Joint National Committee VII and European Society of Hypertension/European Society of Cardiology Guidelines for Evaluating and Treating Hypertension: A Two-Way Road?

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During the first half of the past year, guidelines for hypertension management issued by the Joint National Committee (JNC VII) and by the European Society of Hypertension in conjunction to the European Society of Cardiology (ESH/ESC) have been published in major scientific journals. This article reviews the main features and elements of novelty of these authoritative recommendations. It also highlights the major agreements and disagreements between the two sets of guidelines and their implications for daily clinical practice.

Guidelines for nonpharmacologic and pharmacologic approaches to hypertension treatment were issued for the first time in the middle of the 1970s and periodically updated throughout the following years. This has been the case for the guidelines prepared by the American Committee chosen by the National Institutes of Health, which in 2003 saw their most recent published version (JNC VII) (1). This has been also the case for the European Society of Hypertension/European Society of Cardiology (ESH/ESC), which, although in the past have endorsed the guidelines prepared by the World Health Organization/International Society of Hypertension (WHO/ISH), in 2003 decided to draw up their own recommendations for the European countries (2). Both of these documents have raised interest among experts and clinicians, and a number of similarities and differences have been pointed out and become object of discussion. The present article critically addresses the main features of both guidelines, underlining whenever possible the clinical implication of these recommendations.

JNC VII and ESH/ESC Guidelines: A “Face to Face” Comparison

Major agreements between the two sets of guidelines include a number of important theoretical and practical issues. For example, both the JNC VII and the ESH/ESC Guidelines (1,2) recognize the benefits of antihypertensive treatment in terms of reduction in fatal and nonfatal cardiovascular events. They also agree on the BP measurement procedure as well as on the use and value of ambulatory BP monitoring and home BP readings. Finally, both of the guidelines convey on (1) the BP targets and thresholds for treatment; (2) the use of antiplatelet and lipid-lowering drugs, in conjunction to antihypertensive treatment; (3) the follow-up strategies; and (4) the value and indications of combination drug treatment.

A number of major differences exist between the two guidelines, and several reasons can be advanced for explaining the interest of primary care physicians and health providers for the differences rather than for the similarities between guidelines. Among them, a key one is represented by their economic impact, taking into account that some authors have indicated American guidelines as less costly than the European ones. Although a recent editorial clearly documented this not to be the case (3), other major differences of clinical relevance in the two sets of guidelines exist. General differences include, among others, the main scope of the two guidelines, which seems to be mainly prescriptive in the case of the JNC VII while informative and educational in the case of the ESH/ESC Guidelines. Other general differences refer to the type of the diagnostic procedures to be applied in the clinical practice. Indeed, they seem in the case of the American recommendations to be more simple and thus less expensive but also less adequate to detect the presence and/or the progression of the organ damage (1). This is reflected by the better and more comprehensive evaluation of target organ damage guaranteed by the ESH/ESC Guidelines (2), with obvious favorable implication for the therapeutic approach. A number of other important “diagnostic” and “therapeutic” differences characterize the two above-mentioned guidelines. Given their undisputed clinical relevance, they are discussed separately as follows.

Prehypertension

The JNC Guidelines have unified the BP categories previously defined as “high normal” and “normal” (1). They now call the condition with BP values between 120 and 139 mmHg systolic and 80 and 89 mmHg diastolic “prehypertension” and recommend for this state nonpharmacologic interventions. This
may be justified by the evidence that within this BP range, patients stand a high chance of moving to BP above 140/90 mmHg. However, it should be underlined that defining prehypertension in a large fraction of people who exhibit these BP values might cause anxiety as well as the request of more frequent visits and laboratory examinations, with an adverse impact on both patients’ health and social economic status.

Assessing Total Cardiovascular Risk

The JNC Guidelines do not recommend any quantification of the total cardiovascular risk, based on the degree of BP elevation, additional risk factors, diabetes, organ damage, and associated clinical conditions, as done by other guidelines (1,2,4). Again, the intention is good because assessment of total cardiovascular risk moves guidelines into a higher degree of complexity that may be too difficult to cope with by the practicing physician, yet this assessment may be necessary to take the most appropriate decision about a patient’s treatment. For example, only if patients are at high total cardiovascular risk should effective treatment be instituted quickly and drugs given at lower BP thresholds with the goal of achieving lower targets. Furthermore, only if the total risk is high are additional treatments based on lipid lowering (even at low or normal serum cholesterol levels) and antiplatelet drugs indicated (5,6). Quantification of total cardiovascular risk thus is a procedure that physicians must start using, and failure to recommend so by guidelines eludes their educational role. Total cardiovascular risk quantification is particularly helpful in the “prehypertension” category, which thus can be divided into widely diversified subgroups. That is, those who have a high or very high risk and in whom drug treatment is as necessary as in hypertensive patients; those who have a moderate risk and may benefit from life style changes; and those who have a low risk and do not need any active intervention whatsoever, including the nonpharmacologic one.

First Drug Choice

The JNC Guidelines (1) recommend a diuretic to be used in most hypertensive patients, thereby placing drugs such as β-blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, and angiotensin II antagonists in a subordinate position (7). We find it difficult to agree with this recommendation for several reasons. First, large-scale trials have shown treatment that is based on diuretics but also on β-blockers, ACE inhibitors, calcium antagonists, and angiotensin II antagonists to achieve cardiovascular protection in hypertensive patients (8,9). Second, in most comparison intervention trials, no difference has been found between conventional treatment (i.e., a treatment based on diuretics and β-blockers) and newer drugs on the primary outcome, yet the only two exceptions have not been in favor of conventional treatment, and diuretics lost, although to a marginal degree, a head-to-head comparison with ACE inhibitors in one trial (10). Third, meta-analyses of available trial data (9) suggest that some between-drug differences may exist with regard to prevention of specific cardiovascular diseases such as stroke, myocardial infarction, and heart failure, although not all in favor of diuretics as compared with other drugs. They further show, however, that no between-drug differences exist as far as cardiovascular morbidity, cardiovascular mortality, and total mortality are concerned. Except for a few cases, this is the only information of practical relevance because physicians must speak to their patients in terms of preventing overall morbidity and mortality and not of deciding which of some equally devastating events he or she wants to be more protected from. Fourth, the JNC Guidelines (1) surprisingly fail to acknowledge the potentially negative consequences of the alteration in electrolyte and metabolic profiles induced by diuretics, thereby making a selective use of the data provided by the trial that they take as the most important source of information, i.e., Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT) (11). In ALLHAT, patients who were treated with chlorthalidone showed serum potassium values <3.5 mEq/L four to five times more frequently than patients who were treated with amlodipine or lisinopril. This may be clinically relevant because in the Systolic Hypertension in the Elderly Program Study (12), chlorthalidone-induced serum potassium values <3.5 mEq/L was associated with loss of the cardiovascular protection offered by antihypertensive therapy. In addition, lower serum potassium values that accompany diuretic administration have been reported to increase the rate of sudden death (13), a phenomenon that has not been addressed in ALLHAT. Finally, in ALLHAT, diuretic-treated patients showed a 15 to 40% greater incidence of new-onset diabetes than patients who were given the other two drugs. This is a particular reason for concern because diuretics have shown a diabetogenic effect in several large-scale, prospective, controlled trials that have reported that over 3 to 5 yr, the number of new cases of diabetes is significantly less when patients are treated with ACE inhibitors, calcium antagonists, or angiotensin II antagonists rather than when they are treated with diuretics alone or in combination with β-blockers (Figure 1) (14–21). Because long-term follow-up of patients with treatment-induced diabetes has proved its association with an increased cardiovascular risk (22,23), this has to be taken into account when deciding how to start drug treatment of hypertension. In an elderly patient, the limited life expectancy may make the diabetogenic effect of diuretics (± β-blockers) less important than the need for obtaining early protection by an adequate BP reduction, which diuretics favor. In young or middle-aged patients, however, long-term exposure to an increased chance of becoming diabetic may remove the benefit of BP control and even reduce rather than increase patients’ protection against cardiovascular morbidity or fatal events. At the time when cardiovascular prevention is more and more linked to comprehensive interventions aimed at reducing the total cardiovascular risk (4), failure to consider this problem can hardly be condoned. This applies also to health providers whose wish to save immediately on drug cost has produced long-term negative consequences for cardiovascular prevention.

The diabetogenic effect of conventional treatment deserves a few further remarks. Forts, in ALLHAT (11), data were analyzed on an intention-to-treat basis. However, a considerable number of patients (>20%) did not follow the prescribed treatment regimen but took only or additional drugs that belong to the comparison classes. This makes it likely that on-treatment data would show an even greater difference of new-onset dia-
Assessing Subclinical Organ Damage

The JNC recommendations do not give particular importance to subclinical organ damage (1). This is in contrast with the European guidelines (2), which regard it as a key element for assessing both total cardiovascular risk and benefit of treatment. This is based on the consideration that (1) several measures of organ damage (echographic left ventricular hypertrophy, ultrasonographic assessment of carotid artery wall thickening, modest increases in serum creatinine [or reductions in calculated creatinine clearance]) and microalbuminuria represent a risk factor or marker for cardiovascular disease, (2) subclinical organ damage has a high prevalence in the hypertensive population and thus often can allow proper identification of high-risk patients, and (3) evidence is available that improvement in organ damage by treatment is accompanied by a more favorable prognosis (25,26). This improvement is the real goal of treatment in hypertensive patients who are young, middle-aged, and not at high risk, and in whom a BP reduction is pursued not for preventing an unlikely morbid or fatal event in the following few years but to avoid progression of organ damage that could emerge as an event many years later. Clinically validated measures of organ damage thus offer a long-term perspective that is missed if only evidence from trials is taken into account. Although valuable, this evidence is limited to high-risk patients and covers only a small fraction of life expectancy.

References


