

India Consensus on Hypertension guidelines

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Abstract

A panel discussion and collective opinion on India consensus (IC) on the revised International guideline on hypertension to chart out the management plan was the objective. The panel recommended IC statements on setting up of target blood pressure (BP), factors to be considered, charted out measures for prevention, detection, management, treatment response, associated risks, and other therapeutic outcomes. Noting a lack of evidence-based data from the Indian population, the panel emphasized the need for more awareness among physicians to report to the national registry. The panel proposed widespread screening, catching them young through early screening, diagnosis using ambulatory or home BP monitors (ABPM/HBPM), wider use of the automated office BP manometers and digital manometers for self-monitoring. Identification of high-risk population, initiation of treatment with low dose two-drug therapy/triple therapy if unresponsive to two drugs, regular follow-up, with one visit during the onset of summer and winter, respectively, was recommended. Use of angiotensin receptor blockers/angiotensin-converting enzyme inhibitors along with a diuretic and/or calcium channel blockers was recommended as standard care and suggested individualizing the treatment strategy. Involvement of nurses, pharmacists, and family members to promote treatment adherence was encouraged. **Implications:** Screening must start early (late teens) and aim to identify & prevent microvascular changes. A lower target BP $\leq 120/80$ mmHg and $\leq 130/80$ mmHg be set for those aged ≤ 60 years and ≥ 60 years, though recommended, must be individualized. Use of ABPM and HBPM for diagnosis of hypertension, two drugs from the initial stage is recommended. Importance of patient education, counselling in continuing regular follow up and treatment adherence was emphasized. There is a need for revising the Indian guidelines for hypertension. **Conclusion:** Revised the hypertension guidelines globally, have lowered the normal and optimal Blood pressure. Guidelines issued by European society of Hypertension are more practical to follow but geographical, cultural differences mandate revisions in Indian Hypertension guideline as well. A detailed assessment for the confirmation of the diagnosis, appropriate use of combination medications/fixed drug combinations, prevention of disease complications including minimizing/delaying the development of target organ damage, life style changes, treatment compliance are the focus areas in the disease management.

Key Word: Ambulatory & Home Blood pressure monitors, revised guidelines on hypertension, treatment strategy, target BP, target organ damage.

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INTRODUCTION

The world is witnessing a huge leap in the number of hypertensive patients, with an overall prevalence of 30-45%; an estimated 1.13 billion population globally were hypertensive in 2015, expected to reach 1.5 billion in 2025.¹⁻² Concern is not the increasing number of hypertensive's but the impact on other systems (target organ damage (TOD))³⁻⁴ and disease complications. Reduction in blood pressure (BP) bears a direct relationship with development/progression of disease complication/target organ damage.⁵

Hypertension, a significant risk factor for cardiovascular diseases, is the most challenging clinical condition, not only because of disease-associated complications, morbidity, and mortality but also due to its response to therapy. Presence of comorbidities, and target organ damage demands special attention. Prevention of multi-organ damage (hypertensive nephropathy, coronary artery disease and myocardial infarction (MI), peripheral vascular disease, stroke, hypertensive retinopathy) caused by inadequately controlled hypertension must be the goal of therapy.

Physicians differ in their perspective of treatment of hypertension from aggressive treatment to customized and individualized approach to achieve optimal BP control. Guidelines have attempted to streamline the clinical strategy for the prevention, diagnosis, evaluation, and management. The scope of few of these guidelines is national (Canadian Hypertension Education Program, Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, Australian guidelines), while that of European Society of Hypertension (ESH) guidelines, American Society of Hypertension (ASH)/International Society of Hypertension (ISH) have broader perspective applicable to a broader range of population.

The view on initiating the treatment cut off has undergone significant change from >150 mmHg systolic blood pressure during the 1980s to >130 mm Hg during late 1990s and early 2000s. Mounting evidence of target organ damage and higher mortality with elevated levels (>150 mmHg) of BP resulted in revised cut off to further

lower level of < 120 mm Hg (2017). Besides setting the cut off points for those with other co-morbidities, introduction of new pharmacological agents with convincing evidence of efficacy for the control of hypertension needed update. Keeping these facts in view, these guidelines were revised, sometimes too frequently. All major guidelines (American Heart Association (AHA), American College Cardiology (ACC), European Society of Cardiology (ESC) and ESH) have revised their guidelines in the last one-year.

Significant modifications in the ACC guidelines⁶⁻⁷ (Table 1) include reduced target BP (systolic BP (SBP) <120mmHg, diastolic BP (DBP) < 80 mm Hg); 10-year atherosclerotic cardiovascular disease (ASCVD) risk score to calculate the cardiovascular risk and plan the treatment accordingly is emphasized. Prompt and adequate treatment to achieve the target BP including initiating the therapy with two drugs belonging to the different class for stage 2 hypertension is suggested. However, the views of Clinical Guidelines Committee of the American College of Physicians (ACP) and the American Academy for Family Physicians (AAFP) differ on the revisions by ACC/AHA doubting the effects of the lower target blood pressure.

Revised ESC/ESH guidelines on the arterial hypertension⁸⁻¹⁰ recommend the optimal SBP & DBP to be <120 mm Hg and <80 mm Hg, respectively; definition of hypertension was unchanged in ESH revised guideline,¹¹ but few modifications were made in the existing guidelines and a few new concepts introduced.

Modification ESC/ESH guideline on Hypertension

- Reduced BP targets for elderly (from SBP 140-150 mm Hg to 130-139 mm Hg, DBP <90 mm Hg to <80 mm Hg).
- Use of
 - ❖ Two drugs, preferably single pill combination (SPC),
 - ❖ Spironolactone/diuretic to the existing treatment regimen for resistant hypertension.
 - ❖ Restricted use of device-based therapy.
- Updated
 - ❖ The cardiovascular risk assessment and management (use of SCORE system for risk assessment),
 - ❖ Hypertension-multi organ damage (HMOD) in modifying the cardiovascular (CV) risk and
 - ❖ Use of statin & aspirin as a preventive measure.

Introduction of new concepts in ESC/ESH guideline on Hypertension

- Strengthened the recommendation of ambulatory or home BP monitoring for detection & confirmation of white-coat/masked hypertension.
- Less preference for conservative treatment for elderly.
- Simplification of treatment strategy- choice for the use of two drugs, combination drugs.
- Role of co-morbidities in setting target BP and treatment strategy.
- New target BP & lower safety limits for those on treatment.
- Emphasis on the treatment compliance.
- Charted out the role of nurses, pharmacists, and pharmacy in the treatment strategy.

Table 1 compares the revised guidelines with the previous version

Table 1: Different definitions in different guidelines

Blood Pressure Measurement (mmHg)			ESC Guideline [§]		ACC/ AHA Guidelines		JNC 8	Canadian guidelines
Systolic		Diastolic	Previous	Revised	Previous	Revised		Revised
<120	and	<80	Optimal	Optimal	Normal	Normal	Normal	Terminologies vary based on diabetic status and ambulatory BP monitoring
120-129		<80	Normal	Normal	Pre-HT	Elevated	Pre-HT	
130-139		80-89	High Normal	High Normal	Pre- HT	Stage 1 HT	Pre-HT	
140-159		90-99	Grade 1 HT	Grade 1 HT	Stage 1 HT	Stage 2 HT	Stage 1 HT	
160-179		110-109	Grade 2 HT	Grade 2 HT	Stage 2 HT	Stage 2 HT	Stage 2 HT	
≥180		≥110	Grade 3 HT	Grade 3 HT		Stage 2 HT	Stage 2 HT	
≥140	and	<90	Isolated SBP	Isolated SBP		Classified into stage 1 or 2 based on SBP	---	

[§] No significant change in terminologies

ACC- American College of Cardiology, AHA – American Heart Association, BP- blood pressure, ESC – European Society of Cardiology, JNC - Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, HT- Hypertension, pre-HT – Prehypertension, SBP – Systolic blood pressure

Impact of revised International guidelines on India

Evidences indicate varying prevalence of hypertension among the Indian adults; a meta-analysis of 142 studies from India, revealed higher prevalence (33%) among the urban population than their rural counterparts (25%). This study highlighted an un-ignorable observation that of these hypertensive patients only 25% of rural and 38% of urban hypertensives were under treatment; of these, only 1/10th of rural and 1/5th of urban hypertensive's had their BP under control. Hypertension accounted for 57% stroke and 24% ischemic heart disease.¹² This meta-analysis representing the national data of population >1.3 million and the overall prevalence of hypertension 25% (with definition SBP >140/90mm Hg) indicates that >250 million of our adult population are affected.¹³ Hypertension accounted for an increase of 31% age-adjusted mortality in Indians since the last 25 years, resulting in a significant mortality (1.6 million) and

disability (33.9 million disability-adjusted years),¹⁴ suggesting the importance of preventive role of better control of hypertension in premature deaths. It is affecting not only the lives of urban population, but also spreading into the rural India as evidenced by an increase (23% to 42.2% among the urban population, 11.2 to 28.9% in the rural population).¹⁵ However, the management remained significantly unchanged, highlighting the need to change physician's approach for better control of BP and outcome. Recent changes in the International guidelines stating those with SBP>130 mm Hg and DBP >80 mm Hg as hypertensive, will bring a larger proportion of Indian patients under the definition of hypertension. Lower target BP and change in the range of BP in the classification will result in a 140% increase in hypertensive's in our country, most importantly, significant proportion of younger (18-25 years) patients, rural population and belonging to poor category come under the fold of hypertension,¹⁶ a massive burden on the individual and society for which the country yet to be

ready to face the challenge, with existing limited resources. Confirmation of BP outside the clinic/hospital requiring ambulatory BP monitoring and/home BP monitoring practicality of which is difficult in our population many of whom have inadequate access to a healthcare facility. Considering the huge population, the impact on health and economy is greater requiring active physician and patient involvement to minimize the same. Moreover, India is a country of diversity, various regional factors such as climate, culture etc., dietary habits and varying levels of education must be considered in the management of hypertension. It is necessary that a consensus including these factors be outlined for the evaluation and management of hypertension in Indian population.

METHOD

Zonal level consensus meetings were held at four metro cities of India (Kolkata, Delhi, Chennai and Mumbai) during mid-2018. Forty-two (42) eminent cardiologists from different regions attended one-day panel meeting. Various aspects of the existing Indian guidelines, revised international guidelines, its impact on Indian patients and disease management, the need for revision of Indian guideline was discussed. The Panel recommended its recommendations to the national committee.

Key points discussed

1. Target BP in young patients and elderly Indian patients with hypertension.
2. Detection and confirmation of diagnosis.
3. Use of Ambulatory BP Monitoring and/or Home BP Monitoring to diagnose hypertension.
4. Assessment of cardiovascular risk, target organ damage.
5. Medical management of hypertension, including resistant hypertension.

The Outcome of the consensus meeting

Ensuring adequate data: There is no explicit estimation of prevalence of hypertension, as the available evidence is limited to few regions, but an increasing trend has been noted in the recent years. Though the registry is available, the awareness, less commitment and participation of physicians has made the data not an actual representation of the real Indian scenario; hence, reporting by the physicians must be encouraged. The available evidence is indicating increased prevalence and mortality due to hypertension make it one of the most important non-communicable diseases in India.

The Indian guideline: Current guideline (2016) issued by the Indian Council of Medical Research (ICMR) on the management of hypertension,¹⁷ considers those with Systolic BP 120-129mm Hg and/ diastolic BP of 80-

84mm Hg as normal; those with SBP of 130-139 and/ diastolic BP of 85-89mm Hg as high normal. Persistent elevation of SBP >140 mm Hg and/or DBP >90 mm Hg confirms the diagnosis. Treatment is aimed to achieve a target BP <140/90 mmHg in those aged < 80 years, <150/90 in those above 80 years of age. Considering the increased evidence on the positive association and bidirectional impact of the high BP, inadequate control and higher risk of target organ damage, increased cardiovascular risk, it is necessary to revise the Indian guidelines. SPRINT study by demonstrating the benefits of BP<120/80 mm Hg,¹⁸ formed evidence base for the ACC/AHA for the revised lower target. There is lack of evidence on the beneficial effect of the lower target BP in Indian patients, necessitating the need for population-based studies. Till the availability of proven beneficial effects of lower target BP, panel suggested to follow ECS/EHS guidelines.

Acceptable target BP: Panel members agreed unanimously that guidelines of EHS were more practical however the beneficial effect of lowered target BP in ACC/AHA guidelines in the young cannot be ignored. Hence, it is acceptable to have a target of 140/80 mm Hg for elderly patients (> 60 years) and stringent control to keep the target SBP <120mm Hg in <60 years and DBP must not be lowered below 70 mm Hg for the reason of reduction in the cardiac filling. The classification of hypertension followed in the ESC/EHS guidelines is easy to follow & practice. The concern is that with the revised ACC classification, a larger proportion of population having either normal or high normal BP will now be considered hypertensive which in turn increase the number of patients requiring anti-hypertensive therapy, a direct substantial economic impact on the individual and society, and a psychological effect on the individual and family.

Key expert opinion

- Lower target BP <120/80mm Hg for those aged <60 years.
- Higher target (<140/80 mm Hg) for elderly patients.
- DBP must not to be lowered below 70 mm Hg in all.
- To develop more evidence-based studies.
- Lowering the target BP has a huge adverse economical and psychological impact.

Method of BP Recording: Revised guidelines described the method of measurement of BP and number of readings during their visit to a clinic/physician's office to confirm the high BP/hypertension, without significant deviation from the previous guidelines; however, this revision emphasized on the diagnosis of masked hypertension/white-coat hypertension, which is often

dismissed as normal. Average of BP recordings on three different sittings is taken for the diagnosis of elevated BP or hypertension. Taking an average of two readings (2nd & 3rd recording in a sitting) in the clinic with an adequate gap between is practicable & practiced routinely by all physicians. Also, greater patient load makes it nearly impossible for the physician to check the BP of all patients repeatedly in the clinic, requiring a team effort from the junior doctors and/nursing staff.

Key expert opinions

- Confirmation of diagnosis is by recording BP at 3 visits; average of readings during a visit to be considered to minimize error.
- Emphasis on the diagnosis of white coat & masked hypertension.
- Increased work-load can be reduced by involving the team

Device

Using a mercury sphygmomanometer is a passé now due to environmental toxicity,¹⁹ evidences prove that automated sphygmomanometers/manometer can be used in the clinics.²⁰⁻²² Use of oscillometric sphygmomanometer is recommended but must be tested, validated in our patients. One must consider variation in the reading (5-10mm Hg variation). The use of automated/digital manometers that is tested and standardized is recommended.

Key expert opinions

- Standardized, tested & approved automated digital manometers for monitoring BP.
- Confirmation of white coat/masked hypertension by Ambulatory BP monitoring/home BPM.
- Clinical judgment to correlate the ABPM/ HBPM recordings.
- ABPM of 130/80 mm Hg, with optimal target of 120/70 mm Hg.

As only clinic BP recordings have disadvantages (over-diagnosis of hypertension, inappropriate classification into more severe form than exact, increased chance of overtreatment, for those on treatment, clinic BP will often substantially underestimate the number of patients who are otherwise well controlled and leave many high-risk patients at much higher risk) and masked hypertension itself is a high risk factor, it is recommended that more reliable method of recording the BP (ABPM, HBPM) are followed.

Ambulatory BP monitoring (ABPM) and home BP monitoring (HBPM): To overcome the disadvantages of office BP recordings, revised guidelines suggested the use of ABPM/HBPM and provided correlation of readings of continuous monitoring with office readings to aid the physician. Ambulatory BP monitoring can be an indicator of disease prognosis; a higher set of BP in ABPM has

prognostic evidence of developing hypertension or target organ damage later in life,²³ an advantage not seen with home BPM. HBPM readings have a potential for error, whereas, ABPM records 24 hour recordings resulting in less error. With the presence of target organ damage(s) with normal or elevated BP recorded in the clinic, one must suspect white-coat hypertension. However, practicality of continuous monitoring for all patients suspected to have white-coat/masked hypertension in Indian set up is questionable posing a challenge in rural areas where the access to healthcare is limited. Affordability is another hurdle resulting diagnosis of masked hypertension still a difficult task. In addition, using these devices at home needs some basic understanding, which poses a problem in uneducated/less educated population. Hence, with these limitations, it is clinician's judgment to use ABPM/HBPM for the detection of white-coat/masked hypertension. Ideal situations included but not limited to clinically suspected white-coat/masked hypertension, detection of nocturnal fall in BP particularly in those on anti-hypertensive medications and in resistant hypertension to record the readings at different timings. Availability and affordability of these automated manometers in India are the obstacles;²⁴ making the product locally available at an affordable price may promote its increased use.

Key expert opinion

ABPM/HBPM

- Diagnosis of white coat & masked hypertension.
 - High normal & normal office BP; high risk of ASCVD, features of target organ damage
 - Postural & post prandial hypertension
 - To detect nocturnal change in BP – to identify dippers & non-dippers.
- Clinical evaluation of
 - Resistant hypertension
 - BP control in treated high-risk patients (HBPM)
 - Symptoms consistent with hypotension during treatment (HBPM)
 - Target organ damage (HBPM)
 - Diabetic patients, with ECG changes (HBPM)
- Differential diagnosis
 - Postural hypotension
 - Post-micturition syncope

Limitations of ABPM

- Affordability
- Expensive device as Indian make is not available, dependency on the imported one.

- Need for a standardized, tested, approved local make.

Identifying nocturnal hypertension is as essential as its management. The normal physiological reduction of BP in the night may not be detectable in few (non-dippers) while there may be an increase (reverse dippers) in few that may prove catastrophic, if untreated. Non-dippers and reverse dippers are prone to acute coronary and cerebral events, either stroke or acute myocardial infarction and need aggressive treatment. Treatment strategies need to target all types of nocturnal hypertension; previously only non dippers were considered to have more mortality, but Cuspidi C et al²⁵ did not find any significant difference in the subclinical cardiac and other target organ damage between dippers & non-dippers. This study indicated that dippers are at a similar risk of developing cardiac and other target organ damage, requiring equal attention of physicians.²⁵ In those having a nocturnal rise in BP have increased thickness of the carotid intima media and associated structural and functional left ventricular (LV) abnormalities were noted²⁶⁻²⁷ and are more prone to develop renal failure as indicated by an increased incidence and variable blood pressure recordings being higher during visit to visit. Variability in SBP is associated with an increased risk of cardiovascular events in patients with hypertension irrespective of the baseline risk. Panel suggested to record the BP at night. For 5mm increase in standard deviation of visit to visit systolic blood pressure increases the risk of death due to hypertension and death from all causes (cardiovascular and non-cardiovascular deaths, 10% increase in the death risk).²⁸

Key Expert Opinion

Nocturnal hypertension

- Variable BP, higher during visit-to-visit.
- ABPM/HBPM for detection.
- Identify dippers, non-dippers & reverse dippers.
- Distinguish between nocturnal hypertension and morning hypertension.

Initiating the treatment: Repeat BP recordings are needed for confirmation when the BP is elevated or values are in the range of stage 1 hypertension, but when the repeat readings in a single sitting are in the range of stage 2 hypertension, the physician must consider initiating the treatment.

Key Expert opinion

- **Diagnosis:** Three readings with 1-2 minutes apart, an average of last two readings to be considered. Three office visits are recommended.
- **Screening:** Catch them young: start early; above the age of 18- 30 years once in 5 years, for >30 years, once in 2-3 years, if there is no elevated BP.
- **Causes:** Common: Diabetes mellitus, Renal parenchymal disease, Reno-vascular disease, Primary aldosteronism, Obstructive Sleep Apnoea, Drug/alcohol-induced. Less common: Pheochromocytoma/paraganglioma, Cushing's syndrome, abnormal thyroid function, primary hyperparathyroidism, undiagnosed or repaired Aortic coarctation.
- **Assessment of target organ damage:**
 - Heart – Left ventricular hypertrophy (Sokolov-Lyon index>35 mm, R-wave voltage in lead aVL), early detection of atrial fibrillation, ECG, pulse wave velocity, coronary reserve flow for ischemia. Arteries – Thickness of intima –media and ankle-brachial index.
 - Kidney – Glomerular filtration rate (GFR) and microalbuminuria.
 - Hypertensive retinopathy – Complete ophthalmological examination, funduscopy.
 - Brain–Identification of microbleeds, silent cerebrovascular lesions; MRI is helpful in detecting these changes early.

Revised guidelines emphasized the screening for hypertension. It describes screening tests for the comorbidities, target organ damages and other risk factors (sleep apnoea). It also outlined the necessary basic investigations to be carried out in these patients. Apart from screening for primary causes, secondary causes also to be looked for, particularly for those with resistant hypertension. Screening is necessary for our population at regular intervals for early detection of hypertension. With an increase in the prevalence of young hypertensives the focus must be on the young adults to catch them early. Starting early by screening young adults has a greater beneficial role in the long-term outcome in preventing target organ damage.

Target organ damage, caused by microvascular changes is one of the major complications of uncontrolled hypertension. It is essential to identify these changes early in the course through adequate screening and investigations. Basic laboratory investigations such as blood glucose, electrolytes, creatinine, electrolytes, total & high density lipoprotein (HDL) cholesterol &

glomerular filtration rate, tests for hematuria, micro-albuminuria and albumin: creatinine ratio for nephropathy, complete ophthalmological examination to rule out retinopathy, 12-lead electrocardiograph for underlying cardiac pathology are to be performed.

Key expert opinions

- Start early, catch them young.
- Basic laboratory investigations & Specific tests for target organ damage.
- Screen for primary & secondary causes.

The presence of cardiovascular disease or risk factor (10-year ASCVD risk factor) for the risk stratification (<10%, >10%), to set optimal and target BP and initiation of treatment is highlighted in the revised guidelines. Presence of comorbidities such as diabetes mellitus is a significant risk factor. Asians particularly South Asians are at a higher risk to develop cardiovascular diseases. Revised guidelines give a factor to be multiplied by 0.7 for the East Asians and 1.4 for South Asians. This assessment puts the South Asians at a higher risk of developing cardiovascular disease compared to Caucasians.²⁹ Assessment of risk factor must be adopted in the clinical practice, validated for Indian patients (need to developed) as it will help to treat the patient adequately to achieve and maintain recommended target BP. ASCVD can be calculated using a ASCVD calculator.³⁰ ASCVD score helps the physician to assess the risk level, those with lower risk managed with non-pharmacological approach while those with higher risk initiated pharmacological treatment immediately. Those with low-moderate cardiovascular risk as evidenced by the scoring system, without cardiovascular, renal or target organ damage shall undergo 3-6 months of initial lifestyle intervention, and if unsuccessful in reducing the BP, then antihypertensive treatment shall be initiated. However, those with stage 2 hypertension need immediate treatment.

Treatment with antihypertensive agent depends on the grade of hypertension and ASCVD score risk value. The most critical step is to establish the target at which the therapy is initiated. Those with elevated BP with low ASCVD risk (<10%) are advised lifestyle changes, those with higher BP threshold and greater ASCVD risk is advised pharmacotherapy along with lifestyle changes.

Key expert opinion

10-year ASCVD Score

- Cardiovascular risk assessment (High >10%)
- Target BP and treatment strategy must be based on the risk assessment.
- ASCVD calculator available.
- Not validated for the Indian population.

Management of hypertension: The Primary goal of management of hypertension must aim at achieving an adequate control of BP to prevent, halt, delay or reverse the disease progression & its complications, thereby reducing the overall risk, mortality & morbidity, without compromising the quality of life. Non-pharmacological management applies to all stages of hypertension, and lifestyle changes are advised even for those with normal BP. The surgical approach is reserved only for selected clinical conditions.

Non-pharmacological therapy: The revised guidelines have charted out lifestyle changes with the possible impact on the BP. impact of weight loss has overall beneficial effect; hence hypertensive patients have to be motivated to lose weight. With a healthy diet (Dietary approach to stop hypertension (DASH) dietary pattern), a fall of SBP of 11 mmHg in hypertensives and 3mm Hg in normotensives is expected. Revised guidelines recommend the salt intake to be <1gm -1.5 gm/day; it is expected that with salt restriction, a fall of SBP 5-6 mm Hg in hypertensives and 2-3 mmHg in normotensives. Indian guidelines (ICMR) recommend restricted intake of 1.5gms/day;³¹ despite recommendation, salt intake by Indians remains extremely high, almost 4-5 times the value; hence, it is essential to reduce the sodium intake (stringent control), and increased intake of potassium. Regular physical activity and moderation in alcohol consumption (men \leq 2 drinks/day and women \leq 1 drink/day) for a considerable reduction in BP is emphasized in the revised guidelines.

Key Expert opinions

- Weight loss
- Increased physical activity, regular schedule for exercise (aerobic exercise 30 minutes/day, 5-7 days/week.
 - Homemakers
 - Young adults,
 - Professionals sitting for a long time
- Mind relaxing techniques (Yoga, meditation)
- Healthy diet (DASH pattern)
- Stringent salt control, increased intake of potassium
- Cessation of smoking
- Limiting alcohol intake

Pharmacological Management

Angiotensin converting enzyme inhibitors (ACEIs) & Angiotensin receptor blockers (ARBs) have similar efficacy, total mortality and mortality but ARBs are slightly superior with less adverse events (less drug induced cough), withdrawal³²⁻³³ and protective effect on target organ damage.³⁴⁻³⁶ Among ARBs, telmisartan has shown to have less drug-drug interaction and intra-patient variation (\approx 40-43%)³⁷⁻⁴¹ thus contributing to sustained

blood pressure control over 24 hrs. With well-established efficacy, safety profile, therapeutic benefits beyond numbers, and popularity among the Indian physicians, consensus opined it is still one of the effective drug for hypertension and supported its use. Its pleotropic effects contribute towards the prevention of complications.⁴² Measures to reduce the intra-patient variability (bio-enhanced formulation) will prove its worth. Azilsartan, belonging to angiotensin II receptor type 1 blocker is a recently approved drug in India (2016). It has shown to exert better BP control and tolerated well.⁴³⁻⁴⁴ It can be used either alone or in combination with a diuretic or calcium channel blocker (CCB).⁴⁵ Azilsartan is unique that it is effective in naïve hypertensive patients and also in those unresponsive to other medications including telmisartan and with other co-morbidities,⁴⁴ beneficial pleotropic effect on the cardiovascular system, making it another suitable antihypertensive agent.⁴⁶ Until adequate data on safety and efficacy is available on Indian population, telmisartan retains its position in the treatment ladder.

With treatment evolution, β blockers have a limited role as antihypertensive agent. Atenolol is still in use as antihypertensive in patients with coexisting cardiac

conditions (angina, supra-ventricular arrhythmia, post-myocardial infarction, migraine and anxiety with somatic symptoms) and preferred in younger patients (<60 years) with uncomplicated hypertension. Its efficacy and safety has been proven in the Indian population.⁴⁷ Consensus approved atenolol as add-on hypertensive drug.

Revised guidelines have differed in the decision to use mono-therapy or combination drugs; ESC guidelines advocate the use of two drugs/combination drugs from the beginning, while ACC states use of two drugs/combination drugs to be preferred if there is need to reduce BP ≥ 20 mm Hg. Since many of Indian patients consult the physicians during advanced stages of hypertension, it is recommended to initiate Initiating therapy with a combination of two drugs to hasten the rate of achieving the target BP; studies have shown twice the number of patients with hypertension treated with two drug therapy achieved the target BP compared to those with mono-therapy, supporting the treatment initiation with combination drugs.⁴⁸⁻⁵⁰ Considering the benefits of prescribing two drugs in the better control of hypertension even in the early stages, our consensus suggested to follow this treatment regimen. Table 2 outlines the drug treatment.

Table 2. Drug combinations recommended

Drug regimen	Drug
Step 1- two drug combination	ACE inhibitors/ARB + CCBs or Diuretic
Step 2- three drug combination	ACE inhibitors/ARB + CCBs + Diuretic
Step 3– Triple-drug combination+Spironolactone or other drugs	Triple-drug as above + Spironolactone (25-50 mg once daily) or other diuretic or α adrenergic blocker or β adrenergic blocker

Given the unpredictability of patient behaviour concerning the treatment compliance, administration of two drugs at different timings of the day, combination drugs offers a better choice. Besides, complementary drug mechanisms optimize the efficacy of combination drugs. Low dose combinations of drugs have yielded better control of BP. However, three drug combinations need to be titrated over a period, once stabilized these drugs can be given as a single pill. Single-pill therapy has been found to be effective therapeutically, convenient to the patient and economical.

Among the secondary agents, centrally acting agents can be another group of add-on drugs in those who are not responding to triple-drug therapy or have electrolyte imbalance with diuretics. Centrally acting Selective Imidazoline Receptor Agonists (SIRAs) can be considered in difficult to treat hypertension cases as an add-on therapy with other class of antihypertensive drugs. The experience with this drug is less with Indian

physicians; more evidence on its efficacy and safety will decide its role as antihypertensive in future.

Other agents: Adding a statin along with the antihypertensive treatment has proven beneficial, hence, including statins for those with moderate–high ASCVD risk is recommended. Patients aged >60 years, those with established cardiovascular disease (CVD) (by further reducing risk of myocardial infarction (MI) and stroke, even if BP is well controlled), with any risk factors for hypertension i.e. dyslipidemia, diabetes, low-high density lipoproteins, family history, waist circumference of >90cm, renal dysfunction are ideal candidate for statin therapy. The support for the use of low dose aspirin was not for the primary prevention, but for the secondary prevention. It is cautioned that if the hypertension is uncontrolled, with persisting higher levels of SBP & DBP (SBP>160 mm Hg and DBP>100 mm Hg) aspirin therapy can result in fatal outcomes (cerebral bleed) particularly in older individuals. Challenge is to address the resistant hypertension, which requires a stepwise approach, up

gradation of dose, add-on drugs, regular follow up, monitoring for target organ damage.

Key Expert opinions

Consider

- Two drug therapy or fixed drug combinations of two drugs to initiate treatment.
- ACE inhibitors/ARBs + CCBs/diuretics. In selective conditions, the second drug can include β blockers.
- Three drug combination therapy for uncontrolled hypertension.
- Resistant hypertension may require four drug therapy and stepwise approach.

Drugs

- ACE inhibitors & ARBs have similar efficacy profile, but the latter has an advantage of lesser treatment withdrawal. Drug-induced cough, one of the reasons for withdrawal is less with ARBs.
- Among ARBs, telmisartan has a well-proven safety & tolerability profile;
- Azilsartan, a newer ARB, effective in resistant hypertension, those having poor control with other drugs. Limited data are available on Indian hypertensives.
- Centrally acting agents have limited application; used as an add-on drug in resistant hypertension or in those who cannot tolerate other agents. Drugs belonging to SIRA group have proven beneficial in those with diabetes mellitus, obesity, hyperactive sympathetic nervous system, and resistant hypertension; though it is available since last three decades, data on our population is limited; hence, more studies are required.
- Use of statins is recommended in those with CV risk.
- Judicious prescription of aspirin, considering the risk factors; one has to be cautious about cerebral bleed.

Setting a target BP - Implications

Factors: There is ambiguity in the guidelines about setting a target BP with two widely followed guidelines differing in their view. Shreds of evidences indicate that SBP directly correlates with the mortality than DBP.

Age, coexisting morbidities and the ASCVD score to assess 10-year risk are the major determinants for setting a target BP; for patients aged 18-65 years without comorbidities, it is advisable to maintain the BP at a normal level of <120/80 mmHg. In those >65 years, younger patients with comorbidities (diabetes), the presence of risk factors (h/o stroke, CVD or CAD), the optimal target is SBP <130mm Hg. Maintaining the SBP between 130-140mmHg for elderly patients (>65 years)

and not to reduce below 130 similar to ESC guidelines will be more practical for our patients. For those above 80 years, target SBP of 130-140 to be maintained. This consensus supports the retention of the previous term 'pre-hypertension' not to consider the elevated BP as mentioned in ACC/AHA revision. Prehypertension even at lower range increases the risk of congestive heart disease (CHD) compared to the target BP <120/80 mm Hg.⁵¹

Setting a target BP must be individualized, considering the underlying clinical conditions. Physicians must monitor the response (development of hypotension, ejection fraction, DBP) before setting lower levels, particularly in elderly, cardio compromised conditions.

Key expert opinion

- Major determinants: Age, coexisting morbidities and the 10-year CV risk (ASCVD score)
- SBP is a major risk factor; the optimal target is 120/80mm Hg, not below 110/70 mm Hg.
- The target can be <120/80 mm Hg in young patients; <130/80 mm Hg in elderly (60-80 years); <135/85 in >80 years.
- Individualize the target BP based on adverse effects and quality of life.

For those with elevated BP (120-129/80 mm Hg) or in stage 1 hypertension, if the lifestyle changes bring down the BP to the target BP (<120/80 mm Hg), then the decision to initiate pharmacotherapy is based on the 10-year ASCVD risk score. Mono-therapy for the initiation of the treatment for the elevated and stage 1 hypertension must be the first choice of therapy along with lifestyle modification; for stage 2 hypertension, 2 drug therapy or fixed drug combination of antihypertensive agents is recommended. For resistant hypertension, triple-drug therapy of fixed drug combination (FDC) of 3 drugs is suggested. Adding a secondary agent to the primary depends on the age, existing comorbidities (history of (h/o) myocardial infarction, angina, heart failure, chronic renal failure) and response to therapy.

Combination therapy offers better BP control in addition to other advantages.⁵² Combination of either ACE or ARB, with CCBs/diuretics, is preferred for two drug combination. ACE should not be combined with ARB. The combination should not include drugs belonging to the same group. The use of β blockers is restricted, preferred only in underlying cardiac conditions (MI, angina, Heart failure) and judiciously used after verifying the ejection fraction. The presence of chronic kidney disease (CKD) and in advanced stage, demands addition of a loop diuretic as an add-on drug. For resistant hypertension, aldosterone antagonist (low dose spironolactone) may be added.

BP to be recorded frequently to assess the adequacy of BP control in those who are on treatment; it is recommended to record the BP twice/thrice in a week for the first week to reduce the frequency of recording to once a week till BP is stabilized on treatment. Once maintained, it may be recorded once a month. For uncontrolled hypertension, recording needs to be more frequent. The limiting factor is accessibility to the healthcare facility, particularly in rural areas.

Treatment must be aimed at a gradual reduction in BP, aggressive approach to be discouraged, particularly in elderly patients. If combination drugs are administered, the patient must be monitored for the possible adverse effects. Young, asymptomatic patients, and who can be regularly followed up can undergo aggressive treatment. Prognosis depends on various factors (male, age, smoking, dyslipidemia, diabetic status, obesity & waist circumference, family history, asymptomatic/symptomatic organ damage) and that needs to be considered in setting the treatment goal.

Hypertension accounts for more number of deaths in women. Various stages in women's life teenage & young adult stage, pregnancy, pre-menopause & menopause, witness repeated hormonal changes. Causes for hypertension varies in these stages; renal parenchymal disease, endocrinal causes and congenital heart disease are the causes in young women, while in post-menopausal women, endothelial dysfunction due to genetic causes, hormonal dysfunction, high body mass index (BMI), type 2 diabetes mellitus, sympathetic activation, and renin release are the causes for high BP.⁵³

All these patients need regular follow up; guidelines advise a follow-up once in 3-6 months. It is suggested that review visit must be based on the age of the patient, stage of hypertension, the response to therapy, coexisting illness, the presence of target organ damage, and the accessibility to a healthcare facility. Younger patients requiring aggressive treatment and elderly patients showing irregular response need a frequent follow-up visits. Besides, patients have to be monitored for adverse effects, particularly postural hypotension. It is advisable to have review visit 2-4 weeks in the initial stage, every month till the patient is stabilized, then to have once in 3-6 months. As there is seasonal variation, one visit during early May & November is recommended to make necessary changes in the treatment.

Involving the general practitioners who can monitor the patient during follow up, to be encouraged; they must be trained adequately in common lifestyle disorders.

Health education and counselling the patient have a positive impact on the adherence to treatment and long-term outcome. Involving nurses, pharmacists in imparting the significance of regular intake of medicine and follow-

up, identification of adverse effects, symptoms of target organ damage yield a beneficial effect. Training them to identify and attending emergencies in hypertension (hypertensive crisis) will reduce complications. Patients must be educated to self-monitor using digital BP manometers, report to the nearby health care centre in case of uncontrolled BP, hypertensive crisis and adverse effects. Increasing public awareness will prove beneficial in patient involvement in disease management and improving the treatment compliance.

Major recommendations

1. Encourage evidence-based data on Indian patients with hypertension.
2. Patients with BP $\geq 140/80$ mmHg must be diagnosed as having hypertension requiring medical intervention.
3. Lower target ≤ 120 mmHg must be set for younger patients and higher target for elderly (≥ 65 years). An optimal BP of 120/80 mmHg is preferred in younger patients with lower ASCVD risk and without any comorbidity; otherwise, target BP of 130/80 should be aimed to achieve and SBP can be maintained between 120-130 mm Hg and DBP < 80 mm Hg. Never to lower the DBP < 70 mmHg, particularly in those with coronary artery disease.
4. Automated manometers must be used for the measurement of BP. Diagnosis to be confirmed on persistent high BP $\geq 140/80$ mmHg.
5. In White-coat/masked/nocturnal hypertension, office BP recordings (140/90 mm Hg) must be confirmed by ambulatory/home BPM.
6. Lifestyle modifications must be advised to these patients. Revised guidelines can be followed for our patients.
 - a. Dietary modifications must be followed strictly (stringent restriction of sodium, enhanced intake of potassium). However, seasonal variations must be considered while adopting these changes, particularly in summer; excess sweating during peak summer (in the month of April & May), a slight relaxation of sodium restriction is advised.
 - b. Hot & humid climate, extremes of temperature during summer and winter call for certain modification in the treatment regimen, with winter requirement slightly higher than that of summer.
 - c. Weight reduction for obesity, control measures for smoking and alcohol

- intake, management of other coexisting illness such as metabolic syndrome, dyslipidemia, to be strictly adhered.
7. Initiating the treatment with two drug therapy, rather than mono-therapy is recommended to utilize the complementary drug actions and improve treatment adherence. Add-on drugs may be used if BP is uncontrolled with 2 drugs. Combination of low-dose triple therapy or a single triple pill preferred for those with uncontrolled/unresponsive to two drugs. Choice of drugs is based on the age, severity of the disease, target organ damage, coexisting illness.
 8. Selective imidazoline receptor agonists may be used as an add-on drug, fourth or 3rd line drug; in resistant hypertension, those who have reached a ceiling dose of β blockers or cannot tolerate/contraindicated, and those having edema. Limited data on the usage of compounds of this group demands more studies on its safety & efficacy in the Indian population.
 9. Regular follow up, titration of doses, observation for adverse effects is required for better management and BP control.
 10. Elderly need individualized treatment; whereas aggressive approach may be used for young hypertensive patients. Women need a different strategy due to repeated hormonal changes in various stages of life.
 11. Active involvement of nurses and pharmacists in pursuing the patients to adhere to the treatment.
- Impact and outcome of major recommendation from the consensus is given in table 3.

Table 3. Major Recommendations, possible impact and expected outcome

Key recommendations	Possible Impact	Expected Outcome
<i>Collection of evidence based data</i>	<ul style="list-style-type: none"> • More population-based studies • Reporting cases to national registry 	More robust guidelines
<i>Screening</i>	<ul style="list-style-type: none"> • Early screening – Clinical & Laboratory for primary & secondary causes. • Tests for target organ damage 	Early Identification, better control & prevention/arrest or slow progression of disease progression.
<i>Setting Target BP</i>	<ul style="list-style-type: none"> • Ideal - $\leq 120/80$ mmHg for younger patients. • Population-based studies to prove the beneficial effect of low BP in our population. • Consider various factors – age, gender, occupation, culture (fast/feast), and seasonal variation. 	Redefining the different categories of blood pressure.
<i>Diagnosis</i>	<ul style="list-style-type: none"> • Average of three readings • Confirm by ABPM/HBPM (case specific) • Identification of white-coat/masked/nocturnal/resistant hypertension • Presence of target organ damage. 	Accurate diagnosis. Early identification of risk factors and difficult to treat hypertension.
<i>Management</i>	<ul style="list-style-type: none"> • Lifestyle changes • Pharmacotherapy • Initiation with two drug therapy; add on/triple therapy if needed. • Individualize the treatment strategy. 	Prevention/postponing the development of hypertension and/complications. Better treatment compliance and BP control.
<i>Follow up</i>	<ul style="list-style-type: none"> • Once in 3-6 months, more frequent for those with resistant/ unresponsive hypertension and young patients with low BP target. 	Early detection of complication of hypertension in those who are uncontrolled.
Involvement of support team	<ul style="list-style-type: none"> • Involving family members, nurses & pharmacists 	Family support lead to improved treatment adherence and better control of BP, result in less complications.

CONCLUSION

Indian guideline requires a revision; changes are to be made considering diversity of population, dietary habits, seasonal variations, and affordability. There is a need for real time data on the prevalence, effect of different drugs, associated co-morbidities, and response to therapy in the presence of comorbidities. Use of automated BP

monitors/home based BP monitors to be encouraged. Target BP 120/80 mmHg can be set for young adults requiring tight control and follow a regular follow up; a slightly higher target of $<130/80$, and 135/85 mm Hg can be set for those above 65 years and 80 years, respectively. Setting a target, treatment strategy must be individualized and gender specific.

Therapy can be initiated with two drug therapy in those with >130/90 mmHg. Combination of ACE inhibitors/ARBs with diuretics/CCBs is recommended; ARBs have an advantage of lesser withdrawal rate and drug induced cough compared to ACE inhibitors. Telmisartan has a well-documented efficacy and offers benefits beyond numbers. B-blockers as an add-on drug is reserved for only selected cases, and the evaluation of underlying cardiac condition is a must before its prescription. A comprehensive strategy is to be adopted in the management of hypertension and framing the guidelines accordingly is the need of the hour.

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