Perspectives on Isolated Systolic Hypertension in Elderly Patients

Suman Vardan, MD; Saktipada Mookherjee, MD, FRCP

Until the mid-20th century, clinicians’ concern was directed mainly to the systolic component of blood pressure. Later, however, when systolic blood pressure was found to be elevated with advancing age and decreased compliance of the arterial wall, it began to be considered an inevitable consequence of aging. Based on this belief, physicians often concluded that only the diastolic blood pressure elevation, which reflected peripheral vascular resistance, was harmful, while systolic hypertension was innocuous. Therapeutic intervention was practiced mainly for diastolic hypertension, and research protocols were based on the levels of diastolic blood pressure alone. In the 1950s, even when life insurance companies’ actuarial data revealed that systolic and diastolic blood pressure elevations were hazardous to health, few clinicians took heed. In 1962, the World Health Organization also defined hypertension as a blood pressure level of 165/95 mm Hg or higher for intervention purposes. However, until the 1991 Systolic Hypertension in the Elderly Program (SHEP) trial, many physicians were reluctant to pay credence to the need for therapy of elevated systolic blood pressure. The Framingham Heart Study and other epidemiological data demonstrated that the level of systolic blood pressure in individuals older than 45 years is a better determinant of morbidity and mortality than the diastolic counterpart. Isolated systolic hypertension (ISH), defined as a systolic blood pressure higher than 160 mm Hg with a diastolic blood pressure of 90 mm Hg or lower, is clearly related to stroke, coronary heart disease, heart failure, heart size, renal failure, and decreased renal size. A systolic blood pressure higher than 160 mm Hg doubles all-cause mortality; triples cardiovascular mortality, particularly in women; and increases cardiovascular morbidity by 2.5-fold in both sexes. Even stage 1 ISH between 140 and 159 mm Hg (diastolic blood pressure, ≤90 mm Hg) carries significantly increased cardiovascular morbidity and mortality.

Diagnosis

The systolic blood pressure measured by cuff-mercury sphygmomanometer is comparable with that obtained by simultaneous direct intra-arterial recordings in normal individuals; patients with essential hypertension; and those with ISH. However, Mönckeberg medial sclerosis or calcinosis of the brachial artery was reported to produce a higher systolic pressure by the cuff method than the intra-arterial recording. This phenomenon was suspected by the Osler maneuver (ie, the arterial wall remains palpable even when the cuff pressure has been inflated above the level of the systolic pressure) in as many as 40% of the elderly patients in a small series from a tertiary care referral center. Nevertheless, the utility of this maneuver remains controversial. The diagnosis of ISH is made by exclusion of other causes of wide pulse pressure, ie, aortic regurgitation, severe anemia, thyrotoxicosis, Paget disease of the bones, arteriovenous fistulae, profound bradycardia, and Mönckeberg medial calcinosis.
Prevalence

Isolated systolic hypertension is present in 1.0% of the US population by the age of 55 years, 3.0% by the age of 60 years, 12.5% by the age of 70 years, and 23.6% by the age of 75 to 80 years, especially in women.28 Worldwide prevalence estimates of ISH in those between the ages of 60 and 69 years have varied from 1% in Israel to 24% in Norway.29

Etiopathologic Features of Systolic Hypertension

Attempts have been made to explain ISH because of increased arterial compliance, stroke volume, left ventricular ejection rate, and systemic vascular resistance.1 Arterial stiffness increases in elderly patients with ISH, but one study suggests that an increase in arterial stiffness might be the result rather than a cause of this disorder. Whatever the mechanism of increased stiffness of the arterial system underlying this disorder, the systolic blood pressure increases, while the diastolic blood pressure decreases, resulting in increased pulse pressure. Pulse pressure is independently related to the risk of developing cardiac hypertrophy, myocardial infarction, and cardiovascular mortality.32-34 Reports on stroke volume and cardiac indexes in patients with ISH have been conflicting. Although the average systemic vascular resistance in elderly patients with ISH is similar to that in the normal population of various age groups older than 35 years,30-35-38 in many patients it is considered elevated in relation to respective cardiac outputs.30 Renin-sodium profiling of patients with ISH demonstrates even distribution in the groups with low and normal renin levels.39,40 Contrary to the previously published theory of volume dependency of patients with low-renin hypertension,41 the levels of plasma volume in the elderly patients with low renin levels and ISH were found to be within the normal range.42 The levels of hormones that might be involved in blood pressure regulation, such as plasma aldosterone, atrial natriuretic peptide, norepinephrine, and urinary metanephrines, are normal in patients with ISH.40

Concern of Lowering the Blood Pressure in Elderly Patients

A 20– to 40–mm Hg decrease in systolic blood pressure has been reported in 17% of normotensive, asymptomatic elderly people older than 70 years when they assumed the standing position.42 Thus, increasing orthostatic changes by antihypertensive therapy in elderly patients may be a matter of concern.43 Recent studies in elderly patients with ISH on the hemodynamic and baroreflex response to orthostatic stress have revealed that, following successful antihypertensive therapy, reduction in systolic blood pressure on orthostasis was not significant following short- and long-term therapy, and the patients did not experience any untoward symptoms. Interestingly enough, the hormonal response of renin, aldosterone, atrial natriuretic peptide, and norepinephrine to orthostatic stress in patients with ISH was comparable with that of the normotensive elderly patients and those with essential hypertension.46 Such data should alleviate anxiety about producing symptomatic hypotension in most elderly patients with ISH.

Benefit of Therapy

A reduction in morbidity and mortality in elderly patients with ISH as a result of antihypertensive therapy was suggested based on a nonrandomized trial in the early 1960s.47 Recent data from the SHEP48 and the Syst-Euro49 trials involving more than 9000 patients have shown that therapeutic control of ISH significantly reduces fatal and nonfatal stroke (approximately equal to 40%); clinical myocardial infarction, including coronary death (27%); and sudden deaths (32%) among major cardiovascular events. Absolute risk reduction for total stroke was 30 per 1000; and for major cardiovascular events, 55 per 1000. However, the change in all-cause mortality was only 13%, which was statistically insignificant. Nevertheless, the daily life activity score in these patients improved significantly.50

Approach to Therapy

Most reports suggest that individuals with an elevated systolic blood pressure in hospital clinics or physicians' offices, but with normal levels at home or on 24-hour ambulatory blood pressure monitoring (so-called white coat hypertension; prevalence, 20%), do not need drug therapy with antihypertensive agents. In those with stage 1 systolic hypertension (140-159 mm Hg) who also have increased cardiovascular risk, to our knowledge, no controlled trial has yet been done to demonstrate the benefit of therapy.52 Nevertheless, lifestyle modification, such as weight reduction by diet control, moderation of alcohol intake and dietary sodium, increased physical activity, adequate potassium intake, avoidance of tobacco smoking, and practice of relaxation techniques, should be positively encouraged in the population groups mentioned.32 A similar strategy should also be applied in patients with a systolic blood pressure between 160 and 180 mm Hg for 3 to 6 months before pharmacologic drug therapy is added. In elderly patients with a systolic blood pressure higher than 180 mm Hg, in whom complications may develop more rapidly,32 a combination of lifestyle modifications and drug therapy should be instituted without delay.53
Low-Sodium Diet

The recommended intake of salt in the daily diet is 6 g of sodium chloride or less or 2.5 g or 100 mmol of sodium or less. Most elderly patients with ISH have low or normal plasma renin activity and respond well to a low-salt diet.

Diuretic Therapy

Patients with ISH commonly respond to a low-dose diuretic, either chlorothiazide, 15 mg/d, or hydrochlorothiazide, 12.5 to 25 mg/d. Although a low dose is preferred, hydrochlorothiazide has been given in doses as high as 50 mg/d in the treatment of elderly patients with ISH for 1 year. This has been observed in some studies to be without clinically significant metabolic or symptomatic adverse effects.

Calcium Channel Blocking Agents

These drugs have theoretical advantage in the management of systolic hypertension because they improve arterial compliance and left ventricular diastolic dysfunction, and they can safely be used in patients who also have chronic obstructive lung disease, diabetes, hyperlipidemia, or gout. Calcium channel antagonists (verapamil, diltiazem, and dihydropyridines) have been found to be effective for controlling ISH. Among the long-acting dihydropyridines, isradipine and nitrrendipine have been studied in many such patients and have shown significant reduction in cardiovascular risk. However, short-acting calcium channel blocking agents have been reported to be associated with adverse outcomes; hence, they are no longer recommended.

Angiotensin-Converting Enzyme Inhibitors

This class of agents is effective and well tolerated by elderly patients with ISH. The few patients (10%-15%) unable to tolerate them because of cough may be switched to angiotensin receptor blockers with anticipated efficacy without this complication.

β-Blocking Agents

Propranolol hydrochloride is more effective in younger patients, perhaps reflecting age-related mechanisms. A β blocker as an additional therapy in combination with a diuretic has been effective in reducing cardiovascular risk in elderly patients; however, when used alone, β blockers failed to provide significant risk reduction of coronary artery disease and total mortality in the Medical Research Council trial. These agents as an adjunct may have a role in the elderly patients who also have tachycardia, anagia, or myocardial infarction because of their proved benefit in primary and secondary prevention of coronary events. In patients with ISH and bradycardia, a β blocker with intrinsic sympathomimetic activity may be preferred in the absence of clinical coronary disease.

α-β-Blocker Compound

Labetalol hydrochloride, a combined α-β-adrenergic blocking agent, has been reported to be effective and well tolerated in a randomized, double-blind, placebo-controlled trial of 133 elderly patients with ISH. Therefore, this drug may be considered as an alternative or additional therapy.

The α-β blocker, carvedilol, or the pure α blockers, doxazosin mesylate and terazosin hydrochloride, have not yet been formally used in the treatment of ISH.

Nitrates

Intravenous nitrates lower blood pressure immediately, but tolerance remains a problem. Nevertheless, oral sustained-release isosorbide dinitrate safely reduced the systolic blood pressure in the elderly patients on a long-term basis with no changes in diastolic blood pressure or heart rate.

Centrally Acting Antihypertensive Agents

Methyldopa, until a couple of decades ago, was one of the most commonly used antihypertensive drugs; however, because of frequent drowsiness, tiredness, and orthostatic hypotension, its use in elderly patients is not encouraged.

Clonidine is often well tolerated in many elderly patients, and drowsiness can be avoided by giving the drug at bedtime. However, its use is somewhat limited because of dry mouth (discontinuation rate, 7%) and the possibility of rebound hypertension after its abrupt withdrawal. However, the clonidine patch used once a week may have a much more favorable adverse effect profile and patient compliance.

Reserpine, probably the oldest antihypertensive agent, has central effects as well, but its major hypertensive effect is peripheral. Its efficacy was proved in the earlier Veterans Administration Cooperative Study and in the Hypertension Detection and Follow-up Trial. In the SHEP trial, it was used as an adjunct to chlorothiazide. A concern about increased risk of breast cancer in patients taking reserpine has been refuted, and nasal stuffiness, peptic ulcer disease, and depression are uncommon at presently used doses of 0.1 mg/d. Reserpine is inexpensive and still has a valuable role in the economically challenged groups, while clonidine and methyldopa have not yet been formally used in the treatment of ISH.

A CAUTIONARY NOTE

While treating patients with ISH who are older than 80 years, caution should be exercised when the blood pressure decreases below 145 mm Hg, as chances of stroke may then be increased. In individuals in their mid-80s, the mortality was lowest among those with systolic blood pressures between 148 and 169 mm Hg (and diastolic blood pressures between 70 and 99 mm Hg). Most antihypertensive agents that are effective in controlling ISH in elderly patients also lower their already relatively low diastolic blood pressures. The SHEP study patients undergoing therapy had more often experienced chest pain or heaviness compared with those taking placebo (28.0% vs 21.3%), suggesting the controversial “J-curve phenomenon” (adverse
outcome due to concomitant lowering of diastolic blood pressure level, compromising coronary perfusion.\(^5\) However, the Syst-Euro trial\(^6\) showed 24% less episodes of angina pectoris in patients taking a calcium channel blocking agent, which may be due to its additional anti-ischemic effect. As the impact of concomitant reduction of diastolic blood pressure in these 2 trials has not yet been separately analyzed, it remains unclear if the so-called J-shaped curve of cardiovascular complication exists in relation to therapy of ISH. In addition, the SHEP and Syst-Euro trials have shown that 100 patients with systolic hypertension need to be treated with drug therapy for 2 to 5 years for an absolute benefit in reduction of stroke and major cardiovascular events by 3 and 5 episodes, respectively.\(^7\) Thus, many patients will have to be subjected to drug treatment for “lifelong” pharmacotherapy agents, many of which may cause untoward adverse effects.

More than 3 million people in the United States are estimated to have systolic hypertension, and this number is likely to double in the next 3 to 4 decades.\(^8,9\) A Belgian study\(^10\) has suggested that from 1967 to 1986, decreased salt intake among patients between the ages of 70 and 81 years reduced the prevalence of systolic hypertension by almost one third, with virtual disappearance of severe hypertension (≥220 mm Hg).\(^10\) This observation underscores the potential of dietary salt restriction in reducing the incidence of this common health hazard in the rapidly growing elderly population in our country.

In summary, ISH in elderly patients is not a benign consequence of aging. Prudent control of the systolic blood pressure at levels between 140 and 169 mm Hg, depending on the age of the patient, is desirable.\(^11\) This can be achieved by appropriate lifestyle modifications, a low-salt diet, and judicious use of antihypertensive drug therapy.

Accepted for publication October 26, 1999.

We thank Laurie Mullen, Henry D. Friedman, MD, and Patrick T. Smith, PharmD, for their help.

Reprints: Suman Vardan, MD, Department of Medicine, Veterans Affairs Medical Center and Health Science Center, State University of New York at Syracuse, 800 Irving Ave, Syracuse, NY 13210.

REFERENCES

therapy and its side effects. JAMA. 1983;250:2807-2813.