Cardiology News /Recent Literature Review / First Quarter 2012

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The **Athens Cardiology Update 2012** is slated for April 5-7, 2012

The **HRS** 33rd Meeting will be held in Boston, 9-12/5/12

The **ESC** Congress will be held in Munich, 25-29/8/2012

TCT Meeting will take place in Miami, 22-26/10/12

HCS Meeting to be held in Athens, 1-3/11/12

AHA 2012 is scheduled for Los Angeles, 3-7/11/12

PARTNER Trial (Cohort B): TAVI Remains Cost-Effective for Patients with Severe Aortic Stenosis who are not Candidates for Surgery

The PARTNER trial randomized patients with symptomatic, severe aortic stenosis who were not candidates for surgery to transcatheter aortic valve implantation (TAVI) (n=179) or standard therapy (n=179). Mean costs for the initial TAVI procedure and hospitalization were $42,806 and $78,542, respectively. Follow-up costs through 12 months were lower with TAVI ($29,289 vs $53,621) because of reduced hospitalization rates, but cumulative 1-year costs remained higher ($106,076 vs $53,621). Projection was that over a patient's lifetime, TAVI would increase discounted life expectancy by 1.6 years (1.3 quality-adjusted life-years-QALY) at an incremental cost of $79,837. The incremental cost-effectiveness ratio for TAVI was thus estimated at $50,200 per year of life gained or $61,889 per QALY gained. The authors concluded that TAVI increases life expectancy at an incremental cost per life-year gained well within accepted values for commonly used cardiovascular technologies. (Reynolds MR et al, ***Circulation*** 2012;125:1102-1109).

SCAAR Registry: Lower Risk of Stent Thrombosis & Restenosis with Unrestricted Use of 'New-Generation' Drug-Eluting Stents

A total of 94,384 consecutive stent implantations, including bare metal (BMS, n=64,631), older generation drug-eluting stents (o-DES, n=19,202), and new generation DES (n-DES, n = 10 551) were evaluated in Sweden. Older generation DES comprised Cypher and Cypher Select, Taxus Express and Taxus Liberte, and Endeavor Sprint, while n-DES included Endeavor Resolute, XienceV, Xience Prime, Promus, and Promus Element. A statistically significant lower risk of restenosis was shown for n-DES compared with BMS [adjusted hazard ratio (HR) 0.29] and o-DES (HR 0.62). A lower risk of definite ST was found in n-DES compared with BMS (HR 0.38) and o-DES (HR, 0.57). The risk of death was significantly lower in n-DES compared with o-DES (adjusted HR: 0.77) and BMS (adjusted HR: 0.55). The authors concluded that PCI with n-DES is associated with a 38% lower risk of clinical restenosis, a 43% lower risk of definite ST, and a 23% lower risk of death compared with o-DES (Sarno G et al, ***Eur Heart J*** 2012;33:606-613).

CRT Induced Mechanical Dyssynchrony Presages Increased Mortality

Outcome of heart failure patients (n=290) without significant baseline left ventricular (LV) dyssynchrony, i.e. <60 ms as assessed with tissue Doppler imaging, treated with cardiac resynchronization therapy (CRT), was compared to that of 290 heart failure patients also treated with CRT who showed significant LV dyssynchrony (≥60 ms) at baseline. In the group of patients without significant LV dyssynchrony, median LV dyssynchrony increased from 22 ms at baseline to 40 ms 48 hours after CRT. The cumulative mortality rates at 1-, 2-, and 3-year follow-up of patients with LV dyssynchrony ≥40 ms at 48 hours after CRT implantation were significantly higher when compared with patients with LV dyssynchrony <40 ms (10, 17, and 23 vs. 3, 8, and 10%, respectively; P <0.001). Finally, the cumulative mortality rates at 1-, 2-, and 3-year follow-up of patients with baseline LV dyssynchrony were 3, 8, and 11%, respectively (P = NS vs patients with LV dyssynchrony <40 ms). Induction of LV dyssynchrony after CRT was an independent predictor of mortality (hazard ratio: 1.25; P = 0.009). The authors concluded that in patients without significant LV dyssynchrony, the induction of LV dyssynchrony after CRT may confer less favourable long-term outcome (Auger D et al, ***Eur Hear J*** 2012; 33:913-920).

Catheter Ablation for Atrial Fibrillation: 1 in 20 Patients Experiences a Complication and 1 in 10 are Rehospitalized Within 30 Days

Among 4,156 patients undergoing AF ablation, 5% had complications, most commonly vascular, and 9% were readmitted within 30 days. Older age, female, prior AF hospitalizations, and less hospital experience with AF ablation were associated with higher risk of complications and/or 30-day readmissions. The rate of hospitalization was 38.5% by 1 year and rate of readmission form recurrent AF, atrial flutter, and/or repeat ablation was 21.7% by 1 year and 29.6% by 2 years. The authors concluded that complications occurred

in 1 of 20 patients undergoing AF ablation, and all-cause and arrhythmia related rehospitalizations were common. Older age, female gender, prior AF hospitalizations, and less hospital procedure experience were associated with a higher risk of complications and/or 30-day readmission after AF ablation (Shah RU et al, ***J Am Coll Cardiol*** 2012;59:143–149).

Pediatric Cardiomyopathy Registry: Risk Stratification for Sudden Cardiac Death (SCD) in Children with Dilated Cardiomyopathy (DCM)

Among 1,803 children with a diagnosis of dilated cardiomyopathy (DCM), the 5-year incidence rates were 29% for heart transplantation, 12.1% non-SCD, 4.0% death from unknown cause, and 2.4% for SCD. Of 280 deaths, 35 were SCD, and the cause was unknown for 56. The 5-year incidence rate for SCD incorporating a subset of the unknown deaths was 3%. Patients receiving antiarrhythmic medication were at higher risk of SCD (hazard ratio: 3, $p = 0.025$). Risk stratification based on most recent echocardiographic findings had 86% sensitivity and 57% specificity. Thirty of 35 SCDs occurred in patients who met all these criteria: left ventricular (LV) end-systolic dimension *z*-score >2.6, age at diagnosis younger than 14.3 years, and the LV posterior wall thickness to end-diastolic dimension ratio <0.14. Gender, ethnicity, cause of DCM, and family history were not associated with SCD. The authors concluded that the 5-year incidence rate of SCD in children with DCM is 3%. They proposed the following criteria for prophylactic defibrillator (ICD) implantation: age at diagnosis younger than 14 years, LV dilation, and LV posterior wall thinning (Pahl E et al, ***J Am Coll Cardiol*** 2012;59:607–615)

Percutaneous Revascularization of Unprotected Left Main Remains a Relatively Uncommon Procedure at Most U.S. Centers and is Primarily Reserved for Those at High Risk for Coronary Bypass

A total of 5,627 patients undergoing percutaneous coronary intervention (PCI) for unprotected left main coronary artery (LMCA) stenosis at 693 centers within a National US Registry (2004-2008) were evaluated. Thirty-month mortality and major adverse events with drug-eluting vs bare-metal stents were also compared in a patient cohort ($n = 2,765$) aged $\geq$65 years. PCI was performed in 4.3% of patients with unprotected LMCA stenosis. In-hospital mortality rates ranged from 2.9% for elective cases to 45.1% for emergent/salvage cases. By 30 months, 57.9% of the elderly unprotected LMCA PCI population experienced death, myocardial infarction, or revascularization, and 42.7% died. Patients receiving drug-eluting stents (vs bare-metal stents) had a lower 30-month mortality (hazard ratio-HR: 0.84), but the composite of major adverse events were similar. The authors concluded that in the US, PCI is performed in <5% of patients with unprotected LMCA disease and is generally reserved for those at high procedural risk. Adverse events are common in elderly patients and are related to patient and procedural characteristics, including stent type (Brennan JM et al, ***J Am Coll Cardiol*** 2012;59:648–54).

Renal Sympathetic Denervation (RSD) Reduces Left Ventricular Mass and Improves Diastolic Function in Patients With Resistant Hypertension

A group of 46 patients with resistant hypertension underwent bilateral renal sympathetic denervation (RSD), and echocardiographic results were compared with those of 18 control patients. Besides reduction of systolic and diastolic blood pressure (-22.5/-7.2 mm Hg at 1 month and -27.8/-8.8 mm Hg at 6 months; $p < 0.001$), RSD significantly reduced mean interventricular septum thickness from 14.1 ± 1.9 mm to 13.4 ± 2.1 mm and 12.5 ± 1.4 mm ($p = 0.007$), and LV mass index from 112.4 ± 33.9 g/m^2 to 103.6 ± 30.5 g/m^2 and 94.9 ± 29.8 g/m^2 ($p < 0.001$) at 1 month and 6 months, respectively. The mitral valve lateral E/E´ decreased after RSD from 9.9 ± 4.0 to 7.9 ± 2.2 at 1 month and 7.4 ± 2.7 at 6 months ($p < 0.001$), indicating reduction of left ventricular (LV) filling pressures. Isovolumic relaxation time shortened, whereas LV ejection fraction significantly increased after RSD (baseline: $63.1 \pm 8.1\%$ vs. $70.1 \pm 11.5\%$ at 6 months, $p < 0.001$). No significant changes were obtained in control patients. The authors concluded that in addition to the known effect on blood pressure, it was shown for the first time that RSD significantly reduces LV mass and improves diastolic function, which might have important prognostic implications in patients with resistant hypertension at high cardiovascular risk (Brandt MC et al, ***J Am Coll Cardiol*** 2012;59:901–909).

Atrial Fibrillation (AF) Ablation: Periprocedural Dabigatran Use Increases the Risk of Bleeding or Thromboembolic Complications Compared With Uninterrupted Warfarin Therapy

All 145 patients receiving dabigatran therapy who underwent AF ablation on periprocedural dabigatran, with the dose held on the morning of the procedure, were matched by age, sex, and type of AF with an equal number (n=145) of patients undergoing AF ablation with uninterrupted warfarin therapy over the same period. The mean age was 60 years with 79% being male and 57% having paroxysmal AF. Both groups had a similar

CHADS2 score, left atrial size, and left ventricular ejection fraction. A total of 3 thromboembolic complications (2.1%) occurred in the dabigatran group and none in the warfarin group (p = NS). Dabigatran led to a higher major bleeding rate (6% vs 1%; p = 0.019), total bleeding rate (14% vs 6%; p = 0.031), and combined bleeding and thromboembolic complication rate (16% vs 6%; p = 0.009) compared with warfarin. Dabigatran use was an independent predictor of bleeding or thromboembolic complications (odds ratio: 2.76; p = 0.01) on multivariate regression analysis. The authors concluded that in patients undergoing AF ablation, periprocedural dabigatran use significantly increases the risk of bleeding or thromboembolic complications compared with uninterrupted warfarin therapy (Lakkireddy D et al, ***J Am Coll Cardiol*** 2012;59: 1168–1174).

Out-of-Hospital Deaths Within 30 Days Following Percutaneous Coronary Intervention (PCI) Occur in a Least Expected Group

All 51,695 patients who underwent PCI in New York State from January 1, 2007, and December 31, 2007, who were discharged alive by December 31, 2007 were followed for 30 days after discharge. The in-hospital and 30-day mortality rate for PCI patients was 0.94%, the in-hospital mortality rate was 0.56%, and the mortality rate for deaths that occurred after discharge within 30 days of the procedure was 0.38%. Of the 491 PCI deaths, 199 (40.5%) occurred after discharge. The percentage of short-term (in-hospital or within 30 days) deaths in hospitals with >10 short-term deaths ranged from 15% to 71%. The authors concluded that compared to PCI patients dying in-hospital, patients who died <30 days after discharge were younger, had better ventricular function, were less likely to have had recent myocardial infarctions, and were less likely to have had postprocedural complications. Most deaths in the 30-day group were cardiovascular, and most were cardiac and acute. A small percentage were related to chronic cardiac or vascular disease (Hannan EL et al, ***Am J Cardiol*** 2012;109:47–52).

Decreased LVEF (<40%) Increases the Risk of Stent Thrombosis

Among 5,377 patients undergoing percutaneous coronary intervention (PCI), patients with normal left ventricular ejection fraction (LVEF) (>50%) were compared to those with mild (41% - 50%), moderate (25% - 40%), and severe (<25%) decreases in LVEF. Patients with abnormal LVEF were older and more commonly diabetic and had renal insufficiency and heart failure (p <0.001). These patients demonstrated more angiographically complex lesions and less frequently received a drug-eluting stent. The primary end point (1-year major adverse cardiac events) was significantly increased in patients with lower LVEF (9.7% for normal LVEF vs 20.6% for severely decreased LVEF, p <0.001). Stent thrombosis occurred more frequently in these patients (1.4% for normal LVEF vs 6% for severely decreased LVEF, p<0.001), but clinically driven target lesion revascularization (TLR) did not significantly change across LVEF groups. After adjustment, only moderate and severe LVEF decreases (<40%) demonstrated an association with major adverse cardiac events and stent thrombosis. There was no difference between those receiving only a drug-eluting stent or a bare-metal stent. The authors concluded that decreased LVEF (<40%) is not associated with clinically driven TLR but does increase the risk of stent thrombosis (Sardi GL et al, ***Am J Cardiol*** 2012;109:344–351).

Primary PCI via the Radial Approach is Associated with Lower Short-term Mortality

Ten randomized controlled trials involving 3,347 patients comparing the clinical outcomes of radial and femoral approach in primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) were analyzed. The radial approach was associated with improved survival (odds ratio 0.53) and reduced vascular complications/hematoma (odds ratio 0.35). A nonsignificant trend was found toward reduced major bleeding with the radial approach (odds ratio 0.63). The procedural time with the radial approach was longer by <2 min (mean difference 1.76 min). The authors concluded that in patients undergoing primary PCI, the radial approach is associated with lower short-term mortality. When feasible, the radial approach should be the favored route in primary PCI (Joyal D et al, ***Am J Cardiol*** 2012;109:813– 818).

Use of Bivalirudin and Closure Devices Reduce the Risk for Vascular Complications After Percutaneous Coronary Intervention (PCI)

Among 7,718 patients undergoing PCI via femoral access, 444 (5.8%) had vascular complications (VCs). Compared to those without VCs, patients with VCs were older and had more extensive co-morbidities. Severe blood loss was most frequent in those who had vascular perforation requiring surgical repair or in those who had retroperitoneal bleeding. Overall, <25% of patients with hematoma had severe blood loss. One-year mortality was two-fold higher in patients with minimal or moderate hematocrit decrease and three-fold increased in those

with severe decreases in hematocrit. Stent thrombosis was tripled in patients with VCs and moderate or severe decreases in hematocrit. After adjustment, only patients with VCs and the greater hematocrit decreases had an increased risk for death at 1 year (hazard ratio 1.80). Independent predictors of severe hematocrit decrease included age, female gender, glycoprotein IIb/IIIa inhibitor use, and activated clotting time peak. Bivalirudin and closure devices were independently associated with less frequent severe bleeding. The authors concluded that VCs confer an increased risk for death at 1 year only when associated with severe blood loss. The use of bivalirudin and closure devices seems to reduce the risk for such complications (Romaguera R et al, ***Am J Cardiol*** 2012; 109:75– 81).

In Patients With Out-of-hospital Cardiac Arrest, Early Catheterization (<6 Hours) is Associated With Improved Survival

Among 240 patients with out-of-hospital cardiac arrest caused by ventricular tachycardia or fibrillation, 2 groups were evaluated: those receiving acute catheterization within 6 hours (≤6-hour group, n = 61) and those with deferred catheterization at >6 hours or no catheterization during the index hospitalization (>6-hour group, n = 179). Survival was greater in patients who underwent acute catheterization (72% in the ≤6-hour group vs 49% in the >6-hour group, p = 0.001). Percutaneous coronary intervention (PCI) was performed in 38 of 61 patients (62%) in the ≤6-hour group and 13 of 170 patients (7%) in the >6-hour group (p <0.0001). Neurologic status was similar in the 2 groups. A significantly larger percentage of patients in the acute catheterization group had symptoms before cardiac arrest and had ST-segment elevation on ECG after resuscitation. Age, bystander cardiopulmonary resuscitation, daytime presentation, history of PCI or stroke, and acute ST-segment elevation were positively associated with receiving cardiac catheterization. The authors concluded that in patients with out-of-hospital cardiac arrest, acute catheterization (≤6 hours) was associated with improved survival (Strote JA et al, ***Am J Cardiol*** 2012;109:451– 454).

HORIZONS-AMI trial: in Patients With STEMI Treated With Primary PCI, Triple Antithrombotic Therapy Results in Excess of Bleeding Complications and Premature Discontinuation of Coumadin

The outcomes of patients who received triple therapy (aspirin, thienopyridine, and coumadin) after primary PCI for ST-elevation myocardial infarction (STEMI) were assessed in the Harmonizing Outcomes with Revascularization & Stents in Acute Myocardial Infarction [HORIZONS-AMI] trial. Among the 3,320 patients having primary PCI, 126 (3.8%) were prescribed triple therapy and 3,194 (96.2%) received dual antiplatelet therapy. The most frequent indications for anticoagulation treatment were a severely reduced left ventricular ejection fraction (LVEF) with a large akinetic area, atrial fibrillation (23.8% each), and mural thrombus (23.0%). The assignment to triple therapy was associated with older age, female gender, rhythm disturbances, Killip class >1 on admission, lower LVEF, left anterior descending artery territory infarcts, and final TIMI flow grade <3. Patients treated with triple versus dual therapy had comparable short- and long-term ischemic outcomes but had significantly increased rates of major bleeding during the index hospitalization (17.1% vs 6.5%, p <0.0001), resulting in premature discontinuation of anticoagulation in 14.3% of those patients. The authors concluded that in patients with STEMI treated with primary PCI, the combination of aspirin, thienopyridine, and coumadin results in an excess of bleeding complications and premature discontinuation of coumadin. The risk of adding oral anticoagulation to patients admitted for STEMI should be carefully considered before choosing drug-eluting or bare metal stents (Nikolsky E et al, ***Am J Cardiol*** 2012;109:831–838).

j-Cypher Registry: Late and Very Late Stent Thrombosis Continue to Occur Without Attenuation up to 5 Years with Sirolimus-Eluting Stents

Follow-up at 5 years was obtained in 12,812 patients undergoing implantation of sirolimus-eluting stent (SES). Cumulative incidence of definite stent thrombosis was low (30 day, 0.3%; 1 year, 0.6%; and 5 years, 1.6%). However, late and very late stent thrombosis continued to occur without attenuation up to 5 years after SES implantation (0.26%/y). Cumulative incidence of target lesion revascularization (TLR) within the first year was low (7.3%). However, late TLR beyond 1 year also continued to occur without attenuation up to 5 years (2.2%/y). Independent risk factors of stent thrombosis depended on time of its occurrence. For *early* thrombosis: acute coronary syndrome and target of proximal left anterior descending coronary artery; for *late* thrombosis: side-branch stenting, diabetes mellitus, and end-stage renal disease with or without hemodialysis; and for *very late* thrombosis: current smoking and total stent length >28 mm. The authors concluded that very late stent thrombosis and late TLR are continuous hazards, lasting at least up to 5 years after implantation of the first-generation SES (Kimura T et al, ***Circulation*** 2012;125:584-591).

Everolimus Eluting Stent (EES) is Associated with a Lower Risk of Very Late Stent Thrombosis Compared with Early-Generation Drug-Eluting Stents (DES)

The risk of stent thrombosis was assessed in a cohort of 12,339 patients receiving drug-eluting stents (DES) (3819 sirolimus-SES, 4308 paclitaxel-PES, 4212 everolimus-EES). During follow-up of up to 4 years, the overall incidence of stent thrombosis was lower with EES (1.4 per 100 person-years) compared with SES (2.9; hazard ratio, 0.41; $P<0.0001$) and PES (4.4; hazard ratio, 0.33; $P<0.0001$). The incidence rate per 100 person-years of early (0–30 days), late (31 days–1 year), and very late stent thrombosis amounted to 0.6, 0.1, and 0.6 among EES-treated patients; 1.0, 0.3, and 1.6 among SES-treated patients; and 1.3, 0.7, and 2.4 among PES-treated patients. Differences in favor of EES were most pronounced beyond 1 year. There was a lower risk of cardiac death or myocardial infarction with EES compared with PES directly related to the lower risk of stent thrombosis. The authors concluded that EES is associated with a lower risk of very late stent thrombosis compared with early-generation drug-eluting stents (Raeber L et al, ***Circulation*** 2012;125:1110-1121.)

Risk of Malignant Arrhythmias in Symptomatic Patients with WPW Syndrome Remains Low

Among 8575 symptomatic Wolff-Parkinson-White (WPW) patients with atrioventricular reentrant tachycardia (AVRT) referred for an electrophysiology study, 369 declined catheter ablation and were followed up. After a mean follow-up of 42$\pm$10 months, malignant arrhythmias developed in 29 patients, resulting in presyncope/ syncope (25 patients), hemodynamic collapse (3 patients), or cardiac arrest caused by ventricular fibrillation (1 patient). Of the remaining 340 patients, 168 remained asymptomatic up to 5 years, and 172 had benign recurrence, including sustained AVRT (132 patients) or atrial fibrillation (40 patients). Compared with subjects with no malignant arrhythmias, those with malignant arrhythmias more often exhibited multiple accessory pathways ($P<0.001$), showed shorter accessory-pathway effective refractory period ($P<0.001$) and AVRT triggering sustained pre-excited atrial fibrillation was more frequently inducible ($P<0.001$). The latter two variables were independent predictors of malignant arrhythmias. The authors concluded that symptomatic patients with WPW syndrome generally have a good outcome, and predictors of malignant arrhythmias are similar to those reported for asymptomatic patients with ventricular pre-excitation. (Pappone C et al, ***Circulation*** 2012;125:661-668).

Observational, Propensity Score–matched Study: Percutaneous PFO Closure More Effective than Medical Treatment for the Secondary Prevention of Recurrent Cerebrovascular Events

A total of 308 consecutive patients with cerebrovascular events presumably related to PFO underwent either percutaneous PFO closure (150 patients) or medical treatment (158 patients) and were followed up prospectively for up to 15 years (except for 7 who were lost at follow-up). Analysis of 103 propensity score–matched pairs of patients showed that at a median follow-up of 9 years recurrence was noted in 11 patients with PFO closure (11%) and 22 patients with medical treatment (21%; hazard ratio=0.43; $P=0.033$). The risk of all-cause (6% in both groups) and cardiovascular (3% in both groups) mortality was similar. The authors concluded that PFO closure was more effective than medical treatment for the secondary prevention of recurrent cerebrovascular events among patients with PFO-related transient ischemic attack or stroke (Wahl A et al, ***Circulation*** 2012;125:803-812).

Important Review and Other Articles

Closure of left atrial appendage (Landmesser U & Holmes DR, ***Eur Heart J*** 2012; 33:698-704), Secondary stroke prevention (Meier B et al, ***Eur Heart J*** 2012; 33:705-713), Assessing risk of interventions in valvular heart disease (Rosenhek R et al, ***Eur Heart J*** 2012; 33:822-828), Hypothermia therapy (Delhaye C et al, ***J Am Coll Cardiol*** 2012; 59:197–210), Role of AV node ablation in patients with CRT & AF (Ganesan AN et al, ***J Am Coll Cardiol*** 2012;59:719-726), Update on myocarditis (Kindermann I et al, ***J Am Coll Cardiol*** 2012;59:779-792), Consensus standards for OCT (Tearney GJ et al, ***J Am Coll Cardiol*** 2012;59:1058-1072), Expert consensus 2012 on TAVI (Holmes DR et al, ***J Am Coll Cardiol*** 2012;59:1200-1254), Antiarrhythmic drug therapy for AF (Zimetbaum P, ***Circulation*** 2012; 125:381-385), Atrial fibrillation in athletes (Turagam MK et al, ***Am J Cardiol*** 2012;109:296-302), Epidemiology and genetics of sudden death (Deo R & Albert CM, ***Circulation*** 2012; 125:620-637), Management of atrial fibrillation in patients with structural heart disease (Darby AE & John P. DiMarco JP, ***Circulation*** 2012;125:945-957), Acute coronary events (Arbab-Zadeh A et al, ***Circulation*** 2012;125:1147-1156), Mechanical circulatory support for advanced heart failure (Stewart GC & Givertz MM, ***Circulation*** 2012;125:1304-1315), Sudden death from cardiomyopathies (Sen-Chowdhry S & McKenna WJ, ***Circulation*** 2012;125: 1563-1576).