



WHEN THE 4 GUIDELINES MEET TO TAKE UP THE SILENT KILLER

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ABSTRACT

Background: The initial step to successfully treat hypertension and prevent cardiovascular event is to follow the evidence based medicine through guidelines.

Methods: We have compared the structure and contents of guidelines for hypertension management across countries. The study compares the recommendations of most recent Joint National Committee (JNC 8) 2013, American College of Cardiology & American Heart Association (ACC/AHA) 2017, European Society of Cardiology & European Society of Hypertension (ESC/ESH) 2018 and International Society of Hypertension (ISH) 2020. Study focus on prevalence contrast among the guidelines on when, how and in whom to start the treatment, which is a major health implications of the guidelines.

Results: The four guidelines disagree for the cut of values in definition of hypertension. Information concerning blood pressure measurement, the estimation of cardiovascular risk and the antihypertensive drugs proposed for the initial treatment also varied. Due to difference in cut of values of BP at the definition of hypertension there is a increased chance a patient may be misclassified to one of the four phenotypes of BP measurements from office and out of office, based to which guidelines are followed by the physician.

Conclusion: Guidelines are essential to guide the treatment of hypertension. The differences in guidelines causes a confusion among general practitioners but also to the hypertension experts about the correct approach in use of guidelines in clinical practise.

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INTRODUCTION

Guideline is “a code or rope to aid a passer over difficult or to permit retracting a course which makes sure that climbers stay on the correct and safest path while ascending a mountain”. To guide management of hypertension guidelines are important even though more than 200 guidelines are globally available in India, important ones learned are from North America, Europe, National and International organisations. For the detection and management of hypertension in adult population guidelines have been updated and revised, Joint National Committee 8 (JNC8) in 2013, being followed by The American College of Cardiology and American Heart Association (ACC/AHA) in 2017, Europe and Society of cardiology and European Society of hypertension (ESC/ESH) in 2018 and finally the International Society of hypertension (ISH) at 2020 renewed their guidelines[1,2,3,4].

Definition of hypertension

The definition of hypertension based upon the setting of blood pressure (BP) recommendations was similar for JNC 8 and ESH/ESC guidelines at office, in ambulatory and at home. The ESH/ESC defines hypertension as blood pressure value higher than 140/ 90 mmHg with a target of 130 /80 mmHg only for those at high cardiovascular risk whereas the ASH/ACC defines hypertension when blood pressure is higher than

130/80 mmHg in all adults[1,2]. The ISH guidelines define hypertension when BP values are greater than 140/90 mmHg but cut off value of 130/80 mmHg is considered to be optimal for the whole population and not only for high cardiovascular patients [3]. The AHA/ACC guidelines proposed different out of and for office BP thresholds, they lowered the normal value of office measurement by 10 mmHg and ambulatory or home measurement by 5 mmHg compared to European guidelines.

JNC 8 defines age specific thresholds for the initiation of antihypertensive therapy in an effort to simplify the management of hypertension in adults. The major discord between the guidelines is that the systolic blood pressure treatment thresholds and target BP for individuals aged 60 to 79 years are discrepant. The recommendations of JNC 8 call for relaxing the blood pressure treatment thresholds and targets to < 150 / 90 mmHg whereas recommendations from ACC / AHA, ISH and ESH/ ESC continue to end-rose a target of lower than 140/ 90 mmHg [4]. (Table no.1)

Stages of hypertension

Hypertension is classified into various stages. According to ESH / ESC, AHA/ACC and ISH hypertension is classified into normal, stage 1 and stage 2 whereas in JNC 8 hypertension is classified into one of four categories as normal, pre-hypertension, stage 1 and stage 2 hypertension.

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Table no.1 Diagnosis criteria for hypertension in various guidelines

	ACC/AHA (2017)	ESC/ESH (2018)	JNC 8 (2013)	ISH (2020)
Diagnosis	Defines elevated BP between the range of 120 to 129 mmHg SBP and more than 80mmHg DBP. Hypertension is confirmed once SBP is greater than or equal to 130mmHg and DBP greater than or equal to 80mmHg on repeated examination.	Diagnose and defines hypertension when office SBP values greater than or equal to 140mmHg and / or DBP values greater than or equal to 90mmHg.	In JNC 8, patients 60years or older hypertension is diagnosed when BP is 150/90mmHg or higher. In case of adults younger than 60 years hypertension is diagnosed when higher than 140/90mmHg.	It diagnose & defines hypertension when a person's SBP in office or clinic is greater than or equal to 140mmHg and DBP greater than or equal to 90mmHg on repeated examination. *So systolic hypertension is diagnosed when SBP greater than or equal to 140mmHg and low DBP less than 90mmHg common in young and elderly people.

Abbreviations: SBP= Systolic Blood Pressure; DBP=Diastolic Blood Pressure

Here pre-hypertension is not a disease but identifies those who are likely to progress to stage 1 or stage 2 hypertension [9]. The ACC/AHA guidelines eliminate the category of pre-hypertension, categorising patients as having either elevated (120 -129mmHg and less than 80mmHg) or stage 1 hypertension(130-139 mmHg and 80-89mmHg) [10] (Table no.2). Hypertension is again classified as mask and white coat hypertension in AHA/ACC, ESH/ESC and ISH guidelines.

The ESC/ESH and ISH guidelines recommended that home BP or 24 hour ambulatory blood pressure (ABP) in subjects with high normal BP (130-139/85-89mmHg) is considered as masked hypertension [11]. However the AHA/ACC moved down to the BP range (120-129/75-79mmHg) for masked hypertension. All guidelines recommended to start drug treatment in untreated subjects or reinforce in subjects who are already under treatment [12]. The ESC/ESH, AHA/ACC and ISH recommended home BP or 24 hour ABP (high BP in office but not at home or during 24 hour ABP) for diagnosis and management of white coat hypertension. While the AHA/ACC guidelines do not recommend drug treatment whereas the ESH /ESC and ISH recommended the drug treatment in the subjects in the presence of target organ damage or high cardiovascular risk for white coat hypertension patients[1].

Assessment of cardiovascular risk in hypertensive patients

All other guidelines except JNC 8 agree on the importance of evaluating the cardiovascular risk in patients with hypertension. But a difference is detected on which cardiovascular risk estimation score is proposed by each guideline. The AHA/ACC emphasis on absolute cardiovascular risk computed through AtheroSclerotic CardioVascular Disease (ASCVD) risk calculator, with greater than 10 percentage 10 year risk more aggressive whereas in the ESC/ESH emphasis on absolute cardiovascular risk computed using Systematic Coronary Risk Evaluation (SCORE) system coupled with risk modifiers and assessment of hypertension mediated organ damage with greater than 10 percentage 10 years cardiovascular risk more aggressive[5,6,7,8]. The ISH guidelines encourage the use of different scores in the cardiovascular evaluation of patients with hypertension, especially those taken into account the BP values.

Blood pressure treatment initiation thresholds and on-treatment target

Blood pressure level at which treatment is required is contradicted in these guidelines. All the guidelines focus on two major strategies for BP control in hypertensive patients that are lifestyle interventions and pharmacological therapy.

Table no.2 Classification of hypertension based on blood pressure levels in various guidelines

Hypertension grade	ACC/AHA (2017)	ESC/ESH (2018)	JNC 8(2013)	ISH (2020)
Normal BP	SBP<120mmHg & DBP<80mmHg	SBP<120-129 mmHg & DBP<80mmHg	SBP<120mmHg & DBP<80mmHg	SBP<130mmHg & DBP<85mmHg
Prehypertension	-	-	SBP 120-139mmHg & DBP 80-89mmHg	-
High normal BP/Elevated BP	SBP 120-129mmHg & DBP<80mmHg (Elevated BP)	130-139mmHg of SBP & DBP 85-89mmHg	-	SBP 130-139 mmHg & DBP 85-89mmHg
Stage 1 Hypertension	SBP 130-139mmHg & DBP 80-89mmHg	SBP of 140-169mmHg & DBP 90-99mmHg	SBP of 140-159mmHg & DBP of 90-99mmHg	SBP of 140-159mmHg & DBP 90-99mmHg
Stage 2 Hypertension	SBP>140mmHg & DBP>90mmHg	SBP>160-179mmHg & DBP>100mmHg	SBP >= 160mmHg & DBP>= 100mmHg	SBP>=160mmHg & DBP >=100mmHg

Table no.3 Blood pressure treatment initiation threshold and on-treatment targets in various guidelines

	ISH(2020)	ESC/ESH (2018)	JNC (8)(2013)	AHA/ACC(2017)
Treatment Targets	Treatment to be initiated when BP >or= 140/90mmHg and targets to reduce BP < 130/80 mmHg but individualized in the elderly.	Target ranges based on the age 18-65 years < 140/90 mmHg down BP to 130/80mmHg or lower if tolerated. 65+ years <140/90mmHg down BP to 130/80mmHg if possible or tolerated.	Treatment targets to >= 60 years of age , SBP/DBP treatment initiated at 150/90mmHg and target goal of <150/90mmHg Adult > 18years old & < 60 years old or any adult with diabetes or CKD, SBP/DBP treatment initiated at 140/90mmHg and target goal of < 140/90mmHg.	BP target for treatment is >or= to 130/80mmHg and targets to reduce to < 130/80mmHg.

Abbreviation: BP=Blood Pressure; CKD=Chronic Kidney Disease

According to JNC 8 guidelines individuals greater than 60 years of age with hypertension are recommended for treatment to a goal BP less than 150/90 mmHg whereas less than 60 years of age with hypertension and adults with diabetes or CKD recommended for treatment to a goal BP less than 140/90 mmHg[13]. The ASH/ACC advised to start antihypertensive treatment at the levels of 130 /80 mmHg while the ESH/ ESC and ISH at a level of 140 /90 mmHg[1,2]. (Table no.3) High normal values of BP (130-139 mmHg for SBP and/ or 85-89 mmHg for DBP) the ESH and ISH guideline recommended firstly lifestyle modifications while antihypertensive treatment is usually recommended to patients with very high cardiovascular risk[2,3].

Drug treatment

The JNC 8 guidelines did not recommend drug therapy but lifestyle interventions alone regardless of cardiovascular risk for patients diagnosed with hypertension but not yet treated. The best choice of antihypertensives as first line agents differ in these guidelines. In JNC 8 the initial drug choice is broadened to 4 classes in non-black patients i.e thiazide-type diuretics, calcium channel blockers (CCB), angiotensin converting enzyme inhibitor (ACEI) angiotensin receptor blockers (ARB) and 2 classes in black patients i.e the thiazide-type diuretics or CCBs [13,14].The best choice to start antihypertensive treatment is renin angiotensin aldosterone system inhibitor combined with either CCBs diuretics based on Europeans and Americans[1,2].

The ISH recommended the combinations of renin angiotensin aldosterone system inhibitors with calcium channel blockers and disagreed with the choice of diuretics. All the guidelines disagreed with beta blockers as the first line agent for the initial treatment of hypertension. The ISH guidelines recommended combination of ACE inhibitors and diuretics after stroke in the elderly or those with incipient heart failure or intolerance to calcium channel blocker, as well as combination of ACE inhibitors and CCB in black patients (Table no.4). ISH also introduced for the first time the concept of starting drug combinations at low dose for free or fixed combination and there by increasing to full dose in case BP is still about the target[3]. Table no.4 Drug treatment recommendations in various guidelines

Limitations

All guidelines have their own limitations.JNC 8 did not provide specific recommendations for the use of ambulatory BP monitoring. The relaxing BP targets recommended by the JNC 8 result in higher blood pressure subsequently leading to adverse cardiovascular outcomes. The ESH/ESC 2018 guidelines given much less attention to specific ethics / racial groups whereas AHA/ACC 2017 guidelines recommended similar SBP targets for all patients. The ISH 2020 guidelines recommend the definition of several different BP targets in relation to age, target organ damage and concomitant disease but this may impair the retention of these key concepts of guidelines by physicians with subsequent difficulty in adoption to clinical practice.

Table no 4 Drug treatment recommendations in various guidelines

	ESC/ESH (2018)	AHA/ACC(2017)	JNC8 (2013)
TREATMENT	Smoking cessation, healthy diet/ drinks, reduce salt, alcohol moderation, weight control and regular exercise.	Weight loss for over weight or obese patients with a heart healthy diet, sodium restriction and potassium supplementation within the diet and increased physical activity with a structured exercise program. Reduce alcohol to; men <= 2 drinks daily and women <= 1 drink daily.	Life style modifications are being encouraged by dash diet but don't specify or give detailed information and recommendation on the same.
Life style modifications or interventions	Dual therapy single pill combination (SPC) for most patients usually A+C or A+D (the exceptions are for older patients , those at lower risk & with grade 1 hypertension particularly if SBP is < 150mmHg)	Initial drug therapy comes from one of 4 drug classes *Thiazide diuretics *CCBs *Angiotensin converting enzyme inhibitors and angiotensin receptor blocker unless there is a comorbidity. *In patients with BP > 20/10mmHg above target, two drug therapy either a single pill combination or two separate pills should be initiated. *But avoid combination of any two class of ACEI or ARB or renin inhibitor together.	Nonblack adults with diabetics, first line therapy includes thiazides, CCB, ACEI/ARB. Black adults with diabetics, first line therapy includes thiazides or CCB. Adults with CKD, first line therapy include ACEI/ARB.
Pharmacological treatment Initial drug treatment	A-ACEI or ARB (renin angiotensin aldosterone system inhibitors) C- Calcium channel blocker D- Diuretics	A-ACEI or ARB (Renin angiotensin aldosterone system inhibitors) C- Calcium channel blocker D- Diuretics	If single drug doesn't control BP then start with 2 agents especially if SBP >20 mmHg and if goal is not achieved enhance the adherence to the medication and increase the dose or add 2 nd or 3 rd agent from other anti-hypertensive class.
Further drug treatment	Triple therapy: A+C+D, ideally as single pill combination & four drugs in resistant hypertension Eg: spiranolactone to existing treatment or the additional drug if needed.	Triple combination at low dose or adding an extra anti- hypertensive to treatment regimen.	JNC 8 didn't address the definition of resistant hypertension and neglected to address resistant hypertension although it effects a quarter of hypertensive patients.
Resistant hypertension	Further treatment either through dual full dose combination or combination of A+C or A+C+D.	The addition of low dose Spiranolactone to existing treatment or the addition of further diuretic therapy if intolerant to Spiranolactone or Eplerenone.	

Abbreviations : ACEi= Angiotensin Converting Enzyme inhibitors; ARB=Angiotensin II Receptor Blockers; CCB=Calcium Channel Blockers

These many guidelines can create a dilemma in physicians regarding which guidelines to put into clinical practice.

CONCLUSION

Hypertension is rapidly evolving into a major public health issue and to control this burgeoning epidemic primary care management is essential. Guidelines are essential to guide therapy and provide accurate treatment measures. In this article we have discussed similarities and differences in four major guidelines; JNC 8 2013, AHA/ACC 2017, ESH/ESC 2018 and ISH 2020. All these guidelines agree on the proper method of BP measurement, use of home BP and importance of ambulatory BP monitoring as important for diagnosis. They also promote lifestyle recommendations to control the BP. All the guidelines have restricted use of beta blockers as first line therapy in hypertension. The major disagreements are with the level of BP used for defining hypertension $>130\text{mmHg}$, $>140\text{mmHg}$ or $<150\text{mmHg}$ SBP, flexibility in identifying BP target for treatment and use of initial combination therapy. Patients with borderline hypertension should be studied in future in order to examine increased cardiovascular risk and a measuring of BP can better predict the possibility. All the guidelines agree that control of BP to target is crucial and all pathways should be focused on BP control.

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Declaration of competing interest

The authors declare they have no conflict of interest.

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