Review Article

Blood Pressure Targets in the Hypertensive Elderly

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Abstract

Objective: Hypertension is an important risk factor of cardiovascular disease and increases mortality in the elderly. However, the available medical evidences are both inconsistent and insufficient regarding establishing credible and useful blood pressure (BP) targets in the hypertensive elderly. This review summarizes the existing evidences used for establishing optimal BP targets for this patient population and points out some data inconsistencies which have added to the uncertainty.
Data Sources: We conducted a search for the articles published in English in the PubMed database up to March 2017, with the keywords "hypertension," "elderly," "blood pressure," and "antihypertensive."
Study Selection: Articles that related to BP targeting in the hypertensive elderly were selected for this review.
Results: The selected studies indicated that antihypertensive therapy can substantially reduce the risk of cardiovascular events and mortality, for a subset of the elderly (60 years or older) with systolic BP >160 mmHg. Studies regarding more strict targets yielded mixed findings. For the very old and frail patients (80 years or older), there is a lack of evidence that optimal BP targets and intensive antihypertensives are helpful but in fact may be harmful.
Conclusions: There are solid evidences that patients who are 60–80 years old and in good health have benefited from lowering their BP to below 150/90 mmHg. If well tolerated, the BP target can be further lowered to below 140/90 mmHg. However, for the very old and frail, individualized and careful assessment is crucial. Antihypertensive treatment should be cautious and the adverse effect of drugs requires close monitoring as such treatment can be counterproductive.

Key words: Antihypertensive Treatment; Blood Pressure; Elderly Patients; Hypertension

Introduction

The median population age is trending upward in both industrialized and developing countries. Given the high prevalence of hypertension in the elderly,[1,2] optimal treatment of hypertension has been an increasing public health concern worldwide. Hypertension is associated with target organ damage, such as ischemic heart disease, heart failure, stroke, and chronic kidney disease. Since these effects are life-threatening, the need for more intensive management of hypertension in the elderly has never been greater. However, limited, even contradictory evidences on the management of hypertension in the elderly have created significant debate on proper and credible blood pressure (BP) goals in older patients. Thus, we review the current evidences and then present a consensus summation, while acknowledging, there will always be controversy regarding BP targets in the elderly.

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Pathophysiology and Clinical Features of Hypertension in the Elderly

Arterial stiffness increases with age, and this loss of elasticity is related to the deposit of calcium and collagen in the arterial wall and the degeneration of elastic fibers. Aorta and major arteries are predominantly affected. Consequently, this reduced arterial compliance leads to an elevation of the systolic BP (SBP) and a further decline of the diastolic BP (DBP). Pulse pressure is increased and eventually results in isolated systolic hypertension, which is the most common form of hypertension in the elderly.[3,4]

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Hypertension was deemed to be normal physiological response during aging several decades ago. However, epidemical studies including the Framingham Heart Study have established that hypertension is a strong independent risk factor of morbidity and mortality for cardiovascular diseases throughout life.[1]

The rate of hypertension control among the elderly is much lower than among patients in their middle age.[5] At the same time, comorbidities, including stroke and coronary artery disease, are more common in the elderly patients. As a result, the elderly potentially can achieve a greater benefit than their younger counterparts through antihypertensive treatment.[6] Therefore, better strategies for controlling BP including optimal BP targets are crucial for this patient population.

On the other hand, there have been debate and hesitation about treating hypertensive patients, especially at an older age. The elderly are frailer and carry more hypotension risk. In addition, the autonomic regulation of BP attenuates with aging. Impaired baroreflex sensitivity and vasomotor tone may lead to orthostatic hypotension, which is common among the elderly and is related with cognitive dysfunction and increased mortality.[7] Postprandial hypotension is very common among older patients and has been related with mortality.[8] In addition, more intensive treatment often requires more types and higher doses of antihypertensive agents, which may carry higher risk of adverse reactions. Hypotension caused by antihypertensive agents may increase the risk of acute kidney injury, hospital admission, cognitive impairment, and falls.[9,10]

Finally, the rate of hypotension may be underestimated in clinical practice. A Spanish cross-sectional study enrolled 5066 patients aged 80 years or older with treated hypertension. Using ambulatory BP monitoring as a tool, the investigators detected that more than half of the patients had hypotension.[11]

Recommendations of the Current Guidelines and Relevant Evidence

Recommendations from the current guidelines

Current guidelines provided inconsistent recommendations on BP goals for older patients and there has been debate on the appropriate treatment goals as a result. For example, the Joint National Committee (JNC) 8 guideline recommended treating hypertensive persons aged 60 years or older to a BP goal of <150/90 mmHg.[12] In contrast, the 2014 American Society of Hypertension/International Society of Hypertension guidelines suggested that, for patients older than 80 years, the threshold for starting treatment is at levels ≥150/90 mmHg and the treatment target is <150/90 mmHg.[13] The 2013 European Society of Hypertension/European Society of Cardiology guidelines recommended that, for elderly hypertensives <80 years old or more than 80 years with good physical and mental conditions, the threshold for treatment should be SBP ≥160 mmHg, and the target is between 150 and 140 mmHg.[14] The British 2011 National Institute for Health and Clinical Excellence guidelines recommended that, for patients older than 80 years, the BP target should be <150/90 mmHg.[15] As is evident from the various cited studies, there is a wide variance in what is thought to be acceptable.

Evidence from clinical trials

The inconsistent cutoff value of blood targets between different guidelines reflected the lack of overwhelming evidence on BP targets for the elderly.

In the Systolic Hypertension in the Elderly Program (SHEP) study,[16] 4736 patients older than 60 years were randomized in the ratio of 1:1 to active treatment or placebo group. The baseline SBP was 160 to 219 mmHg. The 5-year average SBP was 155 mmHg for the placebo group and 143 mmHg for the active treatment group. Active treatment reduced the risk of both nonfatal and fatal stroke by 36%, risk of clinical nonfatal myocardial infarction plus coronary death by 27%, and all-cause mortality by 13%. The Syst-Eur study[17] enrolled 4695 patients older than 60 years with SBP 160 to 219 mmHg and DBP lower than 95 mmHg. At a median of 2 years' follow-up, sitting BP for placebo and active treatment groups was 161/84 mmHg and 141/79 mmHg, respectively. Active treatment reduced the total rate of stroke by 42% and all fatal and nonfatal cardiac end points by 26%. All-cause mortality was reduced by a nonsignificant rate of 14%. Similarly, the Syst-China study,[18] which was conducted in Chinese population, enrolled 2394 patients with the same criteria as Syst-Eur study. At 2 years of follow-up, BP for placebo and active treatment groups was 160/84 mmHg and 150/81 mmHg, respectively. Active treatment showed a trend toward reducing cardiovascular mortality and total mortality. The effect was more evident in diabetic patients.

SHEP study, Syst-Eur study, and Syst-China study indicated that, for patients aged 60 years and above with SBP higher than 160 mmHg, lowering SBP to a level around 140–145 mmHg will significantly reduce the risk of cardiovascular and cerebrovascular events, as well as all-cause mortality. Naturally, the question surfaced; will strict BP control to lower targets bring further benefit for the elderly? The answer to this question is relatively uncertain due to mixed findings of the clinical trials.

In the HOPE-3 study,[19] 12,705 participants with a mean age of 66 years at intermediate risk of cardiovascular diseases with baseline mean BP of 138.1/81.9 mmHg were randomly assigned to active treatment or placebo group. The mean decreases from baseline during the trial were 10.0 ± 13.1 mmHg in the active treatment group and 4.0 ± 12.9 mmHg in the placebo group. However, no significant difference was observed in primary outcomes of major cardiovascular events for these patients diagnosed with prehypertension. The result indicated that it is futile

to treat patients with prehypertension, even those with intermediate cardiovascular risk. Two Japanese trials, the JATOS[20] and VALISH,[21] were unable to observe benefit of a more stringent BP target. In the JATOS study, 4418 patients aged 65–85 years, with a baseline SBP of above 160 mmHg, were randomly assigned to strict treatment or mild treatment group. BPs were significantly lower in the strict treatment group compared with the mild treatment group (135.9/74.8 vs. 145.6/78.1 mmHg, respectively), but the incidence of the combined primary end point of cardiovascular disease and renal failure was similar in two groups (86 patients in each group). All-cause deaths were 54 in the strict treatment group versus 42 in the mild treatment group. In the VALISH study, the researchers divided 3260 patients aged 70–84 years with isolated systolic hypertension (sitting BP 160–199 mmHg) into strict (<140 mmHg) and moderate (140–150 mmHg) BP treatment groups. At 3 years, BP in these two groups reached 136.6/74.8 mmHg and 142.0/76.5 mmHg, respectively. The overall rate of the primary composite end point of cardiovascular events was similar between the two groups (10.6/1000 patient-years in the strict treatment group and 12.0/1000 patient-years in the moderate treatment group, hazard ratio: 0.89; $P = 0.38$).

It appears that a further reduction of SBP to around 135 mmHg has gained no additional benefit compared with 140 to 145 mmHg. Accordingly, the JNC 8 expert panel recommended a higher goal of BP control for patients aged 60 years or above based on the JATOS and VALISH studies.[20,21] However, there has been debate on the interpretation of the evidences from these clinical trials. Some experts challenged that there were fewer cardiovascular events in the two studies such that they rejected reaching a conclusion. In contrast, a Chinese study with a much larger patient population revealed a different result. In the FEVER trial, which was conducted in Chinese population, 9800 hypertensive patients with a mean age of 62 years were enrolled.[22] The BP was 137.3/82.5 mmHg in the treatment group and 142.5/85.0 mmHg in the placebo group. The primary end point (fatal and nonfatal stroke) was reduced by 27% in the treatment group. Among secondary end points, all cardiovascular events were reduced by 27% and cardiovascular death by 33% in the treatment group.[22] For patients with higher risk of stroke, strict BP control may be crucial. The SPS3 trial aimed at an even more strict BP target.[23] In this trial, 3020 enrolled patients (average age of 63 years) with recent (within 6 months) symptomatic lacunar infarcts were randomized into treatment groups of a SBP target of 130–149 mmHg or <130 mmHg. After 1 year, mean SBP was 138 mmHg in the higher target group and 127 mmHg in the lower target group. The rate of all strokes was nonsignificantly reduced by 19% ($P = 0.08$) and intracerebral hemorrhage was significantly reduced by 63%.[23]

These studies confirmed that, for patients aged 60 years above with SBP ≥160 mmHg, BP control reduces the risk of stroke, cardiovascular events, and further all-cause mortality. If patients can tolerate more intensive treatment, a lower target for SBP of around 135 mmHg may be helpful. For those who are at a high risk of stroke, the target can be even lower.

Special consideration for the oldest old and the frail

For the oldest old (aged 80 years or older), the ideal treatment goal for BP reduction is more obscure. These very old patients were excluded or underrepresented in most hypertension trials. There has been little solid evidence generated from randomized controlled trials. In a retrospective cohort study of 4000 patients aged 80 years or older with hypertension conducted in the US Veterans Affair Hospitals, patients with higher BP (up to a SBP of 139 mmHg and a DBP of 89 mmHg) were less likely to die during follow-up than those with lower BP.[24] In a cohort analysis of 79,376 patients aged 80 years or older in primary care in England, myocardial infarction and stroke hazards increased with SBP of 145 mmHg or higher, while SBP <135 mmHg was associated with higher mortality rate.[25] These large-scale cohort studies indicated that there may be an J-shape curve of BP and mortality rate for the very old patients. A SBP lower than 135–140 mmHg may be harmful in some patients.

However, these cohort studies are observational and were unable to determine a causal relationship. For example, low BP may be a marker of poor condition, rather than cause of death. To date, the only randomized controlled study investigating antihypertensive therapy in octogenarians or older patients is the HYVET study. The HYVET study[26] assigned 3845 patients aged 80 years or older with SBP ≥160 mmHg. Mean BP at baseline was 173.0/90.8 mmHg. At 2 years, the mean BP was 143.5/77.9 mmHg in the active treatment group and 15.0/6.1 mmHg lower than in the placebo group. Active treatment was associated with a 30% reduction in the rate of fatal or nonfatal stroke, a 23% reduction in the rate of death from cardiovascular causes, and a 21% reduction in all-cause mortality. In addition, in a subgroup analysis of 2636 patients aged 75 years or older who participate in the SPRINT study,[27] the mean SBP was 123.4 mmHg in the intensive treatment group and 134.8 mmHg in the standard treatment group. At a median follow-up of 3 years, the incidence of primary composite outcome of cardiovascular diseases was 34% lower and all-cause mortality was reduced by 33% in the intensive treatment group. The overall rate of serious adverse events showed no difference between treatment groups.

Of note, the patients included in these trials were generally healthier than those observed in the real-world practice. First, the mean age of patients in the HYVET treatment arm was 83.6 years old, with 73% of the patients being 80–84 years old. Patients close to or above 90 years old were insufficiently evaluated. There were evidences that the association between BP and mortality attenuated or even inversed with age. A series of cohort studies conducted in the

Netherlands[28,29] have shown that, for patients aged 85 years and above, hypertension was no longer a risk factor for mortality. Instead, BP lower than 140/70 mmHg and a drop in BP between 85 and 90 years predicted higher mortality. The PARTAGE study enrolled patients living in nursing homes with a mean age of 88 years. In very old individuals living in nursing homes, there was a negative association between SBP, DBP, and mortality.[30]

Moreover, the elderly population are highly heterogeneous, a considerable part of them are with more comorbidities, poor functional capacity, and shorter life expectancy. However, patients with heart failure, elevated serum creatinine level, dementia, and a requirement of nursing care were excluded from the HYVET study.[26] Patients with type 2 diabetes, a history of stroke, recent or advanced heart failure, dementia, expected survival of <3 years, unintentional weight loss, and patients residing in a nursing home were excluded from the SPRINT study. For the frail patients, the benefit of antihypertensive therapy in the long term may be limited and attenuated by a greater risk of adverse effect of drug therapy. In the subgroup analysis of SPRINT study, the intensive treatment insignificantly increased the risk of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or renal failure.[27] For older and frailer patients, the side effect can be magnified.

The assessment of frailty and functional status is crucial for the oldest old. Walking speed can be a convenient index for functional capacity and health status. In a cohort study, 2340 persons aged 65 years and older were measured over a 6-m walk test and classified as faster, slower, or incomplete. After adjusting for confounding factors, there was an association between BP and mortality varied by walking speed. Among faster walkers, those with elevated SBP (≥140 mmHg) had a greater adjusted risk of mortality. Among slower walkers, no such relationship was observed. For those who could not complete the walk test, there was an inverse relationship between BP and risk of death.[31]

Conclusions

There is solid evidence for patients aged 60–80 years in good condition for the benefits of lowering the BP to below 150/90 mmHg. If this treatment regimen is well tolerated, the target can be further aimed at below 140/90 mmHg. For the very old and frail, given the insufficient evidence due to a lack of randomized controlled trials, individualization and careful assessment are crucial before initiating antihypertensive therapy. SBP of 140–150 mmHg appears to be reasonable for patients in good functional status. For those with poor functional capacity, loss of autonomy, short life expectancy, and living in nursing home, antihypertensive treatment should be cautious and the adverse effect of drugs requires close monitoring.

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Conflicts of interest

There are no conflicts of interest.

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