Treating isolated systolic hypertension prevented major cardiovascular events across strata of risk in older patients

Ferrucci L, Furberg CD, Penninx BW, et al. **Treatment of isolated systolic hypertension is most effective in older patients with high-risk profile.** Circulation. 2001 Oct 16;104:1923-6.

QUESTION

In older patients with isolated systolic hypertension (ISH), is blood pressure (BP)–lowering treatment more effective than placebo for preventing major cardiovascular disease (CVD) events in those at high risk than in those at low risk?

DESIGN

Randomized {allocation concealed*}†, blinded (outcome assessors),* placebo-controlled trial with 4.5-year follow-up (subgroup analysis of the Systolic Hypertension in the Elderly Program [SHEP] trial).

SETTING

{5 clinical centers in the United States}†.

PATIENTS

4736 community-dwelling patients who were ≥ 60 years of age and had ISH (systolic BP 160 to 219 mm Hg and diastolic BP < 90 mm Hg assessed and averaged over 2 visits), no atrial fibrillation, and no history of myocardial infarction (MI) or stroke in the past 6 months. Patients taking antihypertensive medications were eligible if their BPs met the entry criteria for ISH after medication withdrawal. 4189 patients (88%) (64% age ≥ 70 y, 58% women) who did not report previous CVD or stroke at baseline and who had complete CVD risk factor data were included in the analysis reported here.

INTERVENTION

Patients were allocated to treatment {*n* = 2365}† or placebo {*n* = 2371}†. ISH treatment was a stepped-care approach: Step 1 consisted of chlorthalidone, 12.5 mg/d, and step 2, of addition of atenolol, 25 mg/d, or reserpine, 0.05 mg/d, if atenolol was not tolerated. Treatment in both groups was increased by doubling the dosage or adding a second-step drug until the BP goal (systolic BP decreased to < 160 mm Hg or by ≥ 20 mm Hg) was reached, side effects precluded an additional step up, or the highest step was reached.

MAIN OUTCOME MEASURE

First-occurring major CVD event (stroke, MI, or congestive heart failure).

MAIN RESULTS

{Analysis was by intention to treat}†. Patients were stratified by sex-specific quartiles of global cardiovascular risk scores. The rate for any major CVD event across strata of risk was lower in the treatment group than in the placebo group ($P < 0.001$). Point estimates for each stratum of risk are shown in the Table. The beneficial trend for treatment across strata was also seen ($P < 0.001$) when MI, stroke, and heart failure were analyzed separately.

CONCLUSION

In older patients with isolated systolic hypertension, blood pressure–lowering treatment prevented major cardiovascular events across strata of risk.

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*See Glossary.

†Information provided by author.

Blood pressure–lowering treatment vs placebo in older patients with isolated systolic hypertension to prevent any major CVD event per 100 patient-y‡

CVD risk group	Treatment	Placebo	RRR (95% CI)	NNT (CI)
1st quartile	1.9	2.5	25% (–14 to 51)	Not significant
2nd quartile	2.6	3.6	29% (1 to 49)	100 (58 to 2485)
3rd quartile	3.0	5.2	43% (24 to 57)	48 (35 to 86)
4th quartile	4.3	7.2	40% (19 to 56)	37 (26 to 77)

‡CVD = cardiovascular disease. Other abbreviations defined in Glossary; RRR and CIs calculated from data in article, and event rates and CIs for NNT provided by author.

COMMENTARY

Using the Multiple Risk Factor Assessment Equation and data generated during the SHEP trial, Ferrucci and colleagues showed that treatment of older patients who have ISH (with each decade of age > 60 years used as an increasing risk factor) prevented major CVD events. SHEP began in 1984 and used an active drug regimen of chlorthalidone plus atenolol or reserpine.

In 1999, the Swedish Trial in Old Patients with Hypertension-2 provided evidence that "newer" drugs (angiotensin-converting enzyme inhibitors and calcium antagonists) for hypertension in the elderly have equivalent BP-lowering effects and equivalent outcomes but possibly more side effects (1) than the more "conventional" drugs used in the SHEP trial. Recent dietary studies show that reduced sodium intake, reduced-fat diets (2), and reduced-sodium diets (3) also lower BP in otherwise-healthy elderly patients in the range of 8 weeks (2) to 30 months (3) and permit reduction in antihypertensive drug dosage (3). Compelling evidence now exists that dietary and drug treatment of hypertension, including ISH, in otherwise healthy elderly patients is beneficial.

Ferrucci and colleagues' retrospective evaluation of data generated during a clinical trial over a decade ago suggests that the higher the cardiovascular risk, the greater the benefit of antihypertensive treatment in older patients.

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