SPRINT and Implications for Target Organ Protection in African Americans

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Background

The Systolic Blood Pressure Intervention Trial (SPRINT) recently published its primary results after the trial was stopped by the director of the National Heart, Lung, and Blood Institute. The decision to halt the trial was based on the recommendation of the trial's Data Safety and Monitoring Board that participants needed to be informed of the differential experience on the primary cardiovascular disease (CVD) outcome (composite consisting of non-fatal myocardial infarction, acute coronary syndrome requiring hospitalization, stroke, acute decompensated heart failure, or cardiovascular death) and all-cause mortality in the two arms of the study.[1] The objectives of SPRINT were to examine the effect of treating patients with elevated blood pressure (BP) to a systolic BP (SBP) target of <120 mm Hg compared with treatment to the usually recommended SBP target of <140 mm Hg on CVD events, all-cause mortality, kidney disease progression, and rate of age-related decline in cognition and incident dementia.[2] While there were significantly higher rates of some adverse events in the lower BP goal group, there were no differences in all serious adverse events. The absolute differences in these adverse events between randomized groups were relatively

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small (<1%-2%), and unlike the CVD events prevented, the conditions were typically not life-altering. Thus, the benefits of the lower SBP target outweighed the harms.[1]

Results of SPRINT Related to African Americans

The results of SPRINT are particularly relevant to African Americans (AA) because of the high rates of hypertension and its complications in this population. SPRINT successfully recruited a diverse cohort of participants.[2, 3] At baseline, self-reported African Americans (AAs) made up 31% of the trial's participants, and 11% were Hispanic.[3] In addition, 28% of participants were aged >75 years, and 28% had chronic kidney disease defined by an eGFR < 60 mL/min/1.73 m^2. AAs had a significantly lower socioeconomic status (SES) as reflected by a lower college graduation rate of 23% compared with 46% for non-AAs *(P*>.001), and 29% compared with 12%, respectively, were either uninsured or on Medicaid *(P*<.0001). Baseline SBP levels were similar: 139.8 mm Hg in AAs compared with 139.6 mm Hg in non-AAs; but, despite AAs being five years younger (64.2 compared with 69.6 years, respectively, *P*<.0001), Framingham Risk Scores were higher in AAs at 17.5 vs 17.3 *(P*<.0001).

At the time of this publication, data collection for some major end-organ outcomes (kidney and brain) continues, and subgroup analyses for many of those already collected have not yet been completed. However, while some of the detailed analyses of the findings in AAs remain to be completed, several important findings describing the cardiovascular outcomes of AAs in SPRINT are now known in advance of the results from additional pending analyses. The hazard ratio (confidence interval) for the primary outcome comparing the <120 mm Hg with the <140 mm Hg goal was .75 (.64 to .89; *P*<.001) and .73 (.60 to .90; *P*=.003) for all-cause mortality. In AAs, the corresponding results were .77 (.55–1.06) and .96 (.65-1.40). The results of tests for interaction were not significant at *P*=.85 for the primary outcome and *P*=.34 for all-cause mortality, after Hommel adjustment for multiple comparisons indicating that the benefit of the lower SBP target also extended to AAs.[1] The final analyses of the renal outcome data by race/ethnicity from SPRINT will be important because of higher rates of renal failure in AA and Hispanic patients.[4] Although the number of total pre-specified renal events was <30 for participants with CKD at baseline (primary renal outcome), the pre-specified secondary renal outcome (30% reduction in eGFR to < 60 mL/min/1.73m^2 in participants without CKD at baseline) was more frequent in those randomized to the <120 mm Hg target arm. In addition, acute kidney injury (AKI) or acute kidney failure (AKF) was reported about 70% *(P*<.001) more frequently in hospital discharge summaries of SPRINT participants treated to the lower SBP target.

The racial breakdown for these renal outcomes is not yet available, and confirmation of the discharge summary reports of AKI/AKF is being formally adjudicated by a blinded end-point committee. The high risk Apo L-1 genotype was present in 10% of SPRINT AA participants.[5] Interestingly, baseline eGFR was higher in AAs (77.4 mL/min/1.73^2 vs 69.2 mL/min/1.73^2 [P<.0001]), and fewer AA SPRINT participants were enrolled with an eGFR below the level that defined CKD.[3] The relationship between these outcomes, participant race, and high risk Apo L-1 genotype will be important in defining the risk benefit of the lower SBP target in AAs.

Upcoming Data Collection and Analyses

Collection of the final data on cognition and magnetic resonance imaging (MRI) is scheduled to be completed by summer 2016. SPRINT will have one of the largest clinical trial databases and experience of the use of cognitive testing in AA patients and is well-positioned to assess the effect of the BP intervention on longitudinal changes in cognitive function. During the final 4-9 months of observation, the blood pressure delta between the two arms is likely to be smaller because the active blood pressure intervention was transferred from the SPRINT clinics back to the participant's provid-

ers. The magnitude of the change in delta and its impact on trial outcomes is unclear at this time.

Projected Impact of SPRINT

SPRINT should shed new light on strategies to reduce heart failure (HF), one of the most frequent, important and lethal forms of end-organ damage from hypertension. AAs have one of the highest rates of HF not preceded by myocardial infarction and much higher rates of HF at younger ages than Whites.[6] In the Atherosclerosis Risk in Communities surveillance study (2005-2012) Black men and women aged 55-64 years had first-time acute decompensated HF event rates that were approximately three times that of White men and women.[7]

Left ventricular hypertrophy was more common in AA SPRINT participants at baseline, 21% compared with 12% (P<.001).

The <120 mm Hg SBP target in SPRINT produced a 38% reduction in decompensated HF and are among the most potent treatment effects seen in the trial. Heart failure in SPRINT was carefully adjudicated by a blinded panel.[2] Left ventricular hypertrophy was more common in AA SPRINT participants at baseline, 21% compared with 12% *(P*<.001). Nearly 60% percent of AAs in SPRINT were between aged 50 to 64 years compared with 32% of non-AAs *(P*<.0001), an age group as noted above where the disparity by race for incident HF is particularly high. Also as noted above, there was a remarkable consistency of treatment effect in the six pre-specified subgroups for the published outcomes. More detailed analyses of heart failure rates by treatment group are underway, including analyses by preserved ejection fraction, reduced ejection fraction, and subgroup analyses by race and ethnicity.

Study Limitations

SPRINT will not provide direct information on the effect of the lower SBP target in AA patients with elevated BP and diabetes since the latter were excluded from the trial. Another challenge will be how to implement the lower targets into the clinical environments where many AAs, Hispanics, low SES, and rural individuals receive care. In addition, BPs in SPRINT were much more carefully measured and more consistent with recommended procedures than currently in use in most clinical practices. If the positive findings in SPRINT are to be realized, greater attention to the measurement of blood pressure and to the management of these patients will be required.

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Conflicts of Interest

No conflicts to report.

Author Contributions:

Research concept and design: Wright, Fine; Acquisition of data: Wright, Fine; Data analysis and interpretation: Wright, Fine; Manuscript draft: Wright, Fine; Acquisition of funding: Wright, Fine; Supervision: Wright, Fine

References

1. Wright JT Jr, Williamson JD, Whelton PK, et al; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103-2116. http://dx.doi.org/10.1056/NEJMoa1511939. PMID:26551272.
2. Ambrosius WT, Sink KM, Foy CG, et al; SPRINT Study Research Group. The design and rationale of a multicenter clinical trial comparing two strategies for control of systolic blood pressure: the Systolic Blood Pressure Intervention Trial (SPRINT). *Clin Trials*. 2014;11(5):532-546. http://dx.doi.org/10.1177/1740774514537404. PMID:24902920.
3. Still CH, Craven TE, Freedman BI, et al; SPRINT Study Research Group. Baseline characteristics of African Americans in the Systolic Blood Pressure Intervention Trial. *J Am Soc Hypertens*. 2015;9(9):670-679. http://dx.doi.org/10.1016/j.jash.2015.06.012. PMID:26320890.
4. Collins AJ, Foley RN, Chavers B, et al. US Renal Data System 2013 Annual Data Report. *Am J Kidney Dis*. 2014;63(1)(suppl):A7. http://dx.doi.org/10.1053/j.ajkd.2013.11.001. PMID:24360288.
5. Langefeld CD, Divers J, Pajewski NM, et al; Systolic Blood Pressure Intervention Trial (SPRINT). Apolipoprotein L1 gene variants associate with prevalent kidney but not prevalent cardiovascular disease in the Systolic Blood Pressure Intervention Trial. *Kidney Int*. 2015;87(1):169-175. http://dx.doi.org/10.1038/ki.2014.254. PMID:25029429.
6. Mozaffarian D, Benjamin EJ, Go AS, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation*.

2015;131(4):e29-e322. http://dx.doi.org/10.1161/CIR.0000000000000152. PMID:25520374.

7. Chang PP, Chambless LE, Shahar E, et al. Incidence and survival of hospitalized acute decompensated heart failure in four US communities (from the Atherosclerosis Risk in Communities Study). *Am J Cardiol*. 2014;113(3):504-510. http://dx.doi.org/10.1016/j.amjcard.2013.10.032. PMID:24342763.