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Hypertension in elderly patients: Treatment reduces mortality, but is underused

■ ABSTRACT

Recently published clinical trials provide compelling evidence of the effectiveness of antihypertensive therapy to reduce cardiovascular mortality. The Sixth Joint National Committee on Detection, Evaluation, and Treatment of Hypertension emphasizes that hypertension is undertreated in this country: only approximately one fourth of hypertensive persons have their blood pressure controlled to the current recommended level of less than 140/90 mm Hg. The point is especially pertinent to elderly patients, most of whom have hypertension. Moreover, most elderly hypertensive persons have systolic hypertension, which has an even stronger association with risk than does diastolic pressure. Current recommendations are reviewed.

■ KEY POINTS

Although increased systolic blood pressure is a stronger risk factor for cardiovascular mortality than increased diastolic pressure, increased pulse pressure may be an even better marker of risk.

Office readings may overestimate true average blood pressure owing to pseudohypertension and "white-coat" hypertension.

The goal of treatment in older persons is to lower the blood pressure to < 140/90 mm Hg if possible.

Initial doses of antihypertensive drugs should be lower in elderly than in younger patients, owing to the risk of orthostatic hypotension.

THE OLDER YOU ARE, the more likely you are to have hypertension—and the less likely you are to have it under control.

Government data^{1,2} show that by age 60 more than half of the population has hypertension, and more than half of hypertensive persons in this age group have isolated systolic hypertension, shown by epidemiologic data to be a stronger cardiovascular risk factor than diastolic hypertension. Yet, only 26% of hypertensive persons over age 60 have their blood pressure controlled to the currently recommended level of 140/90 mm Hg or less, and at age 75 and older the numbers drop to 21% for women and 17% for men.²

Recently published clinical trials provide compelling evidence of the effectiveness of antihypertensive therapy to reduce cardiovascular mortality. This paper summarizes the treatment of hypertension in elderly patients, outlining recent recommendations by the Sixth Joint National Committee on Detection, Evaluation, and Treatment of Hypertension.^{1,2}

■ MOST OLDER PERSONS HAVE HYPERTENSION

More elderly persons have hypertension than do not. The third National Health and Nutrition Examination Survey³ found that the prevalence of hypertension (systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg or under a physician's care for hypertension) in persons aged 60 years and older was:

- 60% in non-Hispanic whites

TABLE 1

Increased risk in elderly patients with hypertension

ENDPOINT	NO. OF PATIENTS	RELATIVE RISK
New coronary events⁴		
Men	664	2.0
Women	1,488	1.6
New atherothrombotic brain infarction¹⁶		
Men	664	2.2
Women	1,488	2.4
Peripheral arterial disease¹⁴		
Men	244	1.7
Women	625	1.5

- 71% in non-Hispanic African Americans
- 61% in Mexican Americans.

Other population studies^{4,5} had roughly similar findings.

Isolated systolic hypertension (an elevated systolic pressure with a normal diastolic pressure) accounts for more than half of cases of hypertension in the elderly.^{4,5} In contrast, most middle-aged persons with hypertension have diastolic or mixed systolic-diastolic hypertension.

■ HYPERTENSION INCREASES CARDIOVASCULAR MORBIDITY AND MORTALITY IN THE ELDERLY

Isolated systolic hypertension and diastolic hypertension are both associated with increased cardiovascular morbidity and mortality in older persons.⁶⁻¹⁷ The higher the systolic or diastolic blood pressure, the greater the morbidity and mortality from cardiovascular disease. Hypertension is the principal risk factor for stroke,^{9,16} and it is also associated with coronary events,^{4,8} peripheral arterial disease,¹⁰⁻¹⁴ and heart failure (TABLE 1).^{9,15}

Of note: Increased systolic blood pressure is a stronger risk factor for cardiovascular morbidity and mortality than is increased diastolic blood pressure.^{2,6} The Cardiovascular Health Study, a 5-year study of 5,202 older men and women, found that a brachial systolic blood pressure higher than 169 mm Hg increased the mortality rate 2.4 times.⁷

An even better marker of risk than either systolic or diastolic blood pressure may be increased pulse pressure. Madhavan et al¹⁸ found that a pulse pressure wider than 63 mm Hg was associated with an increase in cardiovascular events. An increased pulse pressure, found in older persons with isolated systolic hypertension, indicates decreased vascular compliance in the large arteries.

■ ANTIHYPERTENSIVE TREATMENT REDUCES STROKES AND CORONARY EVENTS

A number of clinical trials have demonstrated the benefit of treating both diastolic and isolated systolic hypertension in the elderly.¹⁹⁻²⁵ In general, these studies showed a greater percentage decrease in strokes than in coronary events. MacMahon and Rodgers,²⁶ in a meta-analysis of five studies in the elderly, calculated that antihypertensive treatment decreased the incidence of strokes by 34% and the incidence of coronary heart disease events by 19%. However, cardiac events are much more common than strokes, and antihypertensive treatment will prevent a greater number of coronary events in terms of absolute numbers.

■ HOW TO DIAGNOSE HYPERTENSION

The report of the Sixth Joint National Committee on Detection, Evaluation, and Treatment of Hypertension (JNC VI)¹ defines hypertension as a systolic blood pressure of 140 mm Hg or higher, or a diastolic blood pressure of 90 mm Hg or higher, or both. The number must be the average of at least two blood pressure readings taken at each of at least two visits after an initial screening visit, using a standardized technique.

Stages of hypertension

To gauge the severity of hypertension, JNC VI¹ devised a system of "stages."

Stage 1. 140–159 mm Hg systolic, or 90–99 mm Hg diastolic, or both.

Stage 2. 160–179 mm Hg systolic, or 100–109 mm Hg diastolic, or both.

Stage 3. ≥ 180 mm Hg systolic, or ≥ 110 mm Hg diastolic, or both.¹

If the systolic and diastolic blood pressures fall into different stages, the higher stage is

Take at least 2 readings during at least 3 visits, and find the average

used. Isolated systolic hypertension—a systolic blood pressure of ≥ 140 mm Hg with a diastolic blood pressure of < 90 mm Hg—is staged according to the systolic pressure.

Problems in measuring blood pressure

In some elderly persons, office readings may overestimate the true, average blood pressure, owing to two problems: pseudohypertension and “white-coat” hypertension.

Pseudohypertension is due to excessive vascular stiffness—the calcified brachial artery resists compression by the sphygmomanometer, leading to spuriously high readings.²⁷

White-coat hypertension, ie, an excessive increase in blood pressure in response to the stress of being in a physician’s office, is especially common in older women and particularly affects the systolic blood pressure.²⁸

If office readings are high but the patient does not have target organ damage (ie, heart disease, stroke, transient ischemic attacks, nephropathy, peripheral arterial disease, or retinopathy), consider the possibility that the patient has pseudohypertension or white-coat hypertension. In this situation, blood pressure readings should be obtained outside of the office by self-measurement or by ambulatory monitoring.¹

Stratifying risk

Hypertension is a cardiovascular risk factor, but not the *only* risk factor. Accordingly, JNC VI also recommends a simple risk-factor analysis, as outlined below.

Does the patient have other major cardiovascular risk factors? These are:

- Smoking
- Dyslipidemia
- Diabetes mellitus
- Age older than 60 years
- Male gender
- Postmenopausal status in women
- Family history of cardiovascular disease.

Does the patient have target organ damage (ie, damage due to high blood pressure) **or clinical cardiovascular disease?** These include:

- Left ventricular hypertrophy
- Angina pectoris

- Previous myocardial infarctions
- Previous coronary revascularizations
- Heart failure
- Stroke or transient cerebral ischemic attack
- Nephropathy
- Peripheral arterial disease
- Retinopathy.

Using this information, you can divide patients into three risk groups:

Risk group A. No other risk factors and no target organ damage or clinical cardiovascular disease

Risk group B. One or more risk factors (not including diabetes mellitus) and no target organ damage or clinical cardiovascular disease

Risk group C. Diabetes (with or without other risk factors) or target organ damage or both.

The urgency of beginning antihypertensive drug therapy depends on both the stage of hypertension and the patient’s risk group.

TREATMENT

The goal of treatment of hypertension in older persons is the same as in younger persons—to decrease the blood pressure to $< 140/90$ mm Hg if possible.¹ Further reductions in diastolic pressure seem to be safe,²⁹ although the benefit is not proven.

Although the benefits of antihypertensive treatment in older persons with stage 1 isolated systolic hypertension have not yet been demonstrated, these persons are at increased risk for cardiovascular morbidity and mortality,³⁰ and I believe they should be treated with antihypertensive therapy, especially if they are in risk groups B or C.

Lifestyle modification

Like younger patients, older persons with hypertension should undertake lifestyle modifications. Specifically, they should be instructed to:

- Restrict dietary sodium to 2.4 grams daily
- Lose weight if obese
- Discontinue drugs that increase blood pressure
- Avoid tobacco

A simple risk-factor analysis helps determine whether to start treatment

- Limit alcohol intake to no more than 1 ounce daily in men and no more than one-half ounce daily in women and lighter-weight persons
- Increase aerobic physical activity
- Reduce dietary saturated fat and cholesterol
- Maintain adequate dietary potassium, calcium, and magnesium intake.

When to start drug therapy

Lifestyle modifications alone may suffice for some patients. JNC VI¹ recommends trying lifestyle modification for up to 6 months in persons with stage 1 hypertension in risk group B, and starting antihypertensive drug therapy if this does not reduce the blood pressure to below 140/90 mm Hg.

However, older persons should start antihypertensive drug therapy immediately in addition to lifestyle modifications if they have:

- Stage 2 or 3 hypertension
- Stage 1 hypertension and target organ

damage or evidence of clinical cardiovascular disease or diabetes mellitus.

What drug to use?

JNC VI recommends diuretics or beta-blockers as initial drugs,¹ because these drugs have been found to decrease cardiovascular morbidity and mortality in controlled clinical trials,¹⁹⁻²² whereas few trials have been performed with other classes of agents. I agree with this recommendation.

Older persons with hypertension should receive another drug as initial therapy if they also have any of the conditions listed below:

- Previous myocardial infarction, angina pectoris, myocardial ischemia, or complex ventricular arrhythmias: a beta-blocker is indicated.³¹

- Heart failure: both a diuretic and an angiotensin-converting enzyme (ACE) inhibitor are indicated.^{32,33}

- Diabetes mellitus: an ACE inhibitor is indicated. If the patient cannot tolerate an ACE inhibitor because of cough, rash, or altered taste sensation, an angiotensin II type 1 receptor antagonist should be given. Alternatively, a long-acting dihydropyridine can be effective.³⁴

The JNC VI report includes tables show-

ing the range of doses of different antihypertensive drugs.¹ The lower doses listed in these tables should be used in treating older persons (TABLE 2).

ISOLATED SYSTOLIC HYPERTENSION

Persons with isolated systolic hypertension are the largest subgroup of older persons with hypertension. This group also represents the largest population group inadequately treated at the present time. In an academic geriatrics practice, 30% of persons with hypertension did not have their blood pressure lowered to below 140/90 mm Hg by antihypertensive therapy, and the percentage was the same in patients with isolated systolic hypertension.⁵

The benefit of treating isolated systolic hypertension is well documented. In the Systolic Hypertension in the Elderly Program, isolated systolic hypertension was defined as a systolic blood pressure ≥ 160 mm Hg and the diastolic blood pressure ≤ 90 mm Hg.²² In this randomized, double-blind, placebo-controlled study, chlorthalidone 12.5 mg to 25 mg daily was used as step 1 drug therapy and atenolol 25 mg to 50 mg daily as step 2. At 4.5-years of follow-up, compared with placebo, antihypertensive drug therapy caused a 36% significant reduction in stroke, a 27% significant decrease in nonfatal myocardial infarction plus coronary death, a 33% significant reduction in major cardiovascular events, a 49% significant decrease in heart failure,²⁵ and a 13% insignificant decrease in total mortality.

The Systolic Hypertension in Europe (Syst-Eur) Trial²³ used a slightly different definition of isolated systolic hypertension: a sitting systolic blood pressure ≥ 160 mm Hg with a sitting diastolic blood pressure < 95 mm Hg, and a standing systolic blood pressure ≥ 140 mm Hg. In this randomized, double-blind, placebo-controlled study in older patients, active treatment was started with nitrendipine 10 mg to 40 mg daily and, if necessary, combined with or replaced by enalapril 5 mg to 20 mg daily, hydrochlorothiazide 12.5 mg to 25 mg daily, or both. At 2 years of follow-up, compared with placebo, antihypertensive drug therapy caused a 42% significant reduction in stroke and a 31% significant reduction in all fatal and nonfatal cardiovascular endpoints. In

Start drug therapy immediately in stage 2 or 3 hypertension

TABLE 2

Initial dosages of antihypertensive agents in elderly patients

Thiazide diuretics

Bendroflumethiazide 2.5 mg daily
Benzthiazide 12.5 mg daily
Chlorothiazide 75 mg twice a day
Chlorthalidone 12.5 mg daily
Hydrochlorothiazide 12.5 mg daily
Hydroflumethiazide 12.5 mg daily
Indapamide 2.5 mg daily
Methyclothiazide 2.5 mg daily
Metolazone 0.5 mg daily
Polythiazide 1 mg daily
Quinethazone 25 mg daily
Trichlormethiazide 1 mg daily

Loop diuretics

Bumetanide 0.25 mg twice a day
Ethacrynic acid 12.5 mg twice a day
Furosemide 20 mg twice a day
Torsemide 5 mg daily

Potassium-sparing diuretics

Amiloride 5 mg daily
Spironolactone 25 mg daily
Triamterene 25 mg daily

Alpha 1 receptor blockers

Doxazosin 1 mg daily
Prazosin 1 mg twice a day
Terazosin 1 mg daily

Beta-blockers

Acebutolol 200 mg daily
Atenolol 25 mg daily
Betaxolol 5 mg daily
Bisoprolol 2.5 mg daily
Carteolol 2.5 mg daily
Metoprolol 50 mg daily
Nadolol 40 mg daily
Penbutolol 10 mg daily
Pindolol 5 mg twice a day
Propranolol 20 mg twice a day
Propranolol, long-acting 40 mg daily
Timolol 10 mg twice a day

Alpha-beta blockers

Carvedilol 6.25 mg twice a day
Labetalol 100 mg twice a day

Other adrenergic inhibitors

Clonidine 0.1 mg twice a day
Guanabenz 4 mg twice a day
Guanadrel 5 mg twice a day
Guanethidine 10 mg daily
Guanfacine 1 mg daily
Methyldopa 250 mg twice a day
Reserpine 0.05 mg daily

ACE inhibitors

Benazepril 5 mg daily
Captopril 12.5 mg twice a day
Enalapril 5 mg daily
Fosinopril 10 mg daily
Lisinopril 5 mg daily
Moexipril 3.75 mg twice a day
Quinapril 5 mg daily
Ramipril 1.25 mg daily
Trandolapril 1 mg daily

Angiotensin II receptor blockers

Irbesartan 125 mg daily
Losartan 25 mg daily
Valsartan 80 mg daily

Calcium antagonists

Amlodipine 2.5 mg daily
Diltiazem, sustained release 60 mg twice a day
Diltiazem, extended release 120 mg daily
Felodipine 5 mg daily
Isradipine 1.25 mg twice a day
Nicardipine, sustained release 30 mg twice a day
Nifedipine, long-acting 30 mg daily
Nisoldipine 20 mg daily
Verapamil 40 mg twice a day
Verapamil, long-acting 120 mg daily

SOURCE: ADAPTED FROM THE JNC VI REPORT, REFERENCE 1

addition, there were 14% fewer deaths, 20% fewer myocardial infarctions, 29% fewer cases of heart failure, and 27% fewer deaths due to cardiovascular diseases, but these trends did not achieve statistical significance.

In these studies, no J-curve was clearly defined for either systolic or diastolic blood pressure, ie, no point beyond which further blood pressure reduction was associated with an increase in adverse events.

The JNC VI report recommends thiazide diuretics or beta-blockers in combination with diuretics for treating older persons with isolated systolic hypertension, based on the results from the SHEP study.²² In addition, because of data from the Syst-Eur trial,²³ the JNC VI report also recommends long-acting dihydropyridine calcium antagonists for this indication.¹

LEFT VENTRICULAR HYPERTROPHY

Left ventricular hypertrophy (LVH) is an independent risk factor for coronary events and stroke. In two studies in elderly hypertensive patients in our clinic,^{35,36} we found that LVH increased the risk of coronary events approximately threefold, and the risk of atherothrombotic brain infarction between threefold and fourfold.

A meta-analysis of 109 treatment studies showed that ACE inhibitors were more effective than other antihypertensive drugs in reducing left ventricular mass.³⁷ However, other types of antihypertensive drugs also reduce left ventricular mass. In an echocardiographic substudy of SHEP, at 3-year follow-up, the left ventricular mass index had decreased by 13% in the group receiving

TABLE 3

Reasons to look for secondary hypertension in elderly patients

Onset of diastolic blood pressure > 100 mm Hg after age 60 years
 Exacerbation of hypertension or resistance to a previously effective drug regimen
 Accelerated hypertension
 Diastolic blood pressure > 100 mm Hg despite triple drug therapy
 Increasing renal dysfunction
 Symptoms suggesting pheochromocytoma or other curable types of hypertension
 Spontaneous hypokalemia

active drug treatment (a diuretic-based regimen) and had increased by 6% in the placebo group.³⁸

Prospective studies using different types of antihypertensive drugs are necessary to determine whether regression of left ventricular mass leads to a decrease in cardiovascular morbidity and mortality in older men and women with hypertension.

Renovascular disease is the most common cause of secondary hypertension in the elderly

■ ORTHOSTATIC AND POSTPRANDIAL HYPOTENSION

Antihypertensive drug therapy may cause orthostatic hypotension³⁹ or postprandial hypotension⁴⁰ in older persons, especially in those who are frail or institutionalized. Management of orthostatic and postprandial hypotension in older persons is discussed in detail elsewhere.⁴¹ The dose of antihypertensive drug may need to be decreased or another antihypertensive drug used.

■ SECONDARY HYPERTENSION

Most cases of hypertension in the elderly are primary (ie, idiopathic), but a sizable minority may be secondary (ie, due to an identifiable cause). TABLE 3 lists the reasons for looking for secondary hypertension in older persons. The most common form of secondary hypertension in older persons is atherosclerotic renovascular disease. Using renal duplex ultrasonography, we found proximal renal artery stenosis ($\geq 60\%$ narrowing of the luminal diameter of

the renal artery) in 18 (22%) of 81 older hypertensive patients (mean age 82 years).⁴² Bilateral renal artery stenosis was present in 5 (6%) of the 81 patients.

Medical therapy should be used for treating renovascular hypertension in older persons if blood pressure is controlled and renal function remains stable. Surgical revascularization or percutaneous transluminal renal angioplasty and stent placement should be considered for patients with renovascular hypertension that is refractory to medical therapy. Surgical revascularization may also preserve renal function.



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