Translational Article

Special Issue on the Aging Kidney

Management of Hypertension in the Elderly Population

Raymond V. Oliva and George L. Bakris

1Section of Hypertension, Department of Medicine, Philippine General Hospital, Manila, Philippines.
2ASH Comprehensive Hypertension Center, Department of Medicine, The University of Chicago Medicine, Illinois.

Address correspondence to George L. Bakris, MD, FASN, FASH, The University of Chicago Medicine, 5841 S. Maryland, MC 1027 Rm P-328, Chicago, Illinois 60637. Email: gbakris@gmail.com

Hypertension is common in people aged 65 and older. African Americans and women have a higher prevalence of hypertension than white individuals, and in those aged 70 and older, the hypertension was more poorly controlled than in those aged 60–69. The number of trials available in the elderly population compared with the general population are limited; hence, the database for strong recommendations as to goal blood pressure (BP) are limited. The American College of Cardiology with the American Heart Association has recently published a consensus report of management of hypertension in the elderly population. This review presents an overview of this consensus report and reviews specific studies that provide some novel findings regarding goal BP and progression of nephropathy. In general, the evidence strongly supports a BP goal of less than 150/80 mmHg. The evidence review for the consensus report supports a goal of <150/80 mmHg for the elderly with scant data in those over age 80. However, it was decided to set the goal to less than 140/90 mmHg unless the patient cannot tolerate it and then try for 140–145 mmHg. The data are scant at best for those over age 80 mmHg but some evidence exists for <150/80 mmHg. Diuretics and calcium antagonists are the most efficacious single agents for treatment; however, most patients will require two or more drugs to achieve such goals.

Key words: Elderly adults—Hypertension—Management.

Received February 27, 2012; Accepted May 17, 2012

Decision Editor: Luigi Ferrucci, MD, PhD

The elderly population represents several medical challenges, particularly in the management of hypertension, affecting the success or failure in the treatment of our elderly patients. These individuals have more organ damage or clinical cardiovascular (CV) disease, and they may respond differently to treatment goals of “normal” aged populations. According to the latest National Health and Examination Survey (1), 67% of adults aged 60 and older were found to be hypertensive, and with increasing age, not only it is more likely that someone will develop hypertension, but their risk of dying from CV disease is increased, even during the prehypertensive range (2–4), Figure 1. Despite the relative high incidence of hypertension, the elderly population are not represented in clinical trials as they have upper age limits or do not present age-specific results. The release of the Hypertension in the Very Elderly Trial (HYVET) (5), and the subsequent publication in 2011 of the American College of Cardiology Foundation/American Heart Association Consensus Document on Hypertension in the Elderly (6), changed the management of hypertension particularly in patients older than 80 years. It is but appropriate that issues in this specific population subgroup be put into perspective, particularly in the management of hypertension in the elderly population. However, each patient responds to different treatment, thus, there is a need to individualize hypertension management in the elderly population.

Pathophysiology of Hypertension in the Elderly Population

Age-related blood pressure (BP) elevations derive from changes in the arterial structure and function accompanying aging. The elasticity of the large vessels decreases due to the alteration of the various collagen components in the vessel wall (7). These changes cause increases in the pulse wave velocity, leading to late systolic BP augmentation and increasing myocardial oxygen demand. Reduction of forward flow also occurs, limiting organ perfusion. The arterial stiffness is manifested clinically by the widening of pulse pressure, which is seen commonly in the elderly patients (8,9). Data from the Framingham Heart Study suggest that after age 50, systolic BP continues to increase,
whereas diastolic BP decreases, resulting in the widened pulse pressure (10).

Elderly patients are relatively more salt sensitive due to their reduced ability to excrete a sodium load. This is partly due to the decline in kidney function with age and secondarily due to the reduced generation of the natriuretic substances, such as prostaglandin E2 (PGE2) and dopamine. Progressive renal dysfunction because of glomerulosclerosis and interstitial fibrosis with a reduction of glomerular filtration rate and other renal homeostatic mechanisms leading to increased intracellular sodium, reduced Na–Ca exchange, and volume expansion may also contribute to the pathophysiology of hypertension in the elderly population (11–14).

Secondary causes of hypertension should also be considered in this age group, such as renal artery stenosis (15), sleep apnea (16), primary hyperaldosteronism (17), and thyroid disorders (18). Excess in lifestyle such as overeating or high alcohol consumption as well as medications such as nonsteroidal anti-inflammatory medications can also contribute to the elevation of BP in the elderly patients (4).

### Definition of Hypertension in the Elderly Population

Hypertension is age dependent, and the usual definition of hypertension and target BP levels might not be applicable to the elderly hypertensive population. According to the 2011 consensus of American College of Cardiology Foundation/American Heart Association (6), a clinical diagnosis of hypertension is established by demonstrating a systolic BP of greater than or equal to 140 mmHg, and/or diastolic BP of greater than or equal to 90 mmHg on at least three different BP measurements, taken on two or more than two separate office visits to account for natural variability of BP. BP should also be measured standing for 1–3 minutes to evaluate postural hypotension. In addition, in certain conditions such as chronic kidney disease with proteinuria, a systolic BP of greater than or equal to 130 mmHg may be considered hypertensive.

Isolated systolic hypertension is very common in the elderly and is defined as the presence of systolic BP of greater than or equal to 160 mmHg with a diastolic BP below 90 mmHg (19,20). This condition is associated with a two-to-fourfold increase in the risk of myocardial infarction, left ventricular hypertrophy, renal dysfunction, stroke, and CV mortality.

Criteria to define what an ELDERLY is may also vary. The American College of Cardiology Foundation/American Heart Association decided to define elderly patients in the traditional demographic definition of greater than or equal to 65 years of age, however, recognizing that there are relevant physiological changes among the “young–old” (65–74 years), the “older old” (75–84 years), and the “oldest old” (>85 years old). Aging is a continuous process for both sexes and vascular aging rates may considerably change among individuals as a result of genetic, cultural, environmental, behavioral, and disease-related factors (6). In this article, we decided to follow the traditional definition of more than 65 years old for elderly patients keeping in mind the different pathological changes surrounding this age group.

Although a specific BP level may be used to classify a person as hypertensive, a finite BP level is only a biomarker that is somewhat removed from the complex CV disorder called hypertension (6). Improved descriptors may evolve in the future to define who has the disorder, predict those at risk for adverse outcomes, and better target treatment.

### Blood Pressure Goal in the Elderly Population

The current evidence supports a BP goal of less than 150/80 mmHg in the elderly population. However, present guidelines are based mostly on expert opinion rather than results of clinical trials due to lack of sufficient data from clinical trials involving this age group. The consensus report by the American College of Cardiology/American Heart Association (ACC/AHA) suggests a goal BP of less than 140/90 mmHg in all elderly patients, and for those who cannot tolerate this pressure, 140–145 mmHg. For those older than 80 years, a systolic BP of 140–145 mmHg, if tolerated, is acceptable, but there is no compelling evidence for this level of BP other than the HYVET.

A concern in patients with isolated systolic hypertension is the reduction of diastolic BP after initiation of antihypertensive therapy. Too low a diastolic BP may interfere with coronary perfusion and possibly increase CV risk. The relationship between diastolic BP and CV death, particularly myocardial infarction is like a J-shaped curve, thus excessive reduction in diastolic pressures should be avoided in patients with coronary artery disease who are being treated.
HYPERTENSION IN THE ELDERLY POPULATION

Clinical Trials Involving the Elderly Population

Hypertension clinical trials involving the elderly populations are summarized in Table 1, and the achieved systolic BP is shown in Figure 3. Most patients recruited in these trials prior to HYVET were older than 80 years, limiting information about octogenarians. Results in these trials showed reduction in the incidence of both stroke and CV morbidity, but a trend toward an increase in all-cause mortality. Previous clinical trials showed that lowering BP in the elderly have no effect on overall mortality or on the incidence of fatal or nonfatal myocardial infarction (25,26). However, there was a benefit in stroke outcomes. Thus, clinical practice guidelines prior to HYVET and subsequently the ACC/AHA recommended that in participants aged 80 years and above, “evidence for benefits of anti-hypertensive treatment is as yet inconclusive (22).”

The HYVET in 2008 changed how hypertension in the elderly patient is managed. It randomly assigned to almost 4,000 patients who were 80 years old and above and have systolic BP of more than 160 mmHg to either indapamide or placebo. Results of the HYVET provided clear evidence that BP lowering with treatment using antihypertensive medications is associated with definite CV benefits. The use of indapamide supplemented by perindopril showed reductions in the incidence of stroke, congestive heart failure, and CV fatal events (5).

Stricter BP goals showed no benefit in the CV morbidity and mortality in the elderly populations. The Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS) study showed that the systolic BP goals of less than 140 mmHg did not have any statistically significance in the CV mortality of patients older than 65 years (27).

Treatment Plans in the Management of Hypertension in the Elderly Population

Nonpharmacological Intervention

Lifestyle changes may be the appropriate treatment for mild hypertensive elderly patients (28,29). Interventions include smoking cessation, weight reduction, decrease in mental stress, sodium and alcohol restriction, and increased physical activity. These changes may even reduce the doses of antihypertensive medications (30–32). Weight reduction combined with salt restriction result in greater benefit in elderly patients. In the Trial of Non-pharmacologic Interventions in the Elderly (TONE) (33), the combination of weight loss and sodium restriction showed a drop of 5.3 ± 1.2 mmHg in the systolic BP and 3.4 ± 0.8 mmHg diastolic BP in obese, elderly hypertensive patients. The goal of sodium restriction was 1.8 g/24 h and the goal for weight reduction was 10 pounds.

Other lifestyle changes recommended in the elderly patient include increasing potassium intake, either by fruits and vegetables or pills. Intake of nonsteroidal anti-inflammatory drugs should also be decreased to a minimum, as these patients are more likely to take nonsteroidal anti-inflammatory medications for arthritis and pain. These drugs are known to cause hypertension by inhibiting the production of vasodilatory prostaglandins and may increase BP by as much as 6 mmHg (34,35).

Pharmacological Intervention

According to the 2011 American College of Cardiology Foundation/American Heart Association consensus guidelines, the initial antihypertensive drug should be started at the lowest dose and gradually be increased depending on the BP response up to the maximum tolerated dose. If the response to initial therapy is inadequate after reaching full dose (not necessarily the maximum recommended dose), a second drug from another class should be added. The full dose of the drug is the highest pharmacological dose of drug available, whereas the maximum dose is the highest dose that the person can tolerate without side effects. If the...
Table 1. Summary of Antihypertensive Clinical Trials in the Elderly Patients

<table>
<thead>
<tr>
<th>Clinical Trials</th>
<th>Mean Age of Participants (Age Range)</th>
<th>Number of Patients</th>
<th>Drugs Used</th>
<th>Mean Achieved BP; Control/Placebo (mmHg)</th>
<th>Mean Achieved BP; Treatment (mmHg)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Working Party in High Blood Pressure in the Elderly (EWHPE), 1985 (59)</td>
<td>72 (≥60 y)</td>
<td>840</td>
<td>Hydrochlorothiazide (HCTZ) + triamterene, ± methyldopa</td>
<td>159/85</td>
<td>155/84</td>
<td>Reduction in cardiovascular (CV) mortality</td>
</tr>
<tr>
<td>Coope and Warrender Trial, 1986 (60)</td>
<td>68 (60–79 y)</td>
<td>884</td>
<td>Atenolol ± bendrofluazide</td>
<td>180/89</td>
<td>178/87</td>
<td>Significant reduction in stroke</td>
</tr>
<tr>
<td>Systolic Hypertension in the Elderly Pilot Program (SHEP-P), 1989 (61)</td>
<td>72 (≥60 y)</td>
<td>552</td>
<td>Chlorthalidone ± hydralazine/ reserpine/methyldopa</td>
<td>157/73</td>
<td>141/68</td>
<td>Significant reduction in stroke rates from treatment with a diuretic</td>
</tr>
<tr>
<td>Systolic Hypertension in the Elderly (SHEP) 1991 (62)</td>
<td>72 (≥70 y)</td>
<td>4,736</td>
<td>Chlorthalidone ± atenolol or reserpine</td>
<td>155/72</td>
<td>143/68</td>
<td>Reduction in the incidence of stroke and a trend in the reduction of cardiac events</td>
</tr>
<tr>
<td>Swedish Trial in Old Patients with Hypertension (STOP) 1991 (63)</td>
<td>72 (70–84 y)</td>
<td>1,627</td>
<td>Atenolol ± HCTZ or amiloride</td>
<td>161/97</td>
<td>159/81</td>
<td>Significant reduction in the frequency of fatal and nonfatal stroke and myocardial infarction</td>
</tr>
<tr>
<td>Medical Research Council Trial in the Elderly (MRC) 1992 (64)</td>
<td>70 (65–74 y)</td>
<td>3,496</td>
<td>HCTZ ± amiloride vs atenolol</td>
<td>~169/79</td>
<td>~150/90</td>
<td>Use of diuretics reduce the risk of stroke, coronary, and all CV events</td>
</tr>
<tr>
<td>Cardiovascular Study in the Elderly (CASTEL), 1994 (65)</td>
<td>83 (65–89 y)</td>
<td>665</td>
<td>Clonidine, nifedipine and atenolol 181/97</td>
<td>165.2/85.6</td>
<td></td>
<td>Fixed-dose combination of beta blocker and diuretic reduced mortality</td>
</tr>
<tr>
<td>Shanghai Trial of Nifedipine in the Elderly (STONE), 1996 (66)</td>
<td>67 (60–79 y)</td>
<td>1,632</td>
<td>Nifedipine</td>
<td>155/87</td>
<td>147/85</td>
<td>Significant reduction in stroke and total CV events</td>
</tr>
<tr>
<td>Systolic Hypertension in Europe (Syst-Eur) 1997 (19)</td>
<td>70 (260 years)</td>
<td>4,695</td>
<td>Nitrendipine ± enalapril or HCTZ ~161/94</td>
<td>151/79</td>
<td></td>
<td>Significant reduction in stroke and fatal and nonfatal cardiac end points</td>
</tr>
<tr>
<td>Systolic Hypertension in China (Syst-China) 2000 (67)</td>
<td>67 (≥60 y)</td>
<td>2,394</td>
<td>Nitrendipine ± captopril or HCTZ 178/93</td>
<td>151/76</td>
<td></td>
<td>Significant reductions in total strokes, all-cause mortality, and all fatal and nonfatal cardiac end points</td>
</tr>
<tr>
<td>Hypertension in the Very Elderly Trial (HYVET) 2000(5)</td>
<td>84 (80–105 y)</td>
<td>3,845</td>
<td>Indapamide ± perindopril</td>
<td>158.5/84</td>
<td>143/78</td>
<td>Reduction in the rate of fatal and nonfatal strokes, all-cause mortality, death from CV events, and heart failure</td>
</tr>
<tr>
<td>Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS) study group 2008 (27)</td>
<td>75 (65–85 y)</td>
<td>4,418</td>
<td>Efonidipine hydrochloride</td>
<td>145.6/78.1</td>
<td>135.9/74.8</td>
<td>The incidence of strictly lowering BP in the elderly patients showed no statistically significance in CV mortality and renal disease when compared with the mildly treated group</td>
</tr>
<tr>
<td>Valsartan in Elderly Isolated Systolic Hypertension (VALISH) study 2010 (68)</td>
<td>76 (70–84 y)</td>
<td>3,079</td>
<td>Valsartan</td>
<td>142/76.1</td>
<td>136.6/74.8</td>
<td>BP targets &lt;140 mmHg are safely achievable in relatively healthy subjects of &gt;70 y of age, but the study was underpowered to definitely determine whether strict control was superior to less stringent BP targets</td>
</tr>
</tbody>
</table>

Note: ALLHAT = Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial; Australia HTN = HTN-hypertension; CA = calcium antagonist; CONVINCE = Controlled Onset Verapamil Investigation of Cardiovascular End Points Trial; EWPHE = European Working Party on Hypertension in the Elderly; INVEST = International Verapamil SR-Trandolapril study; LVD = left ventricular dysfunction.
person is having no therapeutic response or had significant side effects, a drug from another class should be substituted. In fact, most elderly patients require two or more drugs to achieve the recommended goals in clinical trials. Either a diuretic or calcium antagonist may be an initial drug or a diuretic should be one of the first two agents when starting combination drugs. When BP is more than 20/10 mmHg above goal, the recommendation is to initiate with two antihypertensive medications, with one of the choices is a diuretic. Single-pill combinations that incorporate logical doses of two agents may enhance convenience and compliance in elderly patients (6). A proposed algorithm is seen in Figure 2 in the management of hypertension in this age group. However, there is still a need for individualization of treatment, thus treatment options should be carefully considered in the elderly population. The benefits of lowering BP must be weighed with the risks of side effects and the concomitant morbidity of the patient.

Thiazide diuretics such as hydrochlorothiazide, chlorthalidone, and bendrofluazide are recommended for initiating therapy (22). Diuretics cause an initial reduction of intravascular volume, peripheral vascular resistance, BP in more
than 50% of patients, and are basically well-tolerated and inexpensive (36,37). However, they can cause hypokalemia, hypomagnesemia, and hyponatremia and are therefore not recommended in patients with baseline electrolyte abnormalities. Serum potassium should be monitored and supplementation should be given if needed (6). Indapamide, a nonthiazide sulfonamide diuretic, may also be used in the elderly population (5).

Calcium antagonists are well suited for elderly patients whose hypertensive profile is based on increasing arterial dysfunction secondary to decreased atrial and ventricular compliance. This class of drugs dilates coronary and peripheral arteries in doses that do not severely affect myocardial contractility (38–41). They hold promise in the treatment in the elderly population. Most adverse effects relate to consequences of vasodilation including ankle edema, headache, and postural hypotension. First-generation drugs, such as nifedipine, verapamil, and diltiazem should be avoided in patients with left ventricular dysfunction. Nondihydropyridines can precipitate heart blocks in the elderly with underlying conduction defects (42).

Renin–angiotensin–aldosterone system blockers, such as angiotensin-converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers, and direct renin inhibitors, may be used in the elderly population (43–45). Theoretically as aging occurs, there is a reduction in the angiotensin levels, thus ACE-Is may not be an effective medication for hypertension in the elderly population; however, several clinical trials have shown otherwise. The use of ACE-Is is beneficial in the reduction of morbidity and mortality in patients with myocardial infarction, reduced systolic function, heart failure, and reduction in the progression of diabetic renal disease and hypertensive nephrosclerosis (46–49). In elderly patients with hypertension and diabetes, angiotensin receptor blockers are considered first-line treatment and as an alternative to ACE-I in patients who cannot tolerate the latter (50). Finally, it appears that use of a blocker of the renin–angiotensin system may provide greater benefit on CV and renal risk reduction than use of a diuretic based on data from the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial, a large outcome trial of 11,506 people with a mean age of 68 years. Although there are very few data on kidney disease in the elderly population, ACCOMPLISH trial (51) did provide some evidence worthy of being tested in a prospective trial, that is, that a calcium antagonist/ACE-I combination led to fewer people going on dialysis than a diuretic/ACE-I combination; an effect that could not be explained by differences in BP (Figure 4). It must be noted that those older than 70 years tend to drink small amounts of fluid and hence, this makes them more vulnerable to decline in kidney function by renin–angiotensin–aldosterone system blockade;
thus, it is recommended that they increase their fluid intake to prevent dehydration.

The clinical benefits of beta blockers as monotherapy in uncomplicated elderly patients are poorly documented. They may have a role in combination therapy, especially with diuretics. Beta blockers have established roles in hypertensive patients complicated by certain arrhythmias, migraine headaches, senile tremors, coronary artery disease, or heart failure (52,53). Nebivolol, a selective beta-1 blocker with nitric oxide properties, does not show any associated symptoms of depression, sexual dysfunction, dyslipidemia, and hyperglycemia in the elderly population, unlike earlier generation of beta blockers (54,55).

Potassium-sparing diuretics are useful when combined with other agents. Aldosterone-blocking agents like spironolactone and eplerenone reduce vascular stiffness and systolic BP (56–58). They are also useful for hypertensive patients with heart failure or primary hyperaldosteronism. Gynecomastia and sexual dysfunction are the limiting adverse events or reactions in men using spironolactone but are less frequent with eplerenone. The epithelial sodium transport antagonists (amiloride, triamterene) are most useful when combined with another diuretic.

Other agents, such as alpha blockers, centrally acting drugs (eg, clonidine), and nonspecific vasodilators (eg, minoxidil) should not be used as first-line treatment in the elderly hypertensive patient. Instead, they are reserved as part of a combination regimen to maximize BP control after other agents have been deployed (6).

Conclusion

The elderly population is increasing, and the dilemma in treatment is aggravated by the changes in their physiology and arterial structure brought about by aging. Thus, there is a need to give extra care in this age group of patients. The advent of the 2011 consensus guidelines delineates for doctors the management of hypertension in this age group, but it is the prerogative of the physician to individualize treatment, as every elderly hypertensive patient may react differently to the treatment. It is our goal to not just decrease the risk of CV diseases brought about by elevated BPs but to prolong their lives as well.

Funding

This article had no funding support from any federal or private agency or group and is solely the work of the authors.

References


