Editorial

Orthostatic Hypotension and Intensive Blood Pressure Treatment

No Need to Worry?

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The SPRINT (Systolic Blood Pressure Intervention Trial) demonstrated that intensive blood pressure control to systolic blood pressure <120 mm Hg is superior to routine management with a target of <140 mm Hg.[1] As a result, the current American hypertension guidelines quickly lowered their blood pressure treatment target for most patients.[2] Given that orthostatic hypotension is a potential risk factor for cardiovascular disease with a prevalence of >20% in the elderly,[3,4] these new targets have led to increasing concern on whether this would lead to increased risk of coronary heart disease, stroke, or falls. Reassuringly, later, post hoc analyses from SPRINT demonstrated that lower blood pressure target actually reduced the risk of orthostatic hypotension, despite a slight increase in the risk of hypotension and syncope without injurious falls.[5] However, the impact of lower blood pressure targets on the relation between orthostatic hypotension and cardiovascular disease remains unknown.

In their study, Juraschek et al[6] used data from 8792 SPRINT study participants to assess the contribution of orthostatic hypotension to cardiovascular disease or adverse events and to examine if orthostatic hypotension detected in the setting of intensive treatment (systolic blood pressure goal <120 mm Hg) was associated with greater risk of cardiovascular disease events compared with orthostatic hypotension in the setting of standard treatment (systolic blood pressure goal <140 mm Hg). The authors defined orthostatic hypotension as a ≥20 mm Hg drop in systolic blood pressure or a ≥10 mm Hg drop in diastolic blood pressure with or without symptoms. During a median follow-up of 3 years, the incidence of orthostatic hypotension was similar in the 2 groups—5.7% in the standard treatment group and 5.0% in the intensive treatment group. Orthostatic hypotension in either group was not associated with higher risk of cardiovascular disease events, syncope, electrolyte abnormalities, injurious falls, or acute heart failure. However, as in the prior SPRINT publication,[5] orthostatic hypotension was associated with 1.77-fold risk of hypotension-related hospitalizations or emergency department visits and 1.94-fold risk of bradycardia, but these associations did not differ significantly by treatment group. The authors concluded that no down-titration of antihypertensive medication is needed in case of symptomless orthostatic hypotension even in the setting of a lower blood pressure goal.

Using data from a large, randomized clinical trial, Juraschek et al[6] provide novel insight into how to react to orthostatic hypotension in the setting of hypertension treatment. However, the study has some limitations and its results may not be generalizable to all populations. Most importantly, the vast majority of patients had asymptomatic orthostatic hypotension, which is rarely screened for clinical practice. Due to the low number of patients with symptomatic orthostatic hypotension, which also rendered subgroup analyses impossible, the study does not provide a definite answer as to if intensive antihypertensive therapy is safe or warranted also in patients with symptomatic orthostatic hypotension. The results of Juraschek et al[6] are therefore only generalizable to asymptomatic patients whereas individuals with symptomatic orthostatic hypotension might still benefit from down-titration of antihypertensive therapy. In addition, no subgroup analyses were performed by type of antihypertensive drugs used despite prior studies demonstrating that certain drug classes, such as β blockers, are more strongly associated with orthostatic hypotension than others.[7,8] Furthermore, the number of many outcome events was <20 among individuals with orthostatic hypotension, increasing the probability of false negative findings. Finally, SPRINT has been criticized for using unattended, automated office blood pressure measurements instead of conventional office blood pressure measurements.[9] As the seated measurements in the study by Juraschek et al were performed using automated office blood pressure, the results could have been different if conventional, attended office measurements would have been used for assessing seated blood pressure.[10] Nevertheless, in spite of its limitations, the study by Juraschek et al[6] provides important new information by suggesting that orthostatic hypotension could be a relatively benign phenomenon even in the setting of intensive antihypertensive therapy.

Despite the authors of the current study not observing an association between orthostatic hypotension and cardiovascular outcomes, results from prior studies have also shown opposite results. Namely, a previous meta-analysis by Ricci et

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al[4] with a study sample of 121 913 individuals and a median follow-up of 6 years reported that orthostatic hypotension was associated with a 50%, 41%, and 64% greater risks of all-cause death, coronary heart disease, and stroke, respectively. The differences between the studies by Ricci and Juraschek could be explained by differences in statistical power and study populations—SPRINT included only patients with hypertension aged ≥50 years whereas many of the studies included in the meta-analysis by Ricci et al included also elderly and community-dwelling individuals. Although the results of the current study are compelling, it still remains unclear whether orthostatic hypotension is causally related to increased cardiovascular risk.[6]

The current hypertension guidelines provide no clear treatment targets for patients with seated hypertension and orthostatic hypotension.[2] If a symptomatic patient's hypertension is well controlled, it is often easy to slightly down-titrate antihypertensive therapy. However, treatment decisions for symptomatic, poorly controlled patients or asymptomatic patients with severe orthostatic hypotension have been more complex. Although the results of the current study may not be generalizable to all (symptomatic) patients, the article demonstrates that more-intensive antihypertensive therapy does not lead to increased incidence of orthostatic hypotension or complications of orthostatic hypotension in asymptomatic patients. The major clinical implication of the study is that symptomless orthostatic hypotension should not be considered a cause for down-titrating therapy, even in the setting of intensive antihypertensive therapy. Additional studies should be conducted for (1) defining the optimal treatment target blood pressure in patients with hypertension with symptomatic orthostatic hypotension and (2) determining the role of orthostatic hypotension as a risk factor for cardiovascular disease and other adverse events in symptomatic versus asymptomatic patients.

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