

Managing High Blood Pressure in Older Persons With Decline in Function



Commentary on Mossello E, Pieraccioni M, Nesti N, et al. Effects of low blood pressure in cognitively impaired elderly patients treated with antihypertensive drugs. *JAMA Intern Med.* 2015;175(4):578-585.

Note from Editors: Preliminary findings from SPRINT referenced in this editorial have been released (www.sprintrial.org).

The debate on the optimal blood pressure (BP) targets in older persons, especially those with multiple comorbid conditions or poor functional status, continues. This issue is extremely complex, involving the definition of old age and the physiologic heterogeneity of older persons and their function.^{1,2} Many of the earlier longitudinal and antihypertensive treatment studies included relatively healthy middle-aged (50-60 years) or young-old (65-75 years) persons, whereas more recent studies have included the oldest old (≥ 80 years), who have more comorbid conditions.³⁻⁶ Physiologically, as arteries stiffen with age, systolic BP (SBP) increases, diastolic BP (DBP) tends to flatten or decrease, and pulse pressure is increased.⁷ Increased SBP might be needed to drive blood through stiff arteries, whereas widened pulse pressure might cause more damage to the arterial wall. Lower DBP might decrease coronary blood flow. Importantly, as hypertension persists over time, the capacity of blood vessels (especially in the cerebral circulation) to autoregulate or maintain constant blood flow diminishes, making the brain and possibly other organs more susceptible to surges or decreases in blood flow at higher or lower BPs.^{8,9}

WHAT DOES THIS IMPORTANT STUDY SHOW?

A recent publication in *JAMA Internal Medicine* has shed more light on this complex issue. Mossello et al¹⁰ report on the relationship between low SBP and cognitive performance in a small cohort of 172 elderly (mean age, 79 years) patients cared for in a memory clinic in Florence, Italy. At baseline, most patients had cognitive impairment, a modest burden of vascular disease, and mild limitation of physical function. Patients were divided into 3 tertiles of SBP based on daytime ambulatory BP monitoring: low, ≤ 128 mm Hg; intermediate, 129 to 144 mm Hg; and highest, ≥ 145 mm Hg. The 3 tertiles were well balanced at baseline on age, Mini Mental State Examination (MMSE) score, vascular comorbid conditions, physical function, and percent with dementia. During a 9-month follow-up, there was a clear association between lower daytime SBP and more cognitive decline. Importantly, this association was only observed in patients receiving antihypertensive medications. This

adds strength to the argument that aggressive antihypertensive treatment may have a causal negative impact on cognition in older persons with baseline impairment.

Strengths of this study include the relatively high rate of follow-up, balance of baseline characteristics across BP tertiles, and use of ambulatory BP monitoring to help standardize measurement. Weaknesses include the small cohort drawn from a memory clinic, short follow-up, unblinded data collection, and assessment of cognitive change based entirely on MMSE score. Although the findings of Mossello et al are far from definitive, they add to the increasing literature that suggests there may be an optimal treatment approach to target BP in persons with multiple comorbid conditions and that either too low or too high BPs could be harmful.^{10,11}

HOW DOES THIS STUDY COMPARE WITH PRIOR STUDIES?

Most longitudinal epidemiologic studies have shown that increased BP in middle-aged or young-old persons is associated with higher risk for stroke, coronary disease, and cognitive decline or dementia.^{1,3,12} However, other studies have shown that the strength of the association of elevations in both SBP and DBP with risk for cardiovascular events or mortality lessens with advancing age or even reverses direction in persons older than 80 years.^{4,5} Also, some recent longitudinal studies have seemed to indicate that higher BPs may be advantageous to longevity and function in persons older than 80 years. In the Helsinki Ageing Study, persons older than 80 years showed a 10% mortality improvement for every 10-mm Hg increase in SBP and an 8% improvement for every 5-mm Hg DBP increase.⁶ Similarly, other studies have found that low BP, especially low DBP, in late life is associated with increased risk of dementia, particularly in persons with a history of midlife hypertension.¹²

The landmark SHEP (Systolic Hypertension in the Elderly Program) trial, published in 1991, showed that treatment of SBP > 160 mm Hg for fairly healthy persons aged 60 to 85 years reduced both stroke and

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coronary events without apparent deleterious effect on function. This trial resolved prior controversy regarding treating elevated SBP in older adults⁷ by providing strong support for at least modest SBP control in relatively healthy older adults.^{13,14}

Meta-analyses of similar trials conducted at that time in relatively healthy persons of similar older age groups all showed that treatment of elevated SBP in such persons lowered the risk for subsequent strokes, coronary events, and myocardial infarction, but also revealed a questionable or even adverse impact on total mortality.^{14,15} Also, substantial questions remained whether antihypertensive therapy in persons older than 80 years was of much benefit in terms of reducing either cardiovascular events or total mortality.¹ Of course, the more comorbid conditions that older persons have, the more likely they are to die of some disease in the near term (competing morbidity).

These issues were only partially resolved in 2008 with the publication of the HYVET (Hypertension in the Very Elderly Trial), which showed that antihypertensive treatment of persons older than 80 years with mean SBP of 173 mm Hg reduced both cardiovascular events and all-cause mortality. Critical for generalizability, two-thirds of HYVET participants had to be taken off antihypertensive medication to determine eligibility and baseline SBP was so high that the prior likelihood that a cardiovascular disease death would precede other causes of death was high. The major implication of this study was that relatively healthy persons of advanced age at very high risk from high SBP should be treated. It did not resolve the issue of whether very old persons at more moderate risk or with more comorbid conditions or functional impairment would have much benefit from therapy.¹⁶

In addition, recent cohort and treatment studies have indicated that there may be a U-shaped relationship between BP levels and stroke, coronary events, and mortality. Such reported associations are not necessarily causal because a decline in health status may alter these relationships. Analyses of SHEP data led to questions about whether too aggressive treatment of SBP with lowering of DBP to <70 mm Hg might result in no benefit (but not harm) due primarily to decreased coronary diastolic perfusion.¹¹ Also, Kovesdy et al¹⁷ have reported on a cohort study of more than 150,000 veterans with chronic kidney disease in which there was a U-shaped relationship between SBP and mortality, with optimal BPs of 130 to 159/70 to 89 mm Hg, a finding also noted in other elderly cohorts or kidney disease populations.^{11,17}

WHAT SHOULD CLINICIANS AND RESEARCHERS DO?

Given what we know about the pathophysiology of hypertension, rigid arteries, and decreased vascular

autoregulation in older persons, we believe moderation is in order. Clinicians need to pay more attention to multiple comorbid conditions and functional impairment in managing BP in older persons. Treatment of high BP is always based on a clinical judgment about risk-benefit ratio, and available cohort and longitudinal data suggest that this ratio is altered unfavorably in some older persons.

We desperately need much more data analyzing the impact of functional status on treatment outcomes. It is likely that future treatment algorithms for older persons with hypertension (and many other chronic diseases) will include specific suggestions of risk-benefit stratification based on the patient's self-reported or observed functional status.¹⁸

We believe it is unwise to give overly specific treatment guidelines for persons of advanced age. The U-shaped relationship between BP and cognitive decline¹⁰ or mortality¹⁷ may be more related to the overall health status of the persons studied, but targeting an SBP range of 130 to 145 mm Hg for older persons on antihypertensive therapy is judicious at the current time.

Fortunately, the ongoing SPRINT (Systolic Blood Pressure Intervention Trial), with results expected in 2017, should shed more light on this issue (www.clinicaltrials.gov, NCT01206062). This large study has randomly assigned 9,361 persons older than 50 years (with 2,639 >75 years and 2,646 with chronic kidney disease) to aggressive lowering of SBP to <120 mm Hg versus a less aggressive <140 mm Hg threshold, and will assess the impact of these 2 treatment strategies on cardiovascular disease, kidney outcomes, and cognition outcomes. The SPRINT data will greatly help in decision making, but it is likely that treatment of hypertension in older persons of advanced age with advanced disease will always remain an individualized decision.

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