

# 69th Annual Conference of the Cardiological Society of India (CSI 2017)

## REMOTE HEMODYNAMIC MONITORING IN AMBULATORY HEART FAILURE

Dr Joy M Thomas, Chennai

- Ambulatory heart failure (HF) patients constitute Heart Failure Groups I and II and Class A, B and C. They may be on conventional standard management, may have a device implanted, had an left ventricular assist device (LVAD) implanted or be a heart transplant recipient. Any of these categories are benefited if we are able to predict when they will be heading for a hospitalization.
- The hemodynamic parameters that we should look at include left atrial pressure, autonomic adaptation in the form of heart rate and vagal nerve activity, fluid accumulation by thoracic impedance and body weight increase.
- These parameters can be measured with remote monitoring devices and acted upon to treat and delay or avoid the oncoming hospitalization.
- These devices have been tested in clinical trials: COMPASS HF, TELE HF, TIMI HF, HOMEOSTASIS and CHAMPION.
- In monitoring patients with LVADs, there is difficulty in assessing the parameters because of continuous flow devices compared to the natural pulsatile flow that has been seen all along in native hearts. Compromises have been made by assessing Doppler derived pressures whose accuracy is questionable and less than desirable.
- Newer monitoring devices use integrated flow probes that, by a feedback mechanism, are able to control the output monitor data as well.
- Newer challenges will be to create “smart pumps” that are able to integrate right ventricular pressures, filling and flow; and to integrate them with left ventricular functions will be the monitoring device of the future with artificial intelligence thrown in.

## AN UPDATE ON HYPERTENSION TREATMENT

Dr PK Biswas, Kolkata

- High blood pressure (BP) is the single largest risk factor for disease burden worldwide.<sup>1</sup>

- In India, high BP has emerged as a leading risk factor for mortality.<sup>1</sup>
- It is predicted that the burden of hypertension in India is expected to almost double from 118 million in 2000 to 213.5 million by 2025.<sup>2</sup>
- The 2017 clinical practice guidelines on hypertension recommend non-pharmacological interventions as the treatment of choice for adults with stage 1 hypertension but otherwise at low risk of atherosclerotic cardiovascular disease (ASCVD).<sup>3</sup>
- Antihypertensive drug therapy along with non-pharmacological therapy is recommended for adults with stage 1 hypertension at a high risk for ASCVD.<sup>3</sup>
- The 2017 treatment guidelines suggest a diuretic, angiotensin-converting enzyme inhibitor (ACEI), angiotensin II receptor blocker (ARB) or calcium channel blocker (CCB) as acceptable first stage agents, but identifies thiazide diuretics and CCBs as good options for monotherapy.<sup>3</sup>
- In spite of various effective treatments of hypertension being available, novel therapies are required to reduce the elevated BP, improve BP control, treat resistant hypertension and reduce the associated cardiovascular (CV) risk factors.
- Azilsartan is a new ARB with better clinical BP-lowering effects compared to other ARBs with good tolerance.<sup>4</sup>

**References:** <sup>1</sup>Roy A, et al. *BMJ Open*. 2017;7(7):e015639. <sup>2</sup>Kearney PM. *Lancet*. 2005;365(9455):217-23. <sup>3</sup>Whelton PK. *JAMA*. Nov 20 2017. <sup>4</sup>Shetty M, et al. *Int J Contemp Med Res*. 2017;4(6):1262-4.

## PCSK9 INHIBITORS AS ADD-ON TO STATINS: EVIDENCE BASE FOR CURRENT CLINICAL UTILITY

Prof Dr PC Manoria, Bhopal

- PCSK9 is a new validated target for lipid management. PCSK9 is an enzyme expressed in the liver and produces lysosomal degradation of low-density lipoprotein cholesterol (LDL-C) receptors, which are the prime pathway for hepatic clearance of LDL-C from the blood. PCSK9 inhibition will

therefore decrease LDL-C and atherogenicity. Two fully humanized monoclonal antibodies against PCSK9 (evolocumab and aliorcumab) have been approved for clinical use and they have consistently decreased LDL-C by 40-60% in various trials. They have a favorable effect on other lipoproteins also and interestingly they also decrease lipoprotein(a) [Lp(a)] by ~25%. Evolocumab is given as 1 mL subcutaneous (SC) injection 140 mg biweekly or 420 mg monthly. Aliorcumab is used in doses 75 mg biweekly or 150 mg monthly. Bococizumab trials SPIRE I and II have been prematurely terminated because of neutralizing antibodies, but the later trial had shown reduction in CV events by 21%.

- The landmark secondary prevention FOURIER trial with evolocumab released in 2017 has passed on three unprecedented big messages: It has evoked a new concept of super low LDL i.e., 25 mg/dL never heard before; evolocumab has incredible safety; evolocumab showed incremental benefit on top of statins.
- There was an incremental 15% reduction in the primary efficacy endpoint of CV death, myocardial infarction (MI), stroke and hospitalization for unstable angina or coronary revascularization and a 20% reduction in secondary efficacy endpoint of CV death, MI or stroke. All subsets of patients benefited. The curves were divergent so that number needed to treat (NNT) at 1 year was 74 and at 2 years it dropped to 50. It seems that if the trial was followed for a longer period of time, the benefit would have increased further.
- PCSK9 monoclonal antibodies have emerged as a new star on the horizon of lipid management. They are indicated in three subsets of patients: Patients with ASCVD not achieving LDL-C goals, familial hypercholesterolemia, statin intolerance.
- As per WHO, dyslipidemia accounts for 50% of all CV events. We know from CTT meta-analysis that high-intensity statin therapy decreases LDL-C by 1 mmol and this translates into reduction of CV events by 20-24%. PCSK9 inhibitors decrease LDL-C by additional 1 mmol and they will decrease CV events by another 20%. Thus, when used together, they will decrease CV events by 40-45% and we will be able to minimize lipid atherogenicity to very great extent. Thus, after witnessing the statin era for last 30 years, we are now heading for another revolution after statin therapy.

## SURGICAL OPTIONS FOR HOCM

Dr Ganeshkrishnan Iyer, Bengaluru

- Septal myectomy is the gold standard, where expertise is available.
- Septal myectomy has better long-term benefits.
- Alcohol septal ablation is an alternative for patients who are poor surgical candidates.

## IV IRON, NOT ORAL, IMPROVES FUNCTIONAL CAPACITY IN HF PATIENTS

Dr Puneet Rastogi, Gwalior

Last year, two new studies testing iron supplementation in patients with HF yielded opposite findings. The two studies - IRONOUT with oral iron and EFFECT-HF with IV ferric carboxymaltose - evaluated similar endpoints. A convenient and easy-to-use oral iron supplement failed to show any improvement in functional capacity and other endpoints, while IV iron complex tested in HF patients with and without anemia significantly improved peak oxygen uptake (VO<sub>2</sub>) when compared with standard of care. Oral iron does not work in patients with HF because it is not adequately absorbed. In addition to EFFECT-HF, two previous studies, FAIR-HF and CONFIRM-HF, have shown that IV iron supplementation can improve 6-minute walk distance and quality-of-life and decrease HF hospitalizations.

## NUCLEAR IMAGING IS PASSÉ: CMR IS THE NEW "GOLD STANDARD"

Dr Johann Christopher, Hyderabad

- Valvular regurgitation can be assessed by multiple imaging modalities.
- 2D Echo is the first-line investigation for valvular regurgitation. It has complex algorithms and significant inter-observer variability.
- Magnetic resonance imaging (MRI) has a very simple algorithm of the regurgitant volume being the difference of the total stroke volume (LV/RV) and the forward volume (AO/PA), both of which are directly measured without any geometric assumptions. MRI scanners are now available across the length and breadth of the country. The scan requires only 1 hour and is extremely cost-effective.
- Cardiac MRI is a noninvasive and nonradiation-based technique. It looks at wall thickness, myocardial perfusion, delayed enhancement and contractile reserve.

- I would consider cardiac MRI as the gold standard for the assessment of valvular regurgitation.

### **CARDIOVASCULAR POLYPILL: RATIONALE, EVIDENCE AND PROGRESS TO DATE**

**Dr Mark Huffman, Chicago**

- Rather than being a panacea for all, polypills represent the most effective and scalable intervention for improving adherence to multidrug therapy for initiation, step-up or substitution indications.
- Polypill trials have been generally designed to demonstrate bioequivalence rather than differences in clinical outcomes; high quality “usual care” seen in trials limits power. Polypills are essential medicines for secondary ASCVD prevention, especially among low adherers, and the growth of polypill suggests an opening of the marketplace for these combinations.

### **CHEMOTHERAPY-INDUCED CARDIAC DYSFUNCTION: HOW TO PREVENT IT?**

**Prof Dr Geetha Subramanian, Varanasi**

- Choose the less cardiotoxic drugs or the less cardiotoxic combinations (including radiotherapy).
- Choose chemotherapy doses with less risk of cardiotoxicity.
- Accumulative dose and the schedule of chemotherapy are important factors for cardiotoxicity.
- Prepare chemotherapy with a lower potential cardiotoxicity effect, for instance in anthracyclines with continuous infusions or altered delivery systems (i.e., Liposomal doxorubicin).
- Try to detect and properly control CV risk factors.
- Start CV treatment with an ACEI (or ARB) and a  $\beta$ -blocker in high-risk patients or in patients with low normal heart function, as well as in patients with a reduced or recovered ejection fraction.
- Dexrazoxane has been shown to prevent LVEF in patients treated with doxorubicin, and should be considered in high-risk patients.

### **HDL AND CVD RISK: THE CURRENT UNDERSTANDING**

**Dr Akshay Mehta, Mumbai**

- Observational studies have shown an inverse relationship between the amount of high-density lipoprotein cholesterol (HDL-C) represented

by its blood level and incidence of coronary heart disease (CHD). This finding (besides the ease of its measurement) has placed HDL-C in the position of an important risk factor.

- However, two streams of information suggest that though it may be epidemiologically related to cardiovascular disease (CVD), it is not causally related. Thus although it is an important risk marker, it may not be a causally related risk factor.
- One is the series of negative therapeutic trials and the other is multiple Mendelian randomization studies, which have shown lack of correlation between levels of HDL-C and incident CHD. In fact, these studies have shown that it is not the ‘amount’ of cholesterol with HDL that is related to CHD incidence but four factors related to the HDL particle that impact the risk of coronary artery disease (CAD) namely, composition, function, size and number of HDL particles.
- Hence future efforts at preventing CHD should concentrate on modifying these aspects of HDL particles, rather than modifying the amount of HDL-C.

### **CONTROVERSIES IN LIPID MANAGEMENT**

**Dr Devendra Prasad Singh, Bhagalpur**

- For decades, statin therapy has been the cornerstone in the management of dyslipidemia. But numerous studies failed to demonstrate a mortality benefit in CVDs.
- In contrast, Mediterranean diet consistently lowers CV events without lowering cholesterol level.
- Framingham studies have shown association of high cholesterol and triglycerides with CVDs. It has been argued that association does not mean causation and many trials show that statins are no good; hence, the controversies.
- Statins are not without side effects; 30% patients taking statins have muscle aches and rarely rhabdomyolysis. Long-term statin therapy causing type 2 diabetes mellitus (T2DM) and dementia, further questions the utility of statin therapy.
- Recent controversy is regarding dosing approach. Fixed-dose-treatment vs. titrating-to-target level - neither of these approaches is inferior.
- CAD is an extremely complex malady. Until the controversies of cholesterol hypothesis vs. alternate mechanism of pathogenesis of atherosclerosis are

settled, statin therapy will stay along with healthy lifestyle, Mediterranean diet and aspirin in the prevention of CVDs.

**MYOCARDIAL INVOLVEMENT IN RHEUMATIC FEVER: DOES IT OCCUR AND WHAT IS ITS RELEVANCE?**

**Prof A George Koshy, Trivandrum**

Traditionally, acute rheumatic fever (ARF) is known to produce pancarditis (endocarditis, myocarditis and pericarditis). Histopathological studies have demonstrated interstitial myocardial infiltrates and Aschoff bodies in ventricular myocardium but significant necrosis is not known to occur. Echocardiographic studies have shown that HF in ARF and carditis is due to endocarditis and consequent mitral and aortic regurgitation. Aortic regurgitation (AR) does not occur in the absence of mitral regurgitation (MR). It is due to a combination of valvulitis, chondritis and annulitis.

The LV systolic function is normal in ARF unlike in viral myocarditis. The left ventricular ejection fraction (LVEF) and shortening fraction are normal. HF and LV dilatation tend to normalize within a short period following valve surgery. Chordal inflammation can lead to lengthening and sometimes rupture leading to prolapse of the anterior mitral leaflet. Chordal rupture can produce flail anterior mitral leaflet and acute severe MR.

High sensitivity cardiac troponins, which are highly sensitive markers of myocardial necrosis, are not significantly elevated in rheumatic carditis. Limited cardiac magnetic resonance studies during the acute phase have also failed to demonstrate significant myocarditis. Studies from South Africa have demonstrated that valve reconstruction and replacement are effective and safe life-saving options in sick children with severe HF following ARF. Clinically significant myocarditis does not occur in acute ARF.

**OPTIMIZING OUTCOMES OF TAVR: ROLE OF IMAGING**

**Dr Partho P Sengupta, USA**

- Ensure patient suitability and selection of device size.
- While computed tomography (CT) remains gold standard, echo can be used for device sizing in selective situation when CT is suboptimal or cannot be done.
- Transthoracic echocardiogram/transesophageal echocardiogram (TTE/TEE) guidance during transcatheter aortic valve replacement (TAVR)

procedures is pivotal for ensuring patient safety and procedure outcomes and follow-up.

**VACCINATIONS IN HF CAN MAKE A LOT OF DIFFERENCE**

**Dr Vitull K Gupta, Punjab**

Vaccination has proved to be one of the most cost-effective disease prevention strategies. Adult vaccination program in India has been at crossroads and is the most ignored area with negligible coverage. Protecting adults by vaccination is yet to be recognized as a preventive strategy in India. HF patients are at increased risk of CV and respiratory related hospitalizations compared with the general public. Vaccination coverage in HF patients is poor and requires sensitization regarding vaccination efficacy and safety. The evidence to date suggests that vaccination represents a low-cost intervention that may be able to prevent the significant morbidity, mortality and system-wide costs associated with HF. HF patients should receive routine adult immunization to decrease the incidence of vaccine-preventable disease. India needs to immediately address the challenge of adult immunization. In the absence of specific vaccination guidelines or schedule for people with cardiac disorders, adult vaccination must become a part of routine immunization because these vaccines can save millions of lives in India alone, especially in chronic diseases including HF.

**HYPERTENSION DURING PREGNANCY: MECHANISMS AND THERAPEUTIC OPTIONS**

**Dr Vitull K Gupta, Punjab**

- Hypertensive disorders of pregnancy, including pre-eclampsia, complicate up to 10% of pregnancies, constituting one of the greatest causes of maternal and perinatal morbidity and mortality.
- Placenta plays a central role in the pathogenesis of pre-eclampsia. The reduced uteroplacental perfusion, which develops as a result of abnormal cytotrophoblast invasion of spiral arterioles, triggers the cascade of events leading to the maternal disorder. Placental ischemia leads to release of soluble placental factors, many of which are classified as anti-angiogenic or pro-inflammatory. Once these ischemic placental factors reach the maternal circulation, they cause widespread activation and dysfunction of the maternal vascular endothelium that results in enhanced formation of endothelin-1 and superoxide, increased vascular sensitivity to angiotensin II and decreased formation of vasodilators such as nitric oxide.



- Current therapy does not ameliorate the placental pathology nor alter the pathophysiology or natural history of pre-eclampsia. Treatment of hypertension in pregnancy does not cure pre-eclampsia but is intended to prevent cerebral hemorrhage and eclampsia and perhaps delay progression of proteinuria. Delivery is the definitive management and is followed by resolution, generally over a few days but sometimes much longer.
- A team approach, involving obstetrician, midwife, neonatologist, anesthetist and physician provides the best chance of achieving a successful outcome for mother and baby. Regular and ongoing reassessment of both the maternal and fetal condition is required.

### DIFFERENT BLEEDING SCORES: A COMPARISON

Dr U Kaul, New Delhi

Pharmacological treatment for patients with CVD, especially acute coronary syndrome (ACS) has considerably improved during the past years. As most drugs which reduce ischemia by way of preventing thrombosis increase bleeding, a balance needs to be maintained. There are several scores to risk stratify these events. The Bleeding Academic Research Consortium (BARC) bleeding score is one of the consensus documents to maintain uniformity in reporting bleeding events. Models are needed to assess a patient's risk for predicting bleeding as well as ischemic complications to assess therapies.

### WHICH NOAC FOR WHICH PATIENT WITH VTE?

Dr Karthikeyan G, Chennai

Non-vitamin K antagonist oral anticoagulants (NOACs) are better alternatives than traditional anticoagulants in the treatment of venous thromboembolism (VTE). Parenteral anticoagulation can be overlapped with an NOAC instead of warfarin. NOACs are effective in the treatment of acute VTE and prevention of recurrence in the long-term and extended-term. But remember, patients with progressive deep vein thrombosis/pulmonary embolism (DVT/PE) with unstable hemodynamics still require conventional therapy with a heparin/fondaparinux with warfarin.

### RECENT ADVANCES IN LOWER LIMB INTERVENTIONS AND PERIPHERAL BRS TECHNOLOGY

Dr NN Khanna, New Delhi

- The superficial femoral artery (SFA) is a challenging artery to treat. Key developments in SFA intervention range from percutaneous transluminal angioplasty (PTA), atherectomy, stent/stent grafts to drug-eluting stents (DES) and drug-coated balloons.
- Indications for stenting include: > Fontaine IIB claudication, non-healing ulcer, limb salvage in cases of impending gangrene.
- Alternative technologies/devices for femoropopliteal artery intervention include covered stent, DES, cryoplasty, excimer laser angioplasty, atherectomy.
- Some trials involving different SFA endovascular therapies include RESILIENT, DURABILITY, ZILVER PTX, IN.PACT SFA, LEVANT 2, DEFINITIVE LE.
- A stent with interwoven nitinol design that is self-expanding and has high radial force and flexibility, can be used for calcified SFA lesions. Stem cell therapy is an emerging treatment modality for management of critical limb ischemia (CLI) in cases where revascularization is not possible.
- Lithoplasty for treatment of calcified SFA/popliteal disease was studied in DISRUPT PAD trial. Potential benefits of bioresorbable scaffolds (BRS) include absence of rigid metallic cage, late lumen enlargement and restoration of vasomotor tone.
- Limitations of first-generation BRS include lower modulus leading to higher recoil, lower yield strength and lower tensile strength leading to increased susceptibility to fractures. Next-generation BRS is designed to improve on all these aspects, with reduced strut thickness.
- Drug-eluting balloon (DEB) efficacy has been proven in short (<9-10 cm) noncalcified *de novo* lesions. DEB could be the first-line strategy for Trans-Atlantic Inter-Society Consensus (TASC) A, B and C *de novo* lesions. For long lesions, the combination of atherectomy and DEB could be a good option.
- Newer percutaneous treatment options are associated with much lower procedural complications and good long-term outcomes.

