



REVIEW ARTICLE

Isolated Systolic Hypertension in Young Patients

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Definition

The international society of hypertension, like other societies, defines isolated systolic hypertension (ISAH) as a brachial arterial pressure value greater than 140 mmHg of systolic values and less than 90 mmHg of diastolic values [1].

The population of young hypertensives has various definitions and cut-off points, ranging from before 30 years of age to 50 years of age. The European guide takes 40 years as the cut-off point to define it [1].

Epidemiology

HTSA is one of the most common forms of arterial hypertension in young patients and in older adults (over 60 years of age) [2].

In people over 60 years of age, around 30% of the types of HTA2 are reported.

Epidemiological data regarding its frequency in young patients have not been evaluated in the South American population in the literature [3].

The reported data is varied and ranges from some reports of 5.2% [4] in the young Asian population to 18.9% in Venice from the HARVEST [5] study.

The ENIGMA study showed that, in 1008 patients from the general population with an average age of 20 years, the most common form of arterial hypertension is HTSA [6].

In the first studies of patients with HTSA, a broad

trend was found, almost exclusively, of male patients, healthy, physically active, non-smokers and generally tall [7,8].

Pathophysiology

The initial description of HTSA in young people was accompanied by an explanation that expressed a benign phenomenon of this elevation in systolic pressure where there was great arterial elasticity, with the ability of peripheral arteries such as the brachial ones to increase the pulse wave, for therefore, a large amplification of this [7,8].

The fact of having this great arterial elasticity led in the studies to observe a higher pulse pressure in the brachial measurement than the central one, with a higher differential pulse pressure. This was also coupled with a pulse wave image with characteristics similar to normotensives.

These patients did not have a high augmentation index, since the reflex wave arrived much more slowly, and in fact the wave propagation speed was slower than normotensive patients [7,8].

These hemodynamic characteristics verified in the initial studies were compatible with the epidemiology demonstrated at the time, where they were mostly male, healthy, non-smokers and tall, explaining their delay in the reflection of the pulse wave [7,8].

Subsequently, in the aforementioned ENIGMA [6] study, the mechanisms involved in this population that lead to HTSA were studied in young patients with an

average age of 20. It was observed that the amplification of the pulse wave vs. normotensive patients was not greater, but instead it was for those with essential hypertension.

The mechanisms involved were not only related to the one mentioned previously, but also in these patients there was an increase in systolic volume and pulse wave velocity (89% of them) compared to normotensive and essential hypertensive patients, and there was no mechanism of increased peripheral resistance well described in essential hypertensive patients [6].

Central arterial pressures (PAC) were higher in patients with HTSA than in normotensive patients, so there was not only this benign mechanism of elevation of systolic figures.

Other mechanisms were implicated in the appearance of HTSA, such as arterial stiffness related to patients with metabolic syndrome [9], leaving other causes such as increased activation of the renin angiotensin system less frequently associated in some observational studies in adolescent patients, which would explain the difference in vascular resistance between systodiastolic hypertensive patients and this special population [10].

Diagnosis and Risk Assessment

The subtypes of arterial hypertension can be divided according to their elevation by office figures, and we can still make a diagnosis of hypertension with several measurements in different consultations with office blood pressure values [1].

Ambulatory measurements

Although the most available are by far the office figures, we also know that ambulatory values have a better long-term prognostic value to detect and predict cardiovascular events, as well as better reproducibility [11].

In a recent study, Citoni, et al. [12] observed that there was a good correlation between office values and 24-hour and daytime systolic values (R0.73 and 0.74, respectively), showing that these patients have a high cardiovascular load in general, and it is not only an elevation phenomenon in the office.

In any case, the measurement of ambulatory pressure in this group of patients is fundamentally relevant despite the good correlation with office values for two reasons:

The first is that in the aforementioned study [12] as well as in the study by Lurbe, et al. [13] a higher percentage of patients with white overalls were found than in other subgroups or than in systodiastolic hypertensive patients. So discarding this entity becomes necessary.

As a second important point, the 24-hour mean arterial pressure in a recent HARVEST analysis is of crucial

importance in predicting long-term elevation of arterial pressure requiring the initiation of pharmacological treatment [14].

In this analysis, it is observed that patients with HTSA vs. normotensive patients have similar risks of evolving to sustained hypertension requiring pharmacological treatment; however, in the subgroup of patients with HTSA who have a 24-hour mean arterial pressure (MAP) with values greater than or equal to 97 mmHg, they have almost double the chances than normotensive patients [14].

This is something that is not the most frequent in patients with HTSA, and in fact, in this study only 29% of them met this condition [14].

Therefore, due to these issues mentioned, the importance of using ambulatory measurements in young patients with HTSA is highlighted.

Central blood pressure measurement

In the evaluation of HTSA, although not as widely available, the measurement of central blood pressure (CBP) has proven to be important in being able to differentiate this heterogeneous population [5].

Once again, the group of Saladini, et al. [5] with the HARVEST study analyzes the patients according to the PAC values; taking 125 mmHg as cut-off point; and showing that patients with lower PAC; they have a similar risk to normotensive patients of developing sustained hypertension requiring pharmacological treatment.

It must be taken into account that in the HARVEST study, they were young patients with no history of previous cardiovascular or renal pathology or diabetes, but they were recruited in the context of suspected grade 1 hypertension, so the normotensive control group were patients who had at least normal-high office blood pressure values [5].

In other studies, patients with elevated PAC have been shown to have greater vascular target organ damage (PWV and augmentation index) than those patients with optimal office values. And in general they have had characteristics similar to those patients who had high normal pressure values in the office [15].

In the same way, another study evaluated patients with HTSA and PAC values less than 125 mmHg vs. those normotensive patients in the office, and found no differences in vascular target organ damage such as PWV [16].

In this context and as the possibilities of accessing PAC measurement are not widely available and difficult to perform routinely, some studies have tried to find predictive variables in patients with HTSA that try to predict that our patient has values of Elevated CAP [17].

In this study, the researchers found that patients with less height (1.78 meters), with greater weight (more than 91 kilos) and with diastolic values (from 80 mmHg) closer to the limit in the office are those who predispose to have this condition [17].

Subclinical target organ evaluation

But in addition to evaluating CAP, it is just as important in HTSA to evaluate subclinical target organ damage. This arises since it has been observed that in some studies patients with HTSA had left ventricular hypertrophy, and even independently of the elevation of central blood pressure [12,18]. Likewise, an increase in the augmentation index (vascular organ damage) has also been observed among patients with HTSA with low PAC vs. normotensive patients [16].

Therefore, as it is a type of arterial hypertension, it would be important to evaluate target organ damage, since it could indicate a greater individual risk for this patient that is not exclusively due to this entity.

Long term forecast

The prognosis of HTSA in young patients has been evaluated in different cohorts where cardiovascular mortality or general mortality was evaluated; and in some also events such as ischemic heart disease or stroke.

In most of them, young patients are considered to be patients between 18-50 years of age.

One of the studies is that of Yano and colleagues [19], which follows up for approximately 30 years and after a model with adjustments for sex, age and other risk factors, a difference is found with an increase in cardiovascular mortality, ischemic heart disease and stroke in HTSA vs. normotensive. An analysis was also performed to predict cardiovascular mortality based on systolic values and, despite not having a very high predictive value, it was significant for this, as were diastolic blood pressure figures.

One of the strengths of this study is the long follow-up of the patients. As a weakness in the study methods, blood pressure was taken using the auscultatory method.

More recently, Lee, Yano and colleagues [20,21] conducted another cohort study with patients between 20-40 years of age in more than 6 million patients in a 13-year follow-up; where similar results were observed. As a particularity in this study, the patients were divided according to office figures, but in this case, they were divided according to the categories of office values according to the AHA 2017 [4].

And to date, at least two more cohorts of the Asian population report similar data where patients with HTSA have a higher adjusted risk of cardiovascular death vs. normotensive patients [4,22,23].

Treatment

Pharmacological antihypertensive treatment in young patients with HTSA has not been studied in a clinical trial, where it demonstrates better results in clinical events. This is probably difficult to do since, due to the cardiovascular risk inherent to the age and comorbidities of the patients, the absolute risk of death and cardiovascular events is low, and too many patients and a long follow-up time would be required for a clinical trial.

The evidence for the treatment of HTSA comes from older adult patients in old studies such as SHEP26 or Syst-Eur [23] where the benefits of pharmacological treatment were shown.

In some indirect evidence from cohorts, the start of pharmacological treatment would seem to reduce the impact of the increase in cardiovascular events in patients with HTSA vs. normotensive; but the study did not have a longitudinal follow-up, nor was it the right design to study this [4].

Currently we can recommend pharmacological treatment only based on an expert recommendation, and in a context of individualization of the patient, where the treatment exceeds the risks and costs [3,24].

Pharmacological treatment will be subject to that patient who, due to the characterization of the type of HTSA, subclinical target organ damage, other cardiovascular risk factors or the response to non-pharmacological treatment, requires it to reduce cardiovascular events since the risk individual absolute value begins to rise above a threshold established by the treating medical specialist.

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