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Hypertension Guidelines for 2017 – The Evidence So Far

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BACKGROUND

The three guidelines that have been instrumental in recent time to have implications in clinical practice in management of hypertension include:

1. ESH guidelines
2. ASH / ISH guidelines
3. JNC VIII Panel Recommendation

Although these guidelines and recommendations have been quite comprehensive there still remain some unanswered questions. There is a possibility of new guidelines or addendum to the existing ones in the year of 2017 with contributions from North America.

EXPECTATIONS FROM THE NEW GUIDELINES

The new recommendations will have to address the following issues for further meaningful insights into what is already known in the previous ones

1. Appropriate targets for systolic BP to reduce cardiovascular mortality in subjects without diabetes
2. Appropriate targets for systolic BP to reduce cardiovascular mortality in subjects with diabetes
3. Safety of aggressive BP lowering in elderly patients
4. Existence of J Curve
5. Method of BP measurement – HBP/OBP/ABPM/ AOBP
6. Clinical Utility of Central Aortic Pressure
7. Recommendations for different ethnicity
8. Clarity on the evidence – RCT based or otherwise and the Strength of the evidence

NEWER EVIDENCE THAT CAN INFLUENCE OR MODIFY GUIDELINES

Systolic Blood Pressure Intervention Trial (SPRINT) was a large National Institutes of Health–sponsored multicenter randomized controlled trial that enrolled 9361 patients with a systolic blood pressure(SBP) of at least 130 mm Hg. The primary goal of SPRINT was to test whether reducing SBP to a lower goal (<120 mm Hg) than currently recommended

(<140 mm Hg) would reduce the occurrence of cardiovascular disease (CVD) and chronic kidney disease(CKD) events. Enrolled patients were 50 years or older with an SBP ≥130 mm Hg and at least one of the following: a history of CVD, stage 3 CKD (estimated glomerular filtration rate 20–59 mL/min/1.73 m2), an intermediate to high risk for CVD other than stroke, orage 75 years or older. A patient was defined as having CVD if they had a prior myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, carotid endarterectomy or carotid stenting, peripheral arterial disease with revascularization, acute coronary syndrome, abdominal aortic aneurysm ≥5 cmwith or without repair, a coronary calcium score >400, or left ventricular hypertrophy.

At 1 year, the mean systolic blood pressure was 121.4 mm Hg in the intensive treatment group and 136.2 mm Hg in the standard-treatment group. The intervention was stopped early after a median follow-up of 3.26 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group than in the standard-treatment group

Trial participants assigned to the lower systolic blood-pressure target (intensive-treatment group), as compared with those assigned to the higher target (standard-treatment group), had a 25% lower relative risk of the primary outcome; in addition, the intensive-treatment group had lower rates of several other important outcomes, including heart failure (38% lower relative risk), death from cardiovascular causes (43% lower relative risk), and death from any cause (27% lower relative risk). Rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls, were higher in the intensive-treatment group than in the standard-treatment group.

LIMITATIONS OF SPRINT TRIAL TO INFLUENCE GUIDELINES

1. There was no evidence of substantial permanent kidney injury associated with the lower systolic blood pressure goal the number of renal events was small and the possibility of a long term adverse renal outcome cannot be excluded.
2. SPRINT excluded participants with diabetes
3. SPRINT excluded persons with prevalent stroke or transient ischemic attack at baseline
4. SPRINT enrolled an older cohort with a mean age of 68 years and may not be applicable to a younger population

5. Intensive treatment group in SPRINT had a non-significant 11% lower incidence of stroke
6. Syncope was more common among participants in the intensive-treatment group than among those in the standard-treatment group (3.5% vs. 2.4%, P = 0.003), as was hypotension (3.4% vs. 2.0%, P<0.001).
7. Higher rate of acute kidney injury or acute renal failure in the intensive-treatment group
8. Electrolyte abnormalities also occurred more often in the intensive (3.1%) than in the standard (2.3%) arm
9. The manner in which BP was measured in the SPRINT trial using an automated manometer (AOBP), an average of 3 office BP readings taken with proper cuff size, participants seated with their back supported, 5 minutes of rest before measurement, and no conversation during the rest period or BP determinations. This is not the standard of clinical practice in most office practice and hypertension clinics globally
10. Significant number of participants were lost to follow up in either arms which can have a impact on the event rates

ACCORD AND ACCORDION STUDY

In the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial a median of 4.9 years of intensive (systolic BP [SBP] <120 mm Hg) versus standard (SBP <140 mm Hg) BP lowering reduced stroke but not mortality or the primary cardiovascular (CV) outcome (nonfatal MI, nonfatal stroke, or CV death) in 4733 people with type 2 diabetes (T2DM) and high CV risk.

The ACCORD Follow-On (ACCORDION) study assessed the long-term effect of this intervention on the incidence of CV events or death. During a median follow-up period of 8.8 years from randomization, the annual rate of the primary outcome (composite of nonfatal MI or stroke or CV death) was 2.03% in the intensive group and 2.22% in the standard group and hazard ratios (CI, p value) for incident outcomes in participants allocated to intensive versus standard BP lowering were 0.91 (0.79, 1.05, p=0.19) for the primary outcome; 1.04 (0.91, 1.19,p=0.59) for death; 0.87 (0.72, 1.06, p=0.16) for nonfatal MI; 0.85 (0.66, 1.10, p=0.22) for stroke; and 0.96 (0.75, 1.23, p=0.74) for CV death.

In conclusion, in patients with T2DM at increased CV risk, 4.9 years of intensive BP lowering did not reduce the rate of a composite of fatal and non-fatal major CV events or mortality over a median follow-up of 8.8 years. The stroke benefit observed during the active intervention did not persist after BP differences waned.

ACCORD trial showed a non-significant 12% lower risk of its primary composite cardiovascular outcome, with a 95%

confidence interval that included the possibility of a 27% lower risk, which is consistent with the cardiovascular benefit observed in SPRINT.

Secondary Prevention of Small Subcortical Strokes (SPS3) Trial

SPS3 compared an SBP treatment target of <130 mm Hg with a target of 130 mm Hg to 149 mm Hg in participants with a recent lacunar stroke, showed a non-significant reduction in recurrent stroke in the group randomized to the lower target

Perspective

Given the totality of the evidence produced by recent clinical trials, although well conducted and with substantial rationale, it looks unlikely that these evidence will unequivocally find its way through the 2017 guidelines. Important studies like ESH-CHL-SHOT trial are underway and likely to address some of these gaps. The year of 2017 will see a more robust effort to lower BP effectively and reduce the patient and physician inertia. To this extent the new data generated has achieved its goal even when the guidelines will persist with the already established blood pressure targets.

REFERENCES

1. Ambrosius WT, Sink KM, Foy CG, et al. The design and rationale of a multicenter clinical trial comparing two strategies for control of systolic blood pressure: the Systolic Blood Pressure Intervention Trial (SPRINT). *Clin Trials* 2014; 11:532–546.
2. The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015; 373:2103– 2116.
3. Cushman WC, Evans GW, Byington RP, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010; 362:1575–1585.
4. SPS3 Study Group Benavente OR, Coffey CS, Conwit R, Hart RG, McClure LA, Pearce LA, et al. . Blood-pressure targets in patients with recent lacunar stroke: the SPS3 randomised trial. *Lancet* 2013; 382:507–515.
5. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension. 1. Overview, metaanalyses and meta-regression analyses of randomized trials. *J Hypertens* 2014; 32:2285–2295.
6. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering treatment on Prevention of heart failure and new-onset heart failure – meta-analyses of randomized trials. *J Hypertens* 2016; 34:373–386.
7. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension Effects at different baseline and achieved blood pressure levels. Overview and metaanalyses of randomized trials. *J Hypertens* 2014; 32:2296–2299.