ARTERIAL HYPERTENSION: THE PRINCIPLES OF ITS TREATMENT ACCORDING TO THE GUIDELINES OF THE EUROPEAN ASSOCIATION OF HYPERTENSION - 2023

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Abstract

Arterial hypertension remains the most common, easily identifiable, and reversible risk factor for coronary artery disease, myocardial infarction, heart failure, ischemic and hemorrhagic cerebrovascular accidents, decline in cognitive functions, renal failure, aortic dissection and diseases of the peripheral arteries. The asymptomatic nature of arterial hypertension in a significant part of patients delays diagnosis, makes it more difficult for patients to adapt to lifestyle modification, regular medication and periodic follow-up. At the time of diagnosis, the assessment of organ damage caused by hypertension, assessment of cardio-vascular risk and other associated diseases should be done. On the basis of arterial pressure values, organ damage caused by hypertension, assessment of cardiovascular risk, associated diseases, the age group of the patient, the hypertension treatment strategy will be built, where the number of drugs to be started, the type of treatment will be determined of them, the arterial pressure values that must be reached and the time that must be reached are determined. In hypertensive patients, the reduction of arterial pressure values to the specified values significantly reduces major cardiovascular events such as myocardial infarction, ischemic and hemorrhagic cerebrovascular accidents, heart failure and mortality from all causes also shows a protective effect against asymptomatic heart damage and kidneys and prevents the decrease of cognitive functions and dementia. Drug treatment of hypertension with two or more drugs combined in one tablet is recommended.

Keywords: Target organs, cardiovascular risk, antihypertensive therapy.

HIPERTENSIONI ARTERIAL: PRINCIPET E TRAJTIMIT SIPAS UDHERREFYESVE TE SHOQATES EUROPIANE TE HIPERTENSIONIT - 2023

Abstrakt

Hipertensioni arterial mbetet faktori i rrezikut më i zakonshëm, lehtësisht i identifikueshëm, dhe i rikthyeshëm për sëmundjet e arterieve koronare, infarktin e miokardit, insufiçiencën kardiake, aksidentet cerebrovaskulare ishemike dhe hemoragjike, rënien e funksioneve konjitive, sëmundjen renale, diseksionin e aortës dhe sëmundjen e arterieve periferike. Natyra asimptomatike e hipertensionit arterial në një pjesë të konsiderueshme të pacientëve, vonon diagnozën, e bën më të vështirë përshtatjen e pacientëve me modifikimin e mënyres së jetesës, marrjen e rregullt të mjekimit dhe ndjekjen periodike të tyre. Në momentin e diagnostikimit

duhet bërë vleresimi i dëmtimit të organeve target, të shkaktuar nga hipertensioni, vlerësimi i riskut kardio-vaskular dhe sëmundjet e tjera shoqëruese. Mbi bazën e vlerave të presionit arterial, dëmtimit të organeve të shkaktura nga hipertensioni, vlerësimit të riskut kardio-vaskular, sëmundjeve shoqëruese, grupmosha e pacientit, do të ndërtohet strategjia e trajtimit të hipertensionit, ku përcaktohet numri i barnave që do të fillohet trajtimi, lloji i tyre, përcaktohen vlerat e presionit arterial që duhet të arihen dhe koha që duhet të arihen. Në pacientët hipertensivë, ulja e vlerave të presionit arterial në vlerat e përcaktuara, ul në mënyrë të rëndësishme eventet madhore kardiovaskulare: si infarkti i miokardit, aksidentet cerebrovaskulare ishemike dhe hemoragjike, insufiçiencën kardiake dhe vdekshmërinë nga të gjitha shkaqet, gjithashtu tregon efekt mbrojtës ndaj dëmtimeve asimptomatike të zemrës dhe veshkave dhe parandalon uljen e fuksioneve kognitive dhe demencës. Rekomandohet trajtimi medikamentoz i hipertensionit me dy ose më shumë barna të kombinuara në një tabletë.

Fjalë kyçe: Organet target, risku kardio-vaskular, antihipertensivët.

Introduction

Hypertension is the most prevalent cardiovascular disorder in the world, and it remains a global problem and the situation is getting worse. The world's population is "aging" and age is the most common risk factor for hypertension. Most hypertensive subjects are diagnosed with primary or essential hypertension. Essential hypertension is a hereditary syndrome that reflects a series of pathological abnormalities, which lead independently or together to an increase in blood pressure. Although secondary causes exists in a small percentage of hypertensive subjects, again they represent a large number of patients. Secondary forms of hypertension account for only a small part of the overall prevalence of hypertension, which is mainly due to primary hypertension. However, their true prevalence is not precisely known, because the available data may be confounded by the selection of studies reported in the literature, the number of undiagnosed cases, and the different definition of secondary forms of hypertension (1,2).
Hypertension is a major cardiovascular risk factor. So, ischemic heart disease is twice as frequent in these subjects, while in 60% of cases with heart failure the only cause is considered high blood pressure, while it's responsible for 50% of cases with Ischemic Insult and in over 80% of cases with hemorrhagic stroke (8). Estimation of total cardiovascular risk is easy in specific subgroups of patients, such as those with a history of existing cardiovascular disease, diabetes melitus, coronary artery disease, or single highly elevated risk factors. In all these situations, the total cardiovascular risk is high or very high, requiring intensive measures that reduces this risk (9). However, a large number of patients with hypertension do not belong to any of the above categories and their identification in low, moderate, high or very high risk requires the use of models to estimate the total cardiovascular risk, so we are able to judge the therapeutic method in accordance with them (9). A further importance is the identification of asymptomatic target organ damage, while asymptomatic alterations associated with hypertension in some organs indicate progression in the installation of cardiovascular disease, which significantly increases the risk beyond that caused by the simple presence of risk factors (1).

Epidemiology

Hypertension is the most prevalent cardio-vascular disorder in the world and according to the WHO, it affects 1.28 billion adults aged 30–79 years worldwide (1), two-thirds living in low- and middle-income countries. The average prevalence of hypertension in adults aged 30-79 years has been reported to be 34% in men and 32% in women (2). In younger ages (<50 years), hypertension is more prevalent in men, while in older age categories (>65 years) it is more prevalent in women(3,4). Systolic arterial pressure increases progressively with age while diastolic arterial pressure increases until the age of 50-60 years, followed by a short period of stability and then we have a subsequent slight decrease. This results in an increase in the difference between systolic and diastolic arterial pressure with age (3).

Definition and classification of hypertension

According to previous 2018 European(5,6,7) and current international guidelines, hypertension is defined based on repeated office values of systolic arterial pressure above 140 mmHg and/or diastolic above 90 mmHg. This definition is arbitrary and has mainly a practical purpose to simplify the diagnosis and decisions for the management of hypertension. In this context, the above threshold values of arterial pressure correspond to the level at which the benefits of intervention exceed those of inaction.

Table 1. Arterial pressure staging

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120-129	and	80-84
High normal	130-139	and / or	85-89
Stage 1 hypertension	140-159	and / or	90-99
Stage 2 hypertension	160-179	and / or	100-109
Stage 3 hypertension	≥180	and / or	≥110
Isolated systolic hypertension	≥140	and	<90
Isolated diastolic hypertension	<140	and	≥90

In addition to the staging of hypertension, which is based on arterial pressure values, we also distinguish the stages of hypertension as follows (1):

Stage 1 : Uncomplicated hypertension (without organ damage caused by hypertension or cardiovascular disease, but including chronic kidney disease stages 1 and 2)

Stage 2 : Presence of organ damage caused by hypertension or stage 3 chronic kidney disease or diabetes.

Stage 3 : Presence of cardiovascular disease or stage 4 or 5 chronic renal disease.

Hypertension and cardiovascular risk assessment

There is a continuous relationship between increased arterial pressure and the risk of cerebrovascular accidents, coronary artery disease, heart failure, and the development and progression of chronic kidney disease (8). This applies to all ages and ethnic groups. It is recommended to evaluate the total cardiovascular risk in every hypertensive patient because of its importance in the management of hypertension (9).

Table 2. Cardiovascular risk according to stage and stage of hypertension

Hypertension disease staging	Other risk factors, HMOD, CVD or CKD	BP (mmHg) grading			
		High-normal SBP 130–139 DBP 85–89	Grade 1 SBP 140–159 DBP 90–99	Grade 2 SBP 160–179 DBP 100–109	Grade 3 SBP ≥ 180 DBP ≥ 110
Stage 1	No other risk factors[a]	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to moderate risk	Moderate to high risk	High risk	High risk
Stage 2	HMOD, CKD grade 3, or diabetes mellitus	Moderate to high risk	High risk	High risk	Very high risk
Stage 3	Established CVD or CKD grade ≥4	Very high risk	Very high risk	Very high risk	Very high risk

	<50 years	60–69 years	≥70 years
	<2.5%	<5%	<7.5%
	2.5 to <7.5%	5 to <10%	7.5 to <15%
	≥7.5%	≥10%	≥15%

Complementary risk estimation in Stage 1 with SCORE2/SCOR2-OP

Abbreviations: CKD chronic kidney disease, CVD cardiovascular disease, HMOD hypertension-mediated organ damage.

Treatment

Lifestyle modification

Adapting a healthy cardiac lifestyle is an important approach to prevent or delay the onset of hypertension, to reduce high blood pressure values, to reduce cardiovascular risk, increase the effectiveness of drug treatment and reduce the number of necessary drugs for blood pressure control(10). The most important and effective lifestyle interventions that have shown a reduction in cardiovascular morbidity and mortality are weight loss, salt reduction, increased potassium intake, regular physical activity, reduced alcohol consumption, smoking cessation, improvement of stress control, reducing exposure to noise and polluted air. Lifestyle modification should be done at every stage or stage of hypertension (11).

Drug treatment

Antihypertensive drugs

Blockers of the renin-angiotensin system:

- Angiotensin-converting enzyme inhibitors (ACEi) such as enalapril, ramipril
- Angiotensin receptor blockers (ARBs) such as valsartan, olmesartan
- Renin inhibitors such as aliskiren, which is no longer used in some European countries.

Calcium channel blockers (CCBs)

- Dihydropyridine CCBs such as amlodipine, lercanidipine
- Non-dihydropyridine CCBs such as verapamil, diltiazem

Diuretics

- Thiazides / thiazides like (T/TL Diuretic) such as hydrochlorothiazide / chlorthalidone, indapamide
- Loop Diuretics such as furosemide, torasemide
- Potassium sparing agents such as amiloride, triamterene

Mineralocorticoid receptor antagonists (MRAs) such as spironolactone, eplerenone
Beta blockers (BBs) such as metoprolol bisoprolol
Alpha 1 blockers such as doxazosin
Centrally acting drugssuch as methyldopa, moxonidine
Vasodilators such as hydralazine, nitrates
Angiotensin and neprilysin receptor inhibitors (ARNIs) such as valsartan / sacubitril which is approved as an antihypertensive in China and Japan
The following five classes are recommended as first-line drugs for the treatment of hypertension, ACEi, ARB, CCB, T/TL diuretics, BB(9). The selection of these five classes is based on the following criteria(1):

1. A proven ability to lower arterial pressure as monotherapy
2. Given that they reduce morbidity and mortality
3. A favorable tolerance and safety profile

Selection of drugs for the treatment of hypertension

According to the guidelines of the European Association of Hypertension 2023, for the most efficient treatment of hypertension, it is suggested to follow these recommendations (1):

1. In most patients, the treatment should start with two drugs combined in one tablet to improve the speed, efficiency and predictability in the control of arterial pressure(9,12,13).
2. Although some two-drug combinations may be used, the preferred two-drug combinations should be an ACEi or ARB with a CCB or a thiazide/thiazide-like diuretic(1,9).
3. A beta blocker can be used at any step of the combination with any of the other first-line classes or in special cases(14).
4. Initial monotherapy is recommended for very high-risk patients with normal to high blood pressure as well as for very elderly and physically weak patients. It may also be considered in low-risk patients with stage 1 hypertension, with systolic blood pressure <150 mmHg(1,15).

5. A combination in one tablet containing an ACEi or ARB + CCB + thiazide/thiazide-like diuretic should be used if combinations of two drugs do not achieve arterial pressure control (at maximum tolerated doses) and if BBs are not indicated.
6. Regardless of the initial choice of treatment, in the end most patients should be on combined treatment, using the combination in one tablet when possible.

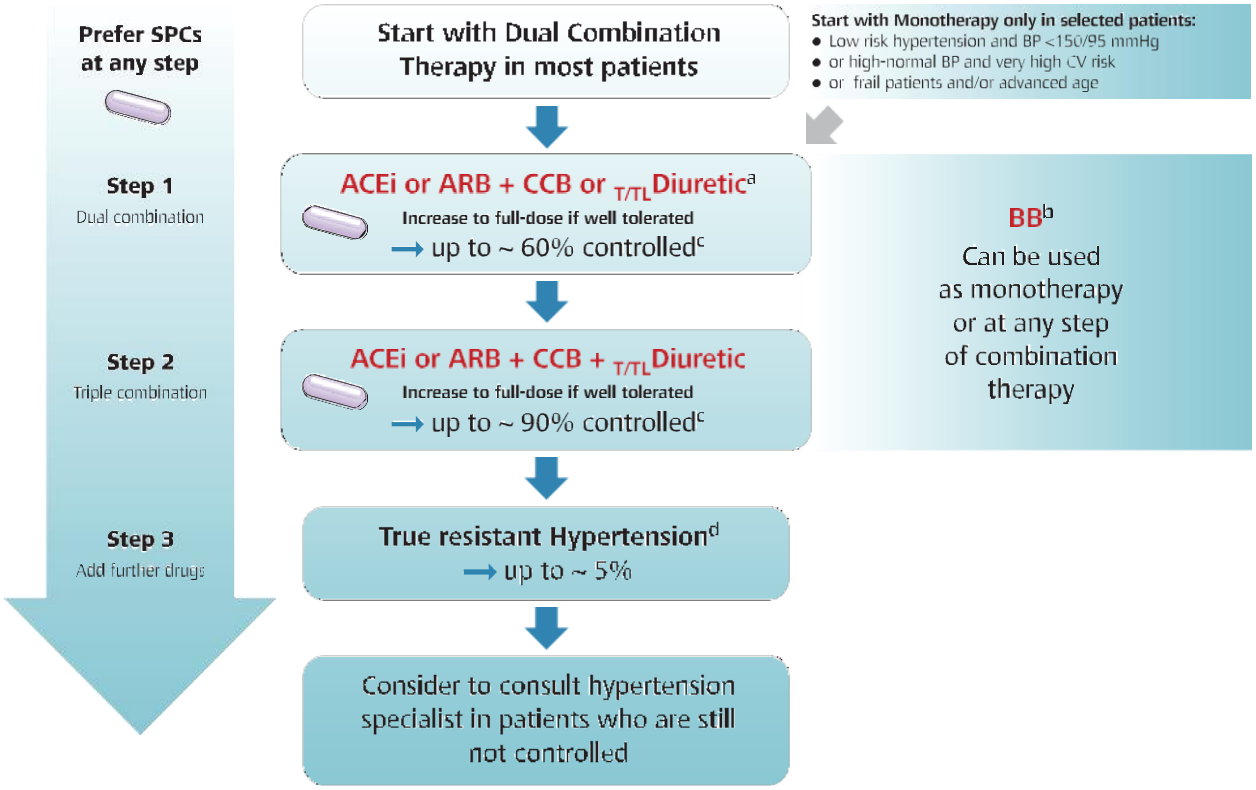
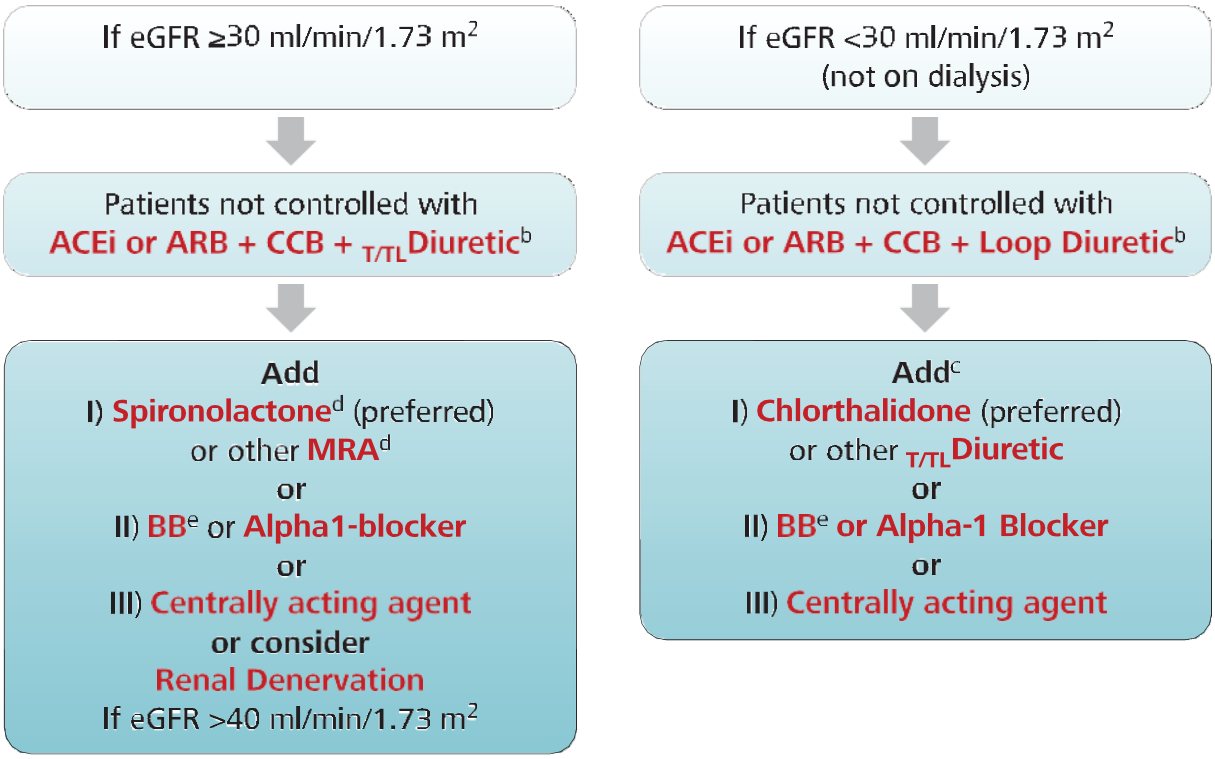


Figure 1. General strategy of arterial pressure treatmentin hypertensive patients

Hypertension resistant to medication

Hypertension is defined as drug-resistant when appropriate lifestyle measures and treatment with optimal or better-tolerated doses of three or more drugs (a thiazide / thiazide-like diuretic, an ACEi or ARB, and a CCB) fail to reduce arterial pressure measured in the office < 140 / 90 mmHg(9). Improper control of arterial pressure must be confirmed by measurements outside the office that show uncontrolled values of arterial pressure during 24 hours (≥ 130 / 80 mmHg). Regular intake of medication and exclusion of secondary hypertension are necessary to determine true resistant hypertension (1).
In patients with resistant hypertension, the fourth line of treatment should be a MRA, spironolactone (16). When MRAs are not tolerated or contraindicated, doxazosin or a centrally acting drug can be used as an alternative (17).

Figure 2. The strategy of reducing arterial pressure in resistant hypertension



If eGFR is <30 ml /min/1.73 m², loop diuretics are the first line instead of thiazide / thiazide-like diuretics in the treatment of hypertension (18).

Renal denervation

Renal denervation can be considered as an alternative treatment of resistant hypertension in patients with eGFR > 40 ml /min/1.73 m² in whom medical control of arterial pressure has not been achieved(19).

Conclusion

Hypertension remains a silent killer. We need to know very well the pathophysiology, its clinic, in order to go as soon as possible to the correct diagnosis, which guides us towards the right treatment, at the right time. This will reduce the complications of hypertension, i.e. damage to the target organs, reducing the cardiovascular morbidity and mortality.

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