Recent evidence on target blood pressure in patients with hypertension

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Hypertension is a significant risk factor for a variety of cardiovascular diseases, including stroke, coronary artery disease, heart failure, and peripheral arterial disease. Achieving and maintaining a specific target blood pressure (BP) is crucial for effectively reducing the risk associated with these conditions. This involves customizing treatments to meet the individual needs of patients with hypertension, ensuring that each person receives the most appropriate care for their particular circumstances. Previously, based on the findings from the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study conducted over the past decade, the target BP for patients with hypertension was set at <140/90 mmHg, regardless of the patient’s risk profile. However, new insights from re-analyzed data of studies such as the SPRINT (Systolic Blood Pressure Intervention Trial), the STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) study, and ACCORD subgroup reanalysis have led to a change in this approach. These studies support a more aggressive target BP of <130/80 mmHg, especially for high-risk patients. The purpose of this article is to offer a thorough review of these updated recommendations and to explain the reasoning behind the revised target BP guidelines for individuals with hypertension.

Keywords: Cardiovascular risk; Blood pressure; Hypertension

INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of mortality and morbidity worldwide [1]. Hypertension, or high blood pressure (BP), is one of the most prevalent and significant risk factors for CVD [2–4]. Fortunately, individuals can dramatically reduce their risk of developing CVD by controlling hypertension [5–9]. From a cost-effectiveness standpoint, controlling BP is more effective in reducing the risk of cardiovascular disease and mortality than any other medical intervention [10]. Years of intensive research and dedicated human effort have yielded a variety of practical strategies to combat hypertension. These include lifestyle modifications, pharmaceutical treatments, and advanced device therapies [3]. For individuals diagnosed with hypertension, establishing a target BP is crucial. This target acts as a benchmark for health professionals and patients alike, providing a measure to determine whether BP is being managed effectively [11]. The target BP varies depending on the patient’s age, underlying health conditions, and overall cardiovascular risk. Recent major clinical studies have led to a reevaluation and, in many cases, a downward adjust-
ment of the target BP, particularly for high-risk patients. This review summarizes the latest evidence for determining the target BP in the management of hypertension.

**RECENT EVIDENCE FOR TARGET BP**

Numerous randomized studies have established that the threshold for systolic BP (SBP) is 140 mmHg, and for diastolic BP (DBP), it is 90 mmHg. Lowering BP to these levels has been shown to effectively reduce the risk of cardiovascular events [7–9]. In light of this evidence, there is a consensus that the target BP for patients with uncomplicated and low-to-moderate risk hypertension should be <140/90 mmHg. While some studies in the general population have indicated that a target SBP of <130 mmHg can lead to a reduction in cardiovascular events, a target of <140 mmHg is generally considered more reasonable than one of <130 mmHg [4].

While there is limited evidence regarding the optimal DBP targets, it has been suggested that DBP values of 90 and 80 mmHg correspond to SBP values of 140 and 130 mmHg, respectively. Recently, the primary debate surrounding target BP levels has centered on whether to set the target at <140/90 or <130/80 mmHg.

Over the past decade, there has been considerable debate regarding the optimal target BP for patients at high cardiovascular risk. The ACCORD (Action to Control Cardiovascular Risk in Diabetes) study [12] found no significant difference in the incidence of composite cardiovascular events between the intensive treatment group, which had a BP target of SBP <120 mmHg, and the conservative treatment group, with a BP target of SBP <140 mmHg. Although the ACCORD study was limited to patients with diabetes, it was a well-designed randomized trial that specifically addressed target BP. Its findings had a significant impact. Since diabetes is a high-risk factor comparable to CVD [13], the ACCORD study raised questions about the benefits of intensive BP control in high-risk patients. As a result, major guidelines around the world recommended a target BP of <140/90 mmHg, regardless of cardiovascular risk [14,15]. However, numerous observational studies and meta-analyses have suggested that an SBP of <120 mmHg may be optimal for minimizing cardiovascular risk [2,16,17]. Additionally, research has shown that patients with elevated BP (SBP, 120–129 mmHg) or prehypertension (SBP, 130–139 mmHg) are at an increased risk of developing CVD compared to those with normal BP (SBP <120 mmHg) [18].

The ACCORD study [12] utilized a 2×2 design to examine the effects of both glucose and BP control. When analyzing patients with reasonably well-controlled glucose levels separately, it was noted that the risk of cardiovascular events was lower in the intensive treatment group that aimed for a target SBP of <120 mmHg. This evidence has led to consistent recommendations to lower the target BP in high-risk patients. However, due to the absence of supportive evidence from other well-designed randomized trials like ACCORD, there was insufficient data to alter clinical guidelines that demand high-quality evidence. This changed with the release of the SPRINT (Systolic Blood Pressure Intervention Trial) [5] results in 2015 in the United States, which reshaped the approach to target BP for hypertension in high-risk patients. The SPRINT study was a randomized trial that included high-risk patients with a substantial risk of CVD, such as those with existing CVD, older adults, individuals with chronic kidney disease (CKD), and those with a 10-year cardiovascular risk >10%. Participants were divided into two groups with target SBPs of <120 and <140 mmHg, respectively, to compare the risk of cardiovascular events based on the BP-lowering effect. The study found that the intensive treatment group, which maintained a target SBP of <120 mmHg, experienced a significant reduction in cardiovascular events compared to the standard treatment group, which had a target SBP of <140 mmHg (hazard ratio with intensive treatment, 0.75; 95% confidence interval, 0.64–0.89; P<0.001). The benefits of BP reduction were so substantial that the trial was stopped early. The SPRINT study’s findings were particularly credible because the study was conducted under the auspices of the US National Institutes of Health (NIH) without pharmaceutical company involvement, which increased the academic community’s confidence in the results. In 2017, the 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines [19] revised the diagnostic criteria for hypertension from ≥140/90 to ≥130/80 mmHg, based on the SPRINT study.

Subsequent meta-analyses [20] that included the SPRINT study and other research have consistently reported the benefits of intensive treatment for high-risk patients, leading to stronger arguments for lowering the target BP in this population. When patients who met the SPRINT study’s en-
Hypertension should be managed in older adults with appropriate consideration of their unique characteristics [23,24]. Elderly patients typically exhibit increased arterial stiffness, which leads to elevated pulse pressure and a higher incidence of isolated systolic hypertension. They also experience greater BP variability, along with a higher occurrence of masked hypertension and white coat hypertension. Furthermore, older adults often have an increased risk of side effects from antihypertensive medications due to polypharmacy for other coexisting conditions, which raises the potential for drug interactions with antihypertensive treatments. Despite these challenges, the benefits of BP reduction are evident in older adults; therefore, they should not neglect the management of high BP [5,6,25,26]. In the SHEP (Systolic Hypertension in the Elderly Program) study [26], which included 4,736 patients aged 60 years and older with isolated systolic hypertension, reducing SBP from 155 to 144 mmHg using chlorothalidone and/or atenolol led to a 32% decrease in CVD incidence. Similarly, in the HYVET (Hypertension in the Very Elderly Trial) [25] involving 3,845 patients aged 80 years and above, controlling SBP above 160 mmHg with indapamide or perindopril to achieve levels around 140 mmHg resulted in a 23% reduction in CVD incidence compared to the placebo group. For older adults with hypertension, the general target BP is <140/90 mmHg [22]. While some past studies reported no significant difference between maintaining an SBP of <140 and <150 mmHg in older adults, recent research, such as the SPRINT study [5] and STEP study [6], has shown that more aggressive BP control in older adults is even more effective in reducing CVD risk. However, older adults have a higher frequency of side effects from BP reduction than younger individuals. Therefore, particularly in frail older adults, care should be taken not to reduce BP excessively, and potential side effects should be closely monitored [3].

**Patients with high-risk profiles**

For patients with hypertension with asymptomatic organ damage or for those with three or more cardiovascular risk factors, it is recommended to control BP to <130/80 mmHg, even in the absence of complications [11]. The SPRINT study [5], which demonstrated the benefits of BP reduction in patients with high-risk factors, provides strong support for this recommendation.

**Patients with diabetes mellitus**

Hypertension is highly prevalent in patients with diabetes mellitus [23,24]. Elderly patients typically exhibit increased arterial stiffness, which leads to elevated pulse pressure and a higher incidence of isolated systolic hypertension. They also experience greater BP variability, along with a higher occurrence of masked hypertension and white coat hypertension. Furthermore, older adults often have an increased risk of side effects from antihypertensive medications due to polypharmacy for other coexisting conditions, which raises the potential for drug interactions with antihypertensive treatments. Despite these challenges, the benefits of BP reduction are evident in older adults; therefore, they should not neglect the management of high BP [5,6,25,26]. In the SHEP (Systolic Hypertension in the Elderly Program) study [26], which included 4,736 patients aged 60 years and older with isolated systolic hypertension, reducing SBP from 155 to 144 mmHg using chlorothalidone and/or atenolol led to a 32% decrease in CVD incidence. Similarly, in the HYVET (Hypertension in the Very Elderly Trial) [25] involving 3,845 patients aged 80 years and above, controlling SBP above 160 mmHg with indapamide or perindopril to achieve levels around 140 mmHg resulted in a 23% reduction in CVD incidence compared to the placebo group. For older adults with hypertension, the general target BP is <140/90 mmHg [22]. While some past studies reported no significant difference between maintaining an SBP of <140 and <150 mmHg in older adults, recent research, such as the SPRINT study [5] and STEP study [6], has shown that more aggressive BP control in older adults is even more effective in reducing CVD risk. However, older adults have a higher frequency of side effects from BP reduction than younger individuals. Therefore, particularly in frail older adults, care should be taken not to reduce BP excessively, and potential side effects should be closely monitored [3].
tes [27]. Controlling BP in this population is critical, as it significantly reduces the risk of CVD, including coronary heart disease and stroke, which are frequent complications of diabetes [28]. Tight BP management is also beneficial in preventing or slowing the progression of diabetic complications, such as kidney disease and retinopathy [29,30]. In a study that utilized a database from the National Health Insurance Service of Korea (NHIS) [31], approximately 240,000 patients with both hypertension and diabetes were examined. The study found that, in patients under the age of 70 years, lower BP was associated with a decreased incidence of cardiovascular events.

However, debate continues regarding the optimal BP target for patients with diabetes [32]. Among the studies proposing target BP levels for this group, the ACCORD study [13] is particularly noteworthy. This study included 4,733 patients with diabetes who were receiving antihypertensive treatment to achieve SBP targets of either <120 or <140 mmHg. The findings revealed no significant difference in the overall incidence of cardiovascular events and mortality between the two target groups. However, the group that underwent more intensive BP-lowering therapy experienced a higher rate of side effects. As a result, for some time, a BP target of <140/90 mmHg was recommended for patients with diabetes. Several other studies, primarily sub-analyses, have similarly concluded that intensive BP-lowering therapy did not reduce the incidence of cardiovascular events in patients with diabetes [33,34]. Subsequent meta-analysis [35] have shown no difference in CVD incidence in patients with diabetes when the BP target was set below 140 mmHg compared to below 130 mmHg. Therefore, the benefits of intensive BP lowering in the general diabetic population remain unclear.

The current Korean guideline [11] recommends a target BP of <140/90 mmHg for the general diabetic population. However, for patients with diabetes with high-risk factors, such as those with asymptomatic organ damage or at least one CVD risk factor, a more intensive BP-lowering therapy is emphasized, with a target BP set at <130/80 mmHg. This recommendation is informed by reanalyzed data from the ACCORD study [21], which demonstrated that intensive BP reduction reduced cardiovascular risk in high-risk patients, and is in line with criteria from the STEP study [5], as well as findings from the STEP study [6], which included 19% patients with diabetes.

**Patients with CVD**

Based on the SPRINT study [5], a target BP of <130/80 mmHg is recommended in patients with CVD (coronary artery disease, peripheral artery disease, abdominal aortic aneurysm, heart failure, or left ventricular hypertrophy).

**Patients with CKD**

Hypertension is the most prevalent comorbidity in CKD, with its prevalence estimated at 70% to 80% in stage 1 and rising to over 90% in stages 4 and 5, according to office BP measurements [36]. The primary mechanism behind high BP in CKD involves sodium retention and the activation of both the sympathetic nervous system and the renin-angiotensin system, due to a decreased glomerular filtration rate [37]. In patients with CKD, hypertension is a major risk factor for worsening renal function and the onset of CVD [38,39]. The SPRINT study [40] showed that patients with CKD who received intensive BP-lowering treatment (with a target SBP of <120 mmHg) had reduced mortality and cardiovascular risk. This finding led to the 2021 revision of the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [41], which now recommended controlling SBP to <120 mmHg in CKD patients. However, there are limitations in directly accepting the results of the SPRINT study, because the SPRINT study excluded patients with diabetes, younger individuals (under 50 years old), and those with significant proteinuria (>1 g/day), and the BP measurement method used in the study does not align with actual clinical practices [5,42]. In the MDRD (Modification of Diet in Renal Disease) study [43] and the AASK (African American Study of Kidney Disease and Hypertension) study [44], intensive BP reduction targeting an SBP of around 130 mmHg in CKD patients did not significantly impact renal function or cardiovascular outcomes. The MDRD study enrolled 1,585 patients with an estimated glomerular filtration rate (eGFR) of 25 to 55 mL/min/1.73m². The study maintained average measurements of Kidney Disease and Hypertension (MDRD) study [43] and the AASK (African American Study of Kidney Disease and Hypertension) study [44], intensive BP reduction targeting an SBP of around 130 mmHg in CKD patients did not significantly impact renal function or cardiovascular outcomes. The MDRD study enrolled 1,585 patients with an estimated glomerular filtration rate (eGFR) of 25 to 55 mL/min/1.73m². The study maintained average BP below 107 mmHg for those under 60 years and below 113 mmHg for those over 60 years in the usual BP group. In the lower BP group, targets were below 92 mmHg for those under 60 years and below 98 mmHg for those over 60 years. Over an average follow-up of 2.2 years, there was no significant difference in the incidence of end-stage renal disease (ESRD) and death between the usual and lower BP groups.
However, subgroup analyses from both the randomized trial and the extended study indicated that the benefits of a lower BP target on the GFR slope and hard outcomes were primarily evident in patients with proteinuria, especially those excreting more than 1 g/day of protein [45,46]. In the AASK study, 1,094 patients with hypertension with a baseline eGFR of 20 to 65 mL/min/1.73 m² were enrolled. The usual BP group aimed for a mean BP of 102 to 107 mmHg, while the lower BP group targeted <92 mmHg. Over a follow-up of 3 to 6.4 years, the outcomes measured included a decline in eGFR by more than 50%, ESRD, and death. No significant differences were observed between the two groups [44]. However, the impact varied based on baseline proteinuria levels (P=0.02 for interaction), showing a potential benefit for patients with a protein-to-creatinine ratio of more than 0.22 g/g (about 320 mg/day), indicated by a hazard ratio of 0.73 (P=0.01) [47]. Collectively, for CKD patients with relatively high levels of albuminuria, the BP-lowering effect consistently demonstrated in several studies appears to effectively suppress the deterioration of renal function and reduce cardiovascular risk, especially compared to CKD patients with low or no albuminuria [45–47]. Based on these research findings, controlling BP to <130/80 mmHg in CKD patients with prominent albuminuria is recommended. However, it is advised for CKD patients with no or mild albuminuria or general CKD patients to maintain BP at <140/90 mmHg. For CKD patients who also have diabetes, given their higher risk profile akin to high-risk patients with diabetes, it is better to aim for a slightly lower BP of <130/80 mmHg [11].

Patients with stroke

Hypertension is a major risk factor for stroke recurrence and the onset of CVD in stroke patients, making BP control essential in this population [48,49]. Numerous clinical studies have demonstrated limited benefits when SBP was controlled to <130 mmHg in stroke patients [50]. In the PATS (Post-stroke Antihypertensive Treatment Study), 5,665 patients with a history of stroke or transient ischemic

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**Fig. 1.** Target blood pressure. a) Risk factors: age (male ≥45 years, female ≥55 years), family history of early cardio-cerebro-vascular disease (male <55 years, female <65 years), smoking, obesity, dyslipidemia, pre-diabetes and diabetes mellitus. b) Target organs damages: periventricular white matter hyperintensity, microbleeds, asymptomatic stroke, left ventricular hypertrophy, albuminuria, low glomerular filtration rate, atheromatous plaque, carotid-femoral pulse wave velocity >10 m/sec, brachial-ankle pulse wave velocity >18 m/sec, coronary artery calcium score ≥400, hypertensive retinopathy (grade ≥3).

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attack (TIA) were enrolled. Over an average follow-up period of 2 years, the group treated with 2.5 mg of indapamide achieved a BP reduction to 144/87 mmHg, which led to an approximate 30% reduction in recurrent stroke compared to the placebo group, which maintained a BP of 149/89 mmHg [51]. In the PROGRESS (Perindopril Protection Against Recurrent Stroke Study), 6,105 patients with a history of stroke or TIA were administered 4 mg of perindopril, which lowered their SBP from 147 to 138 mmHg. This treatment resulted in a 26% reduction in the risk of major cardiovascular events compared to the placebo group, where SBP remained at 147 mmHg [48]. However, a subsequent study involving 20,332 stroke patients, which used 80 mg of telmisartan to reduce SBP from 144 to 136 mmHg, did not show a decrease in the recurrence of stroke or cardiovascular events compared to the control group, which experienced a reduction from 144 mmHg to 141 mmHg (P>0.05) [52]. In the SPS3 (Secondary Prevention of Small Subcortical Strokes) study [50], 3,020 patients with symptomatic lacunar infarctions confirmed by brain magnetic resonance imaging were analyzed. The study found no difference in the recurrence of stroke or the occurrence of cardiovascular events between the intensive treatment group, which lowered SBP to 127 mmHg, and the standard treatment group, which reduced SBP to 138 mmHg. However, the authors noted a significant 63% reduction in the incidence of hemorrhagic strokes when SBP was controlled to <130 mmHg. Based on these findings, the recommended target BP for general stroke patients is <140/90 mmHg, while for those with lacunar infarction, the target is <130/80 mmHg.

Target BPs are summarized in Fig. 1.

LOWER LIMIT OF THE TARGET BP

The "J curve" hypothesis posits that cardiovascular risk may increase when BP is excessively low [53,54]. This understanding of the J curve is particularly important when determining target BP levels. It is essential to recognize that in patients with CVD, an overemphasis on intensive BP-lowering therapy could result in detrimental effects due to overly reduced BP. When prescribing antihypertensive medications, it is important to consider potential side effects associated with low BP, such as syncope, deterioration of kidney function, and electrolyte imbalances [5,12]. Therefore, it is essential to consider the lower limit of the BP treatment target. Generally, it is recommended to avoid lowering treatment BP to <110/70 mmHg.

Specifically, DBP is vital for maintaining coronary artery blood flow; therefore, caution is advised to prevent reducing DBP to <70 mmHg in older adults, patients with diabetes, and those with coronary artery disease or cardiac hypertrophy [55,56].

CONCLUSIONS

In general, for patients with hypertension with a low risk of CVD, the target BP is <140/90 mmHg. However, recent findings from the SPRINT and STEP trials, as well as a reanalysis of the ACCORD trial, have highlighted the benefits of intensive BP reduction in high-risk patients. These high-risk groups include individuals with high-risk hypertension, CVD, high-risk diabetes, CKD with albuminuria, and lacunar infarction. As a result, the target BP for these patients has been set at <130/80 mmHg. For patients with diabetes, CKD, and a history of stroke, the evidence does not support a uniform target BP of <130/80 mmHg. Instead, it is recommended to consider lowering the target BP to <130/80 mmHg selectively for those with additional high-risk factors. It is crucial to recognize the appropriate target BP for each patient and to implement this knowledge in clinical practice, with the ultimate goal of improving the prognosis for individuals with hypertension.

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