Intensive lowering of blood pressure: Should we SPRINT?

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The publication of the Systolic Blood Pressure Intervention Trial (SPRINT) challenged the conventional approach to hypertension care.[1] SPRINT compared intensive lowering of systolic blood pressure (BP) (systolic BP target ≤ 120 mm Hg) with standard treatment (systolic BP target ≤ 140 mm Hg) in 9361 participants aged 50 years and older who had a high risk for cardiovascular disease but no diabetes, and baseline BP levels of 130–180 mm Hg. Eligible participants had either clinical or subclinical cardiovascular disease (excluding stroke and heart failure), a 10-year Framingham Risk Score of 15% or greater, age 75 years or greater, or chronic kidney disease (estimated glomerular filtration rate 20–60 mL/min/1.73 m^2). After 3.3 years, the trial was stopped early. The mean achieved systolic BP level was 122 mm Hg in the intensive arm and 135 mm Hg in the standard arm. In participants assigned to intensive BP lowering, major adverse cardiovascular events were reduced by 25% (5.2% v. 6.8%; hazard ratio [HR] 0.75, 95% confidence interval [CI] 0.64–0.89; number needed to treat [NNT] of 62 over 3 yr) and all-cause mortality was reduced by 27% (3.3% v. 4.5%; HR 0.73, 95% CI 0.60–0.90; NNT of 90 over 3 yr). Notably, no significant reductions were seen in stroke and myocardial infarction.

The results of SPRINT are consistent with the broader literature. A large meta-analysis of 123 placebo-controlled and treat-to-target trials enrolling more than 613 000 participants found that lowering systolic BP by 10 mm Hg reduces the incidence of major cardiovascular events (HR 0.80, 95% CI 0.77–0.83), coronary heart disease (HR 0.83, 95% CI 0.78–0.88), stroke (HR 0.73, 95% CI 0.68–0.77), heart failure (HR 0.72, 95% CI 0.67–0.78), and all-cause mortality (HR 0.87, 95% CI 0.84–0.91). Importantly, risk reductions are similar when stratified by baseline systolic BP (in quintiles from < 130 to ≥ 160 mm Hg).[2] A second meta-analysis focusing only on treat-to-target trials involving patients at high cardiovascular risk (19 trials; nearly 45 000 participants) also reported consistent findings for major cardiovascular events, myocardial infarction and stroke.[3]

Based on these data, we believe that intensive lowering of systolic BP should be strongly considered for implementation in general clinical practice. But which patients would benefit, and how should it be done? Four key elements of SPRINT must be emphasized or we cannot hope to realize its benefits in practice.

First, SPRINT enrolled participants at high risk for cardiovascular disease, but the SPRINT definition of high risk is not entirely inclusive (e.g., it excludes patients with diabetes, stroke and heart failure). Implementation in this defined subset of patients only would be prudent, and the criteria for assigning high-risk status need to be clearly delineated.[4,5]

Second, BP measurement in SPRINT consisted of an average of three readings using an automated office BP (AOBP) device following a five-minute rest period. When BP is measured in the office setting, contemporary Canadian hypertension guidelines strongly endorse the use of multiple readings taken using electronic devices (specifically, AOBP devices) while the patient is unattended to minimize the white-coat effect.[6,7] Further, mean AOBP measurements read 5–10 mm Hg lower than routine manual BP measurements.[7] Practitioners who continue to use manual office measurements risk excessive BP lowering.

Third, SPRINT used protocolized care algorithms emphasizing long-acting agents (especially renin-angiotensin system blockers, thiazide-like diuretics and calcium channel blockers) used in combination. This approach facilitated BP control by limiting therapeutic inertia and ensuring timely medication titration in response to elevated systolic BP levels, and may explain in part why SPRINT investigators were able to lower BP intensively using an average of 2.8 medications. Additionally,

Key points

- Intensive lowering of blood pressure (BP) (targeting a systolic BP level of 120 mm Hg) should be strongly considered for selected patients who are at high risk for cardiovascular disease.
- Accurate BP measurement using automated devices and frequent follow-up are necessary to safely achieve intensive targets for systolic BP.
- Shared decision-making, individualized assessment of the benefit–risk profile and the feasibility of close follow-up will need to guide use of this approach for individual patients.

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adherent patients were preselected for inclusion in the study, and patients with resistant hypertension were likely underrepresented.

Fourth, residents of nursing homes and participants with a standing BP of less than 110 mm Hg, dementia and life expectancy less than three years were excluded.

It is noteworthy that clinically important adverse effects were often seen with intensive therapy. Although the overall rate of adverse events was similar between groups (1793 events [38.3%] with intensive treatment v. 1736 events [37.1%] with standard treatment), those receiving intensive treatment had significantly more hypotension (2.4% v. 1.4%), syncope (2.3% v. 1.7%), electrolyte abnormalities (3.1% v. 2.3%) and acute kidney injury (4.2% v. 2.5%). These elements underscore the critical importance of appropriate patient selection for intensive BP lowering and that achieving lower systolic targets will involve commensurately intensive clinical and laboratory monitoring to ensure patient safety.

Given the findings of the SPRINT trial and the recent meta-analyses summarized above, targeting a BP of less than 120 mm Hg in high-risk patients would seem sensible. However, BP treatment thresholds and targets in patients aged 80 years and older require special consideration. Currently, initiation of pharmacotherapy is recommended if systolic BP is 160 mm Hg or greater, with a treatment target of less than 150 mm Hg.[8] Participants aged 75 and older formed a prespecified subgroup of SPRINT; intensive reduction of systolic BP substantially reduced major cardiovascular events in this subgroup (7.7% v. 10.9%; HR 0.67, 95% CI 0.51–0.86; NNT of 31). The current threshold of 160 mm Hg and target of 150 mm Hg will need re-examining.

SPRINT does not inform on whether intensive BP lowering is warranted in patients with diabetes, because these individuals were excluded. However, the study's results do provide some insight into why the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, which examined intensive BP lowering in patients with diabetes, showed no benefit.[9] The ACCORD trial was likely underpowered given that it had the same event rate in the standard treatment arm as SPRINT (2.1%) yet only half the number of participants (4733). Furthermore, the ACCORD trial used a complex factorial design, and interaction between these factorial arms has been demonstrated.[10]

SPRINT also excluded participants with a history of stroke, partly because the European Society of Hypertension (ESH) and the Chinese Hypertension League (CHL) are currently conducting the Stroke in Hypertension Optimal Treatment Trial (ESH-CHL-SHOT).[11] The trial is enrolling 7500 patients aged 65 and older with a history of prior stroke or transient ischemic attack. The patients are being randomly assigned to three different BP targets (< 145 to 135 mm Hg v. < 135 to 125 mm Hg v. < 125 mm Hg). Recurrent stroke is the primary end point; results are expected in 2018.

We anticipate some reasonable resistance to the widespread adoption of this approach on the part of both practitioners and patients. More detailed information on adverse effects and additional findings from subgroup analyses as well as cost-effectiveness analyses are needed. Ultimately, shared decision-making, individualized assessment of the benefit–risk profile and the feasibility of close follow-up will need to guide use of this approach for individual patients.

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