Hypertension in the Geriatric Population

A Patient-Centered Approach

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KEYWORDS

• Hypertension • Elderly • Frailty • Guidelines • Goal blood pressure

KEY POINTS

- Goal blood pressure for healthy individuals age 60 to 80 years should be less than 140/90 mm Hg. Results of ongoing, randomized, controlled trials may modify this goal.
- Patients with multiple comorbidities, frailty, and/or diminished functional or cognitive status and those older than 80 years may be treated to a goal of less than 150/90 mm Hg.
- Lifestyle modifications should always be incorporated into antihypertensive therapy.
- The thiazide diuretic chlorthalidone should be the first-line agent for most older, hypertensive patients.

INTRODUCTION

The aging of the "baby boomer" population in conjunction with older individuals living longer means that the aging demographic imperative is a current reality. In 2011, the first of 77 million baby boomers turned 65 and approximately 10,000 Americans turn 65 on a daily basis. Three out of 4 adults older than the age of 65 have 3 or more chronic conditions such as diabetes (DM), obesity, cardiovascular disease, congestive heart failure, atrial fibrillation, stroke, cognitive impairment, renal insufficiency, and, not the least of which, hypertension. With the oldest old, those over 85 years of age, estimated to be the fastest growing part of the population over the next 40 years, the impact of hypertension and its consequences will be enormous.

When addressing the complexities of hypertension in older individuals, several considerations are apparent. When, or even if, treatment should be initiated and/or continued? What is the target blood pressure (BP) and should this be adjusted for

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comorbidities? Are benefits greater in those individuals who are less frail or have better functional status or gait speed than in those who do not? Does the risk of adverse outcomes ever outweigh the benefit? What is the role for nonpharmacologic interventions (exercise, a low-salt diet, and weight loss)? How much of a role does therapeutic inertia on the part of treating physicians play? Should time to benefit be taken into account, especially in those with a limited life expectancy or poor prognosis? Have obstructive sleep apnea and nocturnal hypertension been addressed as potential contributors? Finally, has a goals-of-care discussion taken place with the patient and his or her family in addressing these issues? To address these questions, along with what therapy is to be initiated and how aggressively, one must understand the various mechanisms contributing to hypertension in the older individual.

EPIDEMIOLOGY

Although not considered to be part of the normal aging process, there is a clear age-related increase in BP and in the prevalence of hypertension. According to the Framingham Heart Study,[1] in men and women with normal BP at age 55, 85% will develop hypertension over the next 20 to 25 years of follow-up. The results of the National Health and Nutrition Epidemiologic surveys also document the extremely high prevalence of hypertension among older Americans.[2] Based on their definition of hypertension—the average of 3 readings of 140 mm Hg systolic or greater and/or 90 mm Hg diastolic or greater or receiving antihypertensive medications—the overall prevalence of hypertension for those 65 years of age and older ranged from 50% to 75%. For women over age 75, the prevalence exceeded 75%.

PATHOPHYSIOLOGY

Hypertension in the geriatric population is typically characterized by a high systolic BP (SBP) in the setting of a normal or even decreased diastolic BP (Fig. 1). Both

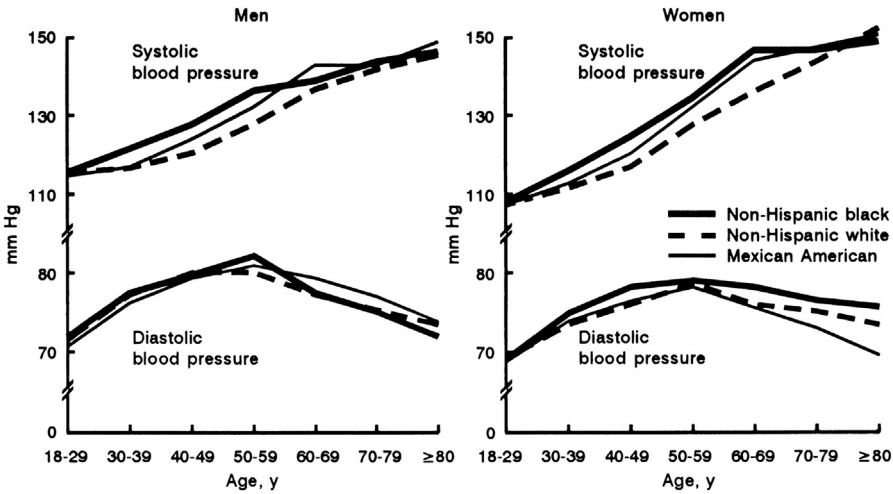

Fig. 1. Systolic and diastolic blood pressure readings by age for non-Hispanic black, non-Hispanic white, and Hispanic men and women from the Third National Health and Nutrition Evaluation Survey. (*From* Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988-1991. Hypertension 1995;25(3):305–13; with permission.)

elevated SBP and elevated pulse pressure (the difference between SBP and diastolic BP) are related to an age-related increase in arterial stiffness. No single factor accounts for this age-related increase in SBP. Although a detailed discussion is beyond the scope of this article, it is worth mentioning these factors, because several may serve as targets for both pharmacologic and nonpharmacologic interventions (**Box 1**). These vascular changes lead to an increase in central arterial stiffness demonstrated by higher arterial pulse wave velocity. Arterial stiffness in turn is believed to be a major contributor to target organ damage and impaired vascular function.

In addition to structural changes in the arteries, there are age-related changes in the autonomic nervous system along with impaired sensitivity of the arterial baroreceptors. As a consequence, a greater change in SBP is needed to elicit the appropriate compensatory response in heart rate and, for a given level of SBP, there is a more pronounced activation of the sympathetic nervous system. Reduced baroreceptor sensitivity has been proposed as a potential contributor to white coat hypertension, loss of the night time "dip" in BP,[3] greater BP variability and postprandial and orthostatic BP changes in the elderly.[4–6]

An age-related decline in renal function is well-documented and is accelerated in the setting of hypertension. A decline in renal cortical blood flow (~10% per decade) results in a loss of functioning glomeruli. Combined with an increase in pulse wave velocity, the remaining glomeruli are exposed to increased pressure transmitted through the small arterioles resulting in increased intraglomerular pressure and further loss of functional glomeruli. The decline in renal blood flow also leads to impaired ability to manage sodium loads. As a result, "salt sensitivity" ensues with an increase in mean arterial pressure of 5 mm Hg or more during a high compared with a low-salt diet.

With advancing age, there are also changes in the renin–angiotensin–aldosterone system associated with increased BP and salt sensitivity. Until end-stage renal disease develops, hypertension in the elderly is characterized by low renin activity. The effects of aldosterone are likely multifactorial (eg, vascular stiffness, central obesity, impaired endothelial function), but increasing levels within the physiologic range may predict the development of hypertension in normotensive subjects.

Box 1
Factors in the age-related increase in blood pressure

Arterial stiffness: Hypertrophy and loss of contractility of vascular smooth muscle cells, fibrosis, collagen deposition, fragmentation of elastic lamina, calcification

Decreased baroreceptor sensitivity

Increased sympathetic nervous system activity

Increased α-adrenergic receptor responsiveness

Endothelial dysfunction: Decreased nitric oxide production

Sodium sensitivity: Decreased ability to excrete a sodium load

Low plasma renin activity

Insulin resistance

Central adiposity

Adapted from Halter J, Ouslander J, Tinetti M, et al, editors. Hazzard's Geriatric Medicine and Gerontology. 6th edition. New York: McGraw-Hill; 2009.

DIAGNOSTIC CONSIDERATIONS

To ensure that appropriate treatment decisions are made, it is imperative that accurate BP measurement take place. Guidelines for accurate BP measurement not only specify appropriate cuff size and type of instrument, but emphasize the need for repeated measurements before making the diagnosis.[7] Indeed, the greater variability of BP in the elderly dictates that the diagnosis of hypertension should be based on the average of at least 3 readings (with the first discarded and subsequent readings averaged) at 3 separate visits over a period of 4 to 6 weeks (provided the presenting BP is not 180/110 mm Hg or greater).

The presence of an auscultatory gap, which is strongly associated with arterial stiffness, may lead to a significant underestimation of the true SBP. The gap represents a temporary loss of Korotkoff sounds between phase 2 and 3 and may span anywhere from a few to greater than 20 mm Hg. The auscultatory gap can be detected by palpating either the radial or brachial artery during rapid manual cuff inflation to a pressure 30 mm Hg above the value where the pulse is no longer palpable. Then, during auscultation for Korotkoff sounds, the cuff is deflated slowly at 1 to 2 mm Hg per second. Determination of BP by using electronic oscillometric devices is not affected by the auscultatory gap because they measure mean arterial pressure, which in turn is used to calculate an estimate of SBP and DBP.[8]

Orthostatic or postural hypotension (a drop in SBP or DBP of $\geq$20 mm Hg or 10 mm Hg, respectively, within 2–3 minutes of standing) was present in 8% of the participants in the Hypertension in the Very Elderly Trial (HYVET),[9] but may be even more prevalent in unselected patients with hypertension.[10] For this reason, supine, sitting, and upright BP should always be obtained and incorporated into treatment decisions because the presence of systolic orthostasis in older individuals with uncontrolled hypertension predicts an increased risk for falls within 1 year.[11]

With the prevalence of office or white coat hypertension in the community reaching 20% to 25%, it is imperative that an accurate diagnosis be reached. This diagnosis applies specifically to untreated individuals with office BPs of 140/90 mm Hg or higher but who have 24-hour ambulatory BP of less than 130/80 mm Hg (awake <135/85 mm Hg, sleep <120/70 mm Hg) or home BP of less than 135/85 mm Hg.[12] Therefore, further evaluation by way of careful home BP or 24-hour ambulatory BP monitoring is indicated in this population. Twenty-four hour BP monitoring not only provides the overall average BP, but has the added advantage of defining daytime and nocturnal averages. Although the 24-hour average correlates with indicators of target organ damage and BP load, the lack of at least a 10% drop in the nocturnal relative to the daytime average BP (nondippers) predicts a greater cardiovascular disease risk compared with the normal dipping pattern.

BLOOD PRESSURE CONTROL AND OUTCOMES

The Prospective Studies Collaboration, a meta-analysis of 61 prospective observational studies evaluating vascular mortality in subjects without vascular disease at baseline, demonstrated a positive association of SBP and DBP with stroke and ischemic heart disease over 4 decades of age from 50 to 59 to 80 to 89. A 20-mm Hg increase in SBP was associated with a 10-fold greater annual absolute stroke risk in patients in their 80s compared with those in their 50s (**Fig. 2**).[13] Based on their findings, the authors state that “blood-pressure-lowering treatment should be considered for a wide range of patients with evidence of occlusive vascular disease, largely irrespective of their current BP or the use of other medication.” Given the increasing incidence of cardiovascular disease in the elderly population, one must consider

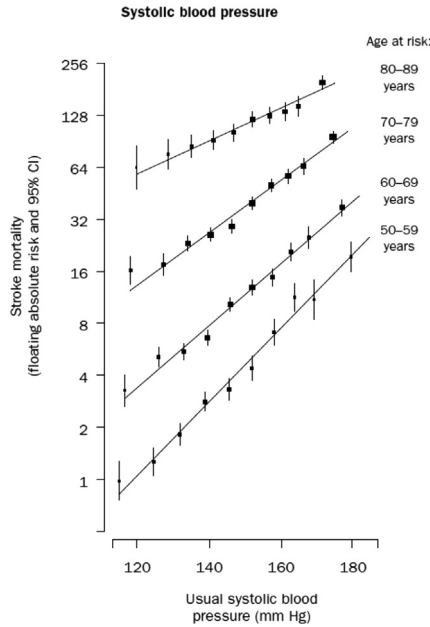

Fig. 2. Stroke mortality rate in each decade of age versus usual blood pressure at the start of that decade. (*From* Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360(9349):1906; with permission.)

that even a modest reduction in relative risk with treating hypertension may lead to a considerable decrease in absolute risk. Multiple hypertension trials in the older populations have supported this conclusion.[9,14–20]

The landmark HYVET demonstrated that antihypertensive therapy in patients over the age of 80 years led to improved outcomes in stroke, cardiovascular events, heart failure, and death with a goal BP of less than 150/80 mm Hg. The HYVET population had fewer comorbid illnesses and was generally healthier than average, such that its results may not generalize to the significant number of older patients with poor functional status, frailty, multiple medical problems, and cognitive impairment/dementia who do not meet inclusion criteria for most randomized, controlled trials. What BP goals should be used in this heterogeneous population and can we identify those who will benefit from achieving lower values through treatment versus those better off left untreated? Although the positive association of high BP and increased cardiovascular risk is maintained into older age, it may diminish or even reverse in those older individuals with poor functional status or those who are frail.

Prospective, population-based cohort studies have found conflicting results, particularly in the oldest old (those $\geq$85 years), and demonstrate an inverse association between hypertension and mortality in higher age groups. In the Leiden 85-plus study, a low SBP ($\leq$150 mm Hg) predicted increased mortality in a 90-year-old population, regardless of their *N*-terminal prohormone of brain natriuretic peptide level.[21] A consistent finding in several studies was an attenuation or even reversal of the association of hypertension and cardiovascular risk in the age range of 75 to 85 years.[22–25]

What might explain the differences in these studies? A potential explanation lies in the differences between study populations. The prospective cohort studies mentioned included individuals with multiple medical problems, dependency in activities of daily living and instrumental activities of daily living, and cognitive and functional impairment, as well as some who were institutionalized, all of which contribute to frailty. By comparison, the Prospective Studies Collaboration included subjects with a higher overall general health status and lesser prevalence of comorbid illnesses.

Gait speed, as a surrogate for frailty in 2340 individuals age 65 and older, was used to predict which subjects might be at greater risk for the adverse effects of hypertension and who subsequently may benefit from intervention.[26] Among those with a faster gait speed (≥0.8 m/s) a SBP of 140 mm Hg or greater was associated with an increased risk for mortality. Among slower walkers, no association between elevated SBP or DBP and mortality was observed. Interestingly, for those who could not complete the walk test an elevated SBP and DBP was independently associated with a lower mortality risk.

Among 4961 community-dwelling adults older than 70 years (mean age, 80) with hypertension and multiple medical comorbidities, use of antihypertensive medication was associated with an increase in serious fall injuries (hip and other major fractures, traumatic brain injuries, joint dislocations). Compared with no medication, the administration of moderate to high doses of any anti-hypertensive was associated with a 30% to 40% increased risk of falls with injury. This association was even stronger among those with a history of previous fall injury.[27]

WHAT DO CURRENT GUIDELINES RECOMMEND?

The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7)[28] was published in 2003 and, in the general population without DM or chronic kidney disease (CKD) recommended the same goal BP of less than 140/90 mm Hg in patients older than 65 years as for younger patients. In 2013, 4 other organizations, including the American Society of Hypertension and International society of Hypertension,[29] European Society of Hypertension and European Society of Cardiology,[30] Canadian Hypertension Education Program,[31] and the American Diabetes Association[32] published their guidelines, each of which promulgates the same less than 140/90 mm Hg target goal (**Table 1**).[33] The 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults:

Table 1
Summary of major hypertension guidelines: Goal blood pressure (mm Hg)

Age (y)	JNC-7[28] (2003)	ASH/ISH[29] (2013)	ESH/ESC[30] (2013)	CHEP[31] (2013)	JNC-8[34] (2014)
<60 y	<140/90	<140/90	<140/90	<140/90	<140/90
60–79	<140/90	<140/90	<140/90	<140/90	<150/90
≥80	<140/90	<150/90	<150/90	<150/90	<150/90

These guidelines apply to patients without chronic kidney disease or diabetes.

*Abbreviations:*ASH/ISH, American Society of Hypertension and International society of Hypertension; CHEP, Canadian Hypertension Education Program; ESH/ESC, European Society of Hypertension and European Society of Cardiology; JNC-7, Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure.

Adapted from Salvo M, White CM. Reconciling multiple hypertension guidelines to promote effective clinical practice. Ann Pharmacotherapy 2014;48:1243.

Report From the Panel Members Appointed to the Eighth Joint National Committee (also known as JNC-8)[34] recommended a goal BP of less than 150/90 mm Hg in patients without DM or CKD between the ages of 60 and 80 years. However, significant controversy surrounds the most recent guidelines and their recommendations not only in the population age 60 to 79 without DM or CKD, but also in women and African Americans.

With regard to raising the goal SBP from 140 to 150 mm Hg in the population between 60 and 80 years of age without DM or CKD, 5 members of the JNC-8 panel published a dissenting opinion.[35] In arguing for a continued goal of less than 140 mm Hg, several points were made. First, an increase in the target SBP to 150 mm Hg in a population at high risk for cardiovascular disease might lead to a reduction in the intensity of anti-hypertensive therapy. Coronary heart disease (CHD) risk increases with age and SBP has a much more significant impact on CHD risk than total cholesterol at older ages. Therefore, a different target BP in individuals age 60 and over compared with those younger than 60 is not justified. In addition, evidence supporting the increased SBP goal in this population was felt to be "insufficient and inconsistent" with that supporting the recommendation for a goal of less than 140 mm Hg in those younger than 60 or over age 60 with DM or CKD. Second, the decline in cardiovascular disease, especially stroke mortality, seen over the last several years might be reversed by a higher SBP goal. Third, the current guidelines are not in keeping with goals put forth in the guidelines from the majority of organizations listed herein.

In African Americans, a population with increased prevalence of CHD, stroke, CKD, and heart failure, the relaxation of the SBP goal to less than 150 mm Hg would likely result in an increase in major adverse cardiovascular outcomes and end-organ damage, especially in elderly blacks and is opposed by the Association of Black Cardiologists. Of note, the 2010 International Society of Hypertension in Blacks consensus statement recommends instituting therapy at BP level of greater than 135/85 mm Hg.[36]

Among patients over age 60 with hypertension in the United States, women represent the majority. Within this population, hypertension is the most significant contributor to heart failure, stroke, DM, CKD, and CHD. Raising the SBP goal to less than 150 mm Hg in women, African Americans, and the healthy older population would negatively impact cardiovascular outcomes and place these populations at unnecessary excess risk.[37]

THERAPY: NONPHARMACOLOGIC TREATMENT OPTIONS

Lifestyle modifications, including weight loss, physical exercise, and a low-salt diet, should be recommended to all patients with hypertension. The Trial of Nonpharmacologic Intervention in the Elderly (TONE)[38] demonstrated that modest reductions in sodium intake (average of 40 mmol/d) and weight loss (average 4 kg) lead to a 30% decrease in the need to reinitiate antihypertensive medication in the intervention group. A reduction in dietary sodium based on the Dietary Approaches to Stop Hypertension (DASH) diet has been shown to reduce BP in untreated hypertensives,[39] prehypertensives,[40] and in older patients with heart failure with preserved ejection fraction.[41] Lifestyle modifications will be adjunctive to pharmacotherapy, lead to improvement in other cardiovascular risk factors such as hyperlipidemia, and may improve physical and cognitive function. Weight loss, aerobic exercise, and reductions in salt and alcohol intake have all demonstrated sustained benefit in BP reduction and each averages a 5 mm Hg reduction in SBP, which is comparable with intervention with a single antihypertensive agent.

PHARMACOLOGIC TREATMENT OPTIONS

In considering the treatment of hypertension in older patients, multiple issues must be taken into account. As discussed, there seems to be a difference in cardiovascular risk and benefit from therapy between those older individuals with preserved functional status and those with impaired function or frailty. In addition, there are concerns related to polypharmacy, potential drug–drug interactions, cognitive impairment, and increasing medical comorbidities. Also, the presence of orthostatic hypotension and sleep apnea need to be taken into consideration. The willingness of the patient and/or their family to monitor home BP values must also be taken into account. Because the benefit of BP lowering is seen within the first year of therapy, a goals-of-care discussion in those with limited life expectancy or on hospice care is imperative.

Given these considerations and current data, we favor the approach to initiating therapy recommended by the EHS/ESC and Canadian Hypertension Education Program (see **Table 1**). The first-line therapeutic class that is recommended by the majority of guidelines in patients over age 60, without compelling medical indications such as DM and coronary artery disease, is a thiazide diuretic. Within this category the preferred agent would be chlorthalidone over hydrochlorothiazide owing to its greater potency and longer half-life, as well as evidence of greater efficacy from multiple randomized, controlled trials.[42] Additional, or second-line agents, would include angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and both dihydropyridine and nondihydropyridine calcium channel blockers. β-Blockers are clearly indicated in those older individuals with underlying coronary artery disease and/or congestive heart failure, but are otherwise not indicated as first-line agents. Recommended approaches to treating the oldest old based on the currently available data have also been proposed with the caveat that they represent subjective views and are not based on firm evidence provided by randomized, controlled trials.[43]

SUMMARY

The approach to hypertension in the geriatric population should be no different than that of other geriatric syndromes. Hypertension in older people represents a heterogeneous physiologic process and should be approached on an individual, case-by-case basis. Given the current level of uncertainty regarding the appropriate SBP goal in the hypertensive patient over age 60 without DM or CKD, data are needed from large, randomized, controlled trials. The ongoing SPRINT (Systolic Blood Pressure Intervention Trial) and ESH-CHL-SHOT (Optimal Blood Pressure and Cholesterol Targets for Preventing Recurrent Stroke in Hypertensives) are two such studies. Both trials will compare a goal SBP of near 140 mm Hg with lower SBP goals. While awaiting these results, we recommend a goal SBP of less than 140 mm Hg in the healthy hypertensive population between the ages of 60 and 80 years and emphasize that risk–benefit considerations be incorporated into decision making in those with poor physical or cognitive function and/or frailty.

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