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INVITED EDITORIAL

Unobserved automated office blood pressure measurement in the Systolic Blood Pressure Intervention Trial (SPRINT): systolic blood pressure treatment target remains below 140 mmHg

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The Systolic Blood Pressure Intervention Trial (SPRINT) enrolled 9300 participants age 50 years and older without diabetes or previous stroke in ~100 expert medical centres and clinical practices throughout the USA.[1] Between 2010 and 2013, the SPRINT investigators randomly allocated the study participants into a standard treatment group receiving an average of two different blood pressure (BP) medications to achieve a systolic BP (SBP) target of <140 mmHg, and an intensive treatment group receiving an average of three BP medications to achieve an SBP target of <120 mm Hg. SPRINT was stopped early because of effect. The target SBP of <120 mmHg had reduced rates of the composite primary outcome that included myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes by 25% and the risk of death from all causes by 27%, as compared with the target SBP of <140 mmHg.[2] However, whether the results of the SPRINT study can be implemented into guidelines for the treatment of hypertension and clinical practice for the purpose of aiming at a lower target for SBP than the current SBP target of <140 mmHg is controversial. Here we comment on the measurement techniques for BP that was used in SPRINT and we assess whether it is representative and applicable for practice outside the specific study.

The details of the BP measurement technique in SPRINT have recently been described:[3] 'One aspect that has received only passing mention is the method of measurement of BP. This was performed using automated office BP (AOBP) measurement using an Omron device and measuring BP 3 times *un-observed*. This is critically important, since SBP when measured this way may be 5–10 mm Hg lower than when measured with a manual instrument or even when patients are being observed or talking, or in a room that is not quiet. Thus in community practice, lowering SBP to 120 mm Hg may mean that, if not done according to the correct protocol of AOBP, SBPs could actually be far lower than 120 mm Hg, with unknown consequences.' All sites in SPRINT used the Omron 907 (Omron Healthcare, Lake Forest, IL, USA) which was programmed for 5 min rest, and then BPs was measured three times at 1 min intervals. The Omron device was supplied by the study. The Manual of Operations and central training called for the study personnel to leave the room, and the device was set to 5 min before starting the measurement.

Previous studies in treated hypertensive subjects have shown that SBP by AOBP is comparable with, or even lower than daytime ambulatory SBP, and up to 20 mmHg lower than conventional auscultatory SBP in the office.[4] A recent study carried out in 353 treated hypertensive subjects[5] indicates 16 mmHg. Overall this means that the lower treatment arm in SPRINT translates into SBP <136 mmHg, which is not very different from SBP <140 mmHg, which is the target SBP currently recommended by hypertension treatment guidelines.

The BP measurement technique that was used in SPRINT was thus different from the tecniques used in previous studies in one key element, and that was the fact that other people were out of the room during measurements and the entire resting period prior to measurement. The SPRINT investigators thus were able to avoid the alert reaction or so-called 'white coat' effect. The alert reaction has been described in numerous ways throughout the years; an early observation was the rise in SBP by ~10 mmHg and in diastolic BP by ~6 mmHg just by introducing a conventional cuff measurement of BPs on the opposite arm while continuously taking an intra-aterial BP reading.[6] Similarly, in patients with mild hypertension,

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intra-arterial mean BP increased by ~20 mmHg in reaction to the doctor's unexpected arrival at the bedside.[7] In a subsequent study, the increase in intra-arterial BP associated with doctor's measurement, although decreasing with the duration of the visit, was still on average 12/7 mmHg after 5 min and 11/4 mmHg after 10 min, and virtually identical among four visits.[8] This is not the case for automatic or semi-automatic measurements in the absence of an observer.[9]

The unobserved measurements in SPRINT were no doubt intentional, both for the optimal standardization of measurements and for the quality of SPRINT, and in order to avoid the alert or white coat effect without depending on ambulatory BP measurements. However, the implications thereof are that BPs taken in SPRINT cannot be directly compared with BPs in other trials, and that the treatment arm <120 mmHg in SPRINT compares with a higher SBP value close to 140 mmHg in other trials. Thus, the SBP target in the treatment of hypertension remains unchanged at <140 mmHg.

The BP measurement technique is one of the many puzzling aspects of SPRINT. We have previously[10,11] pointed out several other points of interest that must be taken into account when assessing the true nature of SPRINT and whether the results from SPRINT are usful in daily clinical work.

Conflict of interest: S.E.K. has received modest honoraria for consultancy and lecturing from Bayer, Merck, and Takeda. G.M. reports no relevant conflicts of interest.

References

1. Ambrosius WT, Sink KM, Foy CG, Berlowitz DR, Cheung AK, Cushman WC, Fine LJ, Goff DC Jr, Johnson KC, Killeen AA, Lewis CE, Oparil S, Reboussin DM, Rocco MV, Snyder JK, Williamson JD, Wright JT Jr, Whelton PK; 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). *ClinTrials* 2014;**11**:532–546.
2. The SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC Jr, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;**373**:2103–2116.
3. Schiffrin EL, Calhoun DA, Flack JM. SPRINT proves that lower is better for non-diabetic high-risk patients, but at a price. *Am J Hypertens* 2016;**29**:2–4.
4. Myers MG, Godwin M, Daves M, Kiss A, Tobe SW, Kaczorowski J. Measurement of blood pressure in the office: recognizing the problem and proposing the solution. *Hypertension* 2010;**55**:195–200.
5. Filipovský J, Seidlerová J, Kratochvíl Z, Karnosová P, Hronová M, Mayer O Jr. Automated compared to manual office blood pressure and to home blood pressure in hypertensive patients. *Blood Press* 2016; http://dx.doi.org/10.3109/08037051.2015.1134086
6. Lund-Johansen P. Hemodynamics in early essential hypertension. *Acta Med Scand* 1967;**181**(Suppl 482):2–101.
7. Mancia G, Bertinieri G, Grassi G, Parati G, Pomidossi G, Ferrari A, Gregorini L, Zanchetti A. Effects of blood pressure measurements by the doctor on the patient's blood pressure and heart rate. *Lancet* 1983;**2**:695–698.
8. Mancia G, Parati G, Pomidossi G, Grassi G, Casadei R, Zanchetti A. Alerting reaction and rise in blood pressure during measurement by physician and nurse. *Hypertension* 1987;**9**:209–215.
9. Parati G, Pomidossi G, Casadei R, Mancia G. Lack of alerting reactions to intermittent cuff inflations during noninvasive blood pressure monitoring. *Hypertension* 1985;**7**:597–601.
10. Mancia G. The pros and cons of the systolic blood pressure intervention trial (SPRINT). *JACC* http://www.acc.org/latest-in-cardiology/articles/2015/12/01/10/04/the-sprint-trial-cons.
11. Kjeldsen SE, Narkiewicz K, Hedner T, Mancia G. The SPRINT Study: outcome may be driven by difference in diuretic treatment de-masking heart failure and study design may support systolic blood pressure target below 140 mmHg rather than below 120 mmHg. *Blood Press* 2016;**8**:1–4.