EDITORIAL

Divergence between the new guidelines for arterial hypertension

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Arterial hypertension is an essential risk factor, inducing an accelerated atherosclerosis with major consequences: myocardial infarction, stroke, chronic kidney disease or peripheral artery disease. Diagnosis, evaluation and management become permanent objectives for an efficient hypertension control.

Multiple clinical trials have demonstrated that antihypertensive treatment and the normalization of blood pressure have reduced the rates of mortality and morbidity by cardiovascular complications. The optimal range for blood pressure or therapeutic targets for hypertension control are still a matter of controversy, probably due to the complex structure of the population.

New American ACC/AHA 2017[1] or European ESC/ESH 2018[2] Guidelines have not accomplished a scientific reconciliation in the very complex approach to arterial hypertension. The essential differences between the two Guidelines are summarized below:

1. Definition and classification of arterial hypertension
2. Therapeutic targets and indications for fixed-dose combinations of drugs
3. Cardiovascular risk evaluation
4. Blood pressure control in the elderly
5. Management of isolated systolic hypertension.

(1) DEFINITION AND CLASSIFICATION OF ARTERIAL HYPERTENSION

A major controversy between the American and the European involves the definition and classification of arterial hypertension. ACC/AHA define the normal range for blood pressure under 120/80 mmHg, while the high normal is between 120-129/<80 mmHg. The American Guidelines also classify arterial hypertension into two stages: stage I with values between 130-139/80-89 mmHg, and stage II with levels higher than or equal to 140 mmHg for systolic blood pressure and 90 mmHg for diastolic blood pressure[1].

By comparison to the American Guidelines, ESC/ESH do not lower the threshold for the definition of arterial hypertension[2], Thus, for the European, arterial hypertension starts from 140/90 mmHg. An interesting observation is that if for the ESC/ESH levels such as 130-139/85-89 mmHg are high normal, for the ACC/AHA they signify stage I hypertension. The European Guidelines maintain the classification of hypertension into 3 grades. Grade III signifies levels higher than or equal to 180/110 mmHg[1,2].

The reduced threshold for defining hypertension in the American Guidelines is based on the SPRINT trial (*Systollic Blood Pressure Intervention Trial*)[3]. The SPRINT trial included 9361 hypertensive patients aged >50 years, (22% were over 78 years old, 28% had chronic kidney disease) with cardiovascular risk (except for patients with diabetes or stroke, who were not included). Subjects were randomized to intensive antihypertensive treatment, targeting a systolic blood pressure lower than 120 mmHg, or standard therapy, with a therapeutic target lower than 140 mmHg. Patients who obtained levels under 120 mmHg had a 25% drop in cardiovascular events, and mortality was reduced by 27 % after 5 years of treatment. The analysis of the SPRINT trial lead to the conclusion that a systolic

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blood pressure under 120 mmHg is associated with a significant reduction in cardiovascular events and mortality[3].

The decision of the European Guidelines to keep the definition for arterial hypertension (higher than or equal to 140/90 mmHg) is mainly based on the HOPE-3 trial (*Heart Outcomes Prevention Evaluation, Blood pressure and cholesterol lowering in persons without cardiovascular disease at intermediate risk*)[4]. HOPE suggests that antihypertensive therapy in patients with a blood pressure under 140/90mmHg is not associated with a decrement in cardiovascular events (less than 1%). The HOPE-3 trial included 12705 subjects at intermediate cardiovascular risk, without cardiovascular disease, with a follow-up period of 7 years.

Following the revision of the definition for hypertension by the ACC/AHA, its prevalence rises from 34% to 63%[5]. The reclassification of blood pressure (stage 1 by ACC/AHA) will significantly increase cardiovascular risk in these patients, who thus become hypertensive. The American Guidelines will uncover more hypertensive patients and will recommend lifestyle changes or even the initiation of therapy in those in stage I, although the mortality rate in these subjects is not different from that of normotensives[5].

(2) THERAPEUTIC TARGETS AND INDICATIONS FOR FIXED-DOSE COMBINATIONS OF DRUGS

The ACC/AHA Guidelines indicate the same therapeutic targets in patients over 30 years of age and older than 75: less than 130/80 mmHg[6,7]. This conclusion is also derived from the analysis of the SPRINT trial[3], underlining the results of decreasing fatal or nonfatal cardiovascular events. At the same time, it is emphasized that patients with a blood pressure between 130-139 mmHg have a 1.5 – 2 times higher risk of coronary events or stroke when compared with those with an arterial blood pressure under 120 mmHg[3].

European Guidelines recommend starting therapy when blood pressure increases above 140/90 mmHg, and the reduction should not be to lower than 120/70 mmHg (according to age and target organ damage)[2,4]. The ESC/ESH Guidelines indicate the initiation of drug therapy by single-pill combination. The ACC/AHA still considers initial monotherapy, when the therapeutic target should not be lowered by more than 20/10 mmHg. Fixed-dose combinations as initial treatment may be more efficient in controlling blood pressure, given that their effect is synergistic.

(3) CARDIOVASCULAR RISK EVALUATION

European as well as American Guidelines recommend that cardiovascular risk evaluation is an important instrument coordinating the start and intensity of antihypertensive therapy. Managing hypertensive patients should include treating modifiable risk factors, along with treating hypertension. Cardiovascular risk is calculated by mathematical equations, including classic risk factors, (cholesterol, blood pressure, diabetes, smoking, gender, age) in subjects without known cardiovascular disease.

American Guidelines propose calculating cardiovascular risk based on cohort studies: Framingham, Atherosclerosis risk in communities, Cardiovascular health study, Coronary artery Risk Development etc, including African Americans, in order to predict the risk of fatal or nonfatal cardiovascular events[1]. The European Guidelines bases the estimation of cardiovascular risk on the SCORE system (*Systematic Coronary Risk Evaluation*), developed following the analysis of the European population, only taking fatal risk into account.

Treatment initiation or lifestyle changes are considered when the 10-year risk of cardiovascular events exceeds 10%. European, as opposed to American Guidelines, introduce the concept of very high risk (the very high or high cardiovascular risk being additional to the cardiovascular risk calculated by the European SCORE system)[2,8,9].

Very high risk is defined by the existence of documented cardiovascular disease (even if asymptomatic) or by the presence of diabetes mellitus, chronic kidney disease, severe arterial hypertension or familial hypercholesterolemia[2]. Also, the ESC/ESH include target organ damage in this concept: left ventricular hypertrophy, microalbuminuria, arterial stiffness etc[2]. The introduction of the very high risk concept associated to the cardiovascular risk score offers a superior prognostic assessment and monitoring of the morphopathophysiologic evolution of target organ damage.

(4) MANAGEMENT OF ARTERIAL HYPERTENSION IN THE ELDERLY

American Guidelines recommend a therapeutic target of under 130/80 mmHg in the elderly, even older than 80 years of age. This indication is also based on conclusions from the SPRINT study[3], showing that in patients over 75 years old, a reduction in blood pressure under 120 mmHg has diminished fatal or nonfatal cardiovascular events[1]. The European Guidelines recommend a

blood pressure target of 130mmHg (targeting levels under 140mmHg) in the elderly aged 65-80 years de, while in those older than 80 years the target is still under 130 (targeting levels under 140mmHg, if tolerated).

In the SPRINT trial[3], although mortality by cardiovascular events has significantly decreased (cu 25%), the side effects of reducing blood pressure under 120 mmHg occurred more frequently (syncope, kidney failure, electrolyte abnormalities etc.)[10]. Thus, in the American trial, the incidence of arterial hypotension has increased by 66% in subjects older than 65 years treated with calcium channel blockers[10,11].

"The Milan Geriatrics 75%" trial[12,13] has demonstrated that the fall in the risk of mortality in hypertensives over 75 years of age was associated with higher blood pressure levels - 165 mmHg systolic, and 85 mmHg diastolic[7,12]. The side effects of an aggressive therapy are much more accentuated in the diabetic hypertensive elderly patients (diabetics were not included in the SPRINT trial).

(5) MANAGEMENT OF ISOLATED SYSTOLIC HYPERTENSION.

The ACC/AHA Guidelines for arterial hypertension do not approach the subject of isolated systolic hypertension. It is more frequent in the elderly, but also in young people, especially male. The definition is a systolic blood pressure higher than 140 mmHg, with a diastolic blood pressure lower than 90 mmHg. It is essentially a hypertension that may be extrapolated to stage I hypertension with systolic levels between 140-159 mmHg, but with normal diastolic levels.

The target is lowering the systolic blood pressure under 140 mmHg[2]. It is important to diagnose this type of hypertension, as these subjects exhibit cardiovascular risk. Thus, patients with isolated systolic hypertension have a similar cardiovascular risk to patients with high normal blood pressure levels[14]. In time, patients with isolated systolic hypertension develop systolic and diastolic hypertension, too[15].

CONCLUSIONS

The American and European academic societies' Guidelines for arterial hypertension include recommendations that are both similar and significantly divergent at the same time. These disagreements in approach change both the prevalence of arterial hypertension, and the therapeutic approach, including treatment initiation and target levels.

Do these differences benefit the complex and efficient management of the hypertensive patient? How could an agreement be reached between the recommendations of the two Guidelines? This paradigm will probably find a solution in personalized medicine. Young patients with hypertension and no comorbidities should be intensively treated to prevent the development of target organ damage, the American Guidelines being a strong resource in this respect. The elderly with hypertension, frail and with coronary or cerebral comorbidities, in which the myocardial or brain perfusion depend on blood pressure levels, should be approached non-aggressively, and the more conservative European Guidelines could offer a pragmatic solution.

Conflict of interest: none declared.

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