Treatment Thresholds and Targets in Hypertension

Different Readings of the Same Evidence?

Costas Tsioufis, Costas Thomopoulos, Reinhold Kreutz

See related article, pp e13–e115

The new 2017 High Blood Pressure Clinical Practice Guideline released by the American College of Cardiology (ACC) and the American Heart Association (AHA)[1] presents several novel aspects with potential significant impact on hypertension management. Important news of the guideline is related to blood pressure (BP) measurement modalities, BP thresholds for the initiation of nonpharmacological as well as pharmacological treatment, BP targets to pursue to maximize treatment benefits from BP lowering and last but not least a novel definition of hypertension. Overall, this is an important document but its translation into clinical practice seems to pose a huge challenge for clinicians

Redefining Hypertension

According to the novel definition of stage 1 hypertension starting at systolic or diastolic BP values of ≥130 mm Hg or ≥80 mm Hg almost 50% of adults in the US population (and in many other countries around the world) have hypertension, whereas the remaining 50% resides either in the elevated (ie, 120–129 mm Hg) or in the normal systolic BP range (ie, <120 mm Hg). Given that BP thresholds and targets are inevitably related to the hypertension definition, the new selected threshold (ie, 130/80 mm Hg) will introduce an epidemiological revolution that will not remain unquestioned in the United States and around the world. Beyond the immediate overnight striking increase (by 14%) of hypertension prevalence in the United States after the presentation of the new guideline, the incidence rate of hypertension is expected to decrease because of the increased disease duration, as the new diagnosis of hypertension is expected to be anticipated at a younger age. It is, however, questionable whether diagnosing hypertension in younger otherwise healthy subjects by tightening up the hypertension definition will indeed improve prevention strategies, for example, by lifestyle modifications, as intended by the authors of the guideline. In addition, in subjects aged <40 years the recommended mandatory estimation of the 10-year atherosclerotic cardiovascular disease risk for risk stratification and decision-making with the proposed risk calculators is not feasible.

BP Thresholds

It is well accepted that hypertension treatment should generally be initiated at BP levels above the threshold for defining the disease. In treated patients, individual intensification of treatment should be pursued to reach the selected BP goal. In this regard, SPRINT (Systolic Blood Pressure Intervention Trial) has been considered as a suitable trial to provide evidence for the selection process of the threshold to initiate treatment.[1,2] However, in addition to the controversy about the methods of BP measurement in SPRINT,[3] another hidden issue here is the fact, that the results of this trial cannot be used for decision-making on BP thresholds, because patients in SPRINT were already treated at baseline. The new ACC/AHA hypertension guideline suggests that all patients with hypertension should be treated at least with nonpharmacological measures. This does not represent an innovation because healthy lifestyle should be inspired from healthcare systems to the whole population and not only to individuals with hypertension. However, for secondary prevention of recurrent cardiovascular disease events, in patients with diabetes mellitus or chronic kidney disease and for primary prevention in patients with a 10-year calculated atherosclerotic cardiovascular disease risk of 10% or higher, the use of BP-lowering medications is recommended for patients with hypertension (ie, ≥130/80 mm Hg).

Nevertheless, do we have enough evidence to initiate drug treatment in previously untreated subjects with systolic BP 130 mm Hg or higher? A previous meta-analysis suggested that subjects with a systolic BP of 140 mm Hg or higher might be treated with a pharmacological intervention irrespectively of baseline cardiovascular risk.[4] A subgroup analysis of untreated patients residing in the upper tertile of baseline systolic BP in the HOPE-3 trial (Heart Outcomes Prevention Evaluation-3; mean systolic BP of 154 mm Hg) in which the 10-year cardiovascular death rate was 7.1%, corresponding to a 10-year cardiovascular disease rate largely higher than 10% supports these findings.[5] However, the effect of BP lowering in the 2 lower baseline systolic BP tertiles of HOPE-3 (mean systolic BP of 130 mm Hg and a 10-year cardiovascular death rate of 3.7% corresponding to 10-year cardiovascular disease rate well <10%) was not accompanied by treatment benefits.[5]

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the First Cardiology Clinic, Medical School, National and Kapodistrian University of Athens, Hippokration Hospital, Greece (C. Tsioufis); Department of Cardiology, Helena Venizelou Hospital, Athens, Greece (C. Thomopoulos); and Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institut für Klinische Pharmakologie und Toxikologie, Germany (R.K.).

Correspondence to Costas Tsioufis, First Cardiology Clinic, Medical School, National and Kapodistrian University of Athens, Hippokration Hospital, 114 Vas.Sofias Ave, 11527 Athens, Greece. E-mail ktsioufis@hippocratio.gr

(*Hypertension*. 2018;71:966-968.
DOI: 10.1161/HYPERTENSIONAHA.118.10815.)

Hypertension **is available at http://hyper.ahajournals.org**
DOI: 10.1161/HYPERTENSIONAHA.118.10815

Thus, the lack of benefit in subjects randomized in the normotensive tertiles of HOPE-3 trial might be dependent on their low overall cardiovascular risk. Another synthesis of trials was in line with the findings of the HOPE-3 trial.[6] In untreated patients with baseline systolic BP <140 mm Hg the initiation of pharmacological treatment was related to benefits only for stroke. When the analysis was stratified according to overall cardiovascular risk, the stroke benefit was limited to subjects with at least high overall cardiovascular risk and overt underlying cardiovascular disease (secondary prevention).[6]

Based on the above considerations, which have also—at least in part—been taken into account by the new 2017 ACC/AHA guideline,[1] we agree that the use of BP[5] lowering medications might be indeed considered in subjects with baseline systolic BP at 130 mm Hg or higher and a history of overt cardiovascular disease. In contrast, there still remains a lack of evidence to support drug treatment initiation in patients with systolic BP ranging from 130 to 139 mm Hg (ie, stage 1 hypertension according to the new guideline) for primary prevention irrespectively of the calculated overall cardiovascular risk; this applies particularly to young adults, because risk calculation in these subjects seems problematic.

BP Targets

The new proposed hypertension definition together with the selected thresholds to initiate antihypertensive treatment makes the selection of BP target apparently an easy task to fulfill. The BP target of <130/80 mm Hg has been proposed as a reasonable one, even for hypertensive subjects in primary prevention with a low overall cardiovascular risk treated either with lifestyle modifications alone or with a combination of BP-lowering drugs and nonpharmacological interventions. Of interest, the same BP target is extended to all hypertensive subjects either in primary or in secondary prevention, and it is also extended to the elderly and to subjects with diabetes mellitus.[1]

Nonetheless, what is the evidence to date to qualify a systolic BP target of <130 mm Hg for all these subjects? Current evidence indicates that BP lowering by few mm Hg <130 mm Hg is associated with relative treatment benefits for most cardiovascular outcomes compared with a higher attained threshold, though the absolute risk reduction becomes smaller.[7] The same phenomenon has been demonstrated for diastolic BP lowering to <80 mm Hg. This smaller incremental benefit should be considered when deciding the BP target to achieve in the individual patient, especially in front of a possible increase in adverse effects and a consequent decrease in the patient's adherence to the treatment.[8] It has to be highlighted that treatment-related adverse events after BP lowering have not been considered in the new 2017 ACC/AHA guideline.[1] However, in several parts of the guideline report[1] the need of a close follow-up of patients under treatment, including the evaluation of treatment adherence, is emphasized. Whether the general recommendation to pursue a target of <130/80 mm Hg can be extended to special groups of hypertensive patients still remains debatable. Indeed, in patients with diabetes mellitus there is little or no further benefit in lowering systolic BP <130 mm Hg.[8] This observation is in line with the ACCORD trial (Action to Control Cardiovascular Risk in Diabetes)[9] having shown no major cardiovascular outcome benefit (but not any harm) in reducing systolic BP <130 mm Hg with the exception for stroke, although the latter represented only a prespecified secondary outcome.

Much more attention when trying to achieve the novel universal BP target should be paid at the emerging adverse events that may also lead to treatment discontinuation and at the strategies to be implemented in the elderly. Although clinicians cannot evaluate the beneficial effects of BP lowering on outcome incidence in the individual patient, they should be always aware of treatment-related adverse events and subsequent discontinuations that may outweigh the potential benefits of profound BP lowering.[10] This concern is particularly significant for elderly subjects in which BP lowering should be individualized and carefully monitored for incident adverse events.

Concluding Remarks

New guidelines include—depending on personal perspectives—usually positive and negative points. Based on our humble exploration, the same holds true for the new 2017 ACC/AHA High Blood Pressure Clinical Practice Guideline.[1] BP thresholds and targets adopted by the independent Writing Committee after external review are largely based on the existing evidence from randomized clinical trials, meta-analyses, and observational studies.[1] However, because the interpretation of the existing evidence might be different from one observer to another (ie, different reading of the evidence) and various types of bias are triggered by empirical or investigational preconceptions of any writing committee member,[11] there is always enough space for constructive disagreement and criticism. We generally agree with the interpretation of the evidence made by this Writing Committee for most aspects but not for all proposed recommendations about BP thresholds and targets. Most importantly, in our view tightening up the definition of hypertension to label more subjects as hypertensive should be grounded on solid evidence from randomized controlled trials, a requirement that is at present only insufficiently fulfilled.

Sources of Funding

None.

Disclosures

C. Tsioufis received honoraria for consultancy, lectures, and support for research from Sanofi, Menarini, AstraZeneca, Bayer, Boehringer Inh, Novartis, Servier, Phizer, MSD, Amgien, Medtronic, and St. Jude Medical. C. Thomopoulos received consultancy fees from Sanofi and Menarini and lecture honoraria from Menarini, MSD, and Servier. R. Kreutz received honoraria for consultancy, lectures, and support for research from AstraZeneca, Bayer AG, Berlin-Chemie Menarini, Daiichi Sankyo, Sanofi, and Servier.

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Hypertension
Journal of the American Heart Association

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Hypertension. 2018;71:966-968; originally published online April 23, 2018;
doi: 10.1161/HYPERTENSIONAHA.118.10815
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0194-911X. Online ISSN: 1524-4563