

## Hypertension in the elderly: Are we all on the same wavelength?

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elderly to different antihypertensive agents also differs from that of younger patients and may explain some of the disparities in outcomes of trials conducted in elderly patients with hypertension.

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### Abstract

Hypertension is of frequent occurrence in the elderly population. Isolated systolic hypertension (ISH) accounts for the majority of cases of hypertension in the elderly. ISH is associated with a 2-4-fold increase in the risk of myocardial infarction, left ventricular hypertrophy, renal dysfunction, stroke, and cardiovascular mortality. There have been many studies to determine the optimal treatment for hypertension in the elderly. Why, when and how to treat hypertension in the elderly was the scope of the majority of these trials. Despite countless efforts many aspects remain obscure. While a number of novel drugs are being developed, the issue of whether all antihypertensive drugs bestow parallel benefits or whether some agents offer a therapeutic advantage beyond blood pressure control remains of crucial importance. Furthermore, the response of the

### INTRODUCTION

Hypertension is of frequent occurrence in the elderly (age greater than 60 to 65 years), with prevalence as high as 60%-80%<sup>[1,2]</sup>. Isolated systolic hypertension (ISH) accounts for 60%-75% of cases of hypertension in the elderly<sup>[3,4]</sup>. It is defined as a systolic blood pressure (BP) above 160 mmHg, with a diastolic BP below 90 mmHg<sup>[5,6]</sup>. ISH is associated with a 2-4-fold increase in the risk of myocardial infarction (MI), left ventricular hypertrophy, renal dysfunction, stroke, and cardiovascular mortality<sup>[7,8]</sup>. Elevated systolic BP is a more important risk factor for cardiovascular and renal disease than elevated diastolic BP<sup>[9,10]</sup>. Studies have clearly pointed out that lowering systolic BP to < 160 mmHg is markedly beneficial in terms of reducing the risk, however no trial has directly measured the degree of added benefit that would occur at a

systolic BP target < 140 mmHg<sup>[11,12]</sup>. While a number of novel drugs are being developed, an issue of whether all antihypertensive drugs bestow parallel benefit or whether some agents offer a therapeutic advantage beyond BP control remains of crucial importance. Furthermore, the response of the elderly to different antihypertensive agents also differs and may explain some of the disparities in outcomes of trials conducted in elderly patients with hypertension.

## WHY TO TREAT?

As late as the 1970s, the customary belief was to disregard elevated BP in the elderly, despite the fact that the age-related risk of coronary heart disease (CHD) as a consequence of hypertension was evident in various epidemiologic data<sup>[13]</sup>. Now, there is robust evidence that treatment of hypertension in the elderly has a multitude of benefits in terms of morbidity and mortality. Two meta-analyses performed in 1994 clearly demonstrated significant reductions in stroke (35%), stroke deaths (34%), CHD events (including MI, 15%), CHD deaths (25%), all cardiovascular events (29%), cardiovascular deaths (25%), and even all-cause mortality (12%)<sup>[14,15]</sup>. Even more striking was the 5-year number needed to treat (NNT) estimate (which indicates the number of patients needed to treat in order to prevent one event in question and is a means of assessing effectiveness of health care intervention), indicated that fewer than 100 older people required to be treated to prevent one event. These numbers were nearly 10-fold lower than estimates based on the first Medical Research Council Study which involved 35-60-year-old hypertensives<sup>[13]</sup>. Since NNT estimates are inversely proportional to the cost-effectiveness ratio, these meta-analyses inferred that hypertension treatment in the elderly is much more rewarding in terms of cost-effectiveness compared to treatment of the same level of BP in younger individuals. According to an older meta-analysis in both elderly and younger hypertensives, drug treatment largely reduces the number of individuals progressing to higher stages of hypertension, which is not only more difficult and expensive to treat, but also increases cardiovascular risk<sup>[16]</sup>. Data from the Multiple Risk Factor Intervention Trial clearly showed the importance of hypertension as a risk factor for end-stage renal disease<sup>[17]</sup>. Furthermore, a meta-analysis has also shown a 42% reduction in heart failure in elderly patients receiving antihypertensive therapy<sup>[18]</sup>. Finally, left ventricular hypertrophy, an important subclinical disease marker that may be the most powerful of all cardiovascular risk factors, can be substantially improved by antihypertensive therapy: some meta-analyses, based on detection by (admittedly imperfect) electrocardiograms have placed the estimate of effectiveness as high as 35%<sup>[16]</sup>.

## WHEN TO TREAT?

The trials in the 1996 meta-analysis all had baseline mean

systolic pressures of 160 mmHg or more<sup>[19]</sup>. No trials have been performed in patients with ISH with baseline systolic pressure of 140 to 149 mmHg<sup>[20]</sup>. The recommendation to treat such patients is based upon observational studies that show a graded relationship between increasing systolic BP and cardiovascular risk<sup>[21]</sup>. Among elderly patients younger than 80 years of age, antihypertensive therapy is initiated among those with systolic pressures greater than 140 mmHg and/or diastolic pressures greater than 90 mmHg<sup>[22]</sup>. However, there is disagreement as to the threshold systolic BP warranting therapy among elderly patients older than 80 years of age with ISH. Some would initiate antihypertensive therapy at a systolic pressure between 150 and 159 mmHg, while others would only treat patients with a systolic pressure of 160 mmHg or greater<sup>[23]</sup>.

## HOW TO TREAT?

All patients should receive non pharmacologic therapy, particularly dietary salt restriction and weight loss in obese patients. Drug therapy should be started if lifestyle changes fail after trying for at least 3 to 6 mo, unless compelling evidence for treatment exists<sup>[22]</sup>. A potential limiting factor to the use of antihypertensive drugs is that orthostatic (postural) and/or postprandial hypotension is common among elderly hypertensive patients<sup>[24,25]</sup>. The 2007 American Heart Association statement on the treatment of BP in ischemic heart disease, the 2007 European Society of Hypertension/European Society of Cardiology guidelines on the management of hypertension, and meta-analyses from 2008 and 2009 concluded that the amount of BP reduction and not the choice of antihypertensive drug is the key determinant of reduction in cardiovascular risk in both younger and older patients with hypertension<sup>[26-29]</sup>. In general, three classes of drugs are considered first-line therapy for the treatment of hypertension in elderly patients: low-dose thiazide diuretics (e.g. 12.5-25 mg/d chlorthalidone), long-acting calcium channel blockers (most often dihydropyridines), and angiotensin converting enzyme inhibitors or angiotensin II receptor blockers<sup>[30-32]</sup>. A long-acting dihydropyridine or a thiazide diuretic is generally preferred in elderly patients because of increased efficacy in BP lowering<sup>[30]</sup>. There is evidence that, in the absence of a specific indication for use,  $\beta$ -blockers should not be considered for primary therapy of hypertension, particularly in elderly patients<sup>[33]</sup>. They may be worse than other agents for the prevention of stroke, particularly among smokers, and perhaps for mortality<sup>[33-36]</sup>. With all drugs, orthostatic hypotension should be avoided because of the increased risk of falling in older patients. If the initial dose of an antihypertensive drug does not control the BP, the dose may be increased or a second drug may be added to reduce the risk of dose-related adverse effects of the first drug<sup>[22]</sup>. Most elderly patients ultimately require two or more antihypertensive agents. If the BP is 20/10 mmHg above the goal, combination drug therapy with drugs from two different

classes is indicated as initial therapy<sup>[22]</sup>.

## REFERENCES

- Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, Horan MJ, Labarthe D. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988-1991. *Hypertension* 1995; **25**: 305-313
- Ostchega Y, Dillon CF, Hughes JP, Carroll M, Yoon S. Trends in hypertension prevalence, awareness, treatment, and control in older U.S. adults: data from the National Health and Nutrition Examination Survey 1988 to 2004. *J Am Geriatr Soc* 2007; **55**: 1056-1065
- Franklin SS, Jacobs MJ, Wong ND, L'Italien GJ, Lapuerta P. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. *Hypertension* 2001; **37**: 869-874
- Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. *JAMA* 1996; **275**: 1571-1576
- National Institute for Health and Clinical Excellence. Hypertension: management of hypertension in adults in primary care (NICE clinical guideline update). Available at: <http://www.nice.org.uk>
- National High Blood Pressure Education Program Working Group Report on Hypertension in the Elderly. National High Blood Pressure Education Program Working Group. *Hypertension* 1994; **23**: 275-285
- Izzo JL, Levy D, Black HR. Clinical Advisory Statement. Importance of systolic blood pressure in older Americans. *Hypertension* 2000; **35**: 1021-1024
- Young JH, Klag MJ, Muntner P, Whyte JL, Pahor M, Coresh J. Blood pressure and decline in kidney function: findings from the Systolic Hypertension in the Elderly Program (SHEP). *J Am Soc Nephrol* 2002; **13**: 2776-2782
- He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. *J Hypertens Suppl* 1999; **17**: S7-S13
- Neaton JD, Wentworth D. Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316 099 white men. Multiple Risk Factor Intervention Trial Research Group. *Arch Intern Med* 1992; **152**: 56-64
- Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. *JAMA* 1991; **265**: 3255-3264
- Kostis JB, Davis BR, Cutler J, Grimm RH, Berge KG, Cohen JD, Lacy CR, Perry HM, Blafox MD, Wassertheil-Smolter S, Black HR, Schron E, Berkson DM, Curb JD, Smith WM, McDonald R, Applegate WB. Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. SHEP Cooperative Research Group. *JAMA* 1997; **278**: 212-216
- Kannel WB, Gordon T, Schwartz MJ. Systolic versus diastolic blood pressure and risk of coronary heart disease. The Framingham study. *Am J Cardiol* 1971; **27**: 335-346
- Insua JT, Sacks HS, Lau TS, Lau J, Reitman D, Pagano D, Chalmers TC. Drug treatment of hypertension in the elderly: a meta-analysis. *Ann Intern Med* 1994; **121**: 355-362
- Mulrow CD, Cornell JA, Herrera CR, Kadri A, Farnett L, Aguilar C. Hypertension in the elderly. Implications and generalizability of randomized trials. *JAMA* 1994; **272**: 1932-1938
- Moser M, Hebert PR. Prevention of disease progression, left ventricular hypertrophy and congestive heart failure in hypertension treatment trials. *J Am Coll Cardiol* 1996; **27**: 1214-1218
- Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African-American and white men. 16-year MRFIT findings. *JAMA* 1997; **277**: 1293-1298
- Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, Lemaitre RN, Wagner EH, Furberg CD. Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. *JAMA* 1997; **277**: 739-745
- Staessen JA, Gasowski J, Wang JG, Thijs L, Den Hond E, Boissel JP, Coope J, Ekblom T, Gueyffier F, Liu L, Kerklikowske K, Pocock S, Fagard RH. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. *Lancet* 2000; **355**: 865-872
- Chaudhry SI, Krumholz HM, Foody JM. Systolic hypertension in older persons. *JAMA* 2004; **292**: 1074-1080
- Pastor-Barriuso R, Banegas JR, Damián J, Appel LJ, Guallar E. Systolic blood pressure, diastolic blood pressure, and pulse pressure: an evaluation of their joint effect on mortality. *Ann Intern Med* 2003; **139**: 731-739
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; **289**: 2560-2572
- Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ. Treatment of hypertension in patients 80 years of age or older. *N Engl J Med* 2008; **358**: 1887-1898
- Vanhanen H, Thijs L, Birkenhäger W, Tilvis R, Sarti C, Tuomilehto J, Bulpitt C, Fagard R, Staessen JA. Associations of orthostatic blood pressure fall in older patients with isolated systolic hypertension. Syst-Eur Investigators. *J Hypertens* 1996; **14**: 943-949
- Applegate WB, Davis BR, Black HR, Smith WM, Miller ST, Burlando AJ. Prevalence of postural hypotension at baseline in the Systolic Hypertension in the Elderly Program (SHEP) cohort. *J Am Geriatr Soc* 1991; **39**: 1057-1064
- Turnbull F, Neal B, Ninomiya T, Algert C, Arima H, Barzi F, Bulpitt C, Chalmers J, Fagard R, Gleason A, Heritier S, Li N, Perkovic V, Woodward M, MacMahon S. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. *BMJ* 2008; **336**: 1121-1123
- Rosendorff C, Black HR, Cannon CP, Gersh BJ, Gore J, Izzo JL, Kaplan NM, O'Connor CM, O'Gara PT, Oparil S. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. *Circulation* 2007; **115**: 2761-2788
- Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Struijker Boudier HA, Zanchetti A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellems I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Kjeldsen SE, Erdine S, Narkiewicz K, Kiowski W, Agabiti-Rosei E, Ambrosioni E, Cifkova R, Dominiczak A, Fagard R, Heagerty AM, Laurent S, Lindholm LH, Mancia G, Manolis A, Nilsson PM, Redon J, Schmieder RE, Struijker-Boudier HA, Viigimaa M, Filippatos G, Adamopoulos S, Agabiti-Rosei E, Ambrosioni E, Bertomeu V, Clement D, Erdine S, Farsang C, Gaita D, Kiowski W, Lip G, Mallion JM, Manolis AJ, Nilsson PM, O'Brien E, Ponikowski P, Redon J, Ruschitzka F, Tamargo J, van Zwieten P, Viigimaa M, Waerber B, Williams B, Zamo-

- rano JL. 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). *Eur Heart J* 2007; **28**: 1462-1536
- 29 **Law MR**, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009; **338**: b1665
- 30 **ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group**. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002; **288**: 2981-2997
- 31 **Hansson L**, Lindholm LH, Ekblom T, Dahlöf B, Lanke J, Scherstén B, Wester PO, Hedner T, de Faire U. Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. *Lancet* 1999; **354**: 1751-1756
- 32 **Jamerson K**, Weber MA, Bakris GL, Dahlöf B, Pitt B, Shi V, Hester A, Gupte J, Gatlin M, Velazquez EJ. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med* 2008; **359**: 2417-2428
- 33 **Khan N**, McAlister FA. Re-examining the efficacy of beta-blockers for the treatment of hypertension: a meta-analysis. *CMAJ* 2006; **174**: 1737-1742
- 34 **Messerli FH**, Bangalore S, Julius S. Risk/benefit assessment of beta-blockers and diuretics precludes their use for first-line therapy in hypertension. *Circulation* 2008; **117**: 2706-2715; discussion 2715
- 35 MRC trial of treatment of mild hypertension: principal results. Medical Research Council Working Party. *Br Med J (Clin Res Ed)* 1985; **291**: 97-104
- 36 **Carlberg B**, Samuelsson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? *Lancet* 2004; **364**: 1684-1689

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