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More: 17th European Meeting on Hypertension (ESH)

ESH '07: New Consensus Hypertension Guidelines From the European Society of Hypertension/European Society of Cardiology (ESH/ESC)

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Posted 09/17/2007

Presenting the New European Hypertension Guidelines

The second version of the guidelines for the management of arterial hypertension, produced jointly by the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC), were presented at this year's ESH conference in Milan, Italy. The guidelines represent the work of a joint task force co-chaired by Giuseppe Mancia, MD, PhD (University of Milan-Bicocca, Monza, Italy), for ESH, and Guy De Backer, MD, PhD (University of Ghent, Belgium), for ESC, and have been published in slightly different formats by the 2 organizations.^[1,2] These guidelines supersede the first ESH/ESC guidelines, published in 2003,^[3] and will be incorporated into the latest European Guidelines on Cardiovascular Disease Prevention in Clinical Practice, which will be released during the ESC's annual congress in Vienna, Austria (September 1-5, 2007).^[4]

The new hypertension guidelines are based on the same principles as the 2003 version, with the repeated aim of being educational, rather than prescriptive or coercive. As described by Prof. Mancia, they attempt "to offer the best and balanced recommendations via an extensive and critical review of the literature, but also to provide simple recommendations via condensed position statements."^[5] The data on which the guidelines are based come mainly from clinical trials, but observational and other data sources deemed to be of sufficiently high standard were also considered. Unlike guidelines such as the recent American Heart Association (AHA) recommendations for the treatment of hypertension,^[6] the European recommendations are not classified by level or strength of the evidence on which they are based. The authors felt that this was difficult to apply and could only be applied to therapeutic aspects, Prof. Mancia said.

Definition and Classification of Blood Pressure

The new guidelines use the same blood pressure classification as used in the 2003 version, which itself was based on the 1999 World Health Organization (WHO)/International Society of Hypertension (ISH) classification,^[7] and is similar to that in the sixth report of the Joint National Committee on Prevention, Detection, and Treatment of High Blood Pressure (JNC VI)^[8] rather than JNC 7.^[9]

This latest classification comprises categories of optimal, normal, and high-normal blood pressure, followed by 3 grades of hypertension, and a separate category for isolated systolic hypertension ([Table 1](#)). The 3 grades of hypertension correspond to mild, moderate, and severe hypertension, but these terms are not used, in order to avoid confusion with categories of total cardiovascular risk. Isolated systolic hypertension is graded as 1, 2, or 3 according to the systolic blood pressure (SBP) level, provided that the diastolic blood pressure (DBP) is < 90 mm Hg. When SBP and DBP fall into different categories, the highest category is used in assessing total cardiovascular risk.

As with the previous ESH/ESC guidelines, the authors have again omitted the "prehypertension" category, as defined in JNC 7,^[9] because they believe that it implies that a large part of the population is sick and that this raises anxiety and leads to unnecessary physician visits. The authors also felt that the population of people who would fall into a prehypertension category would be too diverse to allow treatment recommendations for the whole group.

Blood Pressure Measurement

Recommended blood pressure measurement procedures follow the latest ESH practice guidelines.^[10,11] Guidelines coauthor Stéphane Laurent, MD, PhD (Pompidou Hospital, Inserm U652, and University Paris Descartes, France) explained that although office blood pressure should be used as a reference, the guidelines acknowledge that ambulatory blood pressure monitoring (ABPM) may improve prediction of cardiovascular risk in both treated and untreated patients.^[12] They recommend ABPM particularly if office blood pressure measurements vary widely or are unexpectedly high in patients at otherwise low cardiovascular risk; in addition, self-measurement of blood pressure at home is encouraged.

The guidelines point out that blood pressure thresholds for the definition of hypertension differ according to the type of measurement used ([Table 2](#)). The assumption is that most office blood pressure is the traditional brachial measurement; measurement of central blood pressure needs further evaluation in large-scale studies to confirm its prognostic role before it can be recommended for routine use, the guidelines say.

Total Cardiovascular Risk

As before, one of the central themes that the guidelines stress is that the threshold for hypertension, and the need for drug treatment, should be considered as flexible, based on the level and profile of total (global) cardiovascular risk. In line with this, the 2003 classification of cardiovascular risk, as low, moderate, high, and very high to indicate the 10-year risk of cardiovascular morbidity and mortality, is also retained in the 2007 guidelines ([Table 3](#)).

In the assessment of cardiovascular risk, the new guidelines place particular emphasis on identification of target organ damage, and a separate section is devoted to searching for subclinical organ damage. The guidelines note that hypertension-related subclinical alterations in several organs indicate progression in the cardiovascular disease continuum, increasing the risk beyond that due to the simple presence of risk factors, and they recommend measuring for the possible presence of organ damage at various intervals throughout treatment.

The list of renal markers of organ damage has been expanded. Estimates of the creatinine clearance by the Cockcroft-Gault formula^[13] or glomerular filtration rate by the Modification of Diet in Renal Disease (MDRD)^[14] are recommended as more precise assessments of cardiovascular risk in renal dysfunction. Assessment of microalbuminuria is now considered essential in routine testing because it predicts both renal outcomes and cardiovascular events, and urinalysis by dipstick testing is easy and relatively straightforward to carry out, Prof. Mancia said.

Further measurements added to the list of markers of subclinical organ damage include carotid-femoral pulse wave velocity (> 12 m/sec) -- although this technology is not widely available -- and ankle-brachial blood pressure index (< 0.9). Echocardiography is recommended, and a finding of concentric left ventricular hypertrophy is identified as the cardiac structural parameter that most increases cardiovascular risk.

The metabolic syndrome is not regarded in the guidelines as a "pathogenetic entity" but rather as representing "a cluster of risk factors often associated with high blood pressure which markedly increases cardiovascular risk," ie:

- Blood pressure \geq 130/85 mm Hg;
- Low high-density lipoprotein cholesterol: < 1.0 mmol/L (40 mg/dL) in men; < 1.2 mmol/L (46 mg/dL) in women;
- High triglycerides: > 1/7 mmol/L (150 mg/dL);
- Altered fasting glucose: 5.6-6.9 mmol/L (102-125 mg/dL); and
- Abdominal obesity: waist circumference > 102 cm in men; > 88 cm in women.

Antihypertensive Treatment

The guidelines recommend that all patients should be counseled to adopt lifestyle changes, where appropriate; recognizing, however, that compliance is low and blood pressure response variable, the guidelines also recommend close follow-up and urge that drug treatment should be initiated "in a timely fashion" ([Table 4](#)). They emphasize a "flexible threshold" for initiating drug treatment, which should be \geq 140/90 mm Hg for all hypertension patients and < 140/90 mm Hg in high-risk patients, while stressing that drug treatment should never be delayed unnecessarily, especially in patients at higher level of risk.

Drug Therapy Recommendations

In his presentation of the guidelines' recommendations for antihypertensive drug therapy, Prof. Mancia stressed that they reconfirm the conclusion of 2003 that most of the benefit of antihypertensive treatment is due to blood pressure lowering per se and is largely independent of the drugs or class of drugs employed. Thus the guidelines go on to recommend, either as monotherapy or in combination, thiazide-type diuretics (as well as chlorthalidone and indapamide), calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and beta-blockers -- all of which are deemed able to "adequately lower blood pressure and significantly and importantly reduce cardiovascular outcomes."

Regarding beta-blocker as a first-line therapy, the European guidelines differ from the recently released UK national hypertension guidelines update, which removed beta-blockers from consideration as first-line therapy, relegating them to fourth-line treatment only.^[15] Prof. Mancia and the other ESH/ESC guidelines authors believe that the UK decision was unjustified, being mistakenly based on the results of the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA)^[16] in which the combination of a diuretic plus a beta-blocker was less effective in reducing events -- but only, these authors believe, because of a smaller achieved blood pressure reduction. However, these new European guidelines do advise against the use of beta-blockers in patients with metabolic syndrome or at high risk for diabetes.

The guidelines stipulate that the choice of specific drugs or drug combinations should take into account the following considerations:

1. Patient's previous experience with particular drug class(es);
2. The effects of particular drugs on the specific details of a given patient's cardiovascular risk profile;
3. Presence of subclinical organ damage, cardiovascular disease, renal disease, or diabetes;
4. Presence of other disorders that may limit use of particular antihypertensive drug classes;
5. Possible drug interactions;
6. Cost of drugs (but never a consideration over efficacy, tolerability, or protection of the patient);
7. Preference for drugs that have a 24-hour effect with once-daily administration; and
8. Continued attention to side effects.

Prof. Mancia emphasized that because many patients will need to take more than 1 drug over the remaining course of their lifetime, the emphasis on the first-choice drug is often futile. "A vast array of effective and well-tolerated combinations are available," he said. The guidelines recommend a 2-drug combination as initial treatment in patients presenting with grade 2 or 3 hypertension or with high or very high total cardiovascular risk. Fixed combinations are suggested to simplify treatment and improve compliance.

The following 2-drug combinations are recommended because they "have been found to be effective and well tolerated":

- Thiazide-type diuretic and ACE inhibitor;
- Thiazide-type diuretic and ARB;
- CCB and ACE inhibitor;
- CCB and ARB;
- CCB and thiazide-type diuretic; and
- Beta-blocker and CCB.

The "time honored" combination of a thiazide-type diuretic plus a beta-blocker, "although still valid as a therapeutic alternative," should be avoided in patients with the metabolic syndrome or a high risk for diabetes, the guidelines advise.

Special Patient Subsets

Antihypertensive treatment approaches are outlined for special conditions, such as in the elderly or patients with renal dysfunction, diabetes mellitus, metabolic syndrome, cerebrovascular disease, coronary heart disease, and heart failure. Guidelines coauthor Roland E. Schmieder, MD (University of Erlangen-Nürnberg, Germany) outlined new treatment recommendations for patients with the metabolic syndrome (ACE inhibitors, ARBs, CCBs), diabetes mellitus (ACE inhibitors, ARBs) and glaucoma (beta-blockers). [17] ARBs and ACE inhibitors are recommended for prevention or recurrence of atrial fibrillation. All blood pressure-lowering agents are considered appropriate in patients with previous stroke, and ARBs are added to the list of recommended drugs in patients with previous myocardial infarction (along with beta-blockers and CCBs) and heart failure (along with diuretics, beta-blockers, and ACE inhibitors). Treatment of associated risk factors is also covered in the guidelines.

The stated primary goal of treatment is "to achieve maximum reduction in the long-term total risk of cardiovascular disease." Target blood pressures are set as > 140/90 mm Hg in all hypertensive patients and < 130/80 mm Hg in diabetic and high/very high-risk patients

Comments

Invited discussant Lars H. Lindholm, MD, PhD (Umea University, Umea, Sweden), current President of the International Society of Hypertension (ISH) and coauthor of new ISH/World Health Organization (WHO) guidelines to be published shortly, commended the new European guidelines for being "comprehensive and well written and free from speculation." However, Prof. Lindholm, who is a well-known critic of beta-blockers in hypertension,[18-20] criticized their inclusion as first-line treatment, noting that recent guidelines, such as those produced in the United Kingdom[15] and by the AHA,[6] do not include beta-blockers as first-choice antihypertensive treatment. He suggested that the ESH/ESC guidelines list so many groups of patients in whom beta-blockers would be inappropriate that "it might

have been wiser to take them off the list." Prof. Lindholm also questioned the cost of implementing the guidelines, which, he noted, recommend many visits and work-ups.

A second discussant, Suzanne Oparil, MD (University of Alabama at Birmingham School of Medicine), current President of the American Society of Hypertension (ASH), praised the scholarship of the guidelines, while also expressing reservations about their complexity. For primary care physicians it might be better to focus on blood pressure, the most easily modifiable cardiovascular risk factor, rather than including all risk factors and the metabolic syndrome, she suggested. She also noted that in the United States, guidelines cannot omit grading of recommendations according to level of scientific evidence, as in the European guidelines.

Discussion about the divergence between the European and UK guidelines has continued. The British Hypertension Society has recommended that its members continue to follow the current UK guidelines produced by the National Institute for Clinical Excellence (NICE) rather than adopt the European guidelines.^[21] In the July issue of the British journal *Heart*, Jan A. Staessen, MD, PhD (University of Leuven, Leuven, Belgium) and Eoin O'Brien, MD, PhD (The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Ireland), an ESH/ESC guidelines coauthor, made a plea for harmonization of European hypertension guidelines.^[22] "The international opinion leaders know each other and should be able to come together to produce an international consensus guideline on hypertension, which would relieve practitioners from the burden of identifying the differences in policies between the guidelines," they said. "Realistically, we know that international consensus is unlikely, but surely European agreement should be possible, which begs the question as to why there have to be British guidelines within the context of the European Union."

Table 1. Definition and Classification of Blood Pressure Levels

Category	Systolic (mm Hg)	Diastolic (mm Hg)
Optimal	< 120	< 80
Normal	120-129	80-84
High normal	130-139	85-89
Hypertension:		
Grade 1 (mild)	140-159	90-99
Grade 2 (moderate)	150-179	100-109
Grade 3 (severe)	≥ 180	≥ 10
Isolated systolic hypertension*	≥ 140	< 90

*Isolated systolic hypertension graded (1, 2, or 3).

Table 2. Blood Pressure Thresholds for Definition of Hypertension According to Type of Measurement

Type of Measurement	SBP (mm Hg)	DBP (mm Hg)
Office or clinic	140	90
24-hour	125-130	90
Day	130-135	85
Night	120	70
Home	130-135	85

DBP = diastolic blood pressure; SBP = systolic blood pressure

Table 3. Stratification of Cardiovascular Risk

Other Risk Factors, Subclinical Organ Damage or Disease	Blood Pressure				
	Normal	High normal	Grade 1 hypertension	Grade 2 hypertension	Grade 3 hypertension
No other risk factors	Average risk	Average risk	Low added risk	Moderately added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
≥ 3 risk factors, metabolic syndrome, subclinical organ damage or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established cardiovascular or renal disease	Very high added risk	Very high added risk			

Table 4. Initiation of Antihypertensive Treatment

Other Risk Factors, Subclinical Organ Damage or Disease	Blood Pressure				
	Normal	High normal	Grade 1 hypertension	Grade 2 hypertension	Grade 3 hypertension
No other risk factors	No blood pressure intervention	No blood pressure intervention	Lifestyle changes for several months, then drug treatment if blood pressure uncontrolled	Lifestyle changes for several weeks, then drug treatment if blood pressure uncontrolled	Lifestyle changes +immediate drug treatment
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks, then drug treatment if blood pressure uncontrolled	Lifestyle changes for several weeks, then drug treatment if blood pressure uncontrolled	Lifestyle changes +immediate drug treatment
≥ 3 risk factors, metabolic syndrome, subclinical organ damage	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes +drug treatment	Lifestyle changes +drug treatment	Lifestyle changes +immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + drug treatment			
Established cardiovascular or renal disease	Lifestyle changes +immediate drug treatment	Lifestyle changes +immediate drug treatment	Lifestyle changes +immediate drug treatment	Lifestyle changes +immediate drug treatment	Lifestyle changes +immediate drug treatment

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Disclosure: Linda Brookes, MSc, has disclosed no relevant financial relationships.
