Target Blood Pressure Goals for Treating Hypertension in the Elderly: A Review
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Abstract
Hypertension is a common disease in elderly people, and prevalence increases with age. It is associated with substantial morbidity and mortality. Newer, lower definitions of hypertension further increase prevalence. There is no consensus between the hypertension guidelines on the precise definition of the elderly and the target blood pressure (BP) for the elderly. Due to the heterogeneity of this population, the goal of optimum BP regulation is also controversial. In this article, we review current data on hypertensive treatment guidelines, try to define the target BP, optimize treatment strategies in the elderly and summarize the challenges health providers face when dealing with this population.

Key words: Blood pressure, Cardiovascular, Elderly, Geriatrics, Hypertension

Introduction
The 2015 Global Burden of disease study\(^1\) reported that high systolic blood pressure (SBP) was one of the largest contributors to global morbidity and mortality, accounting for 10.2 million (9.16–11.3 million Uncertainty interval [UI]) deaths and 208 million (UI 188–227 million) disability-adjusted life years (DALYs). Most of the burden of high systolic BP (SBP) was due to stroke and ischemic heart disease, with 56.5% (UI 49.0–63.2) and 55.5% (UI 48.0–62.7) of DALYs being attributed to stroke and ischemic heart disease, respectively. The INTERHEART\(^2\) and INTERSTROKE\(^3\) studies also showed similar findings, with hypertension accounting for 34.6% and 17.9% of the population attributable risk for stroke and coronary artery disease, respectively. A systematic review of hypertension in India highlighted the increasing prevalence of hypertension in both rural and urban India.\(^4\) With the decrease in BP levels in the 2018 American Heart Association/American College of Cardiology guidelines\(^5\) and an increase in the number of elderly people, the prevalence of those with hypertension, especially the elderly, is likely to increase.

There are a number of controversies in the management of hypertension in the elderly, such as the optimum BP at which there are maximum preventive benefits and at the same time minimal complications, the categorization of the BP stage, to rule out pseudo hypertension, white-coat hypertension, masked hypertension, orthostatic, postprandial hypertension and exclude secondary causes in cases of resistant hypertension, the choice of first-line therapy, and the role of combination therapy. In addition, many factors, such as high prevalence of several comorbidities, poly-pharmacy, frailty and minimal inclusion of the elderly in hypertension trials, and leave a variety of unresolved clinical issues to clinicians who offer treatment for this age group. The purpose of this review article is to address the difficulties of evaluating and treating hypertension in older adults and to analyze the evidence and recommendations of different professional societies.

Pathophysiology of Age-related Hypertension
Several factors contribute to the development and worsening of existing hypertension in elderly people. These include arterial stiffening, mechanical hemodynamic changes, neuro-hormonal dysregulation, autonomic dysfunction, ageing of the kidneys, and secondary causes of hypertension.\(^6\)
Over time, arterial intimal hyperplasia and damage of the elastic lamellae occur, leading to arterial stiffening. The stiffened arteries have reduced recoil and capacitance, leading to difficulties in dealing with changes in volume during the cardiac cycle. After the age of 60, SBP tends to increase while diastolic BP (DBP) reduces due to a predominant increase in central arterial stiffness. This leads to isolated systolic hypertension, which is more important than elevated DBP as a risk factor for both cardiovascular disease (CVD) and renal disease.[7]

Pulse pressure, rises with age, regardless of mean BP and other factors, and is a marker for large artery stiffness, early vascular ageing and is a risk factor for CVD.[8]

Pseudohypertension, characterized by systolic and DBP \( \geq 10 \text{ mmHg} \) higher than the concurrently measured intra-arterial BP, is a potential cause of hypertension in this age group with a reported prevalence of 4%. This should be taken into account during the treatment of the elderly hypertensives, as false BP due to arterial calcification can lead to over-treatment and increased adverse reactions.[9]

Increased use of home BP monitoring and ambulatory BP monitoring has showed an increased occurrence of “white coat” hypertension and “reversed white coat” hypertension, which is important challenges in determining target BP and optimizing therapy.[10]

Orthostatic hypotension, described as a decrease in SBP by at least 20 mmHg or DBP by at least 10 mmHg within 3 min of standing, is common in elderly people with a prevalence of 18% in older adults and is associated with increased risk of falls and cerebrovascular events.[11] This is due to reduced arterial compliance, decreased sensitivity of the baroreceptors with age and reduced cardiovascular sensitivity to catecholamines. This is further exacerbated by beta-blockers, which are associated with an increased risk of developing orthostatic hypotension because elderly people rely on increased cardiac output due to increased heart rate, as compared to adjustments in their already stiff arteries, to achieve postural homeostasis. However, a randomized clinical trial reported that non-institutionalized elderly patients with SBP <120 mmHg were not associated with a substantially elevated risk of orthostatic hypotension.[12]

Post-prandial hypotension is an under-recognized cause of syncope in geriatric patients. It appears to be related to a reduced response of the autonomic nervous system to meals. Monitoring of ambulatory BP and symptoms can help with the diagnosis. These patients can be managed with increased water intake before eating or having six smaller meals daily instead of three larger meals. Patients with heart failure, end-stage renal disease on hemodialysis, Parkinson’s disease, and autonomic dysfunction are more prone to post-prandial hypotension.[13]

Secondary causes of hypertension, such as atherosclerotic renovascular disease, chronic kidney disease, thyroid disease, obstructive sleep apnea, and drugs such as nonsteroidal anti-inflammatory drugs, anabolic steroids, and antidepressants, are also more prevalent in this population.[9] Pseudo-resistant hypertension due to drug non-adherence due to various causes, such as cognitive decline and lack of social and financial support, is also an important consideration in this age group.[6]

Risk Assessment of Older Adults with Hypertension

In the geriatric population with hypertension, a thorough history, physical examination, and selected investigations should be carried out to determine the global risk of CVD. In addition, the clinical examination should evaluate the global functioning of the patient, including comorbidity, frailty, autonomy, medications, and social and financial support.[14]

Although the same general rules, as for the general hypertensive group apply, certain specificities should be taken into account for older adults. These include (a) risk calculators such as atherosclerotic CVD risk calculator,[15] are standardized for individuals of age 40–75 years, (b) personal rather than family history is of importance, (c) orthostatic hypotension may be a significant contributor to increased cardiovascular risk, (d) assessment of arterial stiffness and intima-media thickness, although of weak evidence, may be of help to better identify risk, (15) (e) presence of other cardiovascular risk factors, such as smoking and high cholesterol, diabetes mellitus, and (f) presence of target organ damage such as left ventricular hypertrophy, stroke, retinopathy, and renal insufficiency.

The risk of functional decline, morbidity, and mortality should also be assessed by the examination. Groups with considerations of risk/benefit balance of aggressive and chronic treatment should also be defined. Functional profiles using tools such as canadian health study and aging frailty scoring system[16] would provide additional objective measures to guide treatment decisions in the frail elderly.

Current evidence: Clinical Trials and Guidelines on Treating Hypertension in the Elderly

While the benefits of BP control are irrefutable, it was not clear whether or not intensive BP reduction was superior to modest control in the geriatric population. Numerous studies have, therefore, assessed the benefits of antihypertensive drug therapy in reducing cardiovascular events in elderly people with hypertension and have sought to obtain an ideal BP target. Some of the studies are described in Table 1.

Earlier studies such as systolic hypertension in the elderly program,[17] systolic hypertension in Europe (Syst-Eur)[18] and hypertension in the very elderly trial[19] showed significant cardiovascular benefits in elderly patients with isolated systolic hypertension for lowering SBP. However, all four of these studies had defined a SBP cutoff of 160 mmHg to initiate treatment.

The systolic blood pressure intervention trial (SPRINT) trial recently demonstrated the benefits of a lower BP target of SBP <120 mmHg even in the subgroup of patients over 75 years of age.[22] However, the SPRINT trial did not include patients with diabetes mellitus, which is a common comorbid condition in the elderly hypertensives. In comparison, the
Table 1: Analysis of studies showing the benefits of different blood pressure targets in elderly patients

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Study characteristics</th>
<th>Initial blood pressure</th>
<th>Target blood pressure (mmHg)</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic hypertension in the elderly program (1989)</td>
<td>Age of included population ≥60 years</td>
<td>SBP level of 160–219 mmHg and DBP less than 90 mmHg</td>
<td>SBP &lt;160 Or reduction of ≤20 mmHg</td>
<td>Antihypertensive drug therapy reduced ischemic stroke by 37%, hemorrhagic stroke by 54%, reduced heart failure by 49% and by 80% in patients with prior myocardial infarction, reduced major cardiovascular events by 32%, as well as all-cause mortality by 13%</td>
</tr>
<tr>
<td>Systolic hypertension in Europe trial (Syst-Eur) (1997)</td>
<td>Age of included population ≥60 years</td>
<td>Sitting SBP: 160 to 219 mmHg</td>
<td>Sitting SBP &lt; 150mmHg</td>
<td>In the median follow-up of 2 years , the incidence of stroke decreased by approximately 42% and cardiovascular endpoints by 31% in the active treatment group.</td>
</tr>
<tr>
<td>Systolic hypertension in China trial (2000)</td>
<td>Age of included population ≥60 years</td>
<td>Sitting SBP: 160 to 219 mmHg</td>
<td>SBP &lt;150 Or reduction of ≤20 mmHg</td>
<td>Stroke rates decreased by 38%, all cardiovascular endpoints by 37% and all-cause mortality by 39% in the active treatment group.</td>
</tr>
<tr>
<td>Hypertension in the very elderly trial (2008)</td>
<td>Age of included population ≥80 years</td>
<td>SBP &gt;160 mm Hg</td>
<td>SBP &lt;150 DBP &lt;80</td>
<td>Blood pressure &lt; 150/80 mmHg decreases risk of fatal stroke, heart failure, any cardiovascular events, and all-cause mortality</td>
</tr>
<tr>
<td>Valsartan in elderly isolated systolic hypertension study (2010)</td>
<td>Age of included population ≥70 years</td>
<td>Sitting SBP 160 to 199 mmHg</td>
<td>Two groups: strict blood pressure control (&lt; 140 mm Hg) and moderate blood pressure control (≥ 140 mm Hg to &lt; 150 mm Hg)</td>
<td>No difference was seen between strict blood pressure (SBP &lt;140 mmHg) control versus mild blood pressure control (SBP 140–150) in terms of composite cardiovascular diseases</td>
</tr>
<tr>
<td>Systolic blood pressure intervention trial (2016)</td>
<td>Age of included population ≥75 years</td>
<td>Systolic blood pressure of 130 mm Hg or higher</td>
<td>Intensive treatment group: SBP target of less than 120 mm Hg Standard treatment group: SBP target of less than 140 mm Hg</td>
<td>Systolic blood pressure target of &lt;120 mmHg was associate with lower rates of cardiovascular events and deaths, as compared to a SBP target of &lt;140 mmHg</td>
</tr>
<tr>
<td>Delgado et al. (2017)</td>
<td>Age of included population ≥80 years</td>
<td>SBP &gt;140 mmHg DBP &gt;90 mmHg</td>
<td>SBP was grouped in 10-mmHg increments from less than 125 to 185 mmHg or more</td>
<td>Patients with systolic blood pressures ranging between 135 and 154 mmHg had the lowest mortality rate</td>
</tr>
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</table>
analysis of the elderly diabetics with hypertension in the action to control cardiovascular risk in diabetes-BP study\textsuperscript{(24)} showed that targeting SBP to less than 120 mm Hg, as compared with less than 140 mm Hg, did not affect the rate of fatal and nonfatal major cardiovascular events. In addition, increased adverse events such as hypotension, syncope, and renal insufficiency, and electrolyte disturbances were also observed in the SPRINT trial in patients who received intensive BP control. These adverse events will reduce the tolerability of therapy, particularly in older adults, which may result in decreased long-term adherence and discontinuation of treatment, masking the beneficial effects of intensive BP control.\textsuperscript{(25)}

Further studies, such as the observational cohort analysis published in 2017 by Delgado \textit{et al.},\textsuperscript{(23)} reported that patients with SBPs ranging from 135 to 154 mmHg had the lowest mortality rate.

This evidence has been incorporated into the recent guidelines and recommendations of various professional societies. A summary of the guidelines for initiation of therapy and target BPs is mentioned in Table 2.

**Management Considerations in the Elderly**

**Non-pharmacological interventions**

Data from the trial of non-pharmacological interventions in the elderly study\textsuperscript{(26)} have suggested that non-pharmacological lifestyle interventions should be promoted as preventive treatment for the development of hypertension and adjunctive therapy in patients already diagnosed with hypertension. Diets such as dietary approaches to stop hypertension and Mediterranean diets which have been proven to be heart-healthy should be recommended. Patients should be advised regarding reduction in sodium consumption (1000 mg/day), potassium supplementation, increased fiber, reduced carbohydrate, increased protein intake,

<table>
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<tr>
<th>Clinical condition</th>
<th>Threshold to initiate medical therapy</th>
<th>Target blood pressure</th>
<th>Initial Drug choices in the elderly</th>
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</thead>
<tbody>
<tr>
<td>JNC – 8\textsuperscript{(26)}</td>
<td>Age ≥ 60 years: SBP ≥150 mmHg or DBP ≥90 mmHg</td>
<td>SBP &lt;150 mmHg and DBP &lt;90 mmHg,</td>
<td>No separate recommendation</td>
</tr>
<tr>
<td>2017 American college of cardiology/American Heart Association\textsuperscript{(5)}</td>
<td>Older persons (≥ 65 years of age; non-institutionalized, ambulatory, community living adults): SBP ≥ 130</td>
<td>SBP &lt; 130 mmHg</td>
<td>No separate recommendation</td>
</tr>
<tr>
<td>2018 European society of cardiology/European society of hypertension\textsuperscript{(27)}</td>
<td>Age ≥80 years: SBP ≥ 160 mmHg</td>
<td>SBP: 130–139 mmHg</td>
<td>No separate recommendation</td>
</tr>
<tr>
<td>National Institute for Health and Care guideline (2019)\textsuperscript{(26)}</td>
<td>Age ≥ 80 years: SBP ≥ 150 mmHg DBP ≥ 90 mmHg</td>
<td>SBP &lt; 150 mmHg DBP &lt; 90 mmHg</td>
<td>In patients &gt; 55 years of age: Calcium channel blocker Thiazide diuretic, if calcium channel blocker is not appropriate or poorly tolerated</td>
</tr>
<tr>
<td>Indian guidelines on hypertension – IV (2019)\textsuperscript{(26)}</td>
<td>Age ≥ 60: SBP &gt;140 mmHg DBP &gt;90 mmHg</td>
<td>SBP: 130–140 mmHg DBP: 80–90 mmHg</td>
<td>No separate recommendation</td>
</tr>
<tr>
<td>Hypertension Canada (2020)\textsuperscript{(29)}</td>
<td>High risk of cardiovascular disease (clinical or subclinical cardiovascular risk, chronic kidney disease, estimated 10-year global cardiovascular risk ≥ 15%, or age ≥ 75 years): SBP ≥130 mmHg</td>
<td>SBP &lt;120 mmHg</td>
<td>Monotherapy with • Thiazide/Thiazide –like diuretic • ACE-I/ARB (in non-black) • Long acting calcium channel blocker Or a single pill combination of • CCB + ACE-I or ARB • ACE-I or ARB + diuretic</td>
</tr>
</tbody>
</table>

ACE-I: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin II receptor blocker
decreased caffeine intake, and weight loss.[6] Aerobic exercises, dynamic resistance exercises, and isometric resistance exercises have shown statistically significant reductions in both SBP and DBP in older adults. However, these reductions have not reached clinically significant thresholds and cannot be recommended as anti-hypertensive mono-therapy in the majority of individuals.[31] Current recommendations also advocate the cessation of smoking, the reduction of stress and the prevention of excessive alcohol intake. Regular home BP monitoring and follow-up through tele-consultation have also been shown to better control BP.

**Pharmacological Therapy: Special Considerations in the Elderly**[14,32,33]

While angiotensin-converting enzyme inhibitor (ACE-I), angiotensin II receptor blockers (ARB), and thiazide diuretics and calcium channel blocker (CCB) have all shown benefit on cardiovascular outcomes in the elderly and have been recommended as first line agents by most professional guidelines [Table 2],[32-30] factors to be evaluated prior to prescription of medicines include comorbidities including renal function and electrolytes, frailty, comprehension, complexity of the treatment, drug interactions and adverse effects, and social support. Table 3 summarizes important considerations while prescribing these drugs.

**Management in the Elderly with Orthostatic Hypotension**

Current guidelines for hypertension do not provide specific recommendations for the diagnosis and management of orthostatic hypertension in the elderly. However, because orthostatic hypertension is common in elderly hypertensives, has been shown to be associated with increased cardiovascular risk, and has not been excluded from clinical trials, similar targets, as for the rest of the elderly hypertensive population may be used. Monitoring of ambulatory BP may be particularly helpful in guiding the subsequent management of this population. There is a lack of evidence that patients with orthostatic hypertension benefit from a specific class of drugs in terms of cardiovascular risk protection. Treatment of orthostatic hypotension should be aimed more at improving symptoms, functional status, quality of life, and prevention of injury. It is reasonable not to lower BP in elderly patients with orthostatic hypotension or recurrent falls. Maintaining the supine SBP <120 mmHg increases the risk of orthostatic hypotension more adverse outcome. Using the diuretics which sometimes exacerbate central hypovolemia should be used with caution in this population.[34]

**Management in the Elderly with Isolated Systolic Hypertension**

The ideal BP targets for patients with isolated systolic hypertension are debated. While various studies have shown that reduction of SBP reduces cardiovascular mortality, aggressive BP lowering may be harmful in elderly patients with isolated systolic hypertension due to the risk of target organ hypoperfusion. Excessive reduction in BP could result in a J-curve phenomenon such that reduction of DBP could increase the risk of coronary heart disease and other adverse events. People aged 65 years and

<table>
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<tr>
<th>Class of drug</th>
<th>Co-morbidities</th>
<th>Precaution</th>
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<tbody>
<tr>
<td>ACE- I/ ARB</td>
<td>Preferred in non-black elderly with ischemic heart disease, heart failure with reduced ejection fraction, diabetes mellitus, chronic kidney disease, dyslipidemia, hyperuricemia, previous strokes, and peripheral vascular disease</td>
<td>Monitor creatinine and potassium Caution when diuretics and aldosterone antagonists are used concurrently Avoid simultaneous NSAID use</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Di-hydro-pyridines calcium channel blockers may be preferred in patients with previous stroke, chronic kidney disease, diabetes mellitus, dyslipidemia, hyperuricemia, peripheral vascular disease Non-dihydropyridine CCBs are preferred in atrial fibrillation for rate control</td>
<td>Avoid non-dihydropyridine CCBs in heart failure, second or third degree heart block and combination with beta-blockers Monitor creatinine and electrolytes Use with caution in the elderly as they are more prone to hyponatremia Increased risk of severe hyponatremia with concomitant use of SSRI antidepressants May worsen existing urinary incontinence</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Preferred in heart failure (loop diuretics), chronic kidney disease (loop diuretics, if CrCl &lt;30 mL/min/1.73 m²), previous stroke and osteoporosis (thiazide)</td>
<td>Monitor creatinine and electrolytes Use with caution in the elderly as they are more prone to hyponatremia Increased risk of severe hyponatremia with concomitant use of SSRI antidepressants May worsen existing urinary incontinence</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Avoid as first-line medications May be used in Ischemic heart disease, atrial fibrillation or thyrotoxicosis</td>
<td>Avoid in second or third degree heart block Avoid combination with non-dihydropyridine CCBs and acetylcholinesterase inhibitors (for Alzheimer’s disease)</td>
</tr>
<tr>
<td>Alpha-blocker</td>
<td>Avoid as first-line medication May have beneficial effect in benign prostatic hypertrophy</td>
<td>Increased predisposition to falls</td>
</tr>
<tr>
<td>Central α-adrenoreceptor agonists</td>
<td>Avoid as first-line medication</td>
<td>High risk of delirium and confusion</td>
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older with SBP of 130 mm Hg or higher or a DBP of 80 mm Hg or higher with lifestyle measures plus antihypertensive drug to lower the BP to less than 130/80 mm Hg. Preferred drugs in the treatment of this subgroup are like CCBs, Thiazide-like diuretics and ACE-I or ARBs being preferred, alone, or in combination. Beta-blockers are avoided due to lack of efficacy in lowering central aortic BP and possible pro-fibrotic effects.[32,35]

Management in the Elderly with Loss of Autonomy or Limited Life Expectancy

This subpopulation includes patients with multiple comorbidities, dementia, several geriatric syndromes, and lack of functional independence. The main objectives of therapy in this group are the preservation of quality of life and the relief of symptoms. SBP of 130–150 mmHg may be targeted in these patients, taking care to avoid lowering SBP to less than 130 mmHg and orthostatic hypotension. De-prescription of anti-hypertensive drugs should be considered as necessary.[14]

Conclusion

There is a lack of consensus between the hypertension guidelines on the definition of elderly people and target BP recommendations for the elderly. The most recent guidelines suggested a treatment goal of 130/80 mmHg in patients older than 65 years. There is also a lack of data on frail elderly people age >85 years. With the lowering of the threshold for diagnosis of hypertension, the increasing survival of the elderly and the increasing prevalence of the disease, this issue is becoming more relevant. There is great benefit in the successful treatment of hypertension in the elderly population. Encouraging lifestyle changes is the first-line treatment. Medications should be started as appropriate. Therapy may, therefore, need to be tailored to these patients, using clinical judgment and a team-based approach, in consultation with the patient, family, and caregivers, until further studies provide more definite answers.

References

Shivashankara and Hande Target BP goals for treating hypertension in the elderly


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