Hypertension (HT) and its complications constitute the most important health condition causing disability and death in old age. The definition of HT is the same for young and old persons. The World Health Organization characterises HT by a systolic blood pressure (SBP) ≥140 mmHg and a diastolic blood pressure (DBP) ≥90 mmHg at any age after 20 years. During ageing, SBP increases gradually. For DBP, the evolution is characterised by an increase until age 55 years and by a decrease after that.\(^\text{10}\)

The relationship between HT and the risk of vascular complications secondary to atherosclerosis is well documented. A particularity of ageing is the evolution of the pulse pressure (PP). PP corresponds to the difference between SBP and DBP, which is normally ≤60 mmHg. Mechanisms responsible for changes in BP are complex. An increase in BP beyond 30 years is seen to have a higher correlation with CVD complications. A rise in SBP with age was long considered to be a natural process in ageing. However, the results of the Framingham Heart Study\(^\text{5}\) changed this perception. Now, SBP is seen to have a higher correlation with CVD risk. This finding draws attention to BP profiles during ageing and the particular problem concerning PP. According to the Framingham study, the higher the SBP, the higher the risk of CVD complications.\(^\text{10}\) However, an inverse correlation exists for DBP: the lower the DBP, the higher the risk. PP is a risk marker and it is important to consider it in elderly hypertensive patients with an equivalent value for SBP, but a higher PP.\(^\text{11}\)

Diagnosing HT
In doctors’ surgeries, if BP measured is ≥140 and/or 90 mmHg, a second measurement should be done during the consultation. If the second measurement differs substantially from the first, a third measurement should be done. The lower of the last 2 measurements is recorded as the clinic BP. To account for the natural variability of BP, at least 3 separate visits are needed to confirm a diagnosis.\(^\text{16}\) In elderly patients, investigating orthostatic hypotension (OHT) is also recommended: BP should thus be measured standing for 1-3 minutes as well. In patients aged >80 years, more than 20% who are hypertensive will suffer from OHT, which is an independent death risk factor for the older population.\(^\text{17}\)

Results of HYVET provided clear evidence that lowering of BP is associated with definite CV benefits for octogenarians.

Another clinical problem in elderly patients is a frequent discrepancy between BP measured in a surgery and the results of ambulatory BP measurement which is named ‘white coat effect’ (WCE). WCE is defined by a difference of more than 20/10 mmHg for SBP and DBP and is especially frequent in these patients.\(^\text{16}\) The risk is over-diagnosis of HT and over-treatment with associated risks. Using out-of-surgery BP readings, particularly home BP measurement, is preferred in such cases. Devices that measure BP with an upper arm cuff are the most reliable. Wrist monitors must be held at the level of the heart with an increased possibility of erroneous readings. Home monitoring of BP (HBPM) is used...
in respect of the ‘rule of 3’: BP is recorded twice daily, ideally early in the morning and late in the evening. For each BP recording, 3 consecutive measurements are done at least 1 minute apart with the person seated. BP recordings are continued for at least 3 days. HT is defined with HBPM by an 18 measures’ average ≥135/85 mmHg. Ambulatory BP Monitoring may be used to confirm the diagnosis of HT and improve the accuracy of the diagnosis compared with current practice, but is difficult to use in elderly patients.

**Initial antihypertensive therapy with single-pill combinations produced more rapid BP control than initial monotherapy in clinical trials.**

**Epidemiology of HT in elderly patients**

The prevalence of HT increases progressively with age. In France, the HT prevalence increases from 45.3% for men and 42.9% for women aged 60 to 69 years to 70.4% and 69.7% above the age of 80 years. In the Framingham study, 90% of participants with a normal BP at the age of 55 years developed HT. In the North American population, HT prevalence is greater in older African Americans, particularly women, than in older whites. Prevalence of self-reported medical professional diagnosis of HT in South Africans age >18 years was 10.4% in 2010. The prevalence increased significantly with age, from <10% in those aged <40 years to approximately 40% in those aged >65 years. HT is the most important risk factor for CVD. In the North American population, an HT antecedent is observed in 69% of patients with incident myocardial infarction, 77% with incident stroke and 74% with incident heart failure. In addition, HT is a major risk factor for atrial fibrillation, chronic kidney disease and diabetes mellitus. Of great concern in South Africa, Norman et al. have reported that 72% of hypertensive diseases, 50% of strokes and 42% of IHD were attributable to HT in adult males and females.

**Does HT remain a risk factor for CVDs in the very old?**

The absolute risk of stroke mortality and CV mortality is related to BP at any age, and particularly in elderly patients. In the Lewington meta-analysis, the relationship is impressive concerning very old persons (≥80 years). With the high prevalence of HT at older ages and the growing number of elderly persons, the management of HT is a particular health problem. The risks associated with HT in elderly populations are not limited to ‘classical’ CVD, but extend to cognitive decline and dementias.

**What investigations for what risks?**

While HT is a risk marker, with the incidence of complications rising significantly with age, the majority of elderly people have asymptomatic HT. Further investigation should be proposed, taking into account age and risk of complications.

**Brain**

The risks concern vascular lesions secondary to atherosclerosis of the extra- and intra-cerebral arteries. There are 3 types of complications: ischaemia with different degrees of severity, haemorrhage, and degenerative disease such as vascular dementia secondary to numerous lacunae (multi-infarct dementia), Alzheimer’s disease and mixed forms of dementia. A clinical examination should include a complete neurological examination and a simple screen of cognitive function with a mini mental state examination (MMSE). Depending on results, further investigations (head CT-scan and/or magnetic resonance imaging) may be indicated.

**Heart**

Associated with HT are CAD and LVH. CAD may be expressed as angina pectoris or it may be clinically silent. A resting electrocardiogram (ECG) may not be sufficient. However, an exercise test is only feasible in particularly active hypertensive older persons. For others, an echocardiography stress test should be performed. For LVH, an ECG may be carried out to screen for LVH using voltage criteria. Echocardiography is undoubtedly far more sensitive than ECG in diagnosing LVH and predicting CV risks.

**Blood vessels**

Ultrasound examination of carotid arteries with the detection of plaques and measurement of the intima-media complex thickness has been shown to predict the occurrence of both stroke and myocardial infarction. Such investigation needs only to be carried out in the context of a cervical systolic murmur or neurological disorders.

**Kidneys**

Kidney damage induced by HT is evaluated on the estimated glomerular filtration rate (GFR) (Cockcroft-Gault formula) and urinary albumin excretion. These two assays should be included in the laboratory tests for the therapeutic management of hypertensive patients.

**Evidence for BP-lowering treatment in the elderly**

Results in different trials showed reduction in the incidence of both stroke and CV morbidity in octogenarians, but no effect or a slight increase in all-cause mortality. Clinical practice guidelines recommend that in participants aged >80 years, ‘evidence for benefits of anti-hypertensive treatment is as yet inconclusive’. The results of the HYVET study were published in 2008. Almost 4 000 patients aged >80 years with an SBP >160 mmHg were randomly assigned to a diuretic (indapamide) or placebo, and if necessary, supplemented by an angiotensin-converting enzyme inhibitor (ACE-1) (perindopril) or placebo to achieve a target SBP of 150 mmHg. The results provided clear evidence
Hypertension in the elderly

Target systolic blood pressure is ≤140 mmHg in patients aged 55 - 79. Target systolic blood pressure is ≤140 mmHg in patients aged ≥80. Achieved values: <140 mmHg for those aged ≤79 are appropriate; 140 - 145 mmHg for those aged >80, if tolerated, is acceptable.

**Stage 1 HT**
- SBP 140 - 159 mmHg or
- DBP 90 - 99 mmHg
- ACE-I, ARB, CA, diuretic, or combination

**Stage 2 HT**
- SBP ≥160 mmHg or
- DBP ≥100 mmHg

Majority will require at least two medications to reach goal if at least 20 mmHg above target. Initial combinations should be considered. The combination of amlodipine with an RAS blocker may be preferred to a diuretic combination, though either is acceptable.

### Compelling indication
- Heart failure
- Post myocardial infarction
- CAD or high CVD risk
- Angina pectoris
- Aortopathy/aortic aneurysm
- Diabetes
- Chronic kidney disease
- Recurrent stroke prevention
- Early dementia

### Initial therapy options*
- THIAZ, BB, ACE-I, ARB, CA, ALDO ANT
- BB, ACE-I, ALDO ANT, ARB
- THIAZ, BB, ACE-I, CA
- BB, CA
- BB, ARB, ACE-I, THIAZ, CA
- ACE-I, ARB, CA, THIAZ, BB
- ACE-I, ARB
- THIAZ, ACEI, ARB, CA

### Blood pressure control

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*Combination therapy

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ACE-I = angiotensin-converting enzyme inhibitor; ALDO ANT = aldosterone antagonist; ARB = aldosterone receptor blocker; BB = beta blocker; CA = calcium antagonist; CAD = coronary artery disease; CVD = cardiovascular disease; DBP = diastolic blood pressure; RAS = renin-angiotensin system; SBP = systolic blood pressure; THIAZ = thiazide diuretic.

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Fig. 1. Principal of treatment of HT – algorithm for the treatment of HT in the elderly.\(^\text{360}\)
that the lowering of BP is associated with definite CV benefits for octogenarians. The trial showed a reduction in incidence of heart failure (64%) all stroke (30%) and all-cause mortality (21%).

Recommendations for management
Non-pharmacological intervention
Lifestyle changes are appropriate in the treatment of mild HT in elderly patients. Important changes are as follows:
- A salt diet of no more and no less than 4 - 5 g salt per day, due to the relationship between excessive salt diet and HT. However, beware of the risk of hyponatraemia with a low salt diet in elderly persons.
- Regular physical activity – walking 20 - 30 min/day.
- Removal of offending substances such as non-steroidal anti-inflammatory drugs.

Other interventions such as cessation of smoking, reduction in alcohol consumption, weight reduction and a decrease in mental stress are recommended.

Pharmacological intervention
The initial anti-hypertensive drug should be started at the lowest dose and gradually increased, depending on the BP response, up to the maximum tolerated dose: ‘start low and go slow’. The same anti-hypertensive drug treatment may be used in patients aged >80 years and those aged 55 - 80 years, taking into account any co-morbidities (Fig. 1).
- Thiazide diuretics (hydrochlorothiazide, chlorothalidone and indapamide) are recommended to start treatment. Thiazide diuretics are generally well-tolerated and inexpensive; but side-effects such as hypokalaemia and hyponatraemia should be monitored regularly (twice a year). Older patients tend to drink small amounts of fluid, and it is recommended that they are encouraged to increase their fluid intake to prevent dehydration, especially during the warm season and during a febrile episode.
- Calcium channel antagonists (CCAs) dilate coronary and peripheral arteries. They have adverse side-effects such as ankle oedema, headache and postural hypotension. First-generation CCAs (nifedipine, diltiazem, verapamil) are contra-indicated in cases of left ventricular dysfunction, conduction defect and heart block. Second-generation dihydropyridine CCAs (amlodipine, nifedipine XL) do not have these side-effects and are commonly prescribed in the elderly population.
- ACE-Is, angiotensin receptor blockers (ARBs) and direct renin blockers have some specific indications such as left ventricular dysfunction and heart failure, diabetic renal disease and hypertensive nephrosclerosis. ACE-Is reduce morbidity and mortality after a myocardial infarction. Cough is frequent (10 - 15%) with ACE-Is, but rare with ARBs. For all 3 drugs, renal function must be monitored before initial use and after each dose modification.
- Beta blockers (BBs) have reduced anti-hypertensive activity when compared with the 3 previous classes. However, BBs have some specific indications such as arrhythmias (atrial fibrillation and ventricular arrhythmias), CAD, heart failure, migraine headaches, and senile tremors. Nebivolol is the only well-documented BB in elderly patients and is certainly better than atenolol.
- Aldosterone-blocking agents such as spironolactone are also useful in the treatment of some hypertensive patients with heart failure and rarely in primary hyperaldosteronism. However, with spironolactone, the risk of hyperkalaemia and renal failure is frequent and is dose-dependent. Special attention is particularly required when combined with ACE-Is. The other potassium-sparing diuretics (amilodipe, triamterene) are often combined with a thiazide.
- Alpha blockers and centrally acting drugs should not be used as first-line treatment. They are useful in patients with HT and benign prostatic hypertrophy.

The prevalence of hypertension increases progressively with age.

Management of anti-hypertensive treatment
The goal of reducing BP is to prevent morbidity and mortality. Randomised trials have focused on determining which anti-hypertensive drugs or drug classes provide optimal protection in very old (≥80 years) hypertensive patients. No difference in morbidity and mortality between anti-hypertensive drug treatment strategies is identified.

Step I: The anti-hypertensive treatment is initiated with a CCA (amlodipine, diltiazem, verapamil) at a low dose (i.e., amlodipine 5 mg), once a day. If a CCA is not suitable because of oedema, headache and postural OHT, a thiazide-like diuretic such as hydrochlorothiazide (12.5 mg once daily) or indapamide 1.5 mg modified release can be used. The results are assessed after a month of treatment. If BP is significantly decreased, the treatment is continued. If BP is insufficiently controlled, the dose of the monotherapy should be increased, or a second drug added.

Step II: Two drugs are needed and recommendations pertain to 2 types of combinations:
1. Calcium channel blocker (CCB) + thiazide-like diuretic
2. ACE-I (or ARB) + CCB (or thiazide)

Step III: Three drugs are needed with a combination of CCB, diuretic and ACE-I or ARB.

For steps II and III, the control of HT may be improved with a combination therapy.
Initial anti-hypertensive therapy with single-pill combinations produced more rapid BP control than initial monotherapy in clinical trials. Egan et al. studied electronic record data obtained from 180 practice sites for 106,621 hypertensive patients. The authors concluded that initial therapy with single-pill combinations provided better HT control than free combinations or monotherapy and may improve and CV outcomes.

What then should be the BP goal in elderly patients?

Current evidence supports an SBP goal of 150 mmHg and a DBP of 80 mmHg without OHT for hypertensive patients aged >80 years. In the ACC/AHA consensus report, an SBP of 140 - 145 mmHg was described as acceptable for those aged >80 years. Higher or lower pressure was associated with increased risk of adverse outcomes, the J-curve phenomenon. In the INVEST sub-study concerning the relationship between CAD and HT, the increased risk of mortality and morbidity associated with lower pressures, especially systolic, as age increased was confirmed, and was greatest in the very old (aged ≥80 years), as well as in the age group 70 - 79 years. Caution is in order when either SBP or DBP are lowered <140 and 70 mmHg, respectively.

HT in elderly patients is common, remains a CV risk factor and is associated with numerous co-morbidities. Since the results of the HYVET trial, it is recommended that hypertensive octogenarians be treated to reduce mortality and morbidities. However, side effects of anti-hypertensive treatments are common in this population.

References


Summary

- The prevalence of HT and associated complications increases with age.
- ISH is more common in older patients. Treating HT in the elderly is effective in reducing morbidity and mortality.
- Initial management should include lifestyle modification. Pharmacotherapy should be initiated if there is insufficient BP control.
- Elderly patients may need more than one agent to control BP.
- Therapy should be individualised and introduced slowly while monitoring for orthostatic hypotension and other drug adverse effects.
- Choice of therapy is guided by clinical assessment and co-morbidities.