

## 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>.

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