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Hypertension highlights during 2016

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The Systolic Blood Pressure Intervention Trial (SPRINT) included a subset of 2,636 adults aged 75 years and older randomized to a systolic blood pressure (SBP) target of <120 mmHg or to <140 mmHg (1). Of the persons randomized to a SBP <120 mmHg, 33.4% were frail. Of the persons randomized to a SBP <140 mmHg, 28.4% were frail. The primary composite outcome of nonfatal myocardial infarction, acute coronary syndrome not resulting in a myocardial infarction, nonfatal stroke, nonfatal acute decompensated heart failure, and cardiovascular death was lowered 34% and all-cause mortality lowered 33% by a SBP <120 mmHg (1). These outcomes were not different in frail persons. These very elderly adults with a SBP <120 mmHg also had a 37% lowering of nonfatal heart failure and a 32% lowering of the primary outcome plus all-cause mortality (1). The absolute rate of serious adverse events was 2.4% in the lower SBP treatment group versus 1.4% in the standard SBP treatment group. Orthostatic hypotension occurred in 21.0% in the lower SBP treatment group versus 21.8% in the standard SBP treatment group (1). This study did not include persons living in a nursing home or persons with diabetes, prior stroke, symptomatic heart failure, or a left ventricular ejection fraction (LVEF) <35% (1).

The American College of Cardiology (ACC)/American Heart Association (AHA) 2017 guidelines will have to answer by expert medical opinion many questions not answered by SPRINT. What should the SBP goal and the diastolic blood pressure (DBP) goal be in adults with diabetes, an acute coronary syndrome, prior stroke or transient ischemic attack, heart failure with a preserved or low LVEF, a LVEF below 35%, younger than 50 years, at low-risk for cardiovascular events, or those living in a nursing home? The 2015 AHA/ACC/American Society of Hypertension scientific statement on treatment of

hypertension in patients with coronary artery disease recommends a blood pressure (BP) goal of <140/90 mmHg in adults with stable angina, an acute coronary syndrome, and heart failure but states that a BP goal of <130/80 mmHg may be appropriate, especially in those with a prior myocardial infarction or stroke or at high risk for developing either (2).

The DBP should not be lowered to <60 mmHg in any adult with coronary artery disease with myocardial ischemia, diabetes, or age older than 60 years of age (3,4). The SBP should not be lowered to <110 mmHg in these adults (3). Cardiovascular risk should be assessed to guide the diagnosis and therapy of hypertension (5). Although many hypertension experts recommend treating patients with cardiovascular risk factors with hypertension to a BP goal of <120/80 mmHg (6), not all recommend this goal (7). Hypertension in high-risk adults could be defined as a BP \geq 130/80 mmHg with a threshold of treatment of 130/80 mmHg with a goal SBP of <120 mmHg (8).

The Orthostatic Hypotension in Diabetics in the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial investigated the prevalence, incidence, and prognostic significance of orthostatic hypotension in the ACCORD BP trial (9,10). The participants in this trial were at high risk for having orthostatic hypotension because they had type 2 diabetes, had hypertension, and were treated with antihypertensive drugs. The persons in this trial were randomized to treatment with antihypertensive drugs to lower the SBP to <120 mmHg or to <140 mmHg. After 1 year, the SBP was 119.3 mmHg with intensive blood pressure control versus 133.5 mmHg with standard antihypertensive drug treatment (9).

At 4 years, the prevalence of orthostatic hypotension was 12.2% in hypertensive diabetics treated to a SBP <120 mmHg

versus 13.5% in hypertensive diabetics treated to a SBP <140 mmHg (9). At 4 years, the incidence of orthostatic hypotension was 9.9% in hypertensive diabetics treated to a SBP <120 mmHg versus 11.0% in hypertensive diabetics treated to a SBP <140 mmHg (9). Orthostatic hypotension was associated with a 62% increase in all-cause mortality and with a 85% increase in heart failure death or hospitalization (9).

A randomized clinical trial using a similar number of participants and design used in SPRINT needs to be performed in older hypertensive diabetics to investigate whether the SBP goal should be <120 or <140 mmHg in hypertensive diabetics (10). The Orthostatic Hypotension in ACCORD BP study reassures us that hypertensive diabetics treated to a SBP goal of <120 mmHg will not have a higher prevalence or incidence of orthostatic hypotension than hypertensive diabetics treated to a SBP goal of <140 mmHg (9,10).

A meta-analysis of 19 randomized antihypertensive drug trials with 44,989 participants demonstrated that persons treated with more intensive BP lowering treatment had a mean BP of 133/76 mmHg compared to 140/81 mmHg with less intensive BP treatment group (11). At 3.8-year mean follow-up, compared with less intensive BP treatment, more intensive BP treatment lowered major cardiovascular events 14%, myocardial infarction 13%, stroke 22%, albuminuria 10%, and retinopathy progression 19% (11).

A meta-analysis of 123 antihypertensive drug trials including 613,815 participants demonstrated that every 10 mmHg decreases in SBP lowered major cardiovascular disease events 20%, coronary heart disease 17%, stroke 27%, heart failure 28%, and all-cause mortality 13% (12).

The Heart Outcomes Prevention Evaluation (HOPE)-3 trial randomized 12,705 participants at intermediate risk who did not have cardiovascular disease with a mean BP of 138.1/81.9 mmHg to receive candesartan 16 mg daily plus hydrochlorothiazide 12.5 mg daily or placebo (13). The decrease in BP was 6.0/3.0 mmHg greater in the BP treatment group than in the placebo group. Median follow-up was 5.6 years. The first coprimary endpoint of a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke was insignificantly lowered 7% by drug treatment (13). The second coprimary endpoint additionally included resuscitated cardiac arrest, heart failure, and revascularization and was insignificantly lowered 5% by drug treatment. Participants in the upper third of SBP (>143.5 mmHg) had a significant reduction in the first coprimary endpoint of 23% and in the second coprimary

endpoint of 28% if they were treated with candesartan plus hydrochlorothiazide (13). Reasons for the difference in results between the SPRINT trial and the HOPE-3 trial are discussed by their investigators (14,15).

The National Heart Foundation of Australia 2016 guideline for management of hypertension recommends ambulatory and/or home BP monitoring if the clinic BP is $\geq 140/90$ mmHg as out-of-clinic BP is a stronger predictor of outcome (16). This guideline also recommends in selected high cardiovascular risk populations a SBP goal of <120 mmHg to improve cardiovascular outcomes. Close follow-up is recommended in these persons to identify treatment-related adverse effects including hypotension, syncope, electrolyte abnormalities, and acute kidney injury (16).

The 2016 Canadian hypertension guideline recommends for high-risk patients aged 50 years and older with SBP levels of 130 mmHg and higher intensive BP management to target a SBP goal of 120 mmHg and lower (17). Intensive BP management should be guided by automated office BP measurements. Clinical indications defining high-risk patients for consideration for intensive BP treatment are clinical or subclinical cardiovascular disease or chronic kidney disease (nondiabetic nephropathy, proteinuria <1 gram/day, estimated glomerular filtration rate 20–59 mL/min per 1.73 m²) or estimated 10-year global cardiovascular risk $\geq 15\%$ or age ≥ 75 years (17). Persons with 1 or more of these clinical indications should consent to intensive BP treatment (17).

At 24-year median follow-up of the Trials of Hypertension Prevention, in which 744 phase I and 2,382 phase II persons were randomized to sodium reduction or control, there was an increased risk of all-cause mortality for high sodium intake and a direct relationship with all-cause mortality, even at the lowest levels of sodium intake (18). The hazard ratio per unit increase in sodium/potassium ratio was 1.13 (18).

Using data from a population-based 11-cohort International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes, a study compared daytime ambulatory blood pressure monitoring with conventional BP measurements in 653 untreated adults with white coat hypertension and 653 normotensive control adults (19). Median follow-up was 10.6 years. This study showed that after accounting for age, the size of the white coat effect was not influenced by the severity of risk for cardiovascular disease or the presence of past cardiovascular disease events (19). The risk of cardiovascular disease in most adults with white coat hypertension was comparable to age- and risk-adjusted normotensive control persons (19).

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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