

The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The Weapons Are Ready

Paolo Verdecchia and Fabio Angeli

Dipartimento Malattie Cardiovascolari, Ospedale R. Silvestrini, Perugia, Italy.

The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) has recently come to light in a short version. A complete version will soon be available. JNC 7 is the last attempt to bridge the big gap between the current availability of potent and well tolerated antihypertensive strategies and their poor implementation in the clinical practice. Some new and important features characterize the JNC 7 document. The aim of the new and challenging definition of «pre-hypertension» (BP 120-139/80-89 mmHg) is to sensitize the general population and health professionals to implement effective strategies for a healthier life in order to prevent hypertension and related cardiovascular disease as early as possible. Stage 3 hypertension has been deleted and merged with stage 2 (systolic ≥ 160 or diastolic ≥ 100 mmHg). BP levels to achieve with treatment («goals») are $< 140/90$ mmHg ($< 130/80$ mmHg in diabetics). To reach the goal, diuretics are recommended for initial treatment «in most subjects with stage 1 hypertension». However, combination of at least 2 drugs is recommended if initial BP is 20/10 mmHg higher than goal BP. Apart from the definition of pre-hypertension and the advice to begin therapy with diuretics in most patients with stage 1 hypertension, JNC 7 shares several positions with the hypertension guidelines recently released by the European Society of Cardiology and European Society of Hypertension. JNC 7 seems to dedicate limited space to stratify the level of cardiovascular risk in the individual subjects on the basis of the different combinations between BP levels and concomitant risk factors. In summary, JNC 7 is an updated and well equipped arsenal of formidable weapons against hypertension and its complications. The stage is now set for an hard task: their effective implementation in the clinical practice with the aim to decrease cardiovascular morbidity and mortality.

Key words: *Hypertension. Guidelines. Stroke. Myocardial infarction. Prevention.*

Correspondence: Dr. Paolo Verdecchia.
Ospedale R. Silvestrini. Dipartimento Malattie Cardiovascolari.
Via S. Andrea Delle Fate, s/n. Perugia. Italy.
E-mail: verdec@tin.it

Full English text available at: www.revespcardiol.org

Séptimo informe del Joint National Committee para la Prevención, Detección, Evaluación y Tratamiento de la Hipertensión Arterial: el armamento está a punto

Recientemente se ha publicado una versión abreviada del Séptimo Informe del Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). Dentro de poco tiempo estará disponible la versión completa. El JNC 7 es el último intento de eliminar la gran distancia que existe entre las estrategias antihipertensivas actuales, potentes y bien toleradas, y su escasa implementación en la práctica clínica. El documento JNC 7 contiene algunos datos nuevos e importantes. El objetivo de la definición del nuevo concepto de «prehipertensión» (presión arterial [PA], 120-139/80-89 mmHg) es la de sensibilizar a la población general y a los profesionales sanitarios para que apliquen, lo antes posible, estrategias efectivas dirigidas hacia una vida más sana a través de la prevención de la hipertensión y de la enfermedad cardiovascular relacionada con ésta. Se ha eliminado la hipertensión de fase 3 y se ha fusionado con la de fase 2 (presión sistólica ≥ 160 mmHg o presión diastólica > 100 mmHg). Los valores de PA a alcanzar con el tratamiento («PA objetivo») son los $< 140/90$ mmHg ($< 130/80$ mmHg en los diabéticos). Para conseguirlo, se recomiendan como tratamiento inicial los diuréticos «en la mayor parte de las personas con hipertensión en fase 1». Sin embargo, cuando la PA inicial es 20/10 mmHg superior a la PA objetivo, se recomienda el tratamiento de combinación con al menos 2 fármacos. Además de la definición de prehipertensión y de la recomendación de iniciar el tratamiento con diuréticos en la mayor parte de los pacientes con hipertensión en fase 1, el JNC 7 contiene diversas recomendaciones relativas a la hipertensión que han sido propuestas recientemente por la European Society of Cardiology y por la European Society of Hypertension. En el JNC 7 se dedica un espacio limitado a la estratificación del valor de riesgo cardiovascular en los pacientes, según diferentes combinaciones entre los valores de la PA y los factores de riesgo concomitantes. En resumen, el JNC 7 es un arsenal actualizado y bien equipado de armas extraordinarias frente a la hipertensión y sus complicaciones. Ahora queda por hacer lo más difícil: su implementación efectiva en la práctica clínica con el objetivo de disminuir la morbilidad y la mortalidad cardiovasculares.

Palabras clave: Hipertensión. Protocolos. Accidente cerebrovascular. Infarto miocárdico. Prevención.

INTRODUCCIÓN

Despite the growing awareness of the high burden associated with hypertension in terms of excess risk of morbidity and mortality worldwide,¹ situation is still nasty. In the U.S., awareness of hypertension among the general population increased from 51% to 73% from years 1976-1980 to years 1986-1991, but thereafter it leveled around 68% (years 1991-1994) and 70% (years 1999-2000). Of greater concern, rate of control of hypertension (blood pressure [BP] <140/90 mm Hg), which had markedly increased from 10% (years 1976-1980) to 29% (years 1988-1991), is now unexpectedly stagnant between 27% (years 1991-1994) and 34% (years 1999-2000).²

The seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), coordinated by the National Heart, Lung, and Blood Institute, has recently come to light in a short version¹ and a more complete version will be published soon.³ JNC 7 is a major challenge, more than appearing on the surface. It is essentially the last major attempt and effort to bridge the gap between the current availability of potent, accurately tested and well tolerated antihypertensive strategies and their poor and inadequate current implementation in the clinical practice.

Several parts of the JNC 7 document resemble prior JNC reports. However, some crucial points of the JNC 7 report deserve mention and even some criticism.

PRE-HYPERTENSION

Subjects with systolic BP 120-139 mm Hg or diastolic BP 80-89 mm Hg (the highest makes faith) are now labeled «pre-hypertensives» (Figure 1). Ironically, a perfectly healthy 19-year old subject with BP persis-

tently 120/80 mm Hg would not be considered «normal,» but «pre-hypertensive.» The concept of «pre-hypertension» clearly arises from the well established evidence of a linear, graded and continuous association between BP and cardiovascular risk without any evidence of a threshold from values of 115/75 mm Hg.⁴ It also comes from the Framingham evidence that a high-normal blood pressure (130-139 mm Hg systolic or 85-89 mm Hg diastolic) is associated with an increased risk of cardiovascular disease and future hypertension.⁵ In the mind of JNC 7 experts, emphasis on «pre-hypertension» is clearly aimed to sensitize general population and health professionals to implement effective and sustained strategies for a healthier life (smoking prevention or cessation, prevention or treatment of overweight, physical activity, etc.). However, in the mind of critics, «pre-hypertension» may be viewed as an unnecessary definition of «nearly disease» even in completely healthy subjects, which might generate anger, anxiety and depression, with potential influences even in the working and family environment. Just to make a comparison with a similar document, the recent European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines⁶ maintained the prior classification of normotension (systolic BP 120-129 mm Hg and diastolic BP 80-84 mm Hg) and high-normal BP (systolic BP 130-139 or diastolic BP 85-89 mm Hg). Probably, the term pre-hypertension would have been more acceptable if limited to subjects with high-normal BP.

STAGES 1 AND 2 ONLY

Stage 3 has been eliminated because the therapeutic strategies in stage 2 and 3 are essentially the same. Therefore, all subjects with systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg now belong to stage 2, which is the highest stage. By contrast, the ESC/ESH guidelines maintain grade 2 (systolic 160-179 or diastolic 100-109 mm Hg) and grade 3 (systolic ≥180 or diastolic ≥110 mm Hg).

TABLE 1. Classification of hypertension according to the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)² guidelines and the European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines⁶

Category	JNC VII			Category	ESC/ESH 2003		
	Systolic (mm Hg)		Diastolic (mm Hg)		Systolic (mm Hg)		Diastolic (mm Hg)
Normal	<120	and	<80	Normal	120-129	and	80-84
Prehypertension	120-139	or	80-89	High normal	130-139	or	85-89
Hypertension				Grade I	140-159	or	90-99
Stage I	140-159	or	90-99	Grade II	160-179	or	100-109
Stage II	≥160	or	≥100	Grade III	≥180	or	≥110

ROLE OF SYSTOLIC BP

JNC 7 recognizes that systolic BP is more important than diastolic BP as a cardiovascular risk factor, except perhaps in younger subjects. Progressive stiffening of large arteries is believed to be an important basic mechanism of the rise progressive in systolic and decrease in diastolic BP after age 55, with consequent widening of pulse pressure (PP) with age.^{7,8} A wide PP may thus reflect already diseased arteries, with adverse prognostic implications.^{7,8} In cross-sectional studies, PP showed a strong direct association with carotid atherosclerosis, left ventricular mass and white matter lesions detected by magnetic resonance imaging.⁹⁻¹¹ From a prognostic standpoint, an association has been noted in several studies between PP and risk of cardiovascular morbid events in different clinical settings and such association was independent of systolic and diastolic BP.¹²⁻¹⁴ Unfortunately, systolic BP control is more difficult to achieve than diastolic control, particularly in the elderly.

CARDIOVASCULAR RISK FACTORS

JNC 7 list several well established cardiovascular risk factors, which include also microalbuminuria or estimated glomerular filtration rate <60 ml/min. The statement is correct in view of the extensive evidence on the independent prognostic impact of microalbuminuria in patients with hypertension.^{5,16} However, at least in the short version published in JAMA,¹ little effort seems devoted to define the level of cardiovascular risk in the individual subject (risk stratification) on the basis of the different combinations between BP levels and concomitant risk factors. In contrast, the ESC/ESH document⁶ defines 5 levels of risk (average risk, low-added risk, moderate added risk, high added risk and very high added risk) on the basis of such combinations. For example, subjects with stage I hypertension would be at low-added risk in the presence of no other risk factors, moderate added risk in the presence of 1-2 other risk factors, high added risk in the presence of 3 or more risk factors, diabetes or target organ damage, or very high added risk in case of associated clinical condition (prior stroke, TIA, coronary artery disease, peripheral vascular disease or retinopathy stage III or IV). As discussed below, implications for treatment seems to be scarcely dependent on concomitant risk factors (apart from the case of diabetes) and mostly oriented on BP levels.

WHO NEEDS ANTIHYPERTENSIVE DRUGS

Subjects «not at goal» with lifestyle modifications should begin drug treatment. Goal means <140/90 mm Hg, with the notable exception of <130/80 in diabetics. Fortunately, the ESC/ESH document endorses

exactly the same goals. Of note, JNC 7 recommends drug treatment in non diabetic subjects with systolic BP \geq 140 mm Hg or diastolic BP \geq 90 mm Hg despite lifestyle modifications even in the complete absence of concomitant risk factors, as well as in the presence of only 1-2 risk factors. This sounds like a quite liberal approach to drug treatment. By contrast, the ESC/ESH document looks a bit more restrictive, by recommending drug treatment in subjects not at goal after at least 3 months of life-style measures in case of moderate added risk (1-2 risk factors in grade 1 hypertension, 0-2 risk factors in grade 2 hypertension), or not at goal after 3-12 months of life style measures in case of low risk (no risk factors in grade 1 hypertension).

WHICH DRUGS?

This is a crucial point. JNC 7 seems to be quite drastic on the surface, but a careful inspection of the entire document reveals flexibility. JNC 7 simply states that in subjects with stage I hypertension, thiazide diuretics should be used «as initial therapy for most patients with hypertension.» The rationale for such position comes from the low cost of diuretics and the evidence that «in most outcome trials including the recently published Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), diuretics have been virtually unsurpassed in preventing the cardiovascular complications of hypertension.» Critics may argue that «unsurpassed» does not mean «superior» and that the ALLHAT trials has several methodological shortcomings.^{17,18} An important shortcoming of ALLHAT was the forced association, by protocol, of lisinopril with atenolol, instead of a diuretic or a dihydropyridine calcium-antagonist (the usual choice in the clinical practice), in subjects resistant to monotherapy. Such policy inevitably led to favor chlorthalidone (which could add atenolol in a pharmacologically appropriate combination) and to punish lisinopril.

At variance with JNC7, the ESC/ESH document considers diuretics, beta-blockers, ACE-inhibitors, calcium antagonists and angiotensin II blockers as suitable drugs for the initiation and maintenance of therapy.⁶ Such a position is based on the lack of evidence of a clear superiority of one single class versus another in the major outcome trials. Notably, the ESC/ESH document adds the statement (box 11) that the choice of drugs will be influenced by many factors including the «cost of drugs.» Thus, the acute physician may interpret such a position (lack of superiority of one class versus another and cost of drug to be taken into account) as very similar, in its essential substance, to that expressed by the JNC 7 document in support of diuretics as first line agents.

Beyond the points of pre-hypertension and initial therapy with diuretics, JNC 7 and ESC/ESH show an

TABLE 2. Main similarities and differences between the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)² guidelines and the European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines⁶

	JNC VII	ESC/ESH 2003
Definition	Prehypertension: 120-139 o 80-89 mmHg	Normotensión: 120-129 and 80-84 mmHg High normal BP:130-139 or 85-89
Treatment	<p>Stage I:Thyazide type diuretic for most; may consider ACE-inhibitor, ARB, β-blocker,CCB or combination</p> <p>Stage II: 2-drug combination for most; Cusually thiazide type diuretic and, AC-inhibitor or ARB or β-blocker or CCB</p> <p>Compelling indications, Heart failure: diuretic, B-blocker, ACE-inhibitor, ARB aldosterone antagonist, Post MI: B-blocker,ACE-inhibitor, aldosterone antagonist, High CV risk: diuretic. B-blpocker, ACE-inhibitor, CCB;Diabetes all classes except aldosterone antagonists; Chronic renal disesease (ACE-inhibitor,ARB); Recurrentprevention: diuretic, ACE inhibitor</p>	<p>Diuretics, B-blockers,CCB suitable for the initiation and manteinance of therapy</p> <p>Need to use 2 or more drugs in combination in order to achieve goal BP</p> <p>Conditions favour ing the use: Heart failure: diuretics, B-blocker, ACE-inhibitor, aldosterone antagonist Post (MI B-blocker,ACE-inhibitor, aldosterone antagonist) Chronic renal disesease (ACE-inhibitor, ARB) a-blockers BPH, hyperlipidemia- B-blockers: pregnancy, tachyarrhythmias, CCB (Dihydropydieas) angina pectory, ISH, PVD, carotid atherosclerosis, elclerly subjects CCB (verapamil, diltiazem): angina carotid atherosclerosis, arrhythmias</p>
BP goal	< 140/90 (< 130/80 in diabetes)	< 140/90 (< 130/80 in diabetes)

apparent agreement over several points. Both recognize that combinations between two or more drugs are needed to normalize blood pressure in many patients. Here, JNC 7 introduces objective criteria by stating that if pre-treatment BP is >20/10 mm Hg above the goal, consideration should be given to begin treatment with 2 agents. Thus, JNC 7 clearly suggests that in all non-diabetic subjects with BP>160 mm Hg systolic or 100 mm Hg diastolic (as well as in diabetics with BP>150 mm Hg systolic or 90 mm Hg diastolic) treatment should begin with 2 drugs.

Another important area of substantial agreement between the JNC 7 and ESC/ESH guidelines regards the preferential indication for specific drugs even for initial therapy. As shown in figure 2, the «compelling indications» for specific antihypertensive drug mentioned by JNC 7² are not substantially dissimilar from the «conditions favoring the use»⁶ of specific drugs mentioned in the ESC/ESH document.

From a purely scientific, and not diplomatic, perspective, it is encouraging to realize that most positions on the diagnosis and treatment of patients with hypertension are not substantially different on the two sides of the ocean.

In conclusion, JNC 7 is an updated and well equip-

ped arsenal of formidable weapons against hypertension and its complications. The stage is now set for a hard task: their effective implementation in the clinical practice.

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