

Update in Hypertension Therapy



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KEYWORDS

- Hypertension • Blood pressure • Therapy • Antihypertensives
- Blood pressure goals • Spironolactone • SGLT-2 inhibitors

KEY POINTS

- Targets for blood pressure control, traditionally less than 140/90 mm Hg, should be reduced to less than 120 mm Hg systolic in patients more than 50 years of age at very high risk for cardiovascular events.
- With few exceptions, first-line therapy for hypertension should be selected from one of 4 classes: thiazide diuretics, dihydropyridine calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs).
- When blood pressure is not controlled on a low dose of a single agent, adding a second agent is more effective than simply increasing the dose of monotherapy.
- ACE inhibitors seem to be superior to ARBs with regard to overall mortality and should be chosen preferentially. ACE inhibitors and ARBs should not be used in combination because of increased adverse events without appreciable benefits.
- Spironolactone is a particularly potent agent for blood pressure reduction in patients with refractory hypertension.

INTRODUCTION

Hypertension affects about 1 in every 3 adults in the United States and more than 1 billion people worldwide, and the prevalence is projected to increase by 60% by 2025.^{1–3} It is the leading global risk factor for mortality, accounting for about 1 out of every 8 deaths worldwide. Hypertension results in an average loss of life of 5 years, and those living with hypertension are more often burdened with morbidities of congestive heart failure, chronic kidney disease, neurologic deficits from stroke, and vision loss.⁴

CLINICAL QUESTION: WHAT ARE THE APPROPRIATE TARGETS FOR BLOOD PRESSURE CONTROL?

Reducing chronically increased blood pressure using medications clearly reduces the incidence of coronary artery disease, stroke, congestive heart failure, and chronic

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kidney disease.⁵⁻⁷ Epidemiologic evidence suggests a profound increase in cardiovascular mortality with increasing blood pressure greater than systolic pressures of 115 mm Hg.⁸ For the past 3 decades, physicians have settled on a target blood pressure of less than 140/90 mm Hg based on a preponderance of epidemiologic studies. However, most randomized controlled trials have not shown convincing benefits for blood pressure reduction below a systolic target of 150 mm Hg.

Several trials have examined the question of the most appropriate systolic targets for blood pressure in different age and risk categories. A Cochrane Review in 2009 examined outcomes differences between groups treated to standard blood pressure targets (<140–160/90–100 mm Hg) versus more intensive control (<135/85).⁹ The investigators identified 7 randomized trials involving more than 22,000 subjects. Despite significant blood pressure differences, there were no differences in outcomes between the groups. In addition, subgroup analyses did not reveal differences among higher risk patients such as those with diabetes mellitus or chronic kidney disease.

The AASK (African American Study of Kidney Disease and Hypertension) trial examined 1094 African American patients with chronic kidney disease, comparing a standard blood pressure target (<140 mm Hg systolic) with a more aggressive blood pressure goal (<130 mm Hg systolic).¹⁰ Despite significant differences in blood pressure achieved between the two groups, there were no differences in the end point of progression of chronic kidney disease or mortality over roughly a decade of follow-up.

The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial was a randomized controlled trial of adults with diabetes and hypertension who were at very high risk for cardiovascular events.¹¹ The investigators enrolled 4733 patients and followed them over approximately 5 years to determine whether pursuing a more aggressive blood pressure target (<120 mm Hg) would result in fewer important cardiovascular events compared with the traditional systolic blood pressure target (<140 mm Hg). The study failed to show improvement in the primary composite end point of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death. The investigators noted a significant reduction in stroke rate with aggressive blood pressure control, but the number needed to treat was large (~450 over 5 years) to prevent a single event. These small gains came with a cost: increased serious adverse events were significantly more common; namely hypotension, electrolyte disturbances, and worsening of serum creatinine levels.

The paucity of evidence supporting more aggressive blood pressure control led the National Expert Panel (JNC 8) to recommend a less stringent target blood pressure of less than 150/90 mm Hg in adults more than age 60 years in their 2014 guidelines.¹² The group continued to recommend a target blood pressure of less than 140/90 mm Hg in younger adults, although this the recommendation of less than 140/90 mm Hg emanated from expert opinion in the absence of randomized trials. The JNC 8 conclusions raised a great deal of debate about appropriate blood pressure targets and left physicians and patients with much uncertainty.

In 2015, the National Heart, Lung, and Blood Institute released results of the Systolic Blood Pressure Intervention Trial (SPRINT), a randomized controlled, open-label trial of intensive versus standard blood pressure control in nondiabetic adults more than 50 years of age.¹³ In the trial, 9361 patients at high risk for cardiovascular events were randomly assigned to standard (<140 mm Hg) versus aggressive (<120 mm Hg) control of blood pressure. Average starting blood pressure in the trial was 139.7 mm Hg, and participants were seen monthly for medication adjustments until their blood pressure target had been reached. The investigators achieved mean systolic blood pressures of 134.6 mm Hg in the standard group and 121.5 mm Hg in the

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