

# The older patient with hypertension: care and cure

Claudio Borghi and Elisa Tartagni

**Abstract:** Hypertension is one of the most important clinical conditions affecting older people. Its prevalence in this group of subjects is above 60% and continues to grow. Isolated systolic hypertension accounts for the majority of cases as systolic blood pressure increases with advancing age, while diastolic blood pressure remains unchanged or even decreases. Nowadays hypertension is a well established risk factor for stroke and cardiovascular disease among older people and its treatment is considered mandatory. The general recommended blood pressure goal in uncomplicated hypertension is less than 140/90 mmHg, even if this target in older people is based mainly on expert opinion. All patients should receive nonpharmacological treatment, in particular reduction in excess body weight when body mass index is greater than 26 kg/m<sup>2</sup> and dietary salt restriction. Older patients with hypertension may also benefit from smoking cessation, physical activity and alcohol restriction. In relation to drug therapy, a low-dose thiazide diuretic could be a good first step. Other first-line drugs are long-acting calcium channel blockers, generally dihydropyridines, and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. The HYVET study showed a specific protective effect of indapamide with or without perindopril in people older than 80 years. Since monotherapy normalizes blood pressure in only 40–50% of cases, a combination of two or more drugs is often required. Moreover the addition of a second drug may reduce the dose-related adverse effects of the first one. Finally, compliance with treatment should always be achieved by giving complete information to patients and simplifying the drug regimen as much as possible.

**Keywords:** elderly, hypertension, indapamide, perindopril, treatment

## Background

Hypertension (HT) remains the most important cause of cardiovascular morbidity and mortality worldwide. As HT is age dependent, with the prolongation of life expectancy it affects more and more older people [Fagard, 2002]: the prevalence of HT in this population is above 60% and continues to grow.

Isolated systolic HT (ISH) accounts for 60–75% of cases of HT in older people [Franklin *et al.* 2001]. It is characterized by systolic blood pressure (SBP) at least 140 mmHg with diastolic blood pressure (DBP) less than 90 mmHg, and consequently high pulse pressure [Mancia *et al.* 2009b]. ISH is associated with a two- to fourfold increase in the risk of myocardial infarction, left

ventricular hypertrophy, renal dysfunction, stroke and cardiovascular mortality [Izzo *et al.* 2000; Young *et al.* 2002].

ISH is an age-related condition, as SBP increases with advancing age and DBP remains unchanged or even decreases after the sixth decade of life [Pinto, 2007]. The increase in arterial stiffness may be attributed to age-related loss of distensibility in the major central arteries [Mitchell *et al.* 2003] when elastic tissue is progressively replaced with collagen [Virmani *et al.* 1991] or to endothelial dysfunction [O'Rourke and Nichols, 2005], caused by free oxygen radicals in the arterial wall and by the upstream effects of reduced distal vascular flow reserve [Kojda and Harrison, 1999].

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'White coat' HT is another common condition in older people [Amado *et al.* 1999], often initially mistaken for ISH. It is caused by a temporary increase in blood pressure through an autonomic neural reaction triggered by the process of measurement. White coat HT is generally thought not to require treatment, however a recent 10-year follow-up study of subjects with this syndrome showed that they may develop sustained HT and may have a worse prognosis than normotensive subjects [Mancia *et al.* 2009a].

Since the average older patient takes more than six prescription drugs, drug interactions should always be considered. Commonly used medications that increase BP are nonsteroidal anti-inflammatory drugs, corticosteroids, erythropoietin, amphetamines, ergotamine and anabolic steroids.

### Drug treatment

For many years physicians have had the mistaken idea that HT was a result of ageing and claimed not to decrease blood pressure levels in order to avoid possible ischemic events and poor oxygenation of the trigger organs. So treatment was not considered to be necessary and no common criteria existed about the therapy.

Today, on the basis of the evidence provided by many trials performed in older patients with HT, the condition is considered a well established risk factor for stroke and cardiovascular disease in this group. Moreover, trials of antihypertensive treatment in older people have shown benefits comparable with those observed in younger or middle aged people and, as the baseline cardiovascular risk is higher in older people, the absolute benefit of treatment is even higher in this group.

The first placebo-controlled study to show the benefit of blood pressure lowering treatment in older people was the European Working Party on High blood pressure in the Elderly (EWPHE) trial, which studied patients between 60 and 97 years of age using hydrochlorothiazide and triamterene [Amery *et al.* 1985]. A few years later the Systolic Hypertension in Europe trial (Syst-Eur) clearly proved the benefits of hypertensive treatment *versus* placebo [Staessen *et al.* 1997], and these positive results were finally extended to patients aged 80 or older with the Individual Data Analysis of Antihypertensive Intervention trials (INDANA) [Gueyffier *et al.* 1999]. This meta-analysis showed a 34% reduction in stroke,

but no benefit in cardiovascular mortality (actually an increase in all-cause mortality was reported). This result can be attributed to the choice of drugs: among very old people, high-dose diuretics may predispose the person to electrolyte disorders and sudden death and  $\beta$  blockers are less effective than angiotensin-converting enzyme (ACE) inhibitors in reducing blood pressure [Dahlöf *et al.* 2005].

More recently the Hypertension in the Very Elderly Trial (HYVET) showed a 21% reduction in overall mortality and a 30% reduction in stroke in patients aged 80 years or older with SBP at least 160 mmHg after treatment for 2 years with a diuretic (indapamide sustained release, 1.5 mg/day) and, if required, an ACE inhibitor (perindopril 2–4 mg/day) [Beckett *et al.* 2008]. This study provided clear evidence about the need to treat HT in this growing population and it has influenced therapeutic guides as well as clinical practice.

Participants in HYVET were generally healthier than those in the general population: they had low overall rates of stroke and death from any cause and at baseline they were generally free of multiple comorbid conditions. All people aged 80 years or older, irrespective of their blood pressure and their general health condition, are at high risk of a cardiovascular event owing to their age alone. However, this does not mean that all would benefit from antihypertensive treatment. The HYVET results support the indication to treatment in very old people with blood pressure over 160 mmHg who do not have cognitive impairment and are not considered to be frail. Further research is needed before clearer recommendations can be proposed for other subjects. Further research is also needed to ascertain if lowering SBP below 150 mmHg in people aged 80 or over is truly beneficial.

### Guidance

According to the recent joint consensus developed by the American College of Cardiology Foundation and the American Heart Association [Aronow *et al.* 2011] the general recommended blood pressure goal in uncomplicated HT is less than 140/90 mmHg. However, this target for older people with HT is based on expert opinion rather than on data from randomized controlled trials and it is unclear whether target SBP should be the same in patients aged 65–79 years as in patients over 80 years of age. However, SBP less

than 130 and DBP less than 65 mmHg should be probably avoided in older people.

The new National Institute for Health and Clinical Excellence (NICE) HT guidelines [McManus *et al.* 2012] agree to offer people aged 80 years and over the same antihypertensive drug treatment as people aged 55–80 years, taking into account any comorbidities. However, they suggest a target clinic blood pressure below 150/90 mmHg in people aged 80 years and over with treated HT and below 145/85 mmHg during waking hours when using ambulatory blood pressure monitoring.

### Nonpharmacological therapy

All patients should receive nonpharmacological therapy, in particular reduction in excess body weight and dietary salt restriction. Weight loss should be a goal considered in any older patient with a body mass index (BMI) greater than 26 kg/m<sup>2</sup> [Stokes, 2009], even if its effect on blood pressure varies from patient to patient. In the trial of nonpharmacologic interventions in the elderly (TONE) the older patients with HT received weight reduction intervention if their BMI was at least 27.8 kg/m<sup>2</sup> [Whelton *et al.* 1998].

As sodium sensitivity increases with age [Weinberger *et al.* 1986], limitation of dietary sodium intake is more effective in controlling HT in older people than in the young [De Wardener and MacGregor, 2002]. Controlled studies in older people with systolic HT have supported the use of a low sodium diet (60–90 mmol per day) for decreasing BP [He *et al.* 2005; Gates *et al.* 2004].

Two trials showed that increased potassium intake significantly lowered BP among older patients with HT [Smith *et al.* 1992; Fotherby and Potter, 1992]. However in older patients with substantially impaired renal function, serum potassium should be monitored when supplementation is given, either by fruits and vegetables or pills.

The Dietary Approaches to Stop Hypertension (DASH) diet, enriched with fruits and vegetables and low in saturated and total fat, showed BP reductions in patients with HT older than 45 years [Svetkey *et al.* 1999].

Calcium and magnesium supplementation results in minimal to no change in BP and there is no evidence that vitamin, fibre or herbal supplements influence BP in older adults.

Alcohol restriction may improve BP control through a dual effect: weight reduction due to decreased intake of calories and also prevention of the weight-independent pressor activity of alcohol.

Finally, older patients with HT may benefit from smoking cessation and physical activity, in particular regular aerobic exercise [Whelton *et al.* 2002]. If the efficacy of long-term exercise training in reversing or preventing arterial stiffness and HT needs further study, it is known that aerobic exercise increases plasma high-density lipoprotein cholesterol and lowers overall cardiovascular risk. If arthritis limits walking or running in older patients, swimming or 'aquarobics' are alternative ways to exercise.

### Limitations of pharmacological treatment

In relation to pharmacological treatment, high caution is required due to alterations in drug distribution and disposal and to presumptive changes in homeostatic cardiovascular control.

In general, if multiple cardiovascular risk factors are present, the use of antihypertensive measures should be taken only in conjunction with the application of other cardiovascular risk management strategies.

Another potential limiting factor to the use of antihypertensive drugs is the high prevalence among older patients with orthostatic or postprandial hypotension [Vanhanen *et al.* 1996; Applegate *et al.* 1991].

A poor prognosis caused by concomitant systemic disease may influence the decision not to treat.

### Drug treatment steps

According to clinical trials [ALLHAT, 2002; London *et al.* 2006] a diuretic is a good first step in treating HT in older people and a thiazide is usually the most suitable to use. It is important to remember that older patients have an increased sensitivity to diuretics and inappropriately high

doses may provoke hypotension or electrolyte disorders. Moreover thiazide prescription in older people could be limited by the frequent coexistence of severe decline in renal function or heart failure, which require loop diuretics. Indapamide, a nonthiazide diuretic used in several HT trials, may be preferred for its metabolic neutrality. Hypokalaemia is less likely to occur when a diuretic is combined with either a potassium-conserving diuretic or an angiotensin inhibitor. Diuretics may be contraindicated in subjects with gout, hyperuricaemia, diabetes or renal impairment.

A calcium channel blocker can be also used at the first step; a dihydropyridine is preferable to a nondihydropyridine if the HT is severe or if there is coincident treatment with a negative inotrope. Alternatively, an ACE inhibitor or an angiotensin II receptor blocker may be given, especially when there are signs of heart failure or left ventricular hypertrophy. Centrally acting sympathetic agonists (such as clonidine) have a limited role in older people because of sedation and other side effects. Use of peripheral  $\alpha$  adrenoceptor blockers is subject to a risk of postural hypotension. If  $\beta$  blockers are part of pre-existing therapy, given for arrhythmia or secondary prevention of myocardial infarction, they should not be discontinued; however, they may show a limited effect on SBP.

The initial antihypertensive drug should be started at the lowest dose and gradually increased to the maximum tolerated dose in relation to BP response. However, monotherapy normalizes BP in only 40–50% of cases and therefore a combination of two or more drugs is often required to achieve the recommended BP goals. A reasonable strategy is to optimize the maximal antihypertensive therapy with two drugs in low doses in order to reduce the risk of dose-related adverse effects of each drug [Taddei *et al.* 2011; Mazza *et al.* 2012].

ISH is often resistant to triple drug combination therapy and SBP is uncontrolled despite good compliance. In this case, patients may benefit from treatment with extended-release isosorbide mononitrate or from the addition of aldosterone to existing therapy [Mancia *et al.* 2009a].

### Complications and compliance

Older patients with orthostatic hypotension may have supine HT at the same time. This combination has been called the hypertension-hypotension

syndrome [Naschitz *et al.* 2006]. The hypotensive component reflects dysautonomia, but also low cardiac output or plasma volume depletion may contribute. The hypertensive component may reflect increased peripheral vascular resistance, caused by drugs used to control orthostatic symptoms or by vascular stiffness arising from longstanding cardiovascular disease.

Coexistence of supine HT and orthostatic hypotension poses a therapeutic dilemma, as treatment of one component of the syndrome can exacerbate the other [Naschitz *et al.* 2006]. Orthostatic hypotension should always be avoided because of the increased risk of falling so careful titration of volume expanders, sympathomimetic agents or  $\beta$  blockers is recommended [Naschitz *et al.* 2006] to control postural symptoms without increasing supine blood pressure.

Compliance with therapy is often difficult to achieve. A large proportion of older patients will discontinue or take the drugs inappropriately and this often results in failing to reach guideline-recommended BP targets and impacts outcomes.

A possible explanation for noncompliance is the asymptomatic state associated with HT that causes unawareness of the pathology and the related risk.

Side effects are another common reason for therapy discontinuation in older people [Borghesi *et al.* 2007; Weber and Wenger, 2007] and, if not correctly informed, patients tend to blame their drugs for any new symptoms they experience.

The complexity of a drug regimen influences compliance too and there is an inverse relationship between the number of daily drug doses and the adherence rate [Claxton *et al.* 2001]. If possible, once-daily agents should be selected and the number of tablets to be taken should be minimized by the use of drug combination tablets.

Finally, if the patient has memory loss, compliance with medication may be difficult to obtain so caregiver's supervision becomes fundamental.

### Conclusion

In conclusion, older patients with HT represent a large, growing and vulnerable part of the general population. Since HT is associated with a higher risk of cardiovascular morbidity and mortality,

there is virtually no cutoff age for treatment. Available clinical trials and official statements can help physicians in HT management, but every single patient deserves careful attention and treatment should be personalized, always considering its impact on quality of life.

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### Conflict of interest statement

The authors declare no conflict of interest in preparing this article.

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