Management of Hypertension in Older Persons

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Antihypertensive therapy has been shown to reduce morbidity and mortality in older patients with elevated systolic or diastolic blood pressures. This benefit appears to persist in patients older than 80 years, but less than one third of older patients have adequate blood pressure control. Systolic blood pressure is the most important predictor of cardiovascular disease. Blood pressure measurement in older persons should include an evaluation for orthostatic hypotension. Low-dose thiazide diuretics remain first-line therapy for older patients. Beta blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and calcium channel blockers are second-line medications that should be selected based on comorbidities and risk factors. (Am Fam Physician 2005;71:469-76. Copyright© 2005 American Academy of Family Physicians.)

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See page 409 for strength-of-recommendation labels.

By 2030, the U.S. population of persons who are older than 65 years is expected to double to more than 60 million.[1] Sixty-five percent of Americans 60 years and older have hypertension, but only 27 percent of these persons have adequate blood pressure control.[2] Furthermore, persons who are normotensive at age 55 have a 90 percent lifetime risk for developing hypertension.[3] This and the presence of other cardiovascular risk factors in older persons (i.e., obesity, left ventricular hypertrophy, sedentary lifestyle, hyperlipidemia, and diabetes) make this population at high risk for morbidity and mortality.[4]

Blood Pressure Measurement

Multiple studies have demonstrated that isolated elevated systolic blood pressure is more prevalent in older persons because of increased large-artery stiffness.[5] Recommendations from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) state that systolic blood pressure should be the primary target for the diagnosis and care of older persons with hypertension.[6-9] Blood pressure should be based on the average of two or more properly measured readings, in the sitting position, on two or more office visits.[6] Accurate measurement of blood pressure in older persons can be challenging because of cardiovascular changes associated with aging. Age-related decreases in baroreflex response may lead to orthostatic hypotension, so blood pressure should be monitored in the sitting and standing positions.[6]

Only 27 percent of patients 60 years and older with hypertension have adequate blood pressure control.

Measurements may be inaccurate because of pseudohypertension, in which the blood pressure cuff fails to compress a calcified artery. This should be considered in patients with resistant hypertension (i.e., patients with inadequate blood pressure control despite treatment with an appropriate three-drug regimen), especially if these patients have symptoms of orthostatic hypotension.[6]

Resistant hypertension may be caused by "white-coat hypertension," and therefore may be transient. Ambulatory blood pressure monitoring may be useful in documenting white-coat hypertension and verifying hypotensive symptoms in patients receiving antihypertensive agents.[6] One study found that ambulatory blood pressure monitoring was a

In older persons, the goal blood pressure recommended by JNC 7 is less than 140/90 mm Hg (less than 130/80 mm Hg for patients with diabetes mellitus or chronic kidney disease), because achieving these values has been associated with a decrease in cardiovascular disease complications.

better predictor of cardiovascular risk than conventional measurements in an older population with isolated systolic hypertension.[10]

Blood Pressure Goals

The goal blood pressure recommended by JNC 7 is less than 140/90 mm Hg (less than 130/80 mm Hg in patients with diabetes mellitus or chronic kidney disease), because achieving these values has been associated with a decrease in cardiovascular disease complications.[6] Although most data support the treatment of older patients with stage 2 isolated systolic hypertension (systolic blood pressure higher than 160 mm Hg), JNC 7 recommends treating older patients with stage 1 isolated systolic hypertension (systolic blood pressure 140 to 159 mm Hg) equally aggressively.[6]

Observational studies and secondary analyses of randomized controlled trials (RCTs) have documented a relationship between a low diastolic blood pressure and an increased risk of coronary events and death (J curve).[11] However, in a reanalysis of the Systolic Hypertension in the Elderly Program (SHEP), there was no definitive evidence of an increase in risk from aggressive use of antihypertensive therapy unless the diastolic blood pressure was lowered to less than 60 mm Hg.[11] Targeting treatment at reducing the pulse pressure is not recommended, because clinically relevant changes in this measurement with antihypertensive therapy have not been documented, nor have any RCTs used this as an end point.[6]

Evidence Supporting Treatment of Hypertension

Since 1985, there have been multiple RCTs and meta-analyses published evaluating the treatment of hypertension in patients older than 60 years. In 2000, a meta-analysis of eight trials was published that included 15,693 older patients with isolated systolic hypertension.[12] Patients were treated with conventional therapy (i.e., thiazide diuretic, beta blocker, calcium channel blocker) or placebo for four years. Active treatment was shown to reduce total mortality (number needed to treat [NNT] = 59), cardiovascular mortality (NNT = 79), fatal or nonfatal cardiovascular events (NNT = 26), and fatal or nonfatal stroke (NNT = 48).[12] A Cochrane review found similar results, concluding that treating healthy older persons with hypertension is highly efficacious.[4] More recent trials have evaluated the effects of different antihypertensive regimens (i.e., angiotensin-converting enzyme [ACE] inhibitors, angiotensin-receptor blockers [ARBs], beta blockers, calcium channel blockers alone and in combination) on the treatment of hypertension in older persons *(Table 1)*.[13-17] Although there were subtle differences among treatments, there were no overall differences in total mortality.

Meta-analyses have documented a sustained reduction in stroke in patients older than 80 years, and a

Strength of Recommendations

Key clinical recommendation	*Label*	*References*	*Comments*
Isolated systolic blood pressure should be the primary target for diagnosis and management in older persons.	B	6	Based on epidemiologic data
The recommended blood pressure goal in older persons is less than 140/90 mm Hg.	A	6	
The recommended blood pressure goal in persons with diabetes or chronic kidney disease is less than 130/80 mm Hg.	A	6	Studies in diabetes mellitus and chronic kidney disease were not specifically in older persons.
There is no age threshold beyond which hypertension should not be treated.	C	6, 12, 17, 19	
Thiazide diuretics are first-line therapy for isolated systolic hypertension, and they should be considered in any antihypertensive regimen in older persons.	A	6	

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, opinion, or case series. See page 409 for more information.

TABLE 1
Recent Evidence Supporting Treatment of Hypertension in Older Persons

Trial	*Mean age (years)*	*Median follow-up (years)*	*Initial blood pressure (mm Hg)*	*Blood pressure after treatment (mm Hg)*	*Regimens*	*Outcomes*
STOP-2[14] (1999)	76	5	194/98	~158/80 in both groups	Beta blocker or thiazide (older drugs) vs. ACE inhibitor or calcium channel blocker (newer drugs)	Regimens did not differ in rates of stroke, cardiovascular events, or mortality. ACE inhibitor better than calcium channel blocker for myocardial infarction (NNT = 26) and congestive heart failure (NNT = 28).
LIFE[15] (2002)	70	4	174/98	~145/81 in both groups	ARB (losartan) vs. beta blocker (atenolol)	ARB better than beta blocker for stroke (NNT = 50) and combined end point of cardiovascular mortality, stroke, and myocardial infarction (NNT = 50). Regimens did not differ in rates of total mortality.
ALLHAT[13] (2002)	67	5	146/84	~134/85 in all groups	Thiazide (chlorthalidone) vs. ACE inhibitor (lisinopril) vs. calcium channel blocker (amlodipine)	Regimens did not differ in combined end point of fatal coronary heart disease or nonfatal myocardial infarction. Thiazide better than calcium channel blocker for congestive heart failure (NNT = 40) and angina (NNT = 67). Thiazide better than ACE inhibitor for stroke (NNT = 111), cardiovascular disease (NNT = 77), congestive heart failure (NNT = 100), or revascularization (NNT = 100). Regimens did not differ in rates of total mortality.
INVEST[16] (2003)	66	2	150/87	~131/77 in both groups	Calcium channel blocker (verapamil) plus ACE inhibitor (trandolapril) vs. beta blocker (atenolol) plus thiazide (hydrochlorothiazide)	Regimens did not differ in rates of cardiovascular outcomes or total mortality.
ANBP2[17] (2003)	72	4	168/91	~142/79 in both groups	ACE inhibitor (enalapril) vs. thiazide (hydrochlorothiazide)	ACE inhibitor better than thiazide for primary end point of all cardiovascular events or total mortality (NNT = 72) and for myocardial infarction (NNT = 125). Regimens did not differ in rates of total mortality.

STOP-2 = Swedish Trial in Old Patients with Hypertension-2 study; LIFE = Losartan Intervention For Endpoint reduction in hypertension study; ALLHAT = Antihypertensive and Lipid-Lowering Treatment to prevent Heart Attack Trial; INVEST = International Verapamil-Trandolapril study; ANBP2 = Second Australian National Blood Pressure study; ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; NNT = number needed to treat.

Information from references 13 through 17.

Older patients are more prone to thiazide-induced dehydration and orthostatic changes, so physicians should check for orthostatic hypotension and suggest measures to prevent falls.

greater benefit in reduction of cardiovascular events in patients older than 70 years.[12,18] The Systolic Hypertension in the Elderly: Lacidipine Long-term (SHELL) study documented a similar benefit in treating hypertension in older persons in three age groups (i.e., 60 to 69 years, 70 to 79 years, and 80 years and older).[19] Although dementia is more common in older patients with hypertension, there is a lack of data supporting the use of antihypertensive agents to prevent cognitive decline.[6]

Special Considerations When Treating Hypertension

JNC 7 recommendations for treating hypertension are similar in the general population and older persons. The key points include: (1) treat isolated systolic blood pressure; (2) thiazide diuretics should be first-line treatment; (3) second-line treatment should be based on comorbidities and risk factors *(Table 2)*[6,21,22]; (4) patients with systolic blood pressure higher than 160 mm Hg or diastolic blood pressure higher than 100 mm Hg usually will require two or more agents to reach goal[6]; (5) treatment should be initiated with a low dose of the chosen antihypertensive agent, and titrated slowly to minimize side effects such as orthostatic hypotension[6]; and (6) weight loss and sodium reduction have been shown to be feasible and effective interventions in older patients with hypertension.[20] Recommended lifestyle modifications are summarized in *Table 3*.[6] JNC 7 recommends adoption of the Dietary Approaches to Stop Hypertension (DASH) diet, which has been shown to produce blood pressure reductions similar to single-drug therapy[21]; (7) to improve adherence with antihypertensive regimens, involve patients in goal setting, and ensure that the patient's cultural beliefs and previous experiences are incorporated in a treatment plan.[6] Simplify the medication regimen, keeping in mind how much it costs.

TABLE 2
STEPS Comparison of Antihypertensive Agents in Older Persons

	Thiazide diuretics	*Beta blockers*	*ACE inhibitors and ARBs*	*Calcium channel blockers*
Safety	Electrolyte disturbance, especially hypokalemia Acute renal insufficiency and dehydration Drug interactions: digoxin (Lanoxin), NSAIDS	Bronchospasm Drug interactions: digoxin, diltiazem (Cardizem CD), verapamil (Calan SR)	Electrolyte disturbances: hyperkalemia (especially in chronic kidney disease) First-dose hypotension and acute renal insufficiency Angioedema Drug interactions: NSAIDS, potassium-sparing diuretics	Nondihydropyridines: atrioventricular block, bradycardia Dihydropyridines: hypotension, reflex tachycardia Drug interactions: cyclosporine (Sandimmune), grapefruit juice
Tolerability	Orthostasis, sexual dysfunction	Sedation, depression, sexual dysfunction	Cough with ACE inhibitor	Peripheral edema, constipation, gingival hyperplasia
Efficacy	Hypertension, isolated systolic hypertension, heart failure, diabetes, patients at high risk for cardiovascular disease, recurrent stroke prevention	Hypertension, heart failure, postmyocardial infarction, patients at high risk for cardiovascular disease	Hypertension, heart failure, postmyocardial infarction, patients at high risk for cardiovascular disease, diabetes mellitus, chronic kidney disease, and recurrent stroke prevention	Hypertension, diabetes, patients at high risk for cardiovascular disease. Symptom control in chronic stable angina, ischemic heart disease, and atrial fibrillation
Price	$	$	$$	$$$
Simplicity	Once daily	One to two times daily	One to two times daily	One to two times daily

ACE = angiotensin-converting enzyme; ARBs = angiotensin-receptor blockers; NSAIDS = nonsteroidal anti-inflammatory drugs.

Information from references 6, 21, and 22.

Specific Agents

THIAZIDE DIURETICS

Several issues should be considered when using thiazide diuretics in older patients *(Table 2)*. Older patients are more prone to thiazide-induced dehydration and orthostatic changes, so physicians should check for orthostatic hypotension and suggest measures for preventing falls. Serum electrolyte levels should be monitored frequently, and hypokalemia should be treated with potassium administration, the addition of a potassium-sparing diuretic like spironolactone (Aldactone), or the use of a combination product such as triamterene/hydrochlorothiazide (Dyazide, Maxzide).[22,23] This is important because in the SHEP trial, older patients with potassium levels less than 3.5 mg per dL (0.9 mmol per L) lost the cardiovascular protective benefit from the thiazide.[24] Although poorly studied, their efficacy may be decreased in patients with chronic kidney disease.[6,22] Uric acid and thiazides compete for excretion at the level of the renal tubule, so caution is necessary in patients with a history of gout.[23] Although thiazide diuretics have been reported to affect serum glucose and lipid levels adversely, there is a decreased incidence of metabolic abnormalities and associated clinical outcomes with low-dose therapy.[13,25]

Patients taking digoxin (Lanoxin) and a thiazide diuretic may be at increased risk of digoxin toxicity because of diuretic-induced electrolyte disturbances.[22] Nonsteroidal anti-inflammatory drugs (NSAIDs) may reduce diuretic and antihypertensive effects of thiazides.[6] When adding an ACE inhibitor or ARB to existing diuretic therapy, there is a possibility of first-dose hypotension and the risk of acute renal insufficiency.[22]

Additional indications for using beta blockers to treat older patients with hypertension include high risk for coronary disease and prevention of second myocardial infarction and heart failure.

BETA BLOCKERS

Beta blockers reduce mortality and morbidity in older patients with hypertension. Additional indications for use of beta blockers in older persons include high risk for coronary disease and prevention of a second myocardial infarction and heart failure *(Table 4)*.[6] Despite the pharmacokinetic and pharmacodynamic differences among various beta blockers, they have similar clinical antihypertensive efficacy. Atenolol (Tenormin), bisoprolol (Zebeta), and metoprolol (Lopressor, Toprol XL) are cardioselective beta blockers with low lipid solubility, and therefore have a preferable side effect profile in older persons.[22]

TABLE 3
Lifestyle Modifications to Manage Hypertension*†

Modifications	*Recommendation*	*Approximate systolic blood pressure reduction (range)*
Weight reduction	Maintain normal body weight (body mass index 18.5 to 24.9 kg per m^2).	5 to 20 mm Hg per 10-kg weight loss
Adoption of DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat.	8 to 14 mm Hg
Dietary sodium restriction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2 to 8 mm Hg
Physical activity	Engage in regular aerobic activity such as brisk walking (at least 30 minutes per day, most days of the week).	4 to 9 mm Hg
Moderation of alcohol consumption	Limit consumption to no more than two drinks (1 oz or 30 mL of alcohol; e.g., 24-oz beer, 10 oz of wine, or 3 oz of 80-proof whiskey) per day in most men and to no more than one drink per day in women and lighter-weight persons.	2 to 4 mm Hg

DASH = Dietary Approaches to Stop Hypertension.

**—For overall cardiovascular risk reduction, stop smoking.*

†*—The effects of implementing these modifications are dose and time dependent and could be greater for some individuals.*

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TABLE 4
Compelling Indications for Specific Antihypertensive Therapy

	Patient population	*Drug of first choice*
Stage 1 hypertension	Patients without compelling indications	Diuretic for most
	Heart failure	Diuretic, ACE inhibitor, beta blocker, ARB, or aldosterone antagonist
	Postmyocardial infarction	ACE inhibitor, beta blocker, or aldosterone antagonist
	High coronary disease risk	Diuretic, beta blocker, ACE inhibitor, or calcium channel blocker
	Ischemic heart disease	Beta blocker or calcium channel blocker
	Diabetes	Diuretic, beta blocker, ACE inhibitor, ARB, or calcium channel blocker
	Chronic kidney disease	ACE inhibitor or ARB
	Recurrent stroke prevention	Diuretic plus ACE inhibitor
	Black patients	Diuretic or calcium channel blocker
	Elderly patients	Diuretic for most; consider ACE inhibitor, ARB, beta blocker, calcium channel blocker, or combination
Stage 2 hypertension	Patients without compelling indication	Two-drug combination for most: diuretic plus ACE inhibitor, ARB, beta blocker, or calcium channel blocker
	Patients with compelling indication	Two-drug combination for most: diuretic plus treatment for stage 1 hypertension

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker.

Adapted with permission from Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003;42:1221.

Beta blockers that are lipophilic (e.g., propranolol [Inderal]) cross the blood-brain barrier, possibly causing more sedation, depression, and sexual dysfunction in older patients.[22] Beta blockers are contraindicated in patients with severe reactive airway disease, especially the nonselective agents (i.e., nadolol [Corgard] and propranolol).[6] Particularly in older patients, beta blockers as a class can cause bradycardia, conduction abnormalities, and development of heart failure if started too aggressively in patients with preexisting left ventricular dysfunction.[6,22,23] Beta blockers should be tapered before discontinuation to minimize the risk of reflex tachycardia. The effects of beta blockers on lipid profiles are transient and of little clinical significance.[25] Beta blockers should be used with caution in combination with other negative chronotropes, such as diltiazem (Cardizem CD, Dilacor XR, Tiazac), verapamil (Isoptin SR, Calan SR), or digoxin.[6,22,23]

ACE INHIBITORS AND ARBS

Pharmacologic inhibition of the renin-angiotensin-aldosterone system can occur by inhibiting the formation of angiotensin II with an ACE inhibitor or by blocking the receptor site with an ARB. ACE inhibitors and ARBs have compelling indications for use in heart failure, diabetes mellitus, and chronic kidney disease *(Table 4)*.[6] ACE inhibitors (i.e., enalapril [Vasotec], lisinopril [Prinivil, Zestril], ramipril [Altace], trandolapril [Mavik]) also have compelling indications for patients after myocardial infarction, patients at high risk for coronary disease, and for recurrent stroke prevention.[6] Studies comparing equipotent doses of ACE inhibitors have shown comparable efficacy and, although debatable, the benefits are believed to be a class effect.[22]

Generally, ACE inhibitors and ARBs are well tolerated, and the incidence of side effects is low *(Table 2)*. Although rare, angioedema can occur at any time during treatment

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and appears to be more frequent in blacks.[13,22,23] Cough occurs in up to 25 percent of patients and may necessitate discontinuation of therapy. ARBs (i.e., candesartan [Atacand], irbesartan [Avapro], losartan [Cozaar], valsartan [Diovan]) are reasonable alternatives for those with ACE inhibitor–associated cough. Generally, it is recommended to avoid ARBs in patients with a history of ACE inhibitor–related angioedema, although there are case reports of this being done safely.[26]

First-dose hypotension is a concern in dehydrated, decompensated patients with heart failure, and those with bilateral renal artery stenosis.[6,22] While these drugs potentially preserve renal function, patients may experience an elevation in serum creatinine levels after starting an ACE inhibitor if renal insufficiency, dehydration, or heart failure is present. Because these conditions are common in older patients, hypotension and renal function should be monitored closely upon initiation. There is no serum creatinine value beyond which an ACE inhibitor should not be used, but an acute elevation in serum creatinine above 30 percent warrants a temporary discontinuation or lowering of the dose.[6,27] Because ACE inhibitors also may cause hyperkalemia, serum electrolytes and creatinine should be monitored periodically, particularly in patients receiving potassium-sparing diuretics.[6,23] Like thiazides, NSAIDs can blunt the antihypertensive activity of ACE inhibitors and ARBs.[6,23]

CALCIUM CHANNEL BLOCKERS

Calcium channel blockers prevent calcium from entering the cells of the arterial vasculature and cause dilation in the coronary arteries and periphery. There are two classes of calcium channel blockers—dihydropyridines and nondihydropyridines—and both are effective treatments for hypertension in older patients.[6] As a group, calcium channel blockers have compelling indications for use in patients at high risk for coronary disease and those with diabetes mellitus *(Table 4)*.[6] Nondihydropyridines (e.g., diltiazem, verapamil) exhibit negative inotropic and chronotropic effects, making them beneficial in atrial fibrillation and supraventricular tachyarrythmias.[22] Dihydropyridines (i.e., amlodipine [Norvasc], felodipine [Plendil]) are safe for use in patients with heart failure, hypertension, or chronic stable angina.[28] Short-acting agents are not recommended in clinical practice.[6]

In comparison with other antihypertensives, systematic reviews generally have found calcium channel blockers to be equivalent or inferior to other antihypertensive agents.[29] In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), amlodipine was found to be inferior to chlorthalidone in preventing heart failure–related events.[13] Calcium channel blockers have been found to be effective in salt-sensitive hypertensive patients, such as blacks and older persons.[6] Interactions with other drugs and food are reported with some calcium channel blockers *(Table 2)*. In particular, grapefruit juice may increase the bioavailability of felodipine significantly leading to profound hypotension, and diltiazem can inhibit the metabolism of cyclosporine (Sandimmune) in transplant patients leading to cyclosporine toxicity.[22,23] The dihydropyridines, especially nifedipine (Adalat CC, Procardia XL), can cause orthostatic hypotension, peripheral edema, and gingival hyperplasia.[6] These are particularly problematic in older patients.[30] Verapamil often is a cause of constipation in older persons.[22,23]

MISCELLANEOUS ANTIHYPERTENSIVE AGENTS

Peripheral alpha blockers, centrally acting agents, and vasodilators have limited use in older persons because of significant side effect profiles. Although these agents have been found to reduce blood pressure effectively, they have not been associated with reductions in morbidity and mortality in patients with hypertension.

Central alpha agonists include clonidine (Catapres), guanfacine (Tenex), methyldopa (Aldomet), and reserpine (Serpasil). These agents act centrally and may cause significant sedation, dry mouth, and depression.[6,22] Many patients experience hypotension in addition to sodium and water retention. Abrupt cessation of high doses of these agents (e.g., greater than 1.2 mg daily of clonidine) may cause rebound hypertension, making them a poor choice for patients with the potential for noncompliance.[22] The clonidine patch (Catapres-TTS), although expensive, is a useful alternative to oral antihypertensive therapy in older patients who are unable to take medications by mouth.[22] Like central alpha agonists, the vasodilators hydralazine (Apresoline) and minoxidil (Loniten) cause sodium and water retention and reflex tachycardia, so they are not useful as monotherapy.[23]

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