14.7% (group B, P = 0.411). All-cause 1-year mortality was 16.2% (A) vs. 17.4% (B, P = 0.8). Stroke occurred in 2.7% (A) vs. 4.3% (B) patients (P = 0.319). No difference (A vs. B) in SR was found among patients with paroxysmal (61.9 vs. 58.3%) or persistent (72 vs. 50%) AF, except in patients with longstanding persistent AF (53.2 vs. 13.9%, P < 0.001). The authors concluded that surgical ablation improves SR presence post-operatively without increasing peri-operative complications. However, this did not translate into improved clinical outcomes at 1 year (Budera P et al, ***Eur Heart J*** 2012; 33: 2644-2652)

Balloon Dilation and Atrial Fibrillation Account for Stroke in TAVI Patients

Among 1061 patients undergoing transcatheter aortic valve implantation (TAVI) with a balloon-expandable (64%) or self-expandable (36%) valve, cerebrovascular events (CVEs) occurred in 54 patients (5.1%) within 30 days (54% acute). The predictors of acute CVEs were balloon postdilation of the valve prosthesis (odds ratio-OR, 2.46) and valve dislodgment/embolization (OR, 4.36); new-onset atrial fibrillation (AF) (OR, 2.76) was a predictor of subacute CVEs. Late (median 12 months) CVEs (35 patients- 3.3%) were predicted by chronic AF (hazard ratio-HR, 2.84), peripheral vascular disease (HR, 2.02), and prior CVEs (HR, 2.04). The authors concluded that in a large cohort of patients undergoing TAVI, acute CVEs were predicted by balloon postdilation and valve dislodgment/embolization, while new-onset AF conferred a higher risk for subacute events. Late events were predicted by history of chronic AF and peripheral and cerebrovascular disease **(**Nombela-Franco L et al, ***Circulation*** 2012;126: 3041-3053).

Thromboaspiration During Primary PCI Reduces Mortality

Thrombus aspiration was performed in 1095 patients of 2567 patients (42.7%) with ST-elevatiom myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI). Post-PCI TIMI 3 flow was more frequently achieved in the thromboaspiration group (odds ratio-OR, 1.92; P = 0.0004). Overall in-hospital and 10-month mortality rates were 4.5 and 9.0%, respectively. Thromboaspiration was associated with a significant reduction in in-hospital (adjusted OR: 0.51, P = 0.027) and longer term mortality (hazard ratio-HR: 0.69, P = 0.028). Reduced longer term mortality was only significant in those with a total ischemic time ≤180 min (P = 0.001). The authors concluded that thrombus aspiration during primary PCI is associated with a significant reduction in mortality, especially in those with a short total ischemic time (Noman A et al, ***Eur Heart J*** 2012; 33, 3054–3061)

Danish Study: Discontinuation of Clopidogrel 1 Year after MI is Associated with an Increased Risk of Death or Recurrent MI

Of 29 268 patients treated with clopidogrel after a first myocardial infarction (MI) (2004-2009) and included in a Danish retrospective nationwide study, who discontinued clopidogrel after 1 year, 3214 (11.0%) experienced death or recurrent MI at a follow-up of 18 months. There were 9819 (33.6%) patients treated only medically and 19 449 (66.4%) patients treated with PCI. At 12 months after the index MI, for patients treated only medically, the risk of death or recurrent MI in the first 90-day period of clopidogrel discontinuation was 1.07 (*P*= 0.79) (adjusted incidence rate ratio-IRR). For patients treated with PCI, the corresponding IRR was 1.59 (*P*= 0.013). The risk of recurrent MI yielded an IRR of 0.77 (*P*= 0.51) for patients treated only medically and 1.87 (*P*= 0.019) for PCI-treated patients. The authors concluded that discontinuation of clopidogrel 12 months after MI is associated with an increased risk of death or recurrent MI in the first 90 days of discontinuation compared with the next 90-day period of discontinuation for patients treated with PCI, but not for patients not treated with PCI (Charlot M et al, ***Eur Heart J*** 2012; 33:2527-2534)

Important Review and Other Articles

Catheter-assisted pulmonary embolectomy (Sobieszczyk P, ***Circulation*** 2012;126: 1917-1922), 2012 ACCF/AHA/HRS Focused Update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities (Tracy CM et al, ***J Am Coll Cardiol*** 2012;60:1297-1313), Third universal definition of myocardial infarction (Thygesen K et al, ***J Am Coll Cardiol*** 2012; 60:1581-1598), Percutaneous treatment of PFO and ASDs (Tobis & Shenoda, ***J Am Coll Cardiol*** 2012; 60:1722-1732), Nonsustained ventricular tachycardia (Katritsis D et al, ***J Am Coll Cardiol*** 2012; 60: 1993-2004), Quantitation of mitral regurgitation (Grayburn PA et al, ***Circulation*** 2012; 126:2005-2017), 2012 ESC/EACTS Guidelines on the management of valvular heart disease (***Eur Heart J*** 2012; 33: 2451-2496), 2012 ESC Guidelines for the management of STEMI (***Eur Heart J*** 2012; 33: 2569-2619), 2012 ESC Guidelines for the management of atrial fibrillation (***Eur Heart J*** 2012; 33: 2719-2747), Low-flow low-gradient aortic stenosis (Pibarot & Dumesnil, ***J Am Coll Cardiol*** 2012; 60:1845-1853), Update on pulmonary embolism (Konstantinides & Goldhaber, ***Eur Heart J*** 2012; 33: 3014-3022), 2012 ACCF/AHA/ ACP/AATS/PCNA/ SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease (Fihn SD et al, ***Circulation*** 2012;126:3097-3137; ***J Am Coll Cardiol*** 2012;60: 2564-2603), AHA Recommendations for the use of mechanical circulatory support **(**Peura JL et al, ***Circulation*** 2012;126:2648-2667), ACCF 2012 Expert Consensus Document on Practical Clinical Considerations in the Interpretation of Troponin Elevations (Newby LK et al, ***J Am Coll Cardiol*** 2012;60:2427-2463), Inflammation in atrial fibrillation (Guo Y et al, ***J Am Coll Cardiol*** 2012;60:2263-2270), Optical coherence tomography (OCT) (Prati F et al, ***Eur Heart J*** 2012; 33:2513-2520)