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High blood pressure at the crossroads: Looking for a Working Definition

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ABSTRACT

Hypertension (HT) is recognized as one of the major risk factors for vascular damage. Although current guidelines recommend an aggressive drug treatment, with blood pressure control goals ever lower, the prevalence of uncontrolled hypertension is still apparently high. It is often forgotten that BP is a very labile hemodynamic parameter, which requires a correct methodology for its measurement, only rarely met, leading to misdiagnosis and wrong hypertensive monitoring. Although arbitrary, the definition of HT has been set at 140/90 mmHg, based on casual BP taken in the office. This register itself can provide useful information beyond systolic and diastolic values, and with a certain hemodynamic meaning (pulse pressure and mean blood pressure). For a proper diagnosis of hypertensive patients it is essential to enhance BP measurement in any area with an strict methodology, and to incorporate into clinical practice new techniques such as 24 hours MAPA and AMPA at home, which still require definition of specific reference objectives. The application of these techniques has led to the emergence of several subgroups of hypertensive patients, such as white-coat hypertension and masked hypertension, which have their peculiarities in relation to the therapeutic management and prognosis. These techniques, together with the publication of new clinical trials using criteria of evidence, have led to the review of the Guidelines for the management of hypertension by modifying the limits of BP for some special clinical situations, and changing the paradigm of the lowest BP is the best, by one underscoring the need for early intervention and control of associated vascular risk factors.

Key words: Arterial hypertension. Definition. Office blood pressure. Ambulatory blood pressure monitoring.

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Hipertensión arterial en su encrucijada: a la búsqueda de una definición operativa

RESUMEN

La hipertensión arterial (HTA) es reconocida como uno de los principales factores de riesgo de daño vascular. A pesar de que las Guías vigentes indican un tratamiento farmacológico agresivo, con objetivos de control de la tensión arterial (TA) cada vez más bajos, la prevalencia de hipertensos no controlados se mantiene aparentemente elevada. Con frecuencia se olvida que la TA es un parámetro hemodinámico muy lábil, que exige para su medición correcta una metodología que se cumple sólo en contadas ocasiones, induciendo un diagnóstico y un seguimiento erróneos del hipertenso. Aun siendo arbitrario el límite elegido, la definición de HTA se ha fijado en 140/90 mmHg, basada en la toma casual de TA en la consulta. Esta propia toma puede proporcionarnos información muy útil, más allá de la tensión arterial sistólica y diastólica, y con un cierto significado hemodinámico (presión del pulso y presión arterial media). Para un correcto diagnóstico del hipertenso, es imprescindible potenciar la toma de la TA en cualquier ámbito con una metodología estricta, y la incorporación a la práctica clínica habitual de nuevas técnicas como la monitorización ambulatoria de la presión arterial (MAPA) de 24 horas y la automedición de la presión arterial (AMPA) en domicilio, que aún precisan de la asignación de valores de referencia específicos. La aplicación de estas técnicas ha llevado a la aparición de varios subgrupos de hipertensos, como la HTA de bata blanca y la HTA enmascarada, que tienen sus peculiaridades en relación con el tratamiento y el pronóstico. Estas técnicas, junto con la publicación de nuevos ensayos clínicos aplicando criterios de evidencia, han llevado a la reconsideración de las Guías para el tratamiento de la HTA, modificando los límites de TA para algunas situaciones clínicas especiales, y cambiando el paradigma de cuanto más baja sea la TA mejor, por el de cuanto antes y más factores de riesgo vascular asociados se controlen mejor.

Palabras clave: *Hipertensión arterial. Definición. Toma casual tensión arterial. MAPA. AMPA.*

INTRODUCTION

Hypertension (HT) is recognised both individually and in populations as one of the main risk factors for vascular damage and in consequence, organ damage: of the heart, kidneys and brain. The WHO, in a globalised, unified

morbimortality risk analysis has identified HT as the main cause of death and one of the main public health problems, greater than other vascular risk factors, such as smoking, hypercholesterolemia, and obesity,[1] even in developing countries.[2]

Over time, in spite of some improvements in knowledge, treatment and control of HT, the prevalence of patients with non-controlled hypertension continues to be high.[3-7] The most recent HT guides, concentrate on the decrease of overall vascular risk, and recommend an aggressive pharmacological treatment, with ever lower target blood pressure values, especially in specific populations, such as diabetics and patients with chronic kidney disease (CKD).[8-10] Treatment seems to be suboptimal.

In this "mad" race to achieve the lowest possible blood pressure values, we have forgotten a key factor, the measurement of blood pressure, the essential basis for the definition of HT. Casual measurement of HT is the most frequently performed test in a medical consultation, but care taken with the technique used is considerably neglected. In our routine, we forget that HT is a very labile haemodynamic parameter that varies from beat to beat, from morning to evening, from sleeping to waking, according to the season, sitting position or standing position. This variability requires that, for correct HT measurement during consultation, a strict method be followed, which unfortunately is only done on few occasions and, therefore, leads to mistaken diagnosis.

Conceptually, HT is defined as that value of blood pressure at which the beneficial effects of acting to control it (minus risks and costs) outweigh the risks and costs (minus benefits) of inaction. However, blood pressure has, at usually seen values, a continuous, gradual, consistent, independent and directly predictive relationship with stroke, coronary disease and progression of chronic kidney disease.[11, 12] There does not appear to be a limit below which there is no further risk reduction. Therefore, the search for a threshold that operatively defines HT is arbitrary, although it is necessary to specify a value at which to begin treating patients clinically, and it should be set at 140/90 mmHg[8,10] in guidelines, by consensus (Table 1).

There have been a series of significant advances over the last few years concerning the search for this value and the reliability of its determination, and, in consequence a correct definition of HT, which have led to a new approach to HT.

CORRECT CASUAL MEASUREMENT OF BLOOD PRESSURE DURING CONSULTATION

BP measurement during medical consultation has been and is the key for HT diagnosis, treatment and to obtain the benefits of a good control, decreasing vascular morbimortality and multiorgan damage. Most of the studies covering these areas have been based on isolated BP measurement during consultation.

However, this measure requires the application of a very precise method, and as it is an isolated measurement, in many cases does not represent the patient's real BP.[13] Small deviations of 5-10 mmHg are common when the patient's attitude or environment suffer small malfunctions that either accumulate or are not possible to overcome, related to the measurement itself, or the health system (waiting, time limitations, devices, motivation and training of medical or auxiliary personnel taking the measurements, etc.). Overestimating BP may lead to inappropriate treatment, with the consequent exposure to side effects, psychological effects due to a mistaken diagnosis and unnecessary costs.[14]

In spite of lacking in sensitivity and specificity and of assessing BP at a single point in time, it continues to be the initial reference value for all patients before classifying them as hypertensive or not hypertensive, and all our efforts must be directed to achieve an optimum measurement, and to use the information obtained in the best possible way. We frequently forget that BP measurement provides valuable information on four components, each one of different haemodynamic significance. Systolic BP (SBP), diastolic (DBP), pulse pressure (PP = systolic minus diastolic) and mean blood pressure (MBP = DBP + [SBP — DBP]/3). There is still uncertainty as to the relationship of these parameters, when taken in an isolated manner, and the prediction of cardiovascular risk. The Framingham Heart Study has shown that age plays an important role in the correlation between BP components and risk, and that the increase of BP correlates with a gradual displacement of predictors from DBP to SBP and PP. Of the 4 components of BP, only DBP has a non-lineal quadratic relation with cardiovascular risk. The evaluation of this risk can improve by applying a model that takes into account BP components with greater physiological significance than traditional individual ones (SBP, DBP). It is necessary to use PP, an indicator of arterial rigidity (pulsatile load), especially in isolated Systolic HT and pre-hypertension and of MAP, indicator of peripheral resistance and of cardiac output (constant flow load).[15] Currently, systemic assessment of this data is only done rarely and only during specialised exams.

To overcome the limitation of isolated BP measurement during medical consultation, we currently have two techniques available to measure BP outside current clinical practice, although they are difficult to apply in large population studies.

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) OVER 24 HOURS

Ambulatory BP monitoring (ABPM) over 24 hours is a technique that makes it possible to carry out multiple BP

Table 1. Definition and classification of blood pressure values according to JNC VII, 20038 and ESH/ESC, 2007[10] criteria

JNC VII (2003)			ESH/ESH (2007)		
Category	**SBP**	**DPB**	**Category**	**SBP**	**DPB**
Normal	<120	<80	Optimum	<120	<80
Pre-hypertension	120-139	80-89	Normal	120-129	80-84
			High normal	130-139	85-89
			Arterial hypertension		
Stage 1	140-159	90-99	Grade 1	140-159	90-99
Stage 2			Grade 2	160-179	100-109
			Grade 3	>180	>110
			Isolated systolic[a]	>140	<90

SBP: Systolic blood pressure (mmHg); DBP: Diastolic blood pressure (mmHg).

[a] Isolated HT, according to the ESH/ESC definition, can be classified in grades 1, 2 and 3, in the same way as systolic-diastolic HT

measurements during an individual's daily activity. In the best possible scenario, BP measured during medical consultation is the mean of 2-3 measurements, whereas with usual ABPM protocols, not only are mean values of 60-70 measurements obtained but also additional information on the circadian pattern, BP elevation on waking, BP variations over 24 hours, their relationship with medication or certain situations, tension load, evolution of heart rate, etc. Furthermore, ABPM decreases sensitivity to the reaction of alarm generated by BP measurement in a clinical environment, an aspect of especial interest in the elderly, in whom BP variability and reaction of alarm are frequently seen clinically. The reproducibility of BP values obtained by ABPM is much greater to those obtained during consultation. Values obtained by ABPM have a better correlation with target organ damage than isolated clinical measurement.[11]

Known indications for ABPM are, among others, white coat hypertension, resistance or poor efficacy of antihypertensive drugs, episodes of hypotension, considerable variability of BP during consultation, and between medical office and home, and discrepancies between BP and secondary organ damage. These indications of use have meant that ABPM, despite the high cost of the equipment, has been shown to be an effective technique to reduce the cost of pharmacological treatment of HT.

Although there is little comparative data and the results show discrepancies, the proportion of hypertensive patients that achieve a satisfactory control of BP is different according to whether BP is measured in the office (limit value: <140/90 mmHg) or with ABPM (limit value: <130/80 mmHg).[16] The Spanish register of ABPM, on a total of 12,897 patients with hypertension treated in primary care centres, shows that, at least, half of the patients diagnosed with HT are normotense when evaluated using ABPM (51.6%), in comparison with isolated casual BP measurement in the office (23.6%) and, what is also important, ABPM detected masked HT in 5.4%[17] of patients. When an analysis was performed of these mistaken estimates, it was seen that BP is more frequently underestimated in the elderly, women and obese patients, or when BP is measured in the morning, whereas it is overestimated in the young, men, non-obese patients, smokers or when it is measured in the evening.[17] Similar findings as to disparities in percentages of controlled hypertensive patients have been described in the elderly Spanish hypertensive population.[18] These results must be prudently interpreted, and it is necessary to be cautious when saying that we are controlling HT better than what the numbers obtained during medical visits indicate.[17]

The addition of ABPM to conventional measurement methods during consultation has added new complexity to the process of defining HT, since in the same individual significant differences can be detected between HT measurements during consultation and those outside the consulting offices, differences which have let to subclassifying hypertensive patients in different categories based on the variations in these measurements.

1. *True Normotension*. Normal BP with both methods, and, therefore, efficacy of antihypertensive treatment.
2. *True HT*. Patients with poor blood pressure control with both methods.
3. *«White coat HT", also known as «isolated HT during consultation" or "resistance to consultation"*. Hypertensive in the consulting office and normotensive with ABPM. Extensively studied, it is usually accepted that cardiovascular risk is low.[19,20]
4. *Masked HT, "isolated in the consulting office" or "inverted white coat"*. Patients that are normotensive in the consulting office and hypertensive outside, with ABPM[21] or with home blood pressure measurement.[22] Its

clinical importance is due to the fact that patients are not treated or are inappropriately treated until their condition is detected, and without being aware of it, could be exposed to cardiovascular complications or organ damage, causing unnecessary medical expenses. Bombelli, et al. found that prevalence was similar in men and women, and reported gradual decrease with age and with high BP on consultation visits. The absence of any association with left ventricular hypertrophy (LVH) in this study gives rise to doubt as to the real clinical significance of this phenomenon.[23]

The prevalence of the last two subgroups in the general population is relatively constant in scientific literature (15-20% white coat HT and 10-15% masked HT). Patients with masked HT have a greater probability of cardiovascular complications than patients with true normotensive BP, especially in elderly populations.[24,25] In the Spanish population, prevalence of white coat HT was 27.6% in the elderly, a higher percentage than that seen in other studies performed in populations of lower ages, while 7% of them had masked HTA.[18]

In the PAMELA study, carried out in 1,412 subjects followed for 10 years, it was shown that patients with white coat HT and masked HT were at greater risk of developing future persistent HT, in comparison with normotensive patients (OR: 2.51 and 1.78, respectively; $p < 0.0001$), with similar results based on home BP measurement.[25,26] Both conditions, therefore, cannot be considered innocuous phenomena, but are clinical conditions that require a certain diagnosis and follow-up.

ABPM is clearly indicated in patients with a probability of developing masked HT: > 60 years of age and with high normal SBP in the consulting office (130-140 mmHg), smokers, or men > 70 years of age,[27] as also in patients with normal high BP in the consulting office and a high risk of developing cardiovascular disease (multiple risk factors; evidence of target organ damage; associated morbidity, such as diabetes mellitus or chronic kidney disease, CKD), or with these conditions already diagnosed.

HOME BLOOD PRESSURE MEDICATION (HBPM)

The rapid spread of this method of BP registration has been promoted by several factors: Technical progress, widespread availability and simplicity of use of measuring devices, studies that support the importance of regular BP monitoring, the need to be able to count on the co-responsibility of the patient with hypertension for appropriate control and the recognition of the usefulness of official HT guides. Home BP self-medication (HBPM) is advisable in hypertensive patients who want to participate in their own treatment and, in fact, this is based on their own initiative and also diverse problems such as the use of non-validated devices and errors in measurement methods.

There is no standardised program for patient education for HBPM, but it is essential to recommend they purchase an appropriate device, and to teach them the correct method to measure BP.[28] BP must be monitored at home during the 7 days immediately prior to the visit to the medical office, with, at least, two morning and two evening measurements, and in all cases before drug administration. The BP that must be taken into account for a correct decision is the mean measurement of all these measurements once those taken on the first day are excluded. This scheme must be carried out during all HT phases: Confirmation, diagnosis, treatment and follow-up.[28] The scheme of registrations that must be carried out during the period between visits, and the autonomy of the hypertensive patient in dose adjustment, require major individualization, always with the object of preventing anxiety and unnecessary and compulsive medication.

Currently, all devices available for BP self-measurement, automated or semi-automated, use the oscillometric technique. These devices are widely publicised and sold in pharmacies and supermarkets, in general without any advice from a health professional. Only a few of these devices for self-measurement of BP which are available on the market comply with independent validation criteria. The European Society of Hypertension (ESH) (www.dableducational.org) and the British Hypertension Society (www.bhsoc.org) have established sites on Internet where it is possible to consult an updated list of validated devices for BP measurement.

The cut-off limits for accepted BP levels for conventional *sphygmomanometer*s cannot be directly extrapolated to ABPM, since studies in non-selected populations and in hypertensive patients have shown that BP outside the consulting office is underestimated. Reference values have yet to be defined. Current recommendations for threshold values are based on evidence from meta-analysis,[29,30] observational studies and clinical trials, as well as some guides.[31-34]

1. *Diagnostic Threshold*. Until further data in special populations is available, HT must be diagnosed by ABPM starting at levels of 135/85 mmHg in adults, the elderly and women (including pregnant women).
2. *Therapeutic Threshold*. The target value for home BP that must be achieved with antihypertensive treatment is currently unknown, it is being explored in the HOMED-BP (Hypertension Objective treatment based on Measurement by Electrical Devices of Blood Pressure Study) which is currently ongoing. At this point in time, it is necessary to take into account that small BP variations in the consulting office significantly influence the risk of appearance of cardiovascular events,[35,36] and that the reduction of BP in the consulting office translates into a parallel descent of BP at home. Based on this home-

consulting office relation in the effect of BP decrease,[37] a decrease of SBP of 2 mmHg during ABPM can mean a relative risk reduction of acute stroke of 20%, similar to what is obtained by a decrease of 3 mmHg in the consulting office. The application of experts' recommendations on HBPM in clinical practice requires a close interaction with primary care physicians, in all cases.

Since sufficiently powerful random studies are still pending, the available evidence so far supports the idea that the prognostic value of HBPM is equal or greater to isolated measurement in the consulting office.[38,39]

HOME BLOOD PRESSURE MEDICATION IN COMPARISON WITH AMBULATORY BLOOD PRESSURE MONITORING

The increase of ABPM and HBPM in daily clinical practice are conditioned by a series of factors: Banning of mercury in sphygmomanometers, lack of reliability of BP measurements in the consulting office, technical advances in automatic BP measurement, growing evidence that measurement outside the consulting office is a better way of evaluating cardiovascular risk, and growing recognition of the efficiency of ABPM and HBPM in the treatment of hypertensive patients.[40]

ABPM was the first technique outside the consulting office that demonstrated significant improvement in the management of hypertensive patients. However, its generalised indication has several limitations. High cost of measurement devices; need for training personnel to take measurements, and interference of the procedure with patients' habitual daily activities. HBPM has several advantages in comparison with ABPM, and furthermore, it is less costly, which supports the recommendations for its extensive use in clinical practice. These are complementary techniques, capable of providing very useful information on BP under different conditions and during different periods (Figure 1), and this is recognized by the 2007 Directives of the ESH for the measurement of BP.[13] Although in some studies no statistically significant differences were found between HBPM and ABPM during the day, in general, lower BP values were found with HBPM than with ABPM,[41-43] especially in children and adolescents.[44]

Cost and availability are two arguments that have great influence on the choice of BP measurement. BP measurement in the consulting office is cheaper than ABPM, and must be carried out during each visit to the physician. The use of ABPM in systematic clinical practice, is limited mainly to specific conditions, due to the cost of these devices and the need for qualified personnel to manage them. Home monitoring shares many advantages with ABPM, and according to some trials could be cost-effective, since the price of HBPM, paid by the patient themselves, does not limit their generalised use in clinical practice, at least in developed countries. Recently a WHO-ESH joint publication contained the specification for the use of HBPM devices in communities in which resources for health care are scarce, which may help to introduce an efficient way of controlling BP in these communities.[45] Decision making for diagnosis and treatment of HT based on ABPM is very efficient, in terms of savings of non-indicated drugs, decrease of number of visits to the consulting office and, if a better control of BP is achieved, prevention of complications due to hypertension.[46]

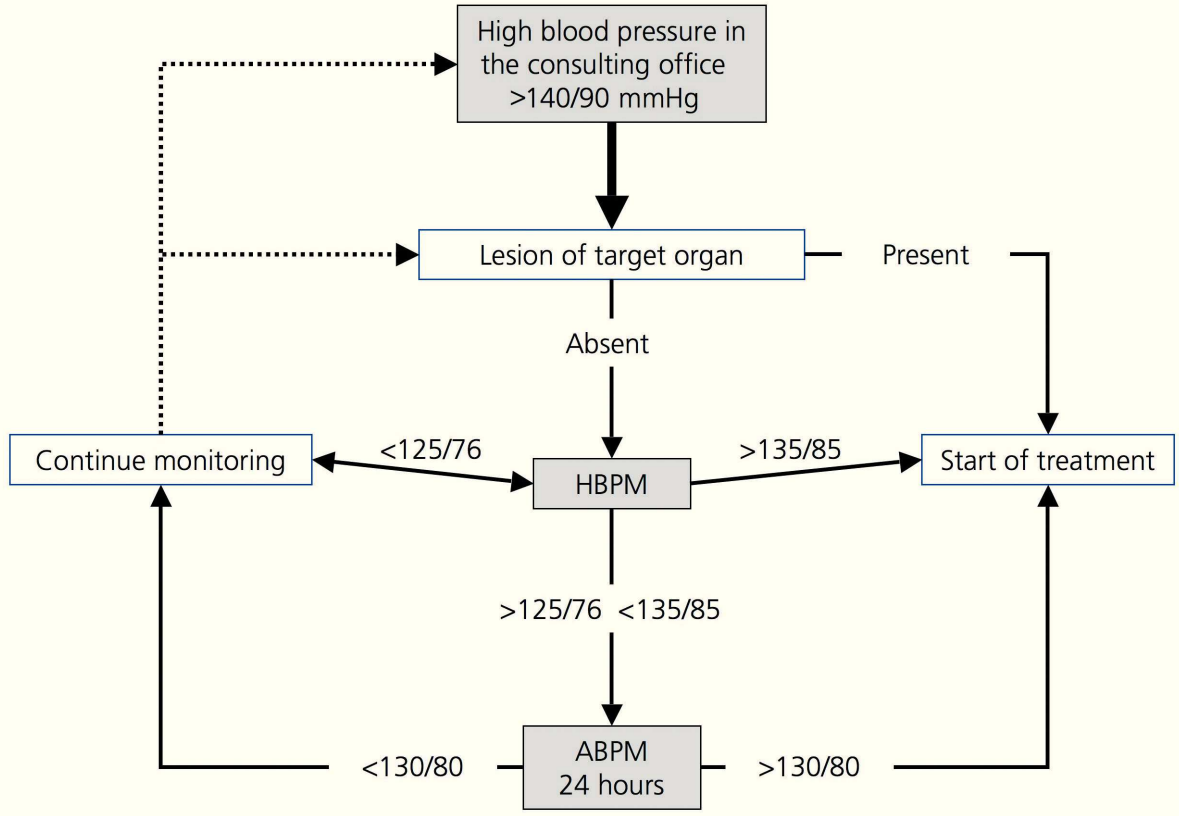
However, there are still many issues to resolve: Better use of all the information provided by correct BP and heart rate measurements; a better definition of reference values, diagnosis and treatment targets; promotion of an international standard protocol for the validation of BP measurement devices; role in the treatment of refractory HT, etc. Future trials of vascular risk should include BP measurement not only by means of conventional methods, but also by ABPM and HBPM.[47-52]

All this data are an indication that in future HT will be treated in a "virtual HT clinic" environment, using ABPM for the initial diagnosis and HBPM with a distance electronic link between patient and physician for maintenance and follow-up.

DEFINITION OF TREATMENT TARGET TO BE ACHIEVED IN HYPERTENSION

In high risk patients, the benefits of lowering SBP below 130 mmHg are centred in the reduction of stroke. The risk of acute myocardial infarction (AMI) is not affected by this limit, and cardiovascular mortality remains unchanged or even increases with greater reductions, behaving as a "J curve" phenomenon, especially in populations with atherosclerosis.[53,54]

A Cochrane systematic review of treatment targets of HT and morbimortality has shown that achieving values of <135/85 mmHg in a general hypertensive population does not provide any added benefit to prolong survival, or reduce the number of cases of stroke, angina, heart failure or CKD, in comparison with the standard target (>140-160/90-100 mmHg).[55] In elderly populations aggressive treatment is not justified (SBP <130 mmHg), and random studies are being carried out to demonstrate the sense in a target value of 130-150 mmHg.[56] Until we have results from specific randomised controlled studies, carried out correctly, the enthusiasm over the slogan "the lower the better" is not justified in the elderly, or in patients with reasonably controlled BP and the risk of stroke is low.



Adapted from Pickering TG. Hypertension 2008;52:1. ABPM: Ambulatory blood pressure monitoring; HBPM: high blood pressure self medication.

Figure 1. Algorythm to assess blood pressure based on one determination in the consulting office and with the support of ABPM and HBPM.

In view of the trials published over the last few years, the ESH reviewed its guide for HT management in 2007, calling attention to the series of very low target values, and while waiting for more evidence, modifying a series of recommendatons[57]:

1. In *all hypertensive patients*, drug treatment *must be started at levels >140/90 mmHg*. There is no evidence that it must be started pre-HT (BP of 130-139/80-89 mmHg).
2. In *any hypertensive patient*, it has been confirmed that there is sufficient evidence to recommend a target BP <140/90 mmHg, both in cases of moderate and high risk patients.
3. In the *elderly hypertensive patient* the target must be set because, even if advisable, there are no randomised studies that support a descent of SBP below 140 mmHg.
4. *High risk diabetic and hypertensive patients*. Previous recommendations of setting a target SBP<130/80 mmHg in these patients could be right, but it is not supported uniformly by available evidence.
5. *High normal BP not complicated by diabetes or prior cardiovascular events*. No proof is available to support the beneficial effects of drug treatment, except for a delay in the onset of HT.
6. *Diabetic patients with normal high BP without LOD* (microalbuminuria or proteinuria). Currently prospective trials do not support treatment with antihypertensive drugs.

To summarise, we must change the concept "the lower the better" for the paradigm "the sooner the better" and, if possible, the more vascular risk factors we can control the better. The aim of achieving optimum BP must not make us forget that the absolute individual risk of developing organ damage depends not only on BP levels, but also on the association of other vascular risk factors and associated clinical disorders. A change is necessary from programs centred in diagnosis and treatment of HT to planning a more efficient use of health resources and a global and real approach to vascular disease prevention associated with HT.[58] Little benefit is obtained from HT control, if our hypertensive patient, for example, has suffered HT for many years without

KEY CONCEPS

1. HT is an essential vascular risk factor and the main cause of death worldwide. However, its definition depends on an arbitrary limit of a very variable haemodynamic parameter, which, in most cases, is determined by an isolated measurement of BP in the consulting office, which is unreliable due to multiple circumstances. All this generates a core of uncertainty that must be swept away by using a strict method for BP measurement, which is only very rarely followed.
2. It is indispensable to have an optimum BP in all places and circumstances, and the measurement of all components, either isolated (SBP and DBP) or haemodynamic (pulse pressure, PP or mean arterial pressure, MAP).
3. The use during routine clinical exam of new techniques for measuring BP, such as ABPM and HBPM, are improving the reliability of BP measurement, which is a key factor for correct diagnosis and treatment of HT.
4. Improvements in BP register, together with new evidence in scientific literature, have lead to a review of the guides for HT treatment, rationalizing the approach to HTA, especially in relation to the targets aimed for when treating certain groups of patients with hypertension.

detection or control, already has established organ damage, continues to smoke, has an uncontrolled metabolic syndrome, etc.

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