

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

## LATEST 2017 HYPERTENSION GUIDELINES

Dr C Venkata S Ram, Australia

- ⦿ The new definition of HT given by AHA/ACC is BP >130/80 mmHg.
- ⦿ Anyone with BP >130/80 mmHg is now considered as having HT.
- ⦿ There is lot of evidence to suggest that any BP >130/80 mmHg can be detrimental to health.
- ⦿ So, the gold standard for HT diagnosis is not 140/90 but 130/80 mmHg. This applies to all age groups and comorbidities.
- ⦿ People with BP >130/80 mmHg should be counseled for lifestyle changes and then, drug treatment. So, the new cut-off between normal and high BP is 130/80 and not 140/90 mmHg.
- ⦿  $\beta$  blockers are now rated as “secondary” drugs for HT, not primary.
- ⦿ First-line drugs for HT are diuretics, CCBs, ACEIs and ARBs.
- ⦿ Among the diuretics, the preferred choice is chlorthalidone, not HCTZ or indapamide.
- ⦿ The new guidelines will change the way medicine will be practiced from now on. The BP should be 130/80 mmHg or lower (*New Recommendation*).

### 5 main points to be emphasized in the new guideline

- ⦿ A strong emphasis on BP measurement.
- ⦿ A new BP classification system.
- ⦿ A new approach to decision making for treatment that incorporates the underlying CV risk.
- ⦿ Lower targets for BP during HT management.
- ⦿ Strategies to improve BP control during treatment with an emphasis on lifestyle approaches.

## CHANGING INDICATIONS OF TAVR

Dr Ashok Seth, New Delhi

*“My daily dilemma is not, which patient should have TAVR but who should have a surgical AVR and why?”*

—Thomas Modine

- ⦿ Expanding indications for TAVR: Intermediate to low risk patients, bicuspid aortic valve, degenerating surgical bioprosthetic valves and AR.
- ⦿ In elderly patients >75 years of age, TAVI is superior to medical therapy in extreme risk patients, noninferior or superior to surgery in high risk patients and noninferior or even superior to surgery when transfemoral access is possible in intermediate risk patients (*2017 ESC/EACTS guidelines for the management of valvular heart disease*).
- ⦿ In patients with severe aortic stenosis at intermediate surgical risk, TAVR was a noninferior alternative to surgery (*N Engl J Med. 2017;376(14):1321-31*).

## NSTEMI ACS MANAGEMENT

Prof Dr Saumitra Ray, Kolkata

- ⦿ All NSTEMI ACS are not the same.
- ⦿ Early risk stratification should guide initial management.
- ⦿ In high or moderate risk patients, early invasive management is useful.
- ⦿ Low risk patients should be treated conservatively with close watch.
- ⦿ DAPT for at least 1 year is the dictum unless very high bleeding risk.
- ⦿ High dose statin is useful.
- ⦿ Total revascularization should be the aim, as opposed to STEMI.

## ACEI REMAINS THE “GOLD STANDARD”

Dr PK Deb, Kolkata

- ⦿ ARB was introduced in 1990 for treatment of HT and subsequently used for HFrEF.
- ⦿ As compared to ACEI, ARBs were not found to be superior in reducing all-cause mortality or HF hospitalizations in symptomatic HF (*JACC. 2002;39(3):463*).
- ⦿ In 2004, controversy surfaced with the reports that ARBs may increase MI and patients need to be told about this (ARB-MI Paradox). A flow of

controversial editorials continued to question the safety of ARBs.

- Patients intolerant to ACEI due to hyperkalemia, worsening of renal function or hypotension may have a similar response to ARB also.
- The PARADIGM study in 2014 introduced angiotensin-neprilysin inhibition, following a fast track mechanism: 2014-study published, 2015: FDA approval, 2016: Guidelines updated to include ARNI.
- Questions were raised on the PARADIGM study about the rationale of combining an ARB with a neprilysin inhibitor and not with an ACEI; why was neprilysin inhibitor not used alone; the study design; why was a lower dose of enalapril used in the study; did the impact on efficacy of LCZ696 depend on the patient's baseline characteristics; effect on renal impairment and the efficacy of LCZ696 on changes in BP and types of HF. The cost-effectiveness and the sponsorship bias also came under scrutiny.
- As per ESC 2016 recommendations, ACEI, MRAs and  $\beta$  blockers continue to be standard of care in HF management. Sacubitril/valsartan is recommended as a replacement and not as first-line therapy.
- The 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for HF recommend substituting ACEI/ARB with ARNI. Addition of ACEI with LCZ696 would have been a scientific compulsion, but addition of valsartan with LCZ696 is a sponsor's compulsion. It can be easily concluded that ACEI is the corner stone of HF therapy and is still the Gold Standard.

### CSI POSITION STATEMENT ON MANAGEMENT OF HF IN INDIA 2017

Dr Santanu Guha, Kolkata

- HF presents about a decade earlier in India, most of the burden is <65 years.
- The commonest etiology is CAD followed by idiopathic dilated cardiomyopathy. RHD still contributes 10% of the disease burden.
- There is a need for a statement on HF as it is emerging as an important public health problem in India.
- The purpose of CSI position statement on HF is to provide a single document for the whole country which provides the latest available data from India and also serves as a reference regarding the latest

clinical literature. It is recommendary in nature and carries no statutory status.

- The CSI position statement recommends nonpharmacological therapy including lifestyle modifications, exercise rehabilitation and vaccination.
- The natriuretic peptides represent the gold standard biomarkers in HF. BNP or NT-proBNP "guided therapy" is not routinely recommended in India.
- Pharmacological management of chronic HFrEF recommends ACEI/ARB/ARNI, BB, MRA in all patients; diuretics in symptomatic patients and use of hydralazine, ivabradine and digoxin as complementary.
- Statins are not recommended to be initiated, unless the patient is already on statin. Carnitine/CoQ/ intermittent inotropes/CCB-verapamil/diltiazem are not to be used. All patients with prior or current symptoms of HFrEF regardless of aetiology should be started on ACEI, unless contraindicated.
- Replacement of ACEI with ARNI should be considered in patients who remain symptomatic despite optimal therapy with an ACEI,  $\beta$ -blocker and MRA. In patients who are tolerating ACEI (or ARB) well, replacement by ARNI may be considered on an individual basis.
- Use of  $\beta$  blockers (bisoprolol, metoprolol succinate extended release or carvedilol) is recommended for all patients with current/prior symptoms of HFrEF in absence of contraindications.
- Patients with prior or current symptoms of chronic HFrEF who are intolerant to ACEI (due to cough) are candidates for ARBs.
- $\beta$  blockers and ACEIs can be initiated together as soon as the diagnosis of HFrEF is made.
- Diuretics should be used in HFrEF patients who have evidence of fluid retention and are usually combined with an ACEI (or ARB),  $\beta$ -blocker and MRAs.
- Ivabradine can be considered for symptomatic HF patients who are in sinus rhythm and have resting HR >70 bpm despite maximally tolerated doses of BB, ACEI (ARB) and MRA. Optimal use of device therapy in our country will require better risk stratification methods or lowering of initial device cost.
- Surgery for HF comprises of mitral valve reconstruction, external support, myocyte restoration and replacement, ventricle restoration,

revascularization, mechanical support and heart transplantation.

- CRT can be considered for patient with LVEF <35% and are undergoing placement of a new or replacement pacemaker implantation. It should not be considered in patients whose comorbidities limit expected survival to <1 year; HF with non-LBBB pattern with QRS <150 ms.
- Preventing or delaying onset of HF is a feasible task and should be a priority for our country because of cost-effectiveness. It can be achieved either by targeting those at high risk or promoting healthy lifestyle for entire population.

### WHAT'S TRENDING IN THE MANAGEMENT OF HF IN 2017?

**Dr Ramachandra Barik, Hyderabad**

- The burden of heart failure (HF) in India appears to be high. A conservative estimation of the prevalence of HF in India due to CHD, HT, obesity, diabetes and rheumatic heart disease ranges from 1.3 to 4.6 million, with an annual incidence of 491,600 to 1.8 million.<sup>1</sup>
- There is a need to include new therapies which complement established pharmacological and device-based therapies in the treatment of patients with HF.
- The ACC, the AHA and the Heart Failure Society of America have updated treatment guidelines to incorporate two new pharmacological therapies for HFrEF: Sacubitril-valsartan and ivabradine.<sup>2</sup>
- The guidelines recommend that in patients with chronic symptomatic HFrEF NYHA Class II or III who tolerate an ACEI or ARB, replacement by ARNI (valsartan/sacubitril) will further reduce morbidity and mortality.<sup>2</sup>
- ARNI has shown to reduce the composite endpoint of CV death or HF hospitalization in an RCT comparing the first approved ARNI (valsartan/sacubitril) with enalapril in symptomatic patients with HFrEF tolerating an adequate dose of either ACEI or ARB.<sup>2</sup>
- Focused update on clinical guidelines recommend that ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA Class II-III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDEH, including a β-blocker at maximum tolerated dose and who are in sinus rhythm with a heart rate ≥70 bpm at rest.<sup>2</sup>

○ Ivabradine is a new therapeutic agent that selectively inhibits the I<sub>t</sub> current in the sinoatrial node, providing heart rate reduction.<sup>2</sup>

○ The QUALIFY international registry has also shown that good adherence to pharmacologic treatment guidelines for ACEIs, ARBs, BBs, MRAs and ivabradine, with prescription of at least 50% of recommended dosages was associated with better clinical outcomes during the 5-month follow-up.

○ Continuing global educational initiatives are imperative to emphasize and ensure the implementation of guidelines to optimize drug therapy and prescribing evidence-based doses in clinical practice.

**References:** <sup>1</sup>Huffman MD, et al. Natl Med J India. 2010;23(5):283-8. <sup>2</sup>Yancy et al. Circulation. 2016;134:e282-e293. <sup>3</sup>Komadja M, et al. Eur J Heart Failure. 2017;19(11):1414-23.

### ARNI AS FIRST-LINE THERAPY IN THE MANAGEMENT OF HEART FAILURE

**Dr Bhagirath Raghuraman, Bengaluru**

- Augmentation of the natriuretic peptide systems is a novel approach in the management of HF and a new paradigm in neurohormonal modulation for HFrEF.
- LCZ696 (Sacubitril+Valsartan) is a first in class ARNI, which simultaneously inhibits neprilysin and blocks AT1 receptor.
- Sacubitril, a prodrug inhibits neprilysin → ↑ natriuretic peptide, while valsartan causes direct antagonism of AT II receptors → vasoconstriction, smooth muscle cell proliferation and decreased renal BF.
- ARNI should be prescribed in adult patients with systolic HF, patients with NYHA Class II-IV, LVEF <40% on β-blocker and MRA, eGFR >30 mL/min/1.73 m<sup>2</sup>, SBP >100 mmHg, serum potassium ≤5.2 mmol/L. ARNI should be initiated 36 hours after stopping ACEI, at a dose of 50 mg b.i.d. and doubling the dose every 2-4 weeks till 100 mg b.i.d. is reached. β blockers, MRAs, ivabradine and digoxin can be continued with ARNI, with devices as appropriate. While on ARNI, the patients should be monitored for renal function and serum K. Do not uptitrate if BP >100. BNP is not useful for monitoring as ARNI increases its level.
- ARNI is contraindicated in patients with hypersensitivity to any component, history of angioedema related to previous ACEI or ARB therapy,

along with ACEIs or concomitantly with aliskiren in patients with diabetes. In PARADIGM-HF, LCZ696 was found to be superior to enalapril in patients with HFrEF. LCZ696 also reduced hospitalization risk for HF by 21% ( $p < 0.001$ ) and decreased symptoms and limitations of HF ( $p = 0.001$ ).

- The 2016 ACC/AHA/HFSA focused update recommend ARNI along with a BB and MRA as therapy of patients with HFrEF. The guidelines also recommend that ARNI should replace ACEIs when stable patients with mild-to-moderate HF on these therapies have adequate BP and are tolerating these therapies well.

### HCM: EPIDEMIOLOGY, GENETICS AND RISK STRATIFICATION

Dr Ajay Bahl, Chandigarh

- Hypertrophic cardiomyopathy (HCM) is a common inherited cardiac disorder caused by mutations in cardiac sarcomeric genes.
- Mutations are most commonly found in genes encoding myosin heavy chain (MYH7) and myosin-binding protein C (MyBPC3).
- HCM is the commonest cause of sudden death in young individuals. Sudden death may be the first presentation of HCM.
- Screening of first-degree relatives of the patient should be advised.
- Family screening may be either clinical, ECG and echocardiography based or by genotyping in case a mutation is identified in the proband.
- Risk stratification for sudden death is important since patients at high risk of sudden death may be offered ICD implantation.

### MANAGEMENT ISSUES IN PATIENTS REQUIRING ANTIPLATELETS AND ANTICOAGULATION

Dr Suresh K, Trivandrum

**A 74-year-old diabetic gentleman with fracture hip and positive dobutamine stress echo**

- Hip fracture obviously needs urgent or semiurgent hip surgery.
- Proper preoperative cardiac risk assessment using conventional risk scoring systems helps in planning appropriate management strategy.
- Dobutamine stress echo (DSE) indicates presence of CAD.

- Post-surgical probability of a cardiac event is low even if DSE is positive. If DSE shows high risk features indicative of multivessel/LMCA/proximal LAD disease or large areas of myocardium in jeopardy, consider invasive coronary evaluation and even urgent preop coronary revascularization.
- In general, there is no role for routine prophylactic coronary angiography (CAG) or revascularization in stable CAD awaiting noncardiac surgery. In subjects at risk of, or with proven IHD, aspirin nonadherence/withdrawal triples the risk of MACE.
- DVT prophylaxis following the hip surgery - 28-35 days of added anticoagulants - NOACs have an edge over heparin/VKA.

### PTCA OR CABG IN DIABETES MELLITUS

Prof Sundeep Mishra, New Delhi

- Several pathophysiological factors confer high risk after revascularization.
- Trials reveal higher MACE after revascularization with PCI compared with CABG in patients with triple vessel disease.
- Most of this higher MACE is associated with increased requirement of repeat procedure with PCI.
- However, this risk may not hold true for single vessel disease or with latest generation of stents.
- The risks of death and target vessel MI with PCI are particularly high in insulin-dependent patients with diabetes.
- Even risk of stent thrombosis is higher in these patients.
- In patients with high surgical risk, PCI still remains an option.
- Newer antiplatelets are better than clopidogrel in patients with diabetes.

### HOW CAN WE IN INDIA ADOPT THESE LATEST GUIDELINES

Dr Gurpreet S Wander, Ludhiana

- The term 'prehypertension' used in JNC 7 was not adopted by anyone else and also in Indian guidelines.
- JNC 8 (2014) threshold and targets higher for age >60 was widely criticized.
- Issue of AOBP is important since devices are expensive. The definition and classification of HT does not need to be changed.

- Longevity in India is less than in US and same targets cannot be applied for the frail old individuals.
- Physicians should be oriented towards reducing risk in high risk individuals.
- Two latest guidelines have reacted less strongly to the SPRINT trial than the ACC/AHA. We possibly need to follow this approach.

### DIGOXIN IN HEART FAILURE: “KABHI HAAN, KABHI NAA”

Dr Nagaraj Desai, Mysuru

- Use of digoxin, in some contemporary clinical practices, is rapidly dwindling.
- There are no major studies to reassess the readmission rates, a major issue in current HF practice.
- It may be used in selected individuals only as add-on therapy albeit with well-known caveats like its narrow therapeutic window.
- A typical example may be a patient of systolic HF in AF with faster heart rate who is not responding adequately despite routine guideline directed therapies including RAAS modulators and  $\beta$  blockers.

### ANTIPLATELETS AND ANTICOAGULANTS IN NSTEMI-TOO MUCH CONFUSION: WHICH ONES SHOULD I CHOOSE?

Dr Smit Shrivastava, Kanpur

- Aspirin is for all patients. Loading dose is 162-325 mg of uncoated aspirin; the first tablet should be chewed or crushed to establish a high blood level quickly, should be given as soon as possible to any patient with NSTEMI, irrespective of treatment strategy. There is no evidence that higher doses are more effective and they may lead to greater gastric irritation. Aspirin (75-100 mg o.d.) should be continued indefinitely for secondary prevention.
- P2Y12 inhibitors for all patients. All NSTEMI patients should be treated with a P2Y receptor blocker and aspirin. Timing of administration depends on the choice between invasive or ischemia-guided management strategies. *For invasive strategy:* Ticagrelor 180 mg loading dose is recommended. For patients in whom there is a concern about a need for urgent CABG surgery, the P2Y receptor blocker may be given after diagnostic coronary angiography. If the P2Y receptor blocker is given

after angiography, administer either ticagrelor 180 mg or prasugrel 60 mg. *For ischemia-guided (conservative) strategy:* Ticagrelor 180 mg loading dose is recommended.

- Most patients do not require IV glycoprotein IIb/IIIa inhibitor. Indications for IV glycoprotein IIb/IIIa inhibitor include patients with evidence of ongoing ischemia despite therapy with aspirin + P2Y12 inhibitor for whom invasive approach is planned; and patients who have high-risk features during angiography such as large thrombus burden or intraprocedural thrombotic complication, particularly if they have not received prasugrel or ticagrelor.
- For those patients with a history of GI bleeding, drugs that reduce the risk of recurrent bleeding (e.g., PPIs) should be given.

### PERIPARTUM CARDIOMYOPATHY: CHANGING DEFINITION AND NEWER THERAPIES

Dr Asha Moorthy, Chennai

- Definition of PCPM: Loose definition - Identify more Cases (ESC).
- How common is it? One in 1,500 live pregnancies.
- What are the complications of PPCM? HF, death, arrhythmias, thromboembolism.
- How do we diagnose? ECG, NPs and Echo/CMR or both.
- When to treat PPCM in a lactating mother? Both before and after delivery.
- Natural history of PPCM: High risk of recurrence.
- How to diagnose recurrence of PPCM in a subsequent pregnancy? NPs and Echo.
- What is the role of device therapy in PPCM? Limited role and not before 6 months.

### WHICH NOAC FOR WHICH PATIENT WITH NONVALVULAR AF?

Dr Srinivasa Rao Maddury, Hyderabad

- In clinical trials, non-vitamin K antagonist oral anticoagulants (NOACs) have demonstrated favorable efficacy and safety profiles vs. vitamin K antagonist (VKAs). They are all noninferior to VKA with regards to ischemic stroke and systemic embolization, but superior with regard to preventing systemic bleeding, especially intracranial bleed. They have the advantage of once- or twice-daily dosing and also do not require monitoring of

dosing unlike VKA. But, they differ slightly from each other in their pharmacological properties.

- Rivaroxaban and edoxaban are given once-daily; apixaban and dabigatran given twice-daily. Rivaroxaban needs to be given with food to facilitate gut absorption. Renal clearance for dabigatran is 80%, adaxoban 50%, rivaroxaban 33% and apixaban 25%.
- Dose reductions for NOACs is needed in renal dysfunction. Dabigatran is not recommended with CrCl <30, apixaban <15 mL. Although rivaroxaban and edoxaban are not recommended below CrCl of 15 mL, caution should be exercised if CrCl <30 mL.
- Patients with AF have other comorbidities: HT (70-80%), HF (40%), coronary disease (30%), diabetes (25%); hence they are already taking many pills. If they want to reduce their pill burden, rivaroxaban and edoxaban taken once-daily would be the preferred choices.
- Dabigatran is a prodrug, highly acidic in nature and tends to get activated in GI wall. It produces more GI irritation and may enhance GI bleed in those patients with tendency to GI bleed. So, it may be given with food to minimize the gastric irritation. Dabigatran may not be right choice in these subset of patients.
- Although there is no head-to-head trial comparing different NOACs with each other, from the individual clinical trials with each of the NOAC, dabigatran 150 mg b.i.d. was far superior in preventing ischemic stroke. In RE-LY trial, dabigatran has shown a 34% risk reduction (rivaroxaban and edoxaban 22%, apixaban 22% in ROCKET, ARISTOTEL and ENGAGE AF trials, respectively). Hence, dabigatran may be preferred choice in those who have highest risk ischemic stroke.
- GI absorption of NOACs is influenced by P-glycoprotein(P-gp) in GI tract. Concomitant administration of known P-gp inhibitors e.g., quinidine, verapamil, ketoconazole, cyclosporine, dronedarone, amiodarone and certain macrolide antibiotics influences the plasma levels of NOACs; hence, dose reduction is needed. In the presence of reduced renal function with a NOAC like dabigatran, which has 80% excretion through renal route, a concomitant administration of above drugs is likely to increase plasma levels of dabigatran. Hence, in these situations apixaban which has least renal clearance may be a better choice.

## ONGOING DILEMMAS IN RHD

Dr Vikas Singh, Patna

- Rheumatic heart diseases (RHDs), in spite of having seen a big decline even to the extent of near eradication in some developed countries, is still a major health challenge in our country.
- Involvement of the heart mostly in the form of endocarditis and pericarditis is recognized. Myocardial involvement is missed many times, and requires a careful view in suspected cases.
- Modified Jones Criteria have been the backbone of diagnosis of acute rheumatic fever for decades. But, the availability and advantages of echocardiography cannot be undermined, and it is now a very important tool in the diagnosis and management decisions.
- Leaky valves in adolescents is a cause of concern both for the patient and the treating physicians.
- Reassurance and discussing the natural history with the patient is an important part.
- It is equally important to have a clear idea about the medical management and when to intervene. Most of these conditions can be managed in a fairly nice way at present.

## ACCURATE MEASUREMENT OF BP IS THE KEY TO CONTROL HT

Dr BA Muruganathan, Tamil Nadu

- Accurate measurement of BP, as per protocol, is a must for correct diagnosis.
- Periodic measurement, documentation and follow-up are necessary.
- BP apparatus used for measuring BP should be validated.
- Recent guidelines recommend HBPM as a routine component of BP measurement in most patients with suspected or known HT. HBPM is well-coordinated with organ damage as is the ambulatory BP.
- While ABPM is the current gold standard in the correct diagnosis of HT and/or borderline HT, HBPM should now be considered as an alternative and not complementary, to ABPM for decision making in HT management.
- Doctors must check the BP and whenever required standing BP must be taken and the timing of BP measurement in concordance with medicine to be taken.



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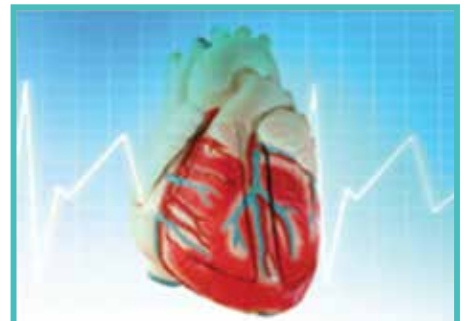
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