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Editorial

On-Treatment Diastolic Blood Pressure: When Is It Too High?

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Hypertension is the most important modifiable risk factor. According to the Korean hypertension factsheet 2021, it affects 28% of the adult population aged 20 or older.[1] Since the cardiovascular events increase with an increase in blood pressure (BP),[2][3] lowering BP is the main goal of hypertension treatment. In clinical practice, the treatment success is often measured with achieved BP, the on-treatment BP.

Surprisingly, determining the cutoff for normal or abnormal BP is challenging because BP is a continuous variable that is unimodally distributed and there is a continuous relationship between BP and cardiovascular outcomes. If the lower BP the better the outcome, what is the BP cutoff at which it becomes dangerous? This fundamental question has led to the endless controversies about BP cutoffs for the diagnosis of hypertension and setting the target BP. A dichotomous cutoff of 140/90 mmHg had been set arbitrarily based on the results of clinical trials and had been widely accepted, until Systolic Blood Pressure Intervention Trial (SPRINT) Study[4] showed intensive BP control led to better outcomes. The following 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guideline recommends BP of <130/80 mm Hg to diagnose hypertension. However, the European Society of Hypertension (ESH), International Society of Hypertension (ISH), and the Korean Society of Hypertension (KSH) still recommend 140/90 mmHg as cutoff for the diagnosis of hypertension.[5]

Another controversy is the role of diastolic BP (DBP). In contrast to isolated systolic hypertension, the term isolated diastolic hypertension is less familiar to many physicians. After initiation of antihypertensive drugs, both systolic BP (SBP) and DBP decrease simultaneously; however, some patients experience a relatively marginal decrease in DBP. What is the clinical relevance of elevated on-treatment DBP in patients who have reached the SBP target? In this issue of the journal, Kim and colleagues[6] investigated the association between cardiovascular events and two different levels, i.e., the JNC7 (SBP <140 mmHg, DBP ≥90 mmHg) or to the 2017 ACC/AHA definitions (SBP <130 mmHg, DBP ≥80 mmHg) of elevated on-treatment DBP in the presence of achieved SBP targets in a nation-wide population-based cohort study comprising 237,592 hypertensive patients. During a median follow-up of 9 years, elevated on-treatment DBP by the JNC7 definition was associated with an 14% increased risk of the composite of death, non-fatal myocardial infarction, or non-fatal stroke but not in those by the 2017 ACC/AHA definition. Elevated on-treatment DBP by

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The data generated in this study is available from the corresponding author upon reasonable request.

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the JNC7 definition was associated with a 42% increased cardiovascular mortality and 19% increased risk for stroke. Elevated on-treatment DBP by the 2017 ACC/AHA definition was only associated with a 10% increased risk for stroke.

There is a gap between the clinical trials and the real-word practice. The populations in the clinical trials are homogenous, selected by strict inclusion and exclusion criteria; whereas those in the real-world practice are a heterogenous group defined by indications and contraindications. The cutoffs derived from the clinical trials are population-specific and, consequently, the generalization to the general population can be problematic. The current by Kim and colleagues[6] is a nationwide population–based study using the Korean National Health Insurance Service database, covering 97% of the Korean population. This is the main strength of the current study. Using this large, real-world data, they showed that elevated on-treatment DBPs according to less intensive BP control (i.e., 140/90 mm Hg) was associated with an increased incidence of major adverse cardiac events (MACEs) which was mainly driven by cardiovascular deaths and stroke, whereas elevated on-treatment DBPs according to the more intensive BP control (i.e., 130/80 mmHg) was only associated with an increased risk of stroke.

Among the clinical outcomes, stroke is especially BP sensitive. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study,[7] targeting a SBP of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the MACE in high-risk diabetic patients. However, stroke could be reduced by 41%. In Heart Outcomes Prevention Evaluation-3 (HOPE-3) study,[8] candesartan 16 mg plus hydrochlorothiazide 12.5 mg per day did not reduce MACE among persons at intermediate risk who did not have cardiovascular disease. However, there was a 20% non-significant reduction in stroke. The current study by Kim and colleagues[6] displays that even in presence of controlled SBP, the elevated on-treatment DBP can increase stroke, emphasizing the importance of on-treatment DBP.

Nonetheless, there are some important issues the current study did not address. Because the study applied 2 different SBP criteria, i.e., 140 mmHg vs. 130 mmHg in each group, it cannot isolate the effect of elevated on-treatment DBP. The differential effect of antihypertensive drugs on outcomes has not been investigated, either. For example, beta-blockers are associated with higher increased risk for stroke compared to other groups of antihypertensive drugs.[9]

It appears that elevated on-treatment DBP is associated with increased cardiovascular events, even after achieving the SBP target. So, the remaining question is: where do we go from here?

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