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Hypertension and Polypharmacy in Elderly Nursing Home Residents: When Less is More

Kalani L. Raphael, MD, Srinivasan Beddhu, MD

Veterans Affairs Salt Lake City Healthcare System, University of Utah School of Medicine, Salt Lake City, UT

The prevalence of hypertension increases with advancing age, such that two-thirds of US adults 60 years or older have hypertension.¹ Hypertension is a major risk factor for cardiovascular disease in older adults,² with nearly 75% of people with first stroke, myocardial infarction, or congestive heart failure having hypertension.³ Whether treating moderate hypertension in older adults, particularly those with extensive comorbid conditions, will reduce adverse events is less certain. Polypharmacy is common in older people and may result in significant complications.⁴

The Hypertension in the Very Elderly Trial (HYVET)⁵ examined whether lowering blood pressure (BP) to <150/80 mm Hg using a thiazide diuretic with or without an angiotensin-converting enzyme inhibitor improved clinical outcomes in individuals older than 80 years. Prior to HYVET, there were concerns that lowering BP might reduce stroke risk yet increase mortality risk in elderly individuals with hypertension. For instance, an observational study of 4,071 ambulatory veterans 80 years or older with hypertension reported shorter survival for those with systolic BP (SBP) < 140 mm Hg, even after adjustment for baseline predictors of death.⁶ However, HYVET showed that lowering BP to <150/80 mm Hg reduced the risks of stroke by 30%, fatal stroke by 39%, heart failure by 64%, and all-cause mortality by 21%.⁵

Notably, older adults residing in nursing homes were excluded from HYVET. Each year, nursing homes provide care to approximately 1.4 million Americans, and the management of hypertension in these elderly and commonly frail individuals is uncertain.

WHAT DOES THIS IMPORTANT STUDY SHOW?

The Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized Very Aged Population (PARTAGE) Study is an observational study of 1,130 frail individuals 80 years and older residing in 72 nursing homes in France and Italy.⁷ A previous publication from this cohort identified an inverse association between SBP and all-cause mortality in adjusted analyses.⁸ Specifically, each 10-mm Hg increase in SBP was associated with a 9% lower risk of all-cause mortality (relative risk, 0.91; 95% confidence interval [CI], 0.84–0.98). In addition, in unadjusted analyses, participants in the lowest tertile of SBP (upper

Address correspondence to Srinivasan Beddhu, MD, University of Utah School of Medicine, 85 N Medical Dr E, Rm 201, Salt Lake City, UT 84112. srinivasan.beddhu@hsc.utah.edu.

bound of ~130 mm Hg) had 30% higher mortality risk compared with those with SBP < 130 mm Hg.

These observations raise the question of whether it is the lower BP per se, the polypharmacy used to lower BP, a combination of both, or some other confounding factor that raises mortality risk. In order to address this question, Benetos et al⁷ reanalyzed the PARTAGE data. Key exclusion criteria were advanced dementia (defined as Mini Mental State Examination score < 12) and a low level of autonomy (defined as activities of daily living score < 2). At the time of study entry, participants self-measured BP 3 times in the morning and 3 times in the evening on 3 consecutive days. The mean of the 18 values was used.

In univariate analyses, SBP < 130 mm Hg (hazard ratio [HR], 1.36; 95% CI, 1.06–1.75, compared with SBP < 130 mm Hg) and taking 2 or more BP medications (HR, 1.28; 95% CI, 0.99–1.65, compared with < 2 BP medications) were both associated with increased mortality risk. There was a significant interaction ($P=0.007$) between these 2 predictor variables with mortality, such that those with SBP < 130 mm Hg who were also taking 2 or more BP medications ($n=227$) had ~80% higher mortality in unadjusted and adjusted analyses compared with the rest of the cohort ($n=900$).

These results are biologically plausible because very low BP and polypharmacy could potentially increase the risk for adverse events and mortality in the elderly. The investigators also used statistical analyses such as propensity score methodology and found similar results. Nonetheless, propensity scores can adjust only for measured confounders and only large randomized controlled trials can balance the unmeasured confounders across the intervention groups. Another major methodological issue with this study is dichotomization of a continuous variable such as SBP because this could lead to misleading interpretation of data. What if most of the events occurred at very low SBPs and not between 110 and 130 mm Hg of SBP? Spline curves of SBP and mortality in those with 0, 1, or 2 or more medications would have been more informative in that regard. Given previously reported results from analyses of 2,340 persons 65 years and older in NHANES (National Health and Nutrition Examination Survey)⁹ showing that frailty modifies the associations of BP with mortality, it is also surprising that measures of physical function, such as gait speed or handgrip strength, are not reported in this study of frail elderly.

HOW DOES THIS STUDY COMPARE WITH PRIOR STUDIES?

SHEP (Systolic Hypertension in the Elderly Program) was a large randomized controlled trial of 4,736 persons 60 years or older (mean age, 72 years) that examined whether antihypertensive drug treatment reduced the risk of nonfatal and fatal stroke in isolated systolic hypertension.¹⁰ The active treatment group achieved a mean SBP of 143 mm Hg versus 155 mm Hg in the placebo group and had 36% lower risk for the primary end point of total stroke, 27% lower risk for the secondary end point of clinical nonfatal myocardial infarction plus coronary death, and 13% lower risk for death from all causes. As discussed, the more recent HYVET also showed in the very elderly (aged > 80 years) that reducing SBP to <150 mm Hg decreased the risk for stroke, heart failure, and all-cause mortality.⁵ Thus, these studies provide evidence to lower SBP to <150 mm Hg in community-dwelling

individuals 60 years or older and form the context of the recent recommendation from members of the Joint National Committee 8.

Whether targeting even lower SBP thresholds in the elderly would be beneficial remains uncertain, with no clinical trials specifically addressing this question to date. In the absence of randomized controlled trials, the evidence from observational data (registries, prospective studies, or secondary analyses of previous randomized controlled trials that studied other questions) suggests a lower limit of SBP goal as 130 to 140 mm Hg.^{3,6-9,11,12} Results from PARTAGE can be considered in this context.

The more definitive answer for optimal SBP threshold in the noninstitutionalized elderly may be provided by the ongoing SPRINT (Systolic Pressure Intervention Trial), a large randomized controlled trial (N = 9,361) funded by the National Institutes of Health that examines SBP goal < 120 mm Hg versus <140 mm Hg.¹³ This study includes a large proportion of elderly (aged >60 years) who were recruited from the outpatient clinics and communities.

WHAT SHOULD CLINICIANS AND RESEARCHERS DO?

Results from PARTAGE importantly highlight the potential harms of lowering SBP to <130 mm Hg with combination antihypertensive therapy among elderly nursing home residents. Because it is unlikely that a large randomized controlled trial will be conducted to determine the intensity of BP reduction in elderly nursing home residents in the near future, PARTAGE results should be incorporated into the clinical judgment of clinicians and in the context of recommendations from expert consensus panels (Box 1) with the caveats discussed previously. PARTAGE further reminds us that consensus recommendations regarding BP management do not specifically address this large subset of the elderly population. The take home message of the PARTAGE Study is that the combination of SBP < 130 mm Hg and combination antihypertensive therapy is associated with mortality risk in elderly nursing home residents. A logical corollary of these findings is that frail elderly institutionalized patients perhaps should not have SBP reduced to <130 mm Hg, particularly if doing so requires more than one antihypertensive medication.

Ultimately, the goal is to identify who will benefit the most and who will be at the most risk from lowering SBP; until we achieve the goal, perhaps less is more in older adults with extensive comorbid conditions.

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Box 1.**Consensus Panel Recommendations for the Management of Blood Pressure in People 80 Years or Older**2011 ACC/AHA²

- Lower SBP to 140–145 mm Hg if tolerated

2013 ESH/ESC¹⁴

- Lower SBP to 140–150 mm Hg if
 - SBP > 160 mm Hg
 - Good mental/physical condition is present

JNC 8^{15,a}

- Lower BP to < 150/90 mm Hg or
- Lower BP to < 140/90 mm Hg in the setting of diabetes mellitus or CKD

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; BP, blood pressure; CKD, chronic kidney disease; ESH/ESC, European Society of Hypertension/European Society of Cardiology; JNC, Joint National Committee; SBP, systolic blood pressure.

^aJNC recommends these targets in persons 60 years or older.