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CARDIOLOGY CORNER

Cardiology News / Literature Review / 2017-2018

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CORONARY ARTERY DISEASE (CAD)

1. Percutaneous coronary intervention in stable angina (ORBITA): A double-blind, randomised controlled trial

ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina) is a blinded; multicenter randomized (1:1) trial of percutaneous coronary intervention (PCI) vs. a placebo procedure for angina relief that was done at five (5) centers in the UK. All patients had severe (≥70%) stenosis in a major epicardial coronary artery and underwent an intensive 6-week medication optimization period, including up-titration from about 1 to 3 medications, with multiple weekly physician consultations. Afterwards they were randomized in the catheterization laboratory to PCI or a sham procedure. The study showed that there was no significant difference on the primary endpoint, incremental improvement in exercise treadmill time (PCI, 28s; sham surgery, 12s). Groups also did not differ in improvements in time to 1-mm ST depression, peak oxygen uptake, Seattle Angina Questionnaire physical function or angina frequency, and quality-of-life score. PCI was associated with a small, significantly greater improvement in ischemia, as measured by wall-motion index score on Dobutamine stress echocardiography (difference,–0.09). This study emphasizes the importance of optimum anti-anginal medication, which should continue to be the first-line therapy. As the authors note, the findings do not imply that patients should never undergo PCI for stable angina and do not apply to acute coronary syndromes (ACS), for which PCI has well-proven benefits. Al-Lamee R et al. *Lancet* 2018;391:31-40. doi: 10.1016/S0140-6736(17)32714-9. Epub 2017 Nov 2.

2. PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock

Culprit-Shock (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) is a multicenter randomized trial in which 706 patients who had multivessel disease (MVD), acute myocardial infarction (AMI), and cardiogenic shock randomly assigned to one of two initial revascularization strategies: percutaneous coronary intervention (PCI) of the culprit lesion only, with the option of staged revascularization of non-culprit lesions, or immediate MV PCI. The trial showed a significant clinical benefit of a culprit-lesion-only strategy with a reduction in the primary end point of 30-day mortality or severe renal failure requiring renal replacement therapy (45.9% culprit-lesion-only PCI vs. 55.4% immediate MV PCI group; p=0.01), which was driven mainly by an absolute 8.2% reduction in 30-day mortality (43.3% versus 51.5%; p=0.03). However, the time to hemodynamic stabilization, the risk of catecholamine therapy and the duration of such therapy, the levels of troponin T and creatine kinase (CK), and the rates of bleeding and stroke did not differ significantly between the two groups. Holger Thiele et al. *N Engl J Med* 2017; 377:2419-2432. doi: 10.1056/NEJMoa1710261. Epub 2017 Oct 30.

3. Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial

The Double Kissing (DK) Crush planned 2-stent technique has been shown to improve clinical outcomes in non-LM bifurcations compared with Provisional Stenting (PS) and in Left Main (LM) bifurcations compared with Culotte stenting technique, but has never been compared with PS in LM bifurcation lesions. In this multicenter (26 centers in 5 countries) randomized trial, percutaneous coronary intervention (PCI) of true distal LM bifurcation lesions (Medina 1.1.1 or 0.1.1) using a planned DK crush 2-stent strategy resulted in a lower rate of target lesion failure (TLF) at 1 year than the PS strategy (5,0% vs. 10.7%, p=0.02). Compared with PS, DK crush also resulted in lower rates of target vessel myocardial infarction (2.9% vs. 0.4%; p=0.03) and definite or probable stent thrombosis (3.3% vs. 0.4%; p=0.02). Clinically driven target lesion revascularization (7.9% vs. 3.8%; p=0.06) and angiographic restenosis within the LM complex (14.6% vs. 7.1%; p=0.10) also tended to be less frequent with DK crush compared with PS. However we must point out that there was no significant difference in cardiac death between the groups. Chen SL, et al. *J Am Coll Cardiol* 2017;70:2605-2617. doi: 10.1016/j.jacc.2017.09.1066. Epub 2017 Oct 30.

STRUCTURAL HEART DISEASE (SHD)

1. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients

SURTAVI (SUrgical Replacement and Transcatheter Aortic Valve Implantation) is a multicenter (26 centers in 5 countries)

randomized trial, which by using Bayesian analytical methods (with a margin of 0.07), among 1746 severe AS patients at intermediate surgical risk (Society of Thoracic Surgeons Predicted Risk of Mortality, 4.5±1.6%) showed that Transcatheter Aortic-Valve Replacement (TAVR) by using the self-expanding device of Medtronic is non-inferior to SAVR, confirming earlier results with the balloon-expandable device of Edwards in PARTNER 2A study. Moreover, surgery was associated with higher rates of acute kidney injury (AKI), atrial fibrillation (AF), and transfusion requirements, whereas TAVR had higher rates of residual aortic regurgitation (AR) and need for pacemaker implantation (PPI). A limitation of the study was the absence of long-term follow-up since a 24-month end-point analysis provides incomplete information about the life cycle of TAVR versus surgical bio-prostheses and that the trial was totally funded by Medtronic. However, the findings of this and PARTNER 2A studies will likely lead to an FDA indication for TAVR in intermediate surgical risk patient population. Reardon MJ et al. *N Engl J Med* 2017;376:1321-1331. doi: 10.1056/NEJMoa1700456. Epub 2017 Mar 17.

2. In-hospital outcomes of transcatheter (TAVR) versus surgical aortic valve replacement (SAVR) in end stage renal disease (ESRD)

In this propensity matched analysis of End Stage Renal Disease (ESRD) patients on hemodialysis (HD) coming from National Inpatient Sample (NIS) undergoing Transcatheter Aortic-Valve Replacement (TAVR) (n=328) or surgery (SAVR) (n=697) between 2012 and 2014 was shown that regardless the treatment modality, patients with AS on HD have high in-hospital mortality. TAVR and SAVR have comparable in-hospital mortality rate however, TAVR was associated with shorter length of stay (LOS) (8 vs. 14 days, p<0.001), lower hospitalization cost ($276,448 vs. $364,280, p=0.01), lower in-hospital complications (60.6% vs. 76%, p=0.003), and higher rate of home discharge (31.4% vs. 17.7%, p=0.004) vs. SAVR. Alkhalil A, et al. *Catheter Cardiovasc Interv* 2018;92:757-765. doi: 10.1002/ccd.27433. Epub 2017 Nov 24.

3. Outcomes With Transcatheter Mitral Valve Repair in the United States: An STS/ACC TVT Registry Report

This is an analysis of the commercial experience in the United States (US) regarding the transcatheter mitral valve repair (TMVR) treatment of mitral regurgitation (MR). The study population consisted of 2,952 patients treated at 145 Centers between November 2013 and September 2015. In 1,867 patients, data were linked to patient-specific Centers for Medicare and Medicaid Services administrative claims for analyses. The acute procedure success was 91.8%. Among the patients with Centers for Medicare and Medicaid Services linkage data, the mortality at 30 days and at 1 year was 5.2% and 25.8%, respectively, and repeat hospitalization for heart failure (HF) at 1 year occurred in 20.2%. Variables associated with mortality or re-hospitalization for HF after multivariate adjustment were: increasing age, lower baseline left ventricular ejection fraction (LVEF), worse post-procedural MR, moderate or severe lung disease, dialysis, and severe tricuspid regurgitation. These findings demonstrate that commercial TMVR is effective and safe procedure. Additionally it may help to determine which patients have favorable long-term outcomes with this therapy. Sorajja P, et al. *J Am Coll Cardiol* 2017;70:2315-2327.doi: 10.1016/j.jacc.2017.09.015.

4. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke

The RESPECT trial is a multicenter, randomized, open-label blinded trial, which enrolled 980 adult patients (between ages 18 and 60 years old) with cryptogenic ischemic stroke (CIS). It was shown that Patent Foramen Ovale (PFO) closure with the Amplatzer PFO Occluder is superior to medical management (aspirin, warfarin, clopidogrel, or aspirin combined with extended-release dipyridamole) in reducing recurrent strokes in patients with presumed CIS and evidence of a PFO on long-term follow-up (>5 years). These results are similar to those noted in the REDUCE and CLOSE trials. An interesting observation was that nearly one third of strokes thought to be cryptogenic likely had another underlying mechanism. In addition, venous thromboembolism (which comprised events of pulmonary embolism and deep-vein thrombosis) was more common in the PFO closure group than in the medical-therapy group. Therefore, according to FDA a strong collaboration between neurologists and cardiologists is required to exclude other causes of strokes. Saver JL et al, for the RESPECT Investigators* *N Engl J Med* 2017;377:1022-1032. doi: 10.1056/NEJMoa1610057.

HEART FAILURE

1. CASTLE-AF: Catheter Ablation vs. Conventional Therapy For Patients With AFib and LV Dysfunction

This trial included 397 patients with symptomatic paroxysmal or persistent atrial fibrillation (AF) and a left ventricular ejection fraction (LVEF) of ≤35% who were randomized to receive radiofrequency catheter ablation or conventional medical treatment. Moreover, all patients had NYHA class II, III, or IV heart failure (HF) and an implantable cardioverter defibrillator (ICD) with Home Monitoring capability. Results showed the composite of all-cause mortality and unplanned hospitalization for worsening HF (primary endpoint) was significantly lower in the ablation group (28.5%) compared to the control group (44.6%) over a median follow-up period of 37.8 months. However, there are certain limitations: (1) The quality of the rate control in the pharmacological group has not been published and there were still active attempts to maintain sinus rhythm in this group. (2) AV nodal ablation was rarely used in CASTLE-AF study. Indeed at 5 years, 20% of the patients randomized to pharmacological rate control were still in sinus rhythm and only 56% had persistent AF. (3) There were potentially significant

differences in patient characteristics between the groups, with a greater incidence of diabetes and ischemic cardiomyopathy. In addition, patients with an LVEF <25% appeared to have no benefit from ablation. Therefore, AF ablation seems to be beneficial in a highly selected group of patients with AF and severe HF in whom antiarrhythmic drugs are not tolerated or ineffective. We expect the results from CABANA and EAST AFNET 4 trial for further details in this interesting topic. Nassir F. Marrouche, MD (PI). CASTLE-AF trial presented on Aug. 27 at the ESC Congress 2017 in Barcelona.

ATRIAL FIBRILLATION

1. 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Non-valvular Atrial Fibrillation: A Report of the American College of Cardiology Clinical Expert Consensus Document Task Force

This is an expert consensus document, which assists clinicians to quickly and effectively decide which peri-procedural management of anticoagulation for patients with non-valvular atrial fibrillation (NVAF) are appropriate. The following key points are important:

- When considering if interrupting anticoagulation is necessary, clinicians should consider the type of oral anticoagulant (vitamin K antagonists [VKAs] with a long half-life vs. direct oral anticoagulants [DOACs] with a shorter half-life), the patient's bleeding risk, the procedural bleeding risk, and any additional clinical information.
- Some procedures (e.g., implantation of pacemakers or ICD) have demonstrated lower bleeding risks when VKA therapy is continued uninterrupted rather than interrupted and heparin bridging is administered.
- To assess a patient's risk of bleeding, elements of the HAS-BLED score (hypertension, abnormal liver or renal function, prior stroke, prior major bleeding or anemia, labile INR for VKA patients, age >65 years, concomitant use of antiplatelet agents or nonsteroidal anti-inflammatory drugs) should be assessed along with any recent bleeding events (within 3 months), platelet abnormalities, elevated INR values for VKA patients, and any prior procedural bleeding history.
- Do not interrupt VKA therapy in patients undergoing procedures with no clinically important risk or low risk of bleeding and no patient-related factors that increase bleeding risk.
- When interrupting VKA therapy, the VKA should be stopped 3-4 days prior to procedure (for INR 1.5-1.9), 5 days prior to procedure (for INR 2.0-3.0), or at least 5 days prior to procedure (for INR >3.0). The INR should be re-checked within 24 hours before the procedure.
- Use of bridging parenteral heparin should only be considered in the following two scenarios: (1) VKA-treated patients at high risk of stroke or systemic embolism (>10% per year), including those with a CHA_2DS_2-VASc score of 7-9 or a recent (within 3 months) ischemic stroke, or (2) VKA-treated patients with a prior stroke or systemic embolism (≥3 months previously) who are not at a significant peri-procedural bleeding risk.
- For patients on DOAC therapy who require interruption of anticoagulation therapy pre-procedurally, the number of doses to be held is determined by the estimated creatinine clearance and the procedural bleeding risk. A standard table should be referenced for this decision-making process. Parenteral heparin bridging is not indicated for DOAC-treated patients.
- Before restarting oral anticoagulant therapy, ensure complete hemostasis. Otherwise, VKA therapy can usually be restarted within 24h and parenteral heparin bridging (if indicated) within 24-72h depending on post-procedural bleeding risk. DOAC therapy should not be reinitiated before 24-72h post-procedure without any parenteral heparin bridging based on post-procedure bleeding risk unless the patient cannot tolerate oral therapy.
- DOAC therapy should not be used in patients undergoing mechanical valve replacement. Doherty JU et al. *JACC* 2017;69:871-898. doi: 10.1016/j.jacc.2016.11.024. Epub 2017 Jan 9.

ARTERIAL HYPERTENSION

1. 2017 Guideline for High Blood Pressure in Adults

The new guidelines is the first comprehensive set since 2003 that addresses a broad spectrum of topics, including BP measurement, secondary hypertension, and managing hypertension in patients with comorbidities. But the big changes – heavily influenced by results of the SPRINT study – are:

1. Newly defined categories are:
   - Elevated blood pressure (BP) (systolic BP 120–129mmHg and diastolic BP <80mmHg)
   - Stage 1 hypertension (systolic BP 130–139mmHg or diastolic BP 80–89mmHg)
   - Stage 2 hypertension (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg)
2. For people with elevated BP, lifestyle modification is recommended.
3. For people with stage 1 hypertension who have known atherosclerotic cardiovascular disease (CVD) or 10-year cardiovascular risk ≥10% (according to the ACC/AHA calculator, which also is used for cholesterol management), both lifestyle modification and drug therapy are recommended. Stage 1 patients with <10% 10-year risk should pursue lifestyle modification only.
4. All people with Stage 2 hypertension should receive medication (in addition to lifestyle modification).
5. The treatment goal for everyone is <130/80 mmHg.

http://www.acc.org/latest-in-cardiology/articles/2017/11/08/11/47/mon-5pm-bp-guideline-aha-2017.