CONSENSUS CONFERENCE

Recommendations for the detection and treatment of hypertension in the elderly

Consensus document by the Spanish Society of Hypertension, the Argentinean Society of Hypertension, the Spanish Society of Geriatrics and Gerontology, the Spanish Society of Geriatric Medicine and the Spanish Society of Nephrology.

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ABSTRACT

Cardiovascular risk increases with age, making adequate diagnosis and management of this condition essential in the elderly. When evaluating the aged hypertensive it is important to take a holistic approach and to evaluate clinical aspects (comorbidity, polypharmacy), functional status (dependences of physical and mental origin) and social conditions (isolation, socio-economic level, and housing). There have been as of yet no studies into the physiological effects of antihypertensive drugs in relation to the aging process or the side-effects of antihypertensive drugs in the elderly, such as incontinence, falls, dehydration or disturbances in the electrical conduction system of the heart. Accordingly, a group of nephrologists, geriatricians, biologists, pharmacists, and hypertensologists met with the aim of analysing the ageing process in detail and gave their recommendations for the management of hypertension in the elderly, taking into account the physiological differences between the aged and the young, as well as medication side-effects which are often not seen in young adults. For instance, as white coat hypertension is more frequent in elderly patients, home blood pressure monitoring (HBMP) and ambulatory blood pressure monitoring (ABPM) should be routinely used in patients older than 65 years of age to aid the diagnosis. The physiological ageing process means the pharmacological treatment of essential hypertension in the elderly in absence of renal or cardiac illnesses should be initiated preferably with renin-angiotensin axis blockers or calcium antagonists. Treatment should be initiated at the minimum recommended dose with progressive increases depending on the therapeutic objective. Beta blockers should be considered as a third line drug, except when special indications exist, as they are less effective than the antihypertensive drug groups in reducing the risk of having a cerebrovascular accident as well as cardiovascular events in the elderly.

Key-Words:
Consensus document; geriatrics; hypertension.

DEFINITION AND CLASSIFICATION

Arterial hypertension, usually defined as a systolic blood pressure (BP) equal to or higher than 140 mmHg and/or a diastolic BP equal to or higher than 90 mmHg, is a cardiovascular disease of complex origin that is diagnosed by means of one key clinical sign; elevated arterial pressure.
The higher the blood pressure, the higher the cardiovascular risk. Defined hypertension values are arbitrary, based on the increased risk to the general population from this BP value onwards (Table I). A balance must be made between the benefits which the treatment offers and the risks involved in not undertaking this treatment, meaning that in certain special populations, hypertension treatment may be necessary when BP values are lower.

In elderly hypertensive patients, the systolic blood pressure (SBP) and the pulse pressure (PP) (the difference between systolic and diastolic pressure) are more important markers of cardiovascular risk than the diastolic blood pressure (DBP).

Studies which have evaluated pulse pressure carefully have concluded that for a determined level of systolic arterial pressure, an inverse relationship between diastolic arterial pressure and cardiovascular risk exists.

Isolated systolic hypertension (SBP higher than 140 mm Hg with a DBP equal to or lower than 90 mm Hg) is frequent in elderly hypertensive male patients and even more frequent in elderly female patients. The importance of ISH lies in the fact that patients with this variety of HBP are at a two to four fold increased risk of having a CVA, myocardial infarction and deterioration in renal function than the normal population.

Pseudohypertension is defined as an elevated arterial pressure (as detected by sphygnometer) despite normal intra-arterial values. This condition should be suspected in elderly patients with difficult to control hypertension, who present with orthostatism, instability, loss of balance or even falls during the course of their hypertensive treatment. The differential diagnosis is made clearer using the Osler technique, which consists of insufflating the cuff above the value of the systolic arterial pressure, while palpating for the radial artery. This manoeuvre is considered positive, and therefore also diagnostic of pseudohypertension, when the radial pulse becomes impalpable due to the great rigidity of the arterial wall in spite of the artery itself still being palpable. If this clinical picture is detected, it is necessary to stop medication and to use other methods for BP assessment, such as the measurement of the intra-arterial pressure to reveal the real blood pressure values.

## EPIDEMIOLOGY

The aging process, the relationship between cardiovascular risk and arterial pressure and the modification of diagnostic values for hypertension, have multiplied the prevalence of HTA in the aged. The absolute rates of hypertension in this cohort have long passed the very high rate of 40% and now reach absolute rates of around 60-70%, with this condition increasing with age. The ISH rate in Spain is 35% in the population aged over 65 and while blood pressure values constantly increase with age, this assumption needs to be clarified:

a) The age-related increase in blood pressure is very evident in developed countries, but there are some under-developed communities which do not experience this age-related increase, raising doubts as to the physiological character of the age-related increase in blood pressure.

b) While the increase in blood pressure is more evident in the systolic values and is more pronounced in elderly females, the above does not apply, with blood pressure tending to stabilise or even decrease. This is clearer for the DBP which tends to slightly decrease from 60-65 years of age onwards than for the SBP, which nevertheless follows the same tendency from 80 years onwards.

## PATHOGENESIS

In humans, aging leads to modifications in the structure and function of the cardiovascular and renal
vascular tree, and this process is intensified by the presence of HBP. Of the three layers that compose the arterial wall (intima, media and adventitia), it is most commonly the intima to which increasing age brings the greatest alterations. This is due to the vascular remodelling induced by elevated arterial pressure as well as other vascular risk factors. With increasing age, lipids accumulate between the elastic fibres, facilitating calcium deposition and making the wall thickness increase with age, to a median estimate of more than 20% per year. There is also hypertrophy and hyperplasia of smooth muscle cells and in addition to this they also synthesise a greater amount of collagen. The cellular matrix is degraded by increased elastase activity, which destroys the elastin leading to an increase in the collagen/elastin ratio and consequently causing loss of elasticity. Therefore, if the normal aorta in the young person acts as a reservoir for the blood volume that is expelled during ventricular systole and maintains constant blood flow, the aging process produces a loss of elasticity, which fundamentally affects the aorta's distensibility, causing the cardiac ejection volume to increase in the zones of fibrosis and an abrupt fall in the diastolic arterial pressure.

The aging process also leads to changes in the heart structure (hypertrophy of the left posterior ventricular wall) either in the mechanical component or in the electrical one. As in the arteries, an increase of the amount of collagen takes place in the subepicardium and subendocardium, making them less soluble, more stable and for that reason more rigid. The increase in the zones of fibrosis is accompanied by calcifications in the valves and valvular rings. In general, in the electrical system this produces a loss of cells from the sinoatrial node and the specific conduction fibres of the bundle of His.

Cardiac output in the elderly is thus diminished as a result of a smaller myocardial contractility, which is accompanied by diminution of the circulating volume. The heart rate does not increase (due to the reduction in the activity of the adrenergic receptors), and therefore there is a reduction in the cardiac output and the systolic volume. In the kidney, the alterations in the small arteries and arterioles are responsible for the focal destruction of nephrons, which in the long term contributes to the development of nephroangiosclerosis. Unaffected nephrons are placed under increased intraglomerular pressure, which produces mechanical expansion through hyperflow and glomerular injury, in this way perpetuating the cycle. The reduction in glomerular filtration in elderly normotensives is about 0.75 ml/min/year. In the eighth decade of life this process can affect up to 40% of the glomeruli. In general, tubular function also loses effectiveness with increasing age. A diminution in the maximal tubular capacity for glucose and phosphate as well as a delay in the elimination of an acute acid overload has been described with increasing age, as has a renal threshold for bicarbonate comparable to that in the young. An alteration of clinical importance is the incompetence of the ascending limb of the loop of Henle to retain the sodium coming from proximal segments of the nephron. The total body potassium is reduced, although the urinary excretion of potassium is lower than in young people.

In the aged, a reduction in the activity of renin-angiotensin-aldosterone system has been observed. The reduction in renin secretion is thought to be secondary to nephroangiosclerosis, but irrespective of its origin, it has also been observed that basal renin levels are low in the elderly and in addition there is a blunted response to postural changes or diuretic intake in this age group. In spite of this, in experimental conditions an increase in the number of angiotensin I receptors in target organs has been observed.

Plasma noradrenalin increases with ages and this is accompanied by a decrease in the sensitivity to catecholamines as a result of the decrease in the number and function of the beta1-receptors; a decrease in the activity of the baroreceptors has likewise been observed. For that reason the adaptation to postural changes, small losses of plasma volume or abrupt arterial pressure changes are slower and less effective in the elderly than in young people and therefore orthostatic hypotension is frequent.

Another difference between the young and the old is the increase in free radicals. It has been proven that the effects of oxidative stress are greater in the cells with a long post-mitotic survival period, as is the case in those of the brain, heart, smooth muscle and kidney, organs, which are affected by HTA.

The increase in arterial pressure has long been considered as an equalizer in maintaining the suitable
perfusion of the organs. Although more than half of the elderly population is hypertensive, the rest is normotensive, and a comparison of these two populations shows that while elderly normotensive people are at a higher risk than normotensive young people, elderly hypertensive people are at a 2-3 times higher risk of cardiovascular complications than elderly normotensives of a similar age and with associated risk factors.

**DETECTION AND DIAGNOSIS OF ARTERIAL HYPERTENSION**

The basic procedure for the detection of arterial hypertension is BP measurement in all patients during medical consultation, as arterial hypertension is a frequently asymptomatic condition. In elderly patients, this procedure is especially required given the high prevalence of HBP in this population group, as well as the low cost and high yield of detecting this condition.

As the case histories of elderly patients are registered at their health centres, at least one visit for measuring arterial pressure should be scheduled in all elderly patients, even those without a documented case history or those with previously normal BP.

As the guidelines for measurement of arterial pressure have been stated in previous documents, such as the Spanish Guideline for the Detection and Treatment of Arterial Hypertension or the Guidelines of the European Society of Cardiology-Arterial Hypertension Society (European HTA Guidelines), we will not repeat them again here.

Should the measurement show a high arterial pressure, this should be confirmed through appropriate means (see below). In any case, the confirmation of the diagnosis implies that several measurements have been taken; at least two or more readings at two or more different visits if taken during consultation. If one or more elevated BP measurements are taken between several normal ones, an annual review must be arranged. The recommended intervals between visits are stated in Table I above.

White coat hypertension is more frequent in elderly patients and affects SBP more frequently than DBP. Home blood pressure monitoring (HBMP) and ambulatory blood pressure monitoring (ABPM) should be routine in patients older than 65 years of age.

### a) HOME BLOOD PRESSURE MONITORING

HBMP is effective and reliable in elderly patients, even in hypertensive patients over 75 years of age with sufficient cognitive capacity, in whom the method shows a greater reliability than the BP measurements taken during the consultation.

To achieve reliable results, the patient must be taught the proper methods of measurement and the need of keeping to a fixed time schedule rather than taking the measurement when they feel like it. Due to its comfort and simplicity, the protocol of 12 measurements (2 in the morning and 2 in the afternoon for 3 working days) seems recommendable. It has been validated, taking as final value the median of the measurements of the last 2 days.

Previous studies have shown that the normal BP value measured by HBMP is the same in the elderly and younger individuals (135/85 mmHg). The apparatuses OMRON HEM 722C and HEM 735C have been validated in elderly people and are therefore recommended in this population group.

For an updated revision of the accepted apparatuses please see the web page of the British Hypertension Society (www.bhsoc.org).

### b) AMBULATORY BLOOD PRESSURE MONITORING

The effectiveness of ABPM in elderly patients has been satisfactorily proven. ABPM is a recommendable procedure in elderly patients, whenever there is suspicion of white coat hypertension, doubts as to the diagnostic classification of the patient or when the results of the HBMP are near the normal limits. Programming and the choice of the type of apparatus do not differ in the young and older patients. Readers interested in this aspect can consult the Recommendations of the European Society of Hypertension.

The definition of arterial hypertension deserves special evaluation. The European Society of Hypertension considers values to be either optimal or probably normal or probably pathological. The lack of clear differentiation regarding the need for treatment between...
these two categories (probably normal and probably pathological) may be the cause of the doubts clinicians have when prescribing treatment, but the recommendations are based on clinical trials carried out up to now16.

The recent recommendations made by the Canadian Society of Hypertension define hypertension as a BP over 135/85 mmHg during activity or as an average of more than 130/80 over 24 hours17.

We think that this definition should be applied to elderly patients if we take into account the following:

1. HBP is the major risk factor associated with age10

2. There is a high rate of progression to established arterial hypertension (BP values during activity 140/90 mmHg) in most of the patients with a BP higher than 135/85 mmHg in the diurnal period18

3. The ARIC study has demonstrated that high blood pressure is associated with a significant increase in morbidity and mortality when compared to optimal blood pressure16

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**EVALUATION OF THE HYPERTENSIVE PATIENT**

The evaluation of elderly hypertensive patients has 6 key points:

1. The holistic approach to the aged hypertensive should, in addition to the clinical aspects (comorbidity, polypharmacy), evaluate the functional status (dependencies of physical and mental origin) and the social conditions (isolation, socioeconomic status, and housing) as they all are key factors in planning therapeutic intervention.

2. Confirm and define the severity of the hypertension according to the European Hypertension Guidelines (Table I)19.

3. Detect cardiovascular risk factors. The following measures are essential in all patients:
   - Enquire as to alcohol and tobacco consumption
   - Measure the abdominal perimeter of the patient (pathological is 102 cm in males and 88 cm in females).
   - Measure glucose, total cholesterol and fractions, as well as triglycerides. A total cholesterol level > 250, a cholesterol-LDL level > 155 or a HDL-cholesterol level < 40 in males and < 48 in females are considered to be pathological.

4. To evaluate the degree of the target organ damage. Occasionally the detection of arterial hypertension can coincide with an acute or subacute event (infarct of myocardial infarction, aneurism, CVA, malignant hypertension) that requires hospital admission. In the rest of the cases it would be thorough to investigate for the presence of target organ injury. (Table II).

5. Decide on the treatment plan (Table III, modified from the European Hypertension Guidelines), because elderly patients have at least one vascular risk factor (age) and in elderly females the number of risk factors is at least 2 (age + menopause). (Figure 1).
6. Check for presence of secondary hypertension. The causes of secondary HTA in the old are not different from other age groups, although the incidence of renal vascular arterial hypertension and suprarrenal adenoma are perhaps higher and therefore one should suspect secondary hypertension in severe HTA. Doppler echography can be useful in excluding renovascular hypertension. Magnetic resonance angiography would be the ideal exploration when these cases are suspected, given the reduction in the renal function that is present in many elderly people and the proven sensitivity and specificity of the technique.

The rest of the cases can be excluded with universally available basic investigations (ions, urea, creatinine, Ca, P, GGT, basic urinary testing, T4 and TSH).

**TREATMENT AIMS**

There is no concrete evidence as to the level of arterial pressure that should be reached in the treatment of essential arterial hypertension in the elderly.

As the subject’s age approaches the maximum life expectancy, the competing factors of mortality increase.
Consequently, the chances of reducing mortality lessen.

Thus, it has been observed that antihypertensive treatment in subjects older than 80 years of age reduces cardiovascular morbidity but not cardiovascular mortality nor mortality in general. Therefore, whereas the objective of antihypertensive treatment in the adult is the reduction of cardiovascular and renal morbidity and mortality, the main objective in the elderly is to increase incapacity-free life expectancy or, if incapacity is present, to optimise function.

Various studies have shown that small reductions (5-6 mmHg) of the diastolic blood pressure significantly reduce cardiovascular morbidity and mortality. Therefore, a BP < 140/90 also seems recommendable for the elderly (Evidence level Ib).

In special population groups (diabetics, cardiology and nephrology patients) lower levels of arterial pressure may be advisable. (Evidence Level Ib)

There is conflicting evidence as to the existence of an increase in mortality if excessive reductions in the diastolic pressure take place. Various interventional studies support this conclusion. Until there is clear evidence, diastolic pressure should not descend below 65 mmHg in old patients. (Evidence Level IIb) In the case of isolated systolic hypertension, the epidemiological evidence demonstrates a greater cardiovascular mortality in patients with simultaneous higher systolic and lower diastolic pressures.

Since the DBP usually responds better to the pharmacological treatment than the SBP, monitoring diastolic pressure is essential and one needs to be careful in all patients to avoid reductions below 65 mmHg, irrespective of the level of systolic pressure. (Evidence level III) The reduction of the DBP levels to around 80 mmHg was accompanied by a significant reduction in morbidity and mortality in the Syst.-Eur study and the Syst.-China study. This is a reasonable objective in most patients (Evidence level IIIb). No data exists on the optimal time intervals for blood pressure reduction. It is recommended that the reductions are made gradually in order to avoid complications.

An initial BP reduction of not more than 20 mmHg seems prudent. If this objective is met and is well tolerated, successive reductions of the arterial pressure can be considered until the target is reached (Recommendation IIIc).

**NON-PHARMACOLOGICAL TREATMENT**

It has been proven that arterial pressure can be controlled by means of lifestyle modifications. Thus, in the TONE trial (Trial of non-pharmacological interventions in the elderly), a total of 975 hypertensive patients between 60 and 80 years of age with BP controlled by monotherapy evaluated the degree of control after withdrawing the antihypertensive drug.

The number of people with controlled BP was 43.6% in the group with salt restricted diet and weight loss, 35% in those that only used one of these measures and 16% in those conventionally treated. These BP reductions were obtained through moderate salt restriction (average 40 mmol/day) or weight loss of 4.7 kg.

Therefore it would be advisable to take the following previous measures in conjunction with drug treatment:

1. Reduction of the calorie intake if overweight.
2. Sodium ingestion of around 100 mmol/day to be achieved by reducing the amount of salt used while eating and avoiding precooked foods, tinned food and sausages. 1.5 g of salt per day may be used, preferably after the food has been cooked, instead of using it during cooking.
3. Increase potassium consumption (fresh fruit, vegetables and cereal products).
4. Increase dietary calcium ingestion (100 g of cheese contains between 700 and 1,180 mg of calcium depending on the type).
5. Daily walking of more than 1/2 hour per day, preferably between 1 and 2 hours. In the non-trained subjects, this objective should be reached gradually.
6. Not more than 30 g of alcohol/day (equivalent to 300 ml of wine, 500 ml of beer or one glass of liquor).
7. Before initiating non-pharmacological measures the socioeconomic conditions of the patient must be considered.

8. The simultaneous and moderate use of several non-pharmacological measures usually gives a better therapeutic result compared to the strict application of a single one of them.


**PHARMACOLOGICAL TREATMENT**

The ideal drug characteristics for the treatment of HBP in the aged are given in Table IV.

In light of the experience gathered through various published clinical trials, various drugs can be used for the initiation of the essential arterial hypertension treatment in the elderly, as they do not only reduce arterial pressure but also cardiovascular morbidity and mortality.

Thiazide diuretics are considered to be the first choice drug, shown in various randomised control trials which have demonstrated a significant reduction of the cardiovascular morbidity and mortality (Evidence Level Ib)\(^27-30\). In these studies beta-blockers were used as second line drugs. Their use as first choice drug for the treatment of the essential HTA in young people has recently been questioned\(^31\).

In the elderly they have added side-effects such as hyponatraemia, urinary incontinence, hypertriglyceridaemia and some clinical trials have shown increased glucose and plasma creatinine as for example the first publication of MRC working party for hypertension in the elderly\(^29\).

Hyponatraemia is one of the most frequent side-effects in the old due to their reduced ability to retain Na\(^32\). Hyponatraemia is a cause of hospital admission, falls and hip fractures in the elderly; all complications which have never been evaluated in clinical trials with people older than 65 years of age. In addition to the personal and familiar consequences for the elderly, hyponatraemia also entails a high cost, a circumstance which has not been accounted for either in clinical trials. For that reason it is necessary

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<table>
<thead>
<tr>
<th>Table IV</th>
<th>Ideal drug characteristics for treatment of the elderly</th>
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<tbody>
<tr>
<td><strong>ACE-inhibitor</strong></td>
<td><strong>Angiotensin receptor blocker</strong></td>
</tr>
<tr>
<td>Reduces peripheral resistance</td>
<td>Yes</td>
</tr>
<tr>
<td>Does not diminish blood flow to vital organs brain, heart and kidney and does not interfere with the self-regulatory mechanisms</td>
<td>Yes</td>
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<tr>
<td>Does not cause bradycardia nor interferes with cardiac conduction system</td>
<td>Yes</td>
</tr>
<tr>
<td>That slows down, halts or reverses the progression of ventricular hypertrophy and thickening of the arterial wall</td>
<td>Yes</td>
</tr>
<tr>
<td>Protects against the progression of renal fibrosis glomerular as well as interstitial</td>
<td>Yes</td>
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<tr>
<td>Does not cause volume depletion</td>
<td>Yes</td>
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<tr>
<td>Does not cause hyponatraemia nor hypokalaemia</td>
<td>Yes</td>
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<tr>
<td>Does not cause insulin resistance nor hyperlipidemias</td>
<td>Yes</td>
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<tr>
<td>Does not cause urinary incontinence</td>
<td>Yes</td>
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<tr>
<td>Has Antioxidant properties</td>
<td>Yes</td>
</tr>
<tr>
<td>Can be used as monotherapy, monodosis and minidosis</td>
<td>Yes</td>
</tr>
<tr>
<td>Maintains apoptotic balance</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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* Thiazide diuretics up to 25 mg/day reduce peripheral resistance, while doses of more than 50 mg/day increase them.

** Loop diuretics increase peripheral resistance.

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to periodically check the blood electrolytes levels in the patients in whom diuretics are indicated, and even more so in the patients who are on a combination of diuretics and saline restriction.

Although diuretic drugs are perceived as cheap, pharma-economical studies have shown different results, with the diuretic being slightly more expensive than angiotensin II receptor antagonists. Perhaps this is the explanation for the discrepancy between therapeutic guidelines and the low acceptance of their indications between doctors.

The use of calcium channels blockers as a therapeutic option in elderly patients is also supported by randomised control trials, which have demonstrated a reduction in mortality and morbidity of cardiovascular origin compared to placebo and other drugs (Evidence Level Ib).

Angiotensin converting enzyme inhibitors were evaluated specifically in the elderly in the Australian National Blood Pressure study. It demonstrated effectiveness similar to diuretics in reducing mortality and cardiovascular events. The same applies to the study STOP2.

Although the HOPE study did not specifically evaluate elderly patients, the subjects’ average age was higher than 65 years. This study showed that ACE-Inhibitors reduce cardiovascular mortality in elderly patients with an elevated cardiovascular risk, meaning these antihypertensive drug groups should be recommended as first-choice drugs in this group of patients. (Evidence Level Ib)

The LIFE study (patients’ average age 72 years) demonstrated that angiotensin receptor antagonists are better than beta-blockers in reducing total cardiovascular mortality. They should also be considered for treatment of the arterial hypertension in the elderly as a first line treatment. (Evidence level Ib) Beta-blockers have been recommended as the drug of choice by the guidelines for the treatment of arterial hypertension. Nevertheless, a meta-analysis of 13 randomised studies of patients with essential HBP with a total of 105 951 patients has compared the protective effect of beta-blockers on target organs with other drugs. 7 studies (27 433 patients) have analysed the effect of treatment with beta-blockers compared to placebo or no pharmacological treatment.

The relative risk of having a cerebrovascular accident was 16% higher in the group receiving beta-blockers (95% CI 4-30%) compared to other drugs. There were no differences relating to myocardial infarctions. In clinical trials, which have compared the effect of beta-blockers to placebo or to no treatment, the relative risk of ACV is reduced 19% (7-29%), approximately half the number previous clinical trials had hoped for. There is no difference in the number of myocardium infarcts and mortality. Particularly in the group of elderly patients beta-blockers were worse than the other hypertensive drug groups in reducing the cardiovascular events.

In summary, the beta-adrenergic receptor blockers do not have to remain as the first choice drug in the treatment of the essential hypertension without complications in the elderly (Evidence level Ia).

A summary of the recommendations is given in Table V.

### Table V
Summary of treatment recommendations

1. The pharmacological treatment of HTA in the aged should be initiated with renin-angiotensin axis blockers, calcium antagonists or diuretics.
2. Treatment should start with the minimum recommended dose with progressive increases depending on the therapeutic objective.
3. Most of the patients need more than one drug to control blood pressure and need a combination of first line drugs.
4. Beta-blockers should be considered as a third line drug, except when special indications exist.
5. The use of fixed combinations is recommended in order to improve therapeutic compliance, as most of the patients will be on multiple medications.
6. Diuretics should be used at the minimum effective dose for the control of the arterial pressure. The combination of drugs is preferable to an increase in the dose of the diuretic.

### Conclusion

Before initiating antihypertensive treatment, it is necessary to design a strategy for effective BP control. Some strategies into compliance, BP control, and possible side effects have been published recently. The regularity of the follow-up depends on the severity of hypertension, the cardiovascular risk factors, organ damage and analytical alterations. Although fixed guidelines do not exist, it is reasonable to establish short periods but for more severe hypertension...
or when several factors coexist, the time interval should vary from 1 to 3-6 months.

**EXPERT COMMITTEE**

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**Acknowledgements**

We are grateful to Mr Mina Hanna for his help in the preparation of the manuscript.

This meeting was supported by a grant of the Spanish Society of Hypertension.

**Conflict of interest statement.** None declared.

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