SNAPSHOT HEMODYNAMICS AND CLINICAL OUTCOMES IN HYPERTENSION

PRECISION IN THE MEASUREMENTS IS KEY

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The recent publication of the Systolic Blood Pressure Intervention Trial (SPRINT) inks the latest chapter in the evolving history of blood pressure management. The trial randomized 9361 nondiabetic hypertensive patients aged >50 years with at least one cardiovascular risk factor (not including stroke) to intensive or standard control (systolic blood pressure <120 or <140 mmHg, respectively). The main conclusion from this large trial was that targeting a systolic blood pressure of <120 mmHg when compared with <140 mmHg resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events were observed in the intensive treatment group. It is also informative to focus on the blood pressure difference achieved between the groups and not just the absolute blood pressure targets. What was accomplished in terms of the independent variable, systolic blood pressure, was a difference of 13.1 mmHg between the 2 groups, which was sustained after the first year of treatment. Importantly, the observed difference in systolic blood pressure was accomplished, whereas the intensive group and the standard group took on average <3 and 2 antihypertensive medications, respectively. This supports the argument that lowering blood pressure can be achieved without an excessive pill burden. This is a relevant practical point, particularly when dealing with people whose systolic blood pressure at study baseline was only moderately elevated on average, 139.7 and 139.7 mmHg in each group. It should be noted, however, that people with difficult-to-control blood pressure were excluded in SPRINT.

This important clinical trial, therefore, raises the critical question of whether we need to be more aggressive than ever before in our blood pressure treatment goals. There is increasing evidence in favor of lower is better from the recent meta-analysis of other studies. Moreover, the SPRINT data suggest clinical benefit even in those individuals aged >75 years and in patients with chronic kidney disease in whom presently such an aggressive blood pressure target is not generally recommended. Of note, less than half of the people in the intensive treatment group reached the systolic blood pressure goal of <120 mmHg. There may be many shades of gray among all the blood pressure changes observed that cannot be appreciated in the dichotomous split of <140 versus <120 mmHg. We do not know what would have happened had this goal been achieved in all intensive group participants. It would not be unexpected to find perhaps improved cardiovascular outcomes but at the expense of more frequent adverse events. Future subgroup analyses may help to understand better the relationship between blood pressure changes and outcomes. For instance, did the >50% of subjects in whom a systolic blood pressure <120 mmHg was attained do as well as the other 50% also in the intensive group? This is just one example of questions that may be further addressed with existing data.

A majority of the discussion after this publication will focus appropriately on the profound effect of the trial on the dependent variables selected as primary and secondary cardiovascular and clinical outcomes. Differences in outcomes after intensive blood pressure control between the SPRINT trial in nondiabetic subjects and the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study in subjects with type 2 diabetes mellitus will be dissected in detail. In fact, several outstanding editorials in Hypertension and elsewhere have already done so. We wish to raise the question of whether the office-based blood pressure is the ideal choice of an independent variable? Let us commend the investigators up front for standardizing the procedure using an automated manometer preset to wait for 5 minutes before taking the blood pressure and completing 3 measurements per clinic visit. But is this enough? Do these numbers provide an accurate enough picture of blood pressure over time to make decisions about long-term therapy with several antihypertensive agents? In the SPRINT trial, after a careful allocation to each treatment group based on monthly visits, blood pressure was measured every 3 months (or every month at the most in the intensive group). Although this is more than reasonable for a clinical trial intended to last 5 years, we wonder what the blood pressure was between visits particularly because there were more episodes of hypotension, syncope, acute kidney injury, and electrolyte abnormalities in the intensive therapy group.

Intermittent office-based cuff measurements have dictated therapy, and there are still >46 million Americans with uncontrolled hypertension. Furthermore, the recent recommendation by the United States Preventive Services Task Force to confirm all new diagnoses of hypertension with an out-of-office measurement also raises the question of office-based cuff pressure reliability alone. The argument that the bulk of our epidemiologic knowledge about blood pressure

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and outcomes, starting with the Framingham study, is based on office blood pressure is hard to dispute, and in fact, the results of the SPRINT study demonstrate how much valuable insight can be derived from snapshot hemodynamics, ie, office blood pressure. There are also many studies, however, that have shown that ambulatory and home-based blood pressure monitoring could be the reference standard to avoid misdiagnosis and overtreatment. Studies have also shown that home blood pressure and particularly 24-hour ambulatory blood pressure are prognostically superior and better for risk profiling than office blood pressure. Home-based blood pressure is an important tool for patient engagement and self-monitoring. Twenty-four–hour ambulatory monitoring has revealed that nighttime blood pressure may be a better predictor of outcomes than daytime pressure in patients with type 1 diabetes mellitus and hypertensive patients. Nighttime blood pressure in itself might provide a more consistent time to assess cardiovascular risk, although data on this are limited. Despite the evidence supporting the advantage of other more comprehensive measurements, the blood pressure snapshot in the clinic is still the standard not only for patient care but also for large clinical studies. We need to wonder what is ahead for the independent variable (blood pressure) in future studies assessing cardiovascular and renal outcomes as dependent variables.

The sphygmomanometer has been a helpful workhorse since its introduction by Karl Ritter von Basch in 1881, but maybe, it is time to move on. Looking ahead continuous noninvasive cuffless blood pressure monitoring is on the horizon. With improvements in sensor technology, we have the ability to pick up high-fidelity pulse waveform signals from extremities to obtain various physiological parameters. These have led to a resurgence of several physiological parameters that correlate with blood pressure. Pulse transit time (the amount of time from left ventricular contraction to pulse waveform acquisition at the distal site) is being looked at as an independent variable to predict blood pressure. Pulse wave velocity has long been known to be a predictor of vascular stiffness better than the brachial blood pressure. Pulse tonometry (counter pressure to measure arterial) and vascular unloading (measuring counter pressure required to maintain constant finger blood volume) are 2 other techniques being attempted to get continuous noninvasive cuffless measurements. Although significant advances have been made in acquiring the pulse waveform signal, the challenge for most of these technologies has been calibration for local perturbations of pressure. Despite the challenges, now more than ever, we have the ability to replace or complement intermittent cuff–based blood pressure measurements with continuous blood pressure monitoring. With 24-hour ambulatory blood pressure monitoring, the important principles of nocturnal hypertension and morning blood pressure surge have been unveiled. It is quite reasonable to predict that devices that will monitor blood pressure continuously and provide additional and comprehensive hemodynamic information will allow to establish better correlations with clinical outcomes and open up new possibilities for cardiovascular and renal disease risk prediction.

The SPRINT trial has offered strong evidence that targeting one independent variable, office systolic blood pressure, can improve clinical outcomes for many people that would not be treated according to current recommendations. This can only emphasize the importance of careful blood pressure measurements in the clinic office, a simple task but one that often is not done properly and with attention to detail. In medicine, we strive to be critical and evidence based with an intention to do no harm. Any decision to target systolic blood pressure <120 mm Hg based on office blood pressure should require precise measurements as the SPRINT investigators did. Keeping this in mind, we also must evolve and ask ourselves if we should still depend so heavily on snapshot hemodynamics when the independent variable is so critically important. To put it simply, better measurements of blood pressure are needed in the future. Much the same way that glycosylated hemoglobin is superior to intermittent blood glucose measurement in assessment of diabetes mellitus control continuous blood pressure monitoring should outperform intermittent blood pressure for hypertension management.

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References

Snapshot Hemodynamics and Clinical Outcomes in Hypertension: Precision in the Measurements Is Key
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