

Lowering High Blood Pressure Is Beneficial in the Very Elderly

Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008;358:1887–98.

Study Overview

Objective. To determine whether antihypertensive therapy reduces the risk of stroke among elderly patients with hypertension.

Design. Multicenter, randomized, double-blind, placebo-controlled trial.

Setting and participants. 3845 patients aged ≥ 80 years from 195 centers in 13 countries with sustained systolic blood pressure ≥ 160 mm Hg at enrollment. Patients with accelerated or secondary hypertension, recent hemorrhagic stroke, existing heart failure, serum creatinine > 1.7 mg/dL, hypo- or hyperkalemia, gout, dementia, nursing home care, or a contraindication to a study medication were excluded. Patients were randomized to either a daily diuretic (sustained-release indapamide, 1.5 mg; $n = 1933$) or placebo ($n = 1912$). If the target blood pressure of $< 150/80$ mm Hg was not reached, patients received an additional angiotensin-converting enzyme inhibitor (perindopril, 2 or 4 mg) or placebo.

Main outcome measures. Fatal or nonfatal stroke. Secondary outcomes were death from stroke, death from cardiovascular causes, development of fatal or nonfatal heart failure, and all-cause mortality.

Main results. During a median follow-up of 1.8 years (range, 0–6.5 years), antihypertensive therapy was associated with a 30% reduction in the rate of fatal or nonfatal stroke (12.4 vs. 17.7 per 1000 patient-years for placebo; $P = 0.06$), a 39% reduction in the rate of death from stroke (6.5 vs. 10.7 per 1000 patient-years; $P = 0.05$), a 23% reduction in the rate of death from cardiovascular causes (23.9 vs. 30.7 per 1000 patient-years; $P = 0.06$), a 64% reduction in the rate of heart failure (5.3 vs. 14.8 per 1000 patient-years; $P < 0.001$), and a 21% reduction in all-cause mortality (47.2 vs. 59.6 per 1000 patient-years; $P = 0.02$). There were fewer serious adverse events among patients receiving antihypertensive therapy as compared with patients receiving placebo (358 vs. 448; $P = 0.001$).

Conclusion. Despite concerns that lowering the blood pressure of hypertensive elderly patients may increase their risk of nonstroke death, antihypertensive therapy has beneficial

effects on several cardiovascular outcomes in this patient population and decreases all-cause mortality rates.

Commentary

Several trials have demonstrated the efficacy of antihypertensive therapy in reducing the risk of stroke and other major adverse cardiovascular events [1,2], but existing guidelines have noted that evidence supporting these benefits in patients aged 80 years and older is lacking [3]. Observational studies have suggested that blood pressure control among patients aged 80 years and older may be associated with increased mortality [4–7]. Whether this “reverse effect” of lower blood pressure on mortality among the very old represented a true effect (perhaps due to increased risks of antihypertensive therapy in this age-group) or an effect of unmeasured confounding (due to comorbid conditions that could lower blood pressure) was unknown. No large randomized trial of antihypertensive therapy among patients aged 80 years and older had previously been conducted.

The current investigation by Beckett and colleagues is the first large, multicenter, randomized, placebo-controlled trial to investigate the effect of antihypertensive therapy on stroke, death, and other cardiovascular outcomes in patients aged 80 years and older. The Hypertension in the Very Elderly Trial (HYVET) was conducted at 195 centers in 13 countries and enrolled patients in the target age-group who had persistent systolic blood pressure greater than 160 mm Hg [8]. In an intent-to-treat analysis, active antihypertensive treatment was associated with significant decreases in the risk of stroke, fatal stroke, fatal cardiovascular events, heart failure, serious adverse events, and all-cause mortality. The trial was terminated earlier than planned due to the unexpected reduction in all-cause mortality.

Although this study provides important evidence to guide antihypertensive therapy for elderly patients with hypertension, there are some limitations. First, the vast majority of patients were recruited in China (1526 patients) and Eastern Europe (2144 patients), where due to survivorship the population older than 80 years may look quite different from a similarly aged population in more developed countries. This may limit the trial’s generalizability to the United States. Second, the exact cause of death was not reliably assessed in all cases, and rapid or unexpected deaths were

designated as deaths from cardiovascular causes. However, concerns about the accuracy of cause of death are attenuated by the significant benefit in all-cause mortality. Finally, only 1 blood pressure target was assessed (< 150/80 mm Hg). Whether an additional blood pressure reduction below the commonly used systolic targets of less than 140 or 130 mm Hg would have added benefits remains unknown.

Applications for Clinical Practice

In the absence of clear contraindications, antihypertensive therapy should be strongly considered among hypertensive patients aged 80 years and older. In light of this study’s findings, the exclusion of older patients from quality measures and pay-for-performance programs targeting blood pressure control should be reconsidered.

—Review by Mark W. Friedberg, MD, MPP

References

1. Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. *Stroke* 2004;35:1024.
2. Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists’ Collaboration. *Lancet* 2000;356:1955–64.
3. Mancia G, De Backer G, Dominiczak A, et al. 2007 guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) [published erratum appears in *J Hypertens* 2007;25:1749]. *J Hypertens* 2007;25:1105–87.
4. Mattila K, Haavisto M, Rajala S, Heikinheimo R. Blood pressure and five year survival in the very old. *Br Med J (Clin Res Ed)* 1988;296:887–9.
5. Langer RD, Criqui MH, Barrett-Connor EL, et al. Blood pressure change and survival after age 75. *Hypertension* 1993;22:551–9.
6. Rastas S, Pirttila T, Viramo P, et al. Association between blood pressure and survival over 9 years in a general population aged 85 and older. *J Am Geriatr Soc* 2006;54:912–8.
7. Satish S, Freeman DH Jr, Ray L, Goodwin JS. The relationship between blood pressure and mortality in the oldest old. *J Am Geriatr Soc* 2001;49:367–74.
8. Bulpitt C, Fletcher A, Beckett N, et al. Hypertension in the Very Elderly Trial (HYVET): protocol for the main trial. *Drugs Aging* 2001;18:151–64.

Copyright 2008 by Turner White Communications Inc., Wayne, PA. All rights reserved.