Defining Hypertension
Role of New Trials and Guidelines

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Introduction

In this perspective, I discuss the rationale for the definition of hypertension and review the evidence for the effect of lowering BP on cardiovascular events and mortality, including landmark studies that compared different levels of BP control on these outcomes. I conclude with the potential treatment implications of the new definition of hypertension and how I incorporate them into my practice. The accompanying perspectives discuss the BP targets for slowing progression of kidney disease and reducing risk for cardiovascular events among those with CKD.

Why Does the Definition of Hypertension Evolve?

The rationale for the continuing evolution of the definition of hypertension is more aggressive lowering of systolic BP among individuals who are hypertensive over the past five decades. Currently, the American Heart Association/American College of Cardiology (AHA/ACC) defines stage 1 hypertension in all adults as a systolic BP level of 130–139 mm Hg or a diastolic BP of 80–89 mm Hg (1). The changing definition of hypertension promulgated in recent AHA/ACC guidelines for diagnosis of hypertension results from focus on linkage between treated BP that results in improved cardiovascular outcomes. For example, as shown in the Systolic Pressure Intervention Trial (SPRINT), targeting lower systolic BP (<120 versus <140 mm Hg) treatment levels in high-risk nondiabetic patient populations improves cardiovascular outcomes and reduces all-cause mortality (2). In addition, in the Heart Outcomes Protection Evaluation 3 Trial, even modest reductions in systolic BP (approximately 6 mm Hg) among (mostly) nondiabetic populations at intermediate risk with highest baseline BP levels also reduce cardiovascular events (3). Thus, the evolving definition of hypertension is related to risk. For example, older individuals with higher systolic BP (with or without diabetes) are at higher risk for cardiovascular events, and lowering systolic BP more aggressively lowers this risk. However, what about the benefit of treating an individual with a systolic BP of 135 mm Hg who is below the age of 50 years old and has no other risk cardiovascular factors (*e.g.*, family history, dyslipidemia, smoking, obesity, kidney disease, *etc.*)? Should they be treated with pharmacologic therapy to lower systolic BP below 130 mm Hg? We do not know the answer to this question. Do we need to know the answer and if so, when?

It is important to note that benefit of BP lowering in clinical trials in both patients with diabetes and nonpatients without diabetes seems to be greatest among those with the highest level of cardiovascular risk as well as those with the highest baseline BP level. Whether future studies of BP lowering will continue to show benefit of further lowering of BP akin to those of cholesterol lowering is unknown. Epidemiologic studies suggest that, like cholesterol lowering, systolic BP lowering is associated with progressive lowering of cardiovascular events (4). Unfortunately, we do not have clinical trials in BP lowering, like those with LDL cholesterol lowering, that show continued reduction in cardiovascular event risk as LDL gets lower and lower. Furthermore, in contrast to LDL cholesterol, we do know that, in addition to important cardiovascular benefits, more aggressive systolic BP lowering can be associated with higher adverse events (2,5). Therefore, it is important to consider not only the benefits of lower BP goals (targets) but also, the potential risks. Individualizing BP treatment regimen is of great importance in everyday clinical practice.

What Is the Evidence?

Landmark clinical trials over the past 50 years have shown the benefit of pharmacologic lowering of BP for reducing cardiovascular event rates, including stroke, myocardial infarction, and heart failure, as well as cardiovascular death and all cause among various hypertensive populations (6–8). The SPRINT was randomized, controlled trial among 9361 nondiabetic hypertensive individuals at high risk for cardiovascular events designed to test the hypothesis that targeting a systolic BP <120 mm Hg would reduce clinical events more than targeting a systolic BP <140 mm Hg. The primary outcome was a composite of myocardial infarction, acute coronary syndrome (nonmyocardial infarction acute coronary syndrome), stroke, acute decompensated heart failure, and cardiovascular disease death. The study was discontinued early for efficacy (median follow-up of 3.26 years), having shown a 25% relative reduction for the composite outcome and a 27% relative risk reduction for all-cause

mortality. Importantly, 28% of the SPRINT participants were ≥75 years of age, 33% were black, 10% were Hispanic, 64% were men, and nearly one third had CKD at entry into the study. The benefit of the more aggressive lowering of BP extended to all of the subgroups. Importantly, the incidence rates of adverse events, including hypotension, syncope, electrolyte abnormalities, new-onset CKD, and AKI episodes, were significantly higher in the aggressive BP control arm. The AHA/ACC Task Force and nine other groups redefined high BP on November 13, 2017 (1). This redefinition represented the first guideline change in 14 years, and it was largely on the basis of the results of the SPRINT (2). On the basis of these data in combination with additional evidence from randomized, controlled trials; registries; and nonrandomized comparative and descriptive studies as well as systematic reviews, among other sources, the AHA/ACC revised the definition of hypertension.

In contrast to the SPRINT results, among patients with type 2 diabetes and hypertension (systolic BP ≥140/90 mm Hg), multiple clinical trials and meta-analyses show that pharmacologic lowering of BP also reduces cardiovascular events, including stroke, heart attack, and cardiovascular death (9). However, the results vary by population and study design. For example, BP lowering in the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation Trial of patients with type 2 diabetes (with and without hypertension) reduced major macrovascular and microvascular events and death (10,11). In contrast, targeting reduction of systolic BP to <120 mm Hg (versus <140 mm Hg) in the Action to Control Cardiovascular Risk in Type 2 Diabetes (ACCORD) Trial did not show an overall benefit on cardiovascular events or mortality. Taken together, these studies have led the American Diabetes Association to recommend treatment for systolic BP ≥140/90 mm Hg (12). Thus, the ADA effectively diagnoses hypertension in type 2 diabetes at this level. This contrasts with the AHA/ACC's new recommendation for the diagnosis of hypertension and reflects in part differing expert opinions surrounding the interpretation of data, primarily derived from clinical trials.

Does One Size Fit All in the Definition of Hypertension?

The AHA/ACC guidelines committee review considered the fact that the SPRINT did not include people with diabetes or stroke in consideration of defining hypertension and recommendations for intervention. The guidelines now define stage 1 hypertension as systolic BP ≥130 mm Hg or diastolic BP ≥80 mm Hg and stage 2 hypertension as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg. In addition, the guidelines provide a thoughtful approach to defining hypertension on the basis of several clinical conditions. Thus, they determined and promulgated thresholds for and goals of pharmacologic therapy in patients with hypertension according to comorbidities. This recommendation indicates that one size does not fit all patients who are hypertensive. Moreover, there are unanswered questions about many of these specific comorbidities. For example, as noted above among those in the ACCORD Trial randomized to aggressive systolic BP lowering, the incidence of stroke was significantly lower compared with among those with less aggressive lowering. The key message is that clinical decision making for treatment of hypertension and target BP should be a shared experience that includes the provider, the patient, and in some cases, family members among others.

What Are the Implications for the New Definition of Hypertension?

First, this new definition carries with it the implication that nearly one half (approximately 46%) of the United States population could be diagnosed with hypertension. Second, although translation into practice by patients and providers will take some time, the new definition will ultimately result in a change in clinical practice.

A lower BP threshold for recommending treatment will ultimately lead to more and potentially earlier intervention approaches, including lifestyle as well as pharmacologic intervention. The long-term benefit versus risk for early intervention is unknown, and although overall, the benefit to the population in terms of cardiovascular outcomes should increase, there is also increased risk for adverse events with broader application of pharmacologic interventions targeting lower BP as illustrated in the SPRINT. Moreover, a new definition of hypertension brings challenges to the clinic with respect to implementation of intervention to a potentially much larger population. Still, I have already implemented changes in my approach, and my approach is to treat each patient individually and apply the guidelines by not only considering the clinical conditions detailed by the guidelines but also, discussing with the patient one by one what is best. Shared decision making with our patients on the benefits and risks of more aggressive BP lowering is important and should be done on an ongoing basis.

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Disclosures

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