Editorial Commentary

SPRINT, or False Start, Toward a Lower Universal-Treated Blood Pressure Target in Hypertension

Murray Esler

Systolic Blood Pressure Intervention Trial (SPRINT) is a parallel group antihypertensive efficacy study, with randomized allocation to 2 groups: intensive treatment (target clinic systolic blood pressure [BP], 120 mm Hg) and standard treatment (target 140 mm Hg systolic BP), and with blinded outcome adjudication.1 Patient selection aimed to assemble a test hypertension population enriched for existing cardiovascular disease, chronic kidney disease, and patients aged >75 years, but with exclusion of diabetics. For the total population tested, in the intensively treated group a reduction in a composite cardiovascular disease end point (the primary outcome), and in all-cause mortality was demonstrated, compared with standard treatment. SPRINT promises to transform the clinical practice of antihypertensive drug prescribing!

In SPRINT, there is a convergence of BP target (here 120 mm Hg systolic) toward the epidemiology linking untreated BP to risk, where incremental cardiovascular risk emerges above a systolic pressure of 100 mm Hg.2 This has of late, subsequent to the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial,3 been held to be not attainable; those with previous hypertension have a cardiovascular memory, in their arterial walls and heart from the years of hypertension exposure, so that it is thought unreasonable to expect to recapitulate the epidemiology of untreated BP risk with antihypertensive drugs. But in SPRINT, empiricism seems to have trumped theory.1

There are more ways than one of viewing the SPRINT findings. One is to consider the results through the prism of a trial directed at specified BP targets. But a second, unspecified way is to interpret trial outcomes comparing the pressure reduction in the 2 groups (means of 18 and 5 mm Hg). With this reorientation in thinking, the larger BP fall in the intensively treated group might be seen as a confounder. Not so, this is the essence of the SPRINT results that the larger BP fall into the unpromising lower registers of BP toward 120 mm Hg in the intensively treated group, actually was beneficial. There is, however, a black hole in SPRINT. This is the exclusion of diabetics, which limits the applicability of the trial.1 This exclusion is explicable logistically, but is a demerit. In clinical practice, diabetes mellitus is so often comorbid with hypertension. Given the evidence from ACCORD,4 SPRINT must not be taken to provide a target BP also for diabetic patients with hypertension. SPRINT did not confirm the disputed therapeutic principle that hypertensive patients particularly at risk, through coexisting illness, will benefit most from adopting a low target BP. Hypertensive patients with coronary artery disease and chronic kidney disease did no better in the intensively treated group than in the hypertensive patients without these adverse features. By trial design, the knowledge base for treating hypertension in diabetes mellitus was not advanced.

The SPRINT trial is based on automated BP measurement in the clinic, and not on ambulatory BP measurements. Some might see this as a failing, but SPRINT joins a long line of historic antihypertensive drug trials using the simpler, and less exact BP measurement system.4,5 This might cause pause, as it is contrary to the arguments that discredit the continuing value of sphygmomanometer readings in the clinic, to the point where in the NICE guidelines6 24-hour ambulatory BP is required to make a diagnosis of hypertension.

Adverse effects were more frequent in the intensively treated group, as might be anticipated. Hypotension, syncopal episodes, acute kidney injury, and serum electrolyte abnormalities (lowered sodium and potassium) were more commonly detected, but certainly not so commonly as to cancel out the major observed benefits. In this context, it is important to note a particular feature of the trial, the modest elevation in average run-in BP in SPRINT (averaging, 139.7 mm Hg), with a contingent modest BP fall to-target in the intensively treated patient group (18 mm Hg). The target of 120 mm Hg systolic established here may, perhaps, not be achievable in all patients, particularly those with much higher initial BP, who need greater BP reduction to achieve this target. In these, the level of serious adverse events might be prohibitively high. It could be a mistake to generalize this target BP to all hypertensive patients, especially for initial therapy of those severely affected.

Has a new universal target BP now been established with SPRINT, a lower validated target than determined elsewhere? That is the crucial question. Or does the lower BP starting point in SPRINT, lower than in most trials, drive the emergence of this low target BP? Within BP on-entry tertiles for the trial, a trend did exist for there to be greater reductions in the primary outcome in the lower tertiles. In short, do we now have a new, lower therapeutic target in hypertension clinical care, or is the target SPRINT-specific? Should 120 mm Hg be the invariable target for those patients with an initial systolic BP of 170 mm Hg, say, or 200 mm Hg? My 45 years of clinical experience in the treatment of patients with more severe grades of hypertension lead me to doubt this.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Hypertension. 2016;67:00-00. DOI: 10.1161/HYPERTENSIONAHA.115.06735.

Hypertension is available at http://hyper.ahajournals.org
DOI: 10.1161/HYPERTENSIONAHA.115.06735
Disclosures

None.

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Hypertension. published online November 9, 2015;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/early/2015/11/09/HYPERTENSIONAHA.115.06735.citation

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