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“Go low” or say “No” to aggressive systolic BP goals?

The SPRINT trial demonstrated the benefits—and risks—of reaching a systolic target <120 mm Hg in non-diabetic patients at high risk for CV events. Here’s who might benefit.

PRACTICE CHANGER

Consider treating non-diabetic patients age ≥ 50 years to a systolic blood pressure (SBP) target <120 mm Hg as compared to <140 mm Hg when the benefits—lower rates of fatal and nonfatal cardiovascular (CV) events and death from any cause—are likely to outweigh the risks from possible additional medication.¹

STRENGTH OF RECOMMENDATION

B: Based on a single, good-quality randomized controlled trial (RCT).

Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103-2116.

ILLUSTRATIVE CASE

A 55-year-old man with hypertension and stage 3 chronic kidney disease (CKD) comes in to your office for routine care. His blood pressure is 135/85 mm Hg, and he is presently taking lisinopril 40 mg daily. Should you increase his antihypertensive regimen?

Hypertension is common and leads to significant morbidity and mortality, but pharmacologic treatment reduces incidence of stroke by 35% to 40%, myocardial infarction (MI) by 15% to 25%, and heart failure by up to 64%.²⁻⁴ Specific blood pressure targets for defined populations continue to be studied.

In patients with diabetes, the ACCORD (Action to Control Cardiovascular Risk in

Diabetes) trial found that more intensive BP targets did not reduce the rate of major CV events, but the study may have been underpowered.⁵ The members of The Eighth Joint National Committee recommended treating patients over age 60 years to BP goals <150/90 mm Hg.⁶ This was based on evidence from 6 randomized controlled trials (RCTs),⁷⁻¹² but there remains debate—even among the members of the Committee—as to appropriate BP goals in patients of any age without CV disease who have BP measurements of 140-159/90-99 mm Hg.¹³

STUDY SUMMARY

Treating to SBP <120 mm Hg lowers mortality

The Systolic Blood Pressure Intervention Trial (SPRINT) was a multicenter RCT designed to determine if treating to lower SBP targets in non-diabetic patients at high risk for CV events improves outcomes as compared to standard care. Patients were at least 50 years of age with SBP of 130 to 180 mm Hg and were at increased CV risk as defined by clinical or subclinical CV disease other than stroke, CKD with glomerular filtration rate (GFR) 20 to 60 mL/min/1.73 m², 10-year risk of CV disease >15% on Framingham risk score, or age ≥ 75 years of age. Patients with diabetes; prior stroke; polycystic kidney disease; significant proteinuria within the past 6 months; symptomatic heart failure within the past 6 months; or left ventricular ejection fraction <35% were excluded.¹



INSTANT POLL

How likely are you to more aggressively treat hypertension in high-risk patients in light of the SPRINT trial findings?

- Not at all likely
- Somewhat likely
- Extremely likely

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Patients (N=9361) were randomly assigned to an SBP target <120 mm Hg in the intensive group or <140 mm Hg in the standard treatment group, in an open-label design. Allocation was concealed. The study protocol encouraged, but did not require, the use of thiazide-type diuretics, loop diuretics (for those with advanced renal disease), angiotensin-converting enzyme inhibitors or angiotensin receptor blocker agents, calcium channel blockers, and beta-blockers. Clinicians could add other agents as needed. All major classes of antihypertensives were used.

Medication dosing adjustments were based on the average of 3 BP measurements taken with an automated measurement system (Omron Healthcare, Model 907) with the patient seated after 5 minutes of quiet rest. Target SBP in the standard therapy group was 135 to 139 mm Hg. Medication dosages were lowered if SBP was <130 mm Hg at a single visit or <135 mm Hg at 2 consecutive visits.¹

The primary composite outcome included the first occurrence of MI, acute coronary syndrome, stroke, heart failure, or death from CV causes. Secondary outcomes were the individual components of the primary composite outcome, death from any cause, and the composite of the primary outcome or death from any cause.¹

■ **Study halted early.** The study was stopped early due to significantly lower rates of the primary outcome in the intensive therapy group vs the standard therapy group (1.65% per year vs 2.19% per year, respectively, hazard ratio [HR] with intensive treatment=0.75; 95% confidence interval [CI], 0.64-0.89; $P<.001$). The resulting median follow-up time was 3.26 years.¹ This corresponds to a 25% lower relative risk of the primary outcome, with a decrease in event rates from 6.8% to 5.2% over the trial period. All-cause mortality was also lower in the intensive therapy group: 3.4% vs 4.5% (HR=0.73; 95% CI, 0.60-0.90; $P=.003$).

The number needed to treat (NNT) over 3.26 years to prevent a primary outcome event, death from any cause, and death from CV causes was 61, 90, and 172, respectively. Serious adverse events occurred more frequently in the intensive therapy group than in

the standard therapy group (38.3% vs 37.1%; HR=1.04; $P=.25$) with a number needed to harm (NNH) of 46 over the study period.¹ (When looking at serious adverse events identified as likely associated with the intervention, rates were 4.7% vs 2.5%, respectively [$P<.001$].) Hypotension, syncope, electrolyte abnormalities, and acute kidney injury/acute renal failure reached statistical significance. The incidence of bradycardia and injurious falls was higher in the intensive treatment group, but did not reach statistical significance. In the subgroup of patients ≥ 75 years of age, 48% in each study group experienced a serious adverse event.¹

Throughout the study, mean SBP was 121.5 mm Hg in the intensive therapy group and 134.6 mm Hg in the standard treatment group. This required an average of one additional BP medication in the intensive therapy group (2.8 vs 1.8, respectively).¹

WHAT'S NEW

Lower SBP produces mortality benefits in those under, and over, age 75

This trial builds on a body of evidence that shows the advantages of lowering SBP to <150 mm Hg^{7,11,12} by demonstrating benefits, including lower all-cause mortality, for lower SBP targets in non-diabetic patients at high risk of CV disease. The SPRINT trial also showed that the benefits of intensive therapy remained true in a subgroup of patients ≥ 75 years of age.

The incidence of the primary outcome in the cohort ≥ 75 years of age receiving intensive therapy was 7.7% vs 10.9% for those receiving standard therapy (HR=0.67; 95% CI, 0.51-0.86; NNT=31). All-cause mortality was also lower in the intensive therapy group than in the standard therapy group among patients ≥ 75 years of age: 5.5% vs 8.04% (HR=0.68; 95% CI, 0.50-0.92; NNT=38).¹

CAVEATS

Many do not benefit from—or are harmed by—increased medication

The absolute risk reduction for the primary outcome is 1.6%, meaning 98.4% of patients receiving more intensive treatment will not



In a group of 1000 patients, an estimated 16 patients will benefit from intensive BP treatment, 22 patients will be seriously harmed, and 962 patients will experience neither benefit nor harm.

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Identifying patients most likely to benefit from more intensive blood pressure targets remains challenging.

benefit. In a group of 1000 patients, an estimated 16 patients will benefit, 22 patients will be seriously harmed, and 962 patients will experience neither benefit nor harm.¹⁴ The difference between how BP was measured in this trial (an average of 3 readings after the patient had rested for 5 minutes) and that which occurs typically in clinical practice could potentially lead to overtreatment in practice.

Also, reducing antihypertensive therapies when the SBP was about 130 to 135 mm Hg in the standard therapy group likely exaggerated the difference in outcomes between the intensive and standard therapy groups, and is neither routine nor recommended in clinical practice.⁶ Finally, the trial specifically studied non-diabetic patients at high risk of CV disease ≥50 years of age, limiting generalizability to other populations.

CHALLENGES TO IMPLEMENTATION

Who will benefit/who can achieve intensive SBP goals?

Identifying patients most likely to benefit from more intensive BP targets remains challenging. The SPRINT trial showed a mortality benefit, but at a cost of increased morbidity.^{1,14}

In particular, caution should be exercised in the subgroup of patients ≥75 years. Despite a lower NNT than the rest of the study population, serious adverse events happened more frequently. Also, this particular cohort of volunteers may not be representative of those ≥75 years of age in the general population.

Additionally, achieving intensive SBP goals can be challenging. In the SPRINT trial, only half of the intensive target group achieved an SBP <120 mm Hg.¹ And in a 2011-12 National Health and Nutrition Examination Survey, only 52% of patients in the general population achieved a BP target <140/90 mm Hg.¹⁵ Lower morbidity and mortality should remain the ultimate goals to the management of hypertension, requiring physicians to carefully assess an individual patient's likelihood of benefit vs harm. **JFP**

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