Cardiovascular and Metabolic Science www.ancam.org.mx

Vol. 33 Suppl. 3
July-September 2022

doi: 10.35366/105184

The detection and study of patient with high blood pressure

Detección y estudio del paciente con hipertensión arterial

José Manuel Enciso-Muñoz, MD* Rafael Olvera-Ruiz, MD‡ Alfredo Manuel Patiño-Llamas, MD§

Keywords:
High blood pressure, paraclinical studies in high blood pressure, cardiovascular risk.

Palabras clave:
Hipertensión arterial, estudios paraclínicos en hipertensión arterial, riesgo cardiovascular.

ABSTRACT

High blood pressure (HBP) is the most important cardiovascular risk factor for cardiovascular disease. Patients with uncomplicated HBP without target organ damage are usually asymptomatic. This leads to significant underdiagnosis of HBP, which contributes to a great extent to the poor control of the hypertensive population, which increases likelihood for complications. In this review, we summarize the clinical presentation of HBP, as well as the role of physical examination, laboratory, and complementary studies as well as the impact of these in the diagnosis of HBP. We also assess the role of HBP in mediating cardiovascular risk, cardiovascular outcomes and pathophysiological changes which lead to impaired vascular and cardiovascular function in patients living with HBP.

RESUMEN

La hipertensión arterial (HTA) es el factor de riesgo cardiovascular más importante para las enfermedades cardiovasculares. Los pacientes con HTA no complicada y sin daños en los órganos diana suelen ser asintomáticos. Esto conduce a un importante infradiagnóstico de la HTA, que contribuye en gran medida al mal control de la población hipertensa, lo que aumenta la probabilidad de complicaciones. En esta revisión, resumimos la presentación clínica de la HTA, así como el papel de la exploración física, el laboratorio y los estudios complementarios, y el impacto de éstos en el diagnóstico de la HTA. También evaluamos el papel de la HTA en la mediación del riesgo cardiovascular, los resultados cardiovasculares y los cambios fisiopatológicos que conducen al deterioro de la función vascular y cardiovascular en los pacientes que viven con HTA.

INTRODUCTION

High blood pressure (HBP) is a cardiovascular disease (CVD), which in turn becomes one of the so-called main cardiovascular risk factors (CVRF), in such a way that it is studied and treated with this double role. Diagnosis of HBP is made with numerical variables, which has given rise to definitions and classifications that vary depending on the criteria of the organizations that are dedicated to their study or their geographical location and have even evolved by modifying the cut-off points to establish the diagnosis according to current epidemiological data and the supervening investigations of its deleterious effects. It is important to establish that its etiopathogenesis is multifactorial.

HBP took a relevant interest during the current COVID-19 pandemic, with proliferating articles about its interaction with COVID-19 disease in 2 main lines:

1. The association between COVID-19 and RAS inhibitors. This raised because there was concern that ACE2, which is upregulated by RAS inhibitors, could promote the proliferation of SARS-CoV-2 and enhance its capability for infection. Fortunately, Matsuzawa et al. clearly demonstrated that RAS inhibitors could be beneficial for the prevention severe forms of COVID-19 patients with HBP.[1]
2. Another hot topic considers that patients with HBP has been identified as the

* Hospital San Agustín. Zacatecas, México, Miembro GREHTA.
‡ Hospital Regional «Dr. Valentín Gómez Farías», ISSSTE. Guadalajara, Jalisco, México, Miembro GREHTA.
§ Hospital General ISSSTE. Zacatecas, México, Miembro GREHTA.

How to cite: Enciso-Muñoz JM, Olvera-Ruiz R, Patiño-Llamas AM. The detection and study of patient with high blood pressure. Cardiovasc Metab Sci. 2022; 33 (s3): s190-s196. https://dx.doi.org/10.35366/105184

most common comorbidity in COVID-19 patients and has shown an association with worse outcomes.[2]

A dramatic consequence of the times of this pandemic has been the regression in the detection and care of CVD, especially the study of population with HBP.[3] In this chapter we address the study of the hypertensive patient as well as the significance of HBP in cardiovascular risk (CVR).

High blood pressure patient clinic

HBP is the most important cardiovascular risk factor for acute coronary syndrome and chronic coronary syndrome, as well as heart failure, renal failure, and peripheral arterial insufficiency. HBP is very common worldwide and has been attributed as leading cause of death, underlining the estimate that said figure will increase by 50% in the next 20 years. It is therefore important to know the clinical presentation of the hypertensive patient.

Clinical manifestations of high blood pressure. Patients with uncomplicated HBP without target organ damage are usually asymptomatic. This leads to significant underdiagnosis of HBP, which contributes to a great extent to the poor control of the hypertensive population, which increases likelihood for complications. Because of this, HBP has been defined as a *silent killer*.[4] Within a minority of patients with HBP who manifest symptoms, headache is the most common manifestation, but it is more in those who know the diagnosis than in those who have the same level of blood pressure but are not aware that they are hypertensive. Stewart et al. reported a 17% prevalence of headaches in unaware hypertensives versus 71% in known hypertensives. In this context, headache appears to be more related to anxiety than to high blood pressure. Cooper et al. observed that the prevalence of headache was similar among patients with diastolic blood pressure of 95 mmHg and among those with 125 mmHg. Weiss et al pointed out that headaches were equally prevalent among hypertensive individuals unaware of their condition and in normotensive individuals. Furthermore, headaches reported during ambulatory blood pressure monitoring were not associated with concomitant increases in blood pressure.[5]

Comparing the symptoms between untreated hypertensive and normotensive patients of similar age, Bulpitt et al. observed a higher prevalence of morning headache, blurred vision, instability, depression and nocturia in the former. In a meta-analysis of 97 prospective randomized placebo-controlled trials, including 24,000 patients, reported that the prevalence of headache was reduced by lowering blood pressure without being related to the type of antihypertensive drug used, which implies that HBP is a reversible cause of headache and that different antihypertensive medications prevent a significant proportion of headaches. The headache is usually fronto-occipital and sometimes wakes the patient up in the early hours of the morning. In severe HBP, occipital headache is more constant and is one of the first symptoms which alerts the patient.

Other manifestations of HBP include epistaxis, tinnitus, dizziness, palpitations, and fatigue. It is useful to know if there has been sexual dysfunction prior to antihypertensive treatment, a topic that is often excluded from medical interviews and which later appears during treatment. Erectile dysfunction may be present in about one third of untreated hypertensive patients and is probably also related to their underlying vascular disease and can be considered one of the first manifestations of endothelial dysfunction. The presence of nocturia should also be interrogated, which can be due to various causes such as benign prostatic hypertrophy, sleep apnea, but it can also mean loss of the ability to concentrate urine, an early sign of kidney disease.[6]

Physical examination of patients with high blood pressure

In most patients with uncomplicated primary HBP, general inspection will not reveal any characteristic signs that differentiate it from a healthy person with normal blood pressure. Anthropometric measurements including weight, height, hip and waist circumference should be performed on all patients, which are essential and useful for detecting abdominal

obesity, which is considered a cardiovascular risk factor independent of body weight.

Blood pressure measurement. It is useful to measure blood pressure in both arms with the standard technique on the first visit. They should be similar, although if there is a time lag between the two measurements there may be differences between 5 and 10 mmHg. If the difference between the arms is greater than 15 to 20 mmHg in the systolic, there may be an atherosclerotic plaque in the circulation of the arm that registers a lower pressure number. The arm with the highest value should always be used for clinical controls.

Ocular fundus. Not very useful in most patients with mild HBP, but the presence of arterial crossings suggests chronicity. Hemorrhages, exudates, and papilledema associated with elevated blood pressure suggest severe end-organ damage and a poor prognosis unless therapy is instituted promptly.

Cardiac exam. Ectopic beats are not uncommon in hypertensive patients, especially if they have left ventricular hypertrophy. Atrial fibrillation may also be found which is of the utmost importance, and heart rhythm disorders must be immediately documented. There may be physical findings of cardiomegaly with strong apical impulse, the second aortic sound is accentuated. A fourth sound is found when there is little compliance of the left ventricular wall, in this context, it is most frequently due to left ventricular hypertrophy. If there is a third sound, it suggests left ventricular dysfunction.

Peripheral pulses. Helpful to evaluate peripheral arterial disease and rule out coarctation of the aorta. Palpation and auscultation of the carotids should also be evaluated to rule out arrhythmias and murmurs that indicate atherosclerotic plaques at that level or irradiation of heart murmurs, as is the case of aortic stenosis.

Abdomen. It is important to auscultate it to rule out murmurs that suggest renal artery stenosis and to palpate it to rule out masses as in polycystic kidney disease. Vigorous pulsations of the aorta may be normal in the young but suggest an abdominal aortic aneurysm in the elderly.[7]

Complementary studies

Also called «paraclinical» studies, they try to complement the most precise information possible in the study of the hypertensive patient. Inappropriately they are often called routine studies, understanding the term routine as the custom, or acquired habit of

Table 1: Comprehensive diagnostic approach

Indispensable		**Optional** (Subsequent or individualized)
Complete blood count		Transthoracic echocardiogram
Serum glucose and HbA1c		Microalbuminuria
Creatinine		Thyroid profile
	←	**Out-of-office blood pressure monitoring**
General urine test		Thorax X-ray
Complete lipid profile		Carotid ultrasound
Serum potassium and sodium		
Electrocardiogram		
Liver function tests	→	

Modified from Am Coll cardiol 2017;23976;DOI:10.1016/j.jacc.2017.07.745, where we propose transferring out-of-office blood pressure monitoring to those that are essential, be it 24-hour ambulatory (arrows) or home self-monitoring according to protocols previously established in the previous chapter of this document. In the same way, liver function tests could be considered as optional and individualized, whose utility in a generalized way could not be so essential, would increase the cost to the patient and are not widely available in our environment.

Table 2: Etiology and way of study.

Condition	Screening test
Chronic kidney disease	Glomerular filtration rate
Aortic Coarctation	Angiotomography
Cushing's syndrome	Dexamethasone suppression test
Pheochromocytoma	Metanephrines in 24-hour urine.
Renal vascular renovascular disease	Renal US with Doppler renal arteries
Primary hyperaldosteronism or Conn syndrome	Aldosterone in 24-hour urine and levels renin/aldosterone
Thyroid/parathyroid disease	Serum TSH and parathyroid

TSH = thyroid-stimulating hormone.

doing something in a certain way, which does not require having to reflect or decide. This implies a practice that over time develops almost automatically, without the need to use reasoning, and implies a practice, without the need intellectual exercise. By putting the word routine before it describes an irrational, biased and tendentious action, not free from certain pecuniary and dichotomous interests, which deviates from the primary academic-scientific interest of studying and establishing the individual pathophysiological mechanisms that will guide the making of the best therapeutic decisions and continue subsequently with the study and follow-up of each patient individually. It is probably better to define them as «basic tests».

Not indicating and not studying basic tests, also represents a highly objectionable failure by the treating physician, lacking interest in the precision of the individual pathophysiological mechanisms of his patient, it is a liable omission. Initiating and continuing treatments in this way, in addition to being improper, irresponsible, will result in poor decisions and poor control of the disease and its complications. The fundamental idea to obtain from paraclinical studies is to have a sufficient idea of the cardiometabolic context in which the patient with HBP finds himself. The American College of Cardiology in 2017 suggests the studies summarized in *Table 1*.

Each of the above studies, both those considered essential and optional, has its relevance and widely documented justification, since any anomaly in each of them modifies important variables that influence blood pressure and should be at the values closest to those desirable for good control of high blood pressure.

Another important purpose with paraclinical studies is the assessment of the possible damage to the target organ because of the multi-organ affectations of HBP, for which it is always recommended to search intentionally for those affectations that constitute the complications themselves, both those that show clinical and subclinical evidence. Thus, when the clinical review and the basic studies establish suspicion of involvement of one or several organs due to HBP or the suspicion of secondary HBP, the following studies have been recommended, which are summarized in *Table 2*.

A recurring theme is the case of the so-called resistant HBP, which is very useful to rule it out. Blood pressure monitoring outside the office in its two aspects, the 24-hour outpatient and home self-monitoring, should always be considered in these patients the possibility of secondary HBP. Frequent causes of resistant HBP include obstructive sleep apnea syndrome (OSAS) should be investigated, chronic kidney disease, renal artery stenosis, whether congenital or atherosclerotic, and infrequent in addition to what is mentioned in the previous table and especially in minors 30 years old coarctation of the aorta or brain tumor.

OSAS and sleep-disorders of breathing deserve special attention due to their frequency, not only do they raise BP, but they also

significantly increase the risk of cardiovascular events. During the awakenings or microarousal episodes, episodes of angina, acute myocardial infarction have been described. Also, OSAS can stimulate heart failure, arrhythmias, and conduction disorders. On the other hand, an association of this syndrome has been described, as well as its severity, with left ventricular hypertrophy, even after adjusting for the BP value. Obesity is a condition associated with patients with OSAS, HBP in general, and resistant HBP since these subjects require more antihypertensive drugs and the probability of achieving adequate control decreases. Compulsory studies include polysomnography, which consists of recording brain activity, breathing, heart rate, muscle activity and blood oxygen levels while sleeping. It is a test indicated for the study of different sleep disorders that is performed at night. Finally, in reference to paraclinical studies, we must mention advances in the study of **vascular function**, which we must have in mind because they indicate the future in the study of the patient with HBP *(Figure 1)*.

Resistant arterial hypertension, cardiovascular risk, and outcomes

Get your facts first, and then you can distort them as much as you please.
Mark Twain

HBP is defined as office blood pressure (BP) record ≥ 140/90, home BP monitoring ≥ 135/85, or ambulatory BP monitoring ≥ 130/80. Cigarette smoking, diabetes, and dyslipidemia are major modifiable risks factors for cardiovascular disease (CVD), there are several mechanisms that induce and increase the cardiovascular risk. In Mexico, HBP is the twelfth cause of death, even though it is also associated with the increased risk for comorbidities such as COVID-19, coronary heart disease (CHD), diabetes mellitus, stroke, and kidney disease. There are short and long-term consequences of HBP. Short-term consequences include stroke, CHD, heart failure (HF), and cardiovascular death; furthermore, long-term consequences include hypertensive cardiomyopathy, HF with preserved ejection fraction, atrial fibrillation, valvular heart disease, aortic syndromes, peripheral arterial disease, chronic kidney disease, dementia, diabetes, and erectile dysfunction.[8] We briefly mention those that in our opinion should be underlined:

1. **Oxidative Stress.** Is an imbalance between free radicals and antioxidants. The immune system produces oxidizing species and by phagocyte activation process reactive oxygen and nitrogen species as a lethal weapon to kill pathogens but also causes cellular damage. Hyperlipidemia, HBP, diabetes, and smoking generate oxidative stress which causes endothelial dysfunction and smooth muscle activation with nitric oxide impairment, increasing tissue angiotensin-converting enzyme, and angiotensin II.[9]
2. **Inflammation.** Chronic inflammation is a long-term stimulus which may last weeks, months, years, or even lifetime, and is characterized by the recruitment of monocytes and lymphocytes accompanied by tissue injury. It and a role in the development and progression of autoimmune disease, infectious disease like COVID-19, metabolic disorders such as atherosclerosis, obesity, and diabetes or hemodynamic disease as HBP, vascular and cardiac disease.[10]
3. **Renin-angiotensin-aldosterone system (RAAS).** RAAS is the cornerstone of blood pressure balance and is found in kidneys, adrenal glands, heart, vasculature, and nervous system. RAAS malfunction produces target organ or vasculature damage and is «the missing link» in long-term catastrophic consequences of HBP. The ying-yang effect of RAAS. Angiotensinogen (1-452 aa) is converted to angiotensin I (1-10 aa) by renin cleavage and is converted to angiotensin II (1-8 aa) by the angiotensin-converting-enzyme (ACE), which has two membrane receptor sites. angiotensin II binds angiotensin I receptor (AT1r) causes vasoconstriction, HBP, inflammation, fibrosis, and proliferation. On the other hand, the angiotensin II receptor (AT2r) is abundantly expressed in both immune and nonimmune cells in fetal tissue. Its

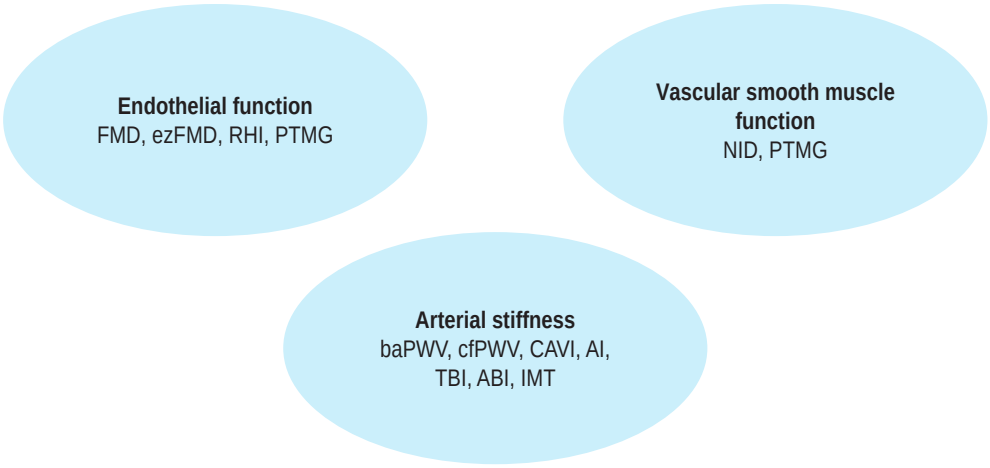

Figure 1: Methods for assessment of vascular function. FMD indicates flow-mediated vasodilation, ezFMD enclosed-zone FMD, RHI reactive hyperemia index, NID nitroglycerine-induced vasodilation, baPWV brachial- ankle pulse wave velocity, cfPWV carotid-femoral PWV, CAVI cardio-ankle vascular index, AI augmentation index, TBI toe brachial pressure index, ABI ankle-brachial pressure index, IMT intima media thickness. Modified from: Mogi M et al.[3]

expression is increased under pathological conditions in adult tissues and counteracting AT1r functions.[11] Angiotensin II is converted to Angiotensin 1-7 by angiotensin-converting enzyme 2 (ACE2) which has only one membrane receptor site located in the lungs, cardiovascular tissues, kidneys, gastrointestinal tract, and adipocyte tissue and is the doorkeeper of COVID-19. The pathways of Angiotensin 1-7 are degradation or stimulation of MAS membrane receptor which produce vasodilatation, vasoprotection, and maybe hypotension by nitric oxide synthase stimulation.

4. **High blood pressure-mediated organ damage.** High blood pressure-mediated organ damage (HMOD) describes functional changes in major organ systems (the heart, the brain, the retina, the kidneys, and the vasculature) and could be evaluated through an electrocardiogram, echocardiogram, computed tomography scan (CTs), or magnetic resonance (MR) for left ventricular hypertrophy (LVH), CTs or MR for brain disease, fundoscopy for retinopathy, estimated glomerular filtration (eGFR) or microalbuminuria (MAU) for kidney disease, carotid-femoral pulse wave velocity (PWV) for arterial stiffness (AS), and ankle-brachial index or carotid intimal-medial thickness for vasculature atherosclerosis (VA). Systolic pressure correlates positively in odds ratio HMOD except in eGFR, diastolic pressure correlates negatively in odds ratio HMOD except in eGFR, and pulse pressure correlates positively in odds ratio HMOD except in eGFR.

Unger et al published the 2020 International Society of Hypertension Global Hypertension Practice Guidelines which recommend a simplified classification of HMOD based on a 60-year-old male patient, but categories of risk will vary according to age and sex *(Figure 1)*. In summary, HBP is a major cardiovascular risk factor linked with chronic degenerative diseases, associated with bad outcomes which leads to the top mortality ranking in the world and each patient must be sufficiently studied to offer the best available therapeutic alternatives.

REFERENCES

1. Matsuzawa Y, Ogawa H, Kimura K, Konishi M, Kirigaya J, Fukui K et al. Renin-angiotensin system inhibitors and the severity of coronavirus disease 2019 in Kanagawa, Japan: a retrospective cohort study. Hypertens Res. 2020; 43 (11): 1257-1266. doi: 10.1038/s41440-020-00535-8.
2. Sheppard JP, Nicholson BD, Lee J, McGagh D, Sherlock J, Koshiaris C et al. Association Between Blood Pressure Control and Coronavirus Disease

2019 outcomes in 45 418 symptomatic patients with hypertension: an observational cohort study. Hypertension. 2021; 77 (3): 846-855. doi: 10.1161/HYPERTENSIONAHA.120.16472.
3. Mogi M, Higashi Y, Bokuda K, Ichihara A, Nagata D, Tanaka A et al. Annual reports on hypertension research 2020. Hypertens Res. 2022; 45 (1): 15-31. doi: 10.1038/s41440-021-00766-3.
4. Sierra C, Aguilera MT. Evaluación clínica del paciente hipertenso. Med Integral. 2001; 37: 210-214.
5. Ocampo DA. Fisiopatología de la hipertensión arterial esencial. n.d. pp. 351-357.
6. Ohishi M, Kubozono T, Higuchi K, Akasaki Y. Hypertension, cardiovascular disease, and nocturia: a systematic review of the pathophysiological mechanisms. Hypertens Res. 2021; 44 (7): 733-739. doi: 10.1038/s41440-021-00634-0.
7. Rosas M, Pastelín G, Vargas-Alarcón G, Martínez-Reding J, Lomelí C, Mendoza-González C et al. Guías clínicas para la detección, prevención, diagnóstico y tratamiento de hipertensión arterial sistémica en México. Arch Cardiol Mex. 2008; 78 (Suppl 2): 5-57.
8. Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. Hypertension. 2020; 75 (2): 285-292. Available in: https://doi.org/10.1161/HYPERTENSIONAHA.119.14240.
9. Lim HS, MacFadyen RJ, Lip GYH. Diabetes mellitus, the renin-angiotensin-aldosterone system, and the heart. Arch Intern Med 2004; 164: 1737-1748. doi: 10.1001/archinte.164.16.1737.
10. Harrison DG, Coffman TM, Wilcox CS. Pathophysiology of hypertension: the mosaic theory and beyond. Circ Res 2021; 128: 847-863. doi: 10.1161/CIRCRESAHA.121.318082.
11. Fatima N, Patel SN, Hussain T. Angiotensin II type 2 receptor: a target for protection against hypertension, metabolic dysfunction, and organ remodeling. Hypertension. 2021; 77 (6): 1845-1856. doi: 10.1161/HYPERTENSIONAHA.120.11941.

Author contributions: Each author contributed important intellectual content during manuscript drafting or revision and accepted accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Funding: The authors received no specific funding for this work.

Conflict of interest/financial disclosure: The authors declare that they have no conflict of interests.

Correspondence:
José Manuel Enciso-Muñoz, MD
E-mail: jmenciso2@hotmail.com
Rafael Olvera-Ruiz, MD
E-mail: rafaelolveraruiz@gmail.com
Alfredo Manuel Patiño-Llamas, MD
E-mail: drpatinoll@hotmail.com