

## Isolated Systolic Hypertension in Young People Is Not Spurious and Should Be Treated

### *Con Side of the Argument*

*Empar Lurbe, Josep Redon*

Isolated systolic hypertension (ISH) in young people, defined on the basis of brachial blood pressure (BP) as a systolic BP (SBP) of at least 140 mmHg with a diastolic BP (DBP) of <90 mmHg, is not an unusual condition and is increasing in prevalence.<sup>1-3</sup> To date, this concept has been confronted with challenges in the mechanisms, clinical relevance, and consequences. Parameters other than brachial BP, such as noninvasive central hemodynamics, have introduced new insights to the condition. Nevertheless, grounded information supporting the long-term consequences is still lacking; therefore, the necessity to decide to treat or not to treat is a matter of concern in clinical practice.<sup>4</sup> The current knowledge of ISH in young people is presented with an emphasis on the elements that are relevant to deciding that treatment is not needed.

#### **Prevalence**

The prevalence of ISH reported among the young ranges widely, from 2% to 8% in population studies, and between 14% and 50% in patients with hypertension.<sup>3</sup> This is a result of the differences in population characteristics, such as age, ethnicity, and obesity. The Enigma study in the UK confirmed that ISH is the most common form of hypertension (HTN) in young adults aged 17 to 27 years, with a prevalence of 8%.<sup>1</sup> Data from the National Health and Nutrition Examination Survey indicate that among younger and middle-aged adults in the US, aged 18 to 39 years, the overall prevalence of ISH between 1988 and 1994 was 0.7%. This reached 1.6% (2.23% in males and 0.92% in females) between 1999 and 2004. Obesity, smoking, and low socioeconomic status seem to be important determinants of ISH among young adults.<sup>2</sup> In

a United States pediatric population of 12- to 16-year olds, the most prevalent hypertensive subtype was ISH.<sup>5</sup> Similarly, in Spanish obese youths, the overall prevalence of ISH was 4%, outnumbering systo-diastolic hypertension (SDH) by a ratio of 2:1.<sup>6</sup> Along with age, ethnicity, and obesity, the number of BP measurements at the time of establishing the diagnosis is a factor which affects the prevalence, the lower the number of measurements the higher the prevalence.<sup>5</sup>

#### **Mechanisms**

In youths with ISH, the mechanisms that produce BP elevation interplay with the high elasticity of the vascular tree, resulting in an elevation of SBP although normal DBP is maintained. Elasticity of the great vessels is particularly relevant in the young, and causes SBP to be considerably higher in upper limb arteries than in the ascending aorta. Therefore, ISH has been attributed to exaggerated pulse pressure amplification from central to peripheral arteries in youths, but is less observed with increasing age. Although not extensively studied, a certain degree of vascular stiffness, assessed by pulse wave velocity has been documented in some of these subjects with ISH.<sup>1</sup> Besides the relevance of elasticity/stiffness, stroke volume (SV) seems to play a role in the elevation of SBP in some cases.<sup>1</sup> Data from the Anglo-Cardiff Collaborative trial<sup>7</sup> report that although pulse pressure amplification is moderately higher in young individuals with ISH as compared with normotensives, SV is markedly higher. Whatever the mechanism, the hemodynamic pattern of these subjects differs from those with SDH, in which the main factor is an increment in the peripheral vascular resistance.

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The Enigma study, which includes a large proportion of normotensive, ISH and SDH, identifies ISH subjects as a heterogeneous population in terms of hemodynamics. Although 28% have a primary elevation of SV, another 20% have primary elevation of pulse wave velocity, and a third group, which accounts for 41% of the subjects, has an elevation of both SV and pulse wave velocity.<sup>1</sup> The potential clinical significance should be considered because an elevated SV in ISH youth has the potential to transform into sustained HTN in the future.<sup>8,9</sup> Whether or not subjects with ISH could be in the first phase of essential HTN is a relevant question with clinical implications, which in the absence of long-term follow-up prospective studies in youth, is still pending an answer. The only data available has come from the Framingham Heart Study in which ISH increases the risk of SDH later in life, although the average age at baseline was 45 years.<sup>10</sup>

### Clinical Relevance

Phenotypic characteristics of subjects with ISH have been reported in several studies; however, other clinically relevant information is rather scarce. The phenotype of being male and relatively tall for one's age is more common in ISH when compared with that for normotensives or even to that for SDH.<sup>1,11,12</sup> The clinical relevance of ISH may be assessed with the study of hypertension-induced early organ damage in the heart, kidney, vessels, or central nervous system. Only a small number of studies are available on the assessment of early organ damage.<sup>12,13</sup> Mahmud and Feely<sup>12</sup> observed normal echocardiographic left ventricular mass in 6 untreated subjects who had a diagnosis of spurious systolic HTN for at least 2 years. Sorof et al<sup>13</sup> have found that in children with ISH, intima-media thickness was higher when compared with that for normotensives, but lower than that in those with SDH.

Prospective studies assessing association between SBP and DBP with future risk for cardiovascular events in young subjects have been published,<sup>14-18</sup> although the number is small and no separate analysis of ISH has been reported in some of them. Studies with no ISH segregation<sup>14,17,18</sup> have been performed mainly in males with a mean age of around 20 years and a follow-up of between 24 to 50 years. SBP in 2 studies,<sup>14,17</sup> and both SBP and DBP in another,<sup>18</sup> are associated with cardiovascular disease mortality. ISH has been separately assessed in 2 studies,<sup>15,16</sup> however, with a threshold to define it of >160 mmHg. Recently, Yano et al<sup>3</sup> have found that among men, ISH subjects have a higher cardiovascular disease mortality than normotensives, but a risk similar to that for high-normal subjects. In contrast, in ISH women, cardiovascular disease mortality is greater than that for high-normal females.

An essential piece of lacking information is the persistence of ISH when BP measurements are repeated over longer periods of time. Visit-to-visit variability, wider in SBP, may be relevant to maintaining the status of ISH over time, and the phenomenon of regression to the mean needs to be taken into account.

### Aortic BP and The Concept of Spurious Hypertension

Besides measurement of BP in the brachial artery, the gold standard for diagnosis and classification of BP conditions,

during the past few years, the assessment of central BP (cBP) has increased, and it seems to be superior to peripheral BP in correlating with the severity of existing cardiovascular disease and the prediction of subsequent events.<sup>19-23</sup> CBP values in the aortic root, calculated from the pulse wave recorded in peripheral arteries using a transfer function, are lower than those obtained in the brachial artery. Central aortic BP and central pulse pressure are more reflective of the BP experienced by major organs, such as the brain, heart, and kidneys, and therefore may have a stronger association with cardiovascular risk. CBP most likely reflects the pressure against which the heart contracts during systole and may play an important role in the development of increased left ventricular mass.

Simultaneous assessment of peripheral and cBP identified a condition that is called pseudo or spurious HTN. It is first described by O'Rourke<sup>11</sup> in 6 young males aged 14 to 23 years. This HTN subtype, spurious systolic hypertension, characterized by a high peripheral SBP with normal central SBP (cSBP), has been attributed to exaggerated pulse pressure amplification from central to peripheral arteries because of increased vascular elasticity, and it is claimed to be probably a benign condition. The differences between central and peripheral pulse pressure, the amplification phenomenon, is driven mainly by differences in vessel stiffness and wave reflection, a phenomenon that is widely observed in young people.

In a later study on this concept, in a subgroup of subjects from the Atherosclerosis Risk in Young Adults study, aged 26 to 31 years, 16.1% of men and only 3 women were diagnosed with spurious hypertension, based on an office ISH and cSBP <124 mmHg in men and <120 mmHg in women.<sup>24</sup> Cardiovascular risk of the ISH subjects is calculated using the 20-year Framingham risk score and comparing it with normotensive and SDH subjects. The risk score, based on DBP, does not significantly differ between spurious and normotensive subjects, although a trend for higher risk is observed in the ISH. Although differences exist when SBP is used to calculate risk, DBP is more recommended in this age group because of the correlation with cardiovascular risk being present only for DBP.

The prognostic value of cSBP in ISH subjects has been explored in a prospective study.<sup>25</sup> In the follow-up of 9.5 years, incident HTN is more common among participants with ISH with high cBP, as compared with those of normotensive individuals. Among ISH subjects with low cBP, the incidence of HTN is only slightly higher than that of normotensive individuals. Therefore, the authors concluded that ISH in young to middle-aged individuals implies a relatively low risk of developing HTN, without the need for treatment when cBP is low.

Classifying cBP as normal or not is a matter of concern because no grounded information exists to define the reference values.<sup>26</sup> In addition to the cBP values, the high variability of the amplification phenomenon between aortic and brachial SBP at all ages<sup>7</sup> leads to a more difficult interpretation.

### Ambulatory BP Monitoring and The Presence of White-Coat

Ambulatory blood pressure monitoring (ABPM) is now considered a keystone in hypertension management. Ambulatory BP monitoring is more reproducible and offers

better prognostic value than do its office BP counterparts.<sup>27</sup> Moreover, it allows for the detection of discordant conditions with different prognostic significance.<sup>28</sup> Therefore, ABPM has the potential to enhance our diagnostic abilities and may aid in decision making and management. Information about ABPM in ISH of the young is practically negligible, and how much the prediction is improved by adding ambulatory to clinic BP is still unanswered.

Further information about ISH can be obtained from comparing ABPM with office BP and cSBP. In our experience, the majority of moderately obese ISH youth with normal cSBP<sup>29</sup> are white-coat, in contrast to the SDH subjects with normal cSBP who are mainly sustained HTN.<sup>6</sup> In the only prospective study using ABPM,<sup>25</sup> 24-hour SBP and the white-coat effect are similar in participants with ISH and with either high or low cBP. In this study, the necessity to start antihypertensive treatment is related to low or high cSBP, using 120.5 mmHg as the threshold, independent of the average of 24-hour ABPM.

### Challenge of Management

Given that ISH is the most prevalent hypertensive subtype in the young, and having the potential for spurious hypertension, it is extremely important to establish recommendations. That notwithstanding, the uncertainties about the mechanisms and the scarcity of long-term follow-up information do not facilitate its management.<sup>30</sup> Therefore, certain information should be considered before making clinical decisions in this population.

First, the question is if ISH is really hypertension and carries cardiovascular risk, or if it simply represents the extreme of the normal pressure wave pattern in youth, where the high amplification between central and peripheral arteries leads to conventional high systolic values that exaggerate the aortic ones. The use of prognostic studies at the time of deciding whether ISH in the young should be treated is rather limited. In these studies, which do not differentiate between ISH and SDH, it is not possible to determine the impact of each HTN class. In the studies in which ISH is analyzed, the age range includes subjects of 18 to 49 years of age, an average of 34 years in the Yano et al study,<sup>3</sup> and 30 to 45 years in the Strandberg study,<sup>16</sup> too wide a range to consider as grounded information for young subjects. In fact, no information is provided concerning the prognostic value of separate age segments. Although Yano et al<sup>3</sup> conducted age-specific analyses, younger or older than 40 years, they showed no significant interaction. This age group, however, is still too old for its data to be useful in young subjects. Likewise, no information about antihypertensive treatment or the presence of other cardiovascular risk factors is available for the long follow-up period of >30 years in both studies.

Second is the relevance of cSBP as the marker of risk. The concept that surrounds whether ISH is a spurious HTN based on cSBP cannot be attributed to all ISH subjects. Whether cSBP is a better prognostic factor than the office SBP counterparts and the relevance of cBP as a marker of risk is questionable. Although the presence of normal values of cSBP may not be enough to qualify subjects as spurious hypertensives because of its possible coexistence with different hemodynamic patterns, high cSBP is not considered to be a marker of

risk that warrants treatment. Furthermore, the reference values of cSBP in this age group can be misleading because of the absence of a large series of subjects.

Third, although most of the adverse outcomes occur in adulthood it has become clear that HTN is a life course problem that may become evident in childhood and can be progressive throughout childhood into adolescence and adulthood. There is a wealth of epidemiological data supporting a correlation between BP in childhood and adolescence with the incidence of hypertension in adulthood.<sup>31–33</sup> Even though an increased risk to develop hypertension has been linked to SBP in childhood, no reference to ISH is made in the Bao et al<sup>31</sup> and Sun et al studies.<sup>32</sup> Recently, Tirosh et al<sup>33</sup> have analyzed the progression of normotensive adolescents into hypertensive adults in a large number of subjects, 26 980. The study demonstrates that BP in late adolescence, 17 years of age, linearly predicts progression to hypertension in young adulthood, at age 42 years. At the same BP level, the risk is higher in males than in females. The risk groups analyzed, however, include combined SBP and DBP, and ISH is not analyzed separately.

Fourth is the recommendation of the Scientific Societies. Current guidelines advocate the initiation of pharmacological treatment based on a global risk calculation.<sup>22</sup> In the case of youth with primary HTN, the presence of organ damage is an indicator to initiate pharmacological treatment.<sup>34,35</sup> Decisions to treat based on global cardiovascular risk deals with the problem of a low absolute risk in young people even with multiple risk factors because risk is assessed for the following 10 to 20 years in the majority of the risk charts or scores. Other approaches such as the relative risk charts,<sup>36</sup> the lifetime risk,<sup>37,38</sup> or the Pooled Cohort Studies Equation<sup>39</sup> are more suitable for young adults, but they are not applicable because they only collect information on people >35 years. In the absence of suitable charts and of early organ damage, the most common situation, the initiation of antihypertensive treatment is not supported.

### Conclusions

To finalize, there is evidence to support avoiding the commencement of antihypertensive treatment precipitously in youths with ISH. Detecting white-coat using 24-hour ABPM, recording normal cSBP, and checking the absence of early organ damage, we have grounded support in the decision of not to treat. Furthermore, in the presence of ISH in 24-hour ABPM and high cSBP, no evidence exists to support introduction of antihypertensive treatment. This decision also takes into account that antihypertensive drugs are costly, produce secondary effects, some of them restrict the engagement in physical sports,<sup>40</sup> and, consequently, reduce one's quality of life. This is all the more relevant in the young, precisely those who have a long life ahead.

Considering ISH as an intermediate phenotype with unpredictable development, follow-up with lifestyle recommendations that pay attention to potential factors of progression such as obesity or excessive salt intake should be given. Further studies must be designed to determine whether ISH is a benign condition or not, which will help to improve its diagnosis and management, restricting and personalizing treatments to those patients that can benefit from it. This will



save considerable cost and effort, lead to substantial long-term benefits, and maintain people active and healthy longer.

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### Disclosures

None.

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## Response to Isolated Systolic Hypertension in Young People Is Not Spurious and Should Be Treated: Con Side of the Argument

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We agree with many of the points made by Lurbe and Redon,<sup>1</sup> which were similar to those raised in our own article. Certainly, the ability to assess central blood pressure (BP) noninvasively has increased our understanding of isolated systolic hypertension (ISH) in young people. However, rather than providing any mechanistic information, assessment of central BP simply highlights that ISH in young people cannot be attributed to exaggerated amplification of a normal central BP, but, instead, is associated with elevated central and brachial systolic BP. In this regard, measurements of cardiac output and stroke volume are more informative and could, potentially, be used to stratify risk in young individuals in the future.

We also agree that studies examining the longer-term risk associated with ISH in the young are required. However, data demonstrating strong tracking of systolic BP from childhood into adulthood,<sup>2,3</sup> together with recent observations demonstrating increased future cardiovascular risk in young-to-middle-aged individuals with ISH,<sup>4</sup> are compelling, and strongly suggest that early, targeted interventions in young people with ISH would be beneficial. Lurbe and Redon<sup>1</sup> argue that in the absence of early organ damage, initiation of antihypertensive therapy is not supported. But should one really wait until organ damage is apparent in a young individual before initiating therapy? Innovative studies targeting therapy toward the key mechanisms underlying ISH in the young are required. Ultimately, these could provide important evidence to guide treatment decisions in young people with ISH, leading to more effective BP control during the life course and the potential to delay, or even prevent the appearance of end-organ damage.

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Con Side of the Argument**  
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# LA HIPERTENSIÓN SISTÓLICA AISLADA EN JÓVENES NO ES ESPURIA Y DEBERÍA SER TRATADA

## *Argumentos en contra*

*Empar Lurbe, Josep Redon*

La hipertensión sistólica aislada (HSA) en personas jóvenes, definida en base a la presión arterial (PA) braquial como una PA sistólica (PAS) de al menos 140 mmHg con una PA diastólica (PAD) <90 mmHg, no es una patología inusual y su prevalencia va en aumento.<sup>1-3</sup> Hasta la fecha, este concepto ha confrontado con los desafíos en los mecanismos, la relevancia clínica y las consecuencias. Parámetros diferentes a la PA braquial, como el monitoreo hemodinámico central no invasivo, han introducido nuevas perspectivas a la patología. No obstante, aún no existen datos fundamentados que avalen las consecuencias a largo plazo; por lo tanto, la decisión de tratar o no esta patología es motivo de preocupación en la práctica clínica.<sup>4</sup> El conocimiento actual respecto de la HSA en jóvenes hace hincapié en los elementos que son relevantes en la decisión de que el tratamiento no es necesario.

### **Prevalencia**

La prevalencia de la HSA informada en jóvenes varía ampliamente del 2% al 8% en estudios poblacionales, y del 14% al 50% en pacientes con hipertensión.<sup>3</sup> Esto ocurre debido a las diferencias en las características poblacionales, como la edad, etnicidad y obesidad. El estudio *Enigma* efectuado en el Reino Unido, confirmó que la HSA es la forma más común de hipertensión (HTN) en adultos jóvenes de entre 17 y 27 años de edad, con una prevalencia del 8%.<sup>1</sup> Datos provenientes de la *National Health and Nutrition Examination Survey* indican que en adultos jóvenes y de mediana edad en los Estados Uni-

dos, de entre 18 y 39 años de edad, la prevalencia general de HSA entre 1988 y 1994 fue del 0,7%. Esta tasa llegó al 1,6% (2,23% en hombres y 0,92% en mujeres) entre 1999 y 2004. La obesidad, el tabaquismo y el nivel socioeconómico bajo parecen ser determinantes importantes de la HSA en adultos jóvenes.<sup>2</sup> En una población pediátrica estadounidense de entre 12 y 16 años de edad, el subtipo de hipertensión más prevalente fue la HSA.<sup>5</sup> De manera similar, en jóvenes obesos españoles, la prevalencia general de HSA fue del 4%, lo que superó a la hipertensión sistólica -diastólica (HSD) en una relación 2:1.<sup>6</sup> Junto con la edad, la etnicidad y la obesidad, la cantidad de mediciones de la PA en el momento de establecer el diagnóstico es un factor que repercute en la prevalencia –cuanto menor es la cantidad de mediciones, mayor es la prevalencia.<sup>5</sup>

### **Mecanismos**

En jóvenes con HSA, los mecanismos que producen elevación de la PA interactúan con la alta elasticidad del árbol vascular, lo que da como resultado una elevación de la PAS, aunque la PAD se mantiene normal. La elasticidad de los vasos de gran calibre es particularmente relevante en los jóvenes, y hace que la PAS sea considerablemente más elevada en las arterias de los miembros superiores que en la aorta ascendente. Por lo tanto, la HSA ha sido atribuida a la exagerada amplificación de la presión de pulso en su travesía desde las arterias centrales a las periféricas en personas jóvenes; no obstante, esto se observa con menor frecuencia a medida que la edad avanza. Aunque

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no ha sido ampliamente estudiado, se ha documentado cierto grado de rigidez vascular evaluada mediante la velocidad de la onda de pulso en algunos de los sujetos con HSA.<sup>1</sup> Además de la relevancia de la elasticidad/rigidez, el volumen sistólico (VS) pareciera cumplir un papel en la elevación de la PAS en algunos casos.<sup>1</sup> Datos provenientes del estudio *Anglo-Cardiff Collaborative Trial*<sup>7</sup> informan que aunque la amplificación de la presión de pulso es moderadamente superior en personas jóvenes con HSA que en personas normotensas, el VS es notablemente superior. Cualquiera sea el mecanismo, el patrón hemodinámico de estos sujetos difiere de aquellos con HSD en que el factor principal es un aumento de la resistencia vascular periférica.

El estudio *Enigma*, que incluye una gran proporción de sujetos normotensos, sujetos con HSA y sujetos con HSD, identifica a los sujetos con HSA como una población heterogénea en cuanto a la hemodinámica. Aunque el 28% tiene una elevación primaria del VS, otro 20% tiene elevación primaria de la velocidad de la onda de pulso y un tercer grupo, que representa al 41% de los sujetos, tiene una elevación tanto del VS como de la velocidad de la onda de pulso.<sup>1</sup> Debería considerarse la potencial significación clínica debido a que el VS elevado en jóvenes con HSA tiene posibilidad de transformarse en HTN sostenida en el futuro.<sup>8,9</sup> Si los sujetos con HSA pueden ubicarse o no en la primera fase de la HTN esencial es una pregunta relevante con implicancias clínicas, que en ausencia de estudios prospectivos de seguimiento a largo plazo, aún no tiene respuesta. Los únicos datos disponibles provinieron del *Framingham Heart Study*, en el que la HSA aumentó el riesgo de HSD en el futuro, a pesar de que la edad promedio en el período inicial fue de 45 años.<sup>10</sup>

### Relevancia clínica

Las características fenotípicas de los sujetos con HSA se han informado en varios estudios; sin embargo, otros datos clínicamente relevantes son bastante escasos. El fenotipo de ser hombre y relativamente alto para la edad es más común en personas con HSA en comparación con normotensos o, incluso, con aquellos con HSD.<sup>11,12</sup> La relevancia clínica de la HSA puede ser evaluada mediante el estudio de daño temprano en órganos inducido por hipertensión, entre ellos, corazón, riñón, vasos o sistema nervioso central. Solo hay a disposición una pequeña cantidad de estudios sobre la evaluación del daño prematuro en órganos.<sup>12,13</sup> Mahmud y Feely<sup>12</sup> observaron mediante ecocardiografía una masa ventricular izquierda normal en 6 personas no sometidas a tratamiento con diagnóstico de HTN sistólica espuria durante al menos 2 años. Sorof et al.<sup>13</sup> hallaron que en niños con HSA, el espesor íntima media fue superior que en niños normotensos, pero inferior que en aquellos con HSD.

Se han publicado estudios prospectivos que evaluaron la relación entre la PAS y la PAD con el riesgo futuro de eventos cardiovasculares en personas jóvenes,<sup>14-18</sup> aunque la cantidad es pequeña y, en algunos de ellos no se ha informado ningún análisis de la HSA por separado. Se llevaron a cabo estudios sin separación de la HSA<sup>14,17,18</sup> principalmente en hombres con una media de edad de aproximadamente 20 años y un seguimiento de entre 24 y 50 años. En 2 estudios, la PAS<sup>14,17</sup> se

relacionó con mortalidad por enfermedad cardiovascular, y en otro estudio, se relacionaron tanto la PAS como la PAD. La HSA se evaluó por separado en 2 estudios,<sup>15,16</sup> sin embargo, el umbral para definirla fue >160 mmHg. Recientemente, Yano et al.<sup>3</sup> hallaron que en hombres, los sujetos con HSA tienen mayor riesgo de mortalidad por enfermedad cardiovascular que los sujetos normotensos, sin embargo, tienen el mismo riesgo que los sujetos con presión normal a alta. Por el contrario, en mujeres con HSA, la mortalidad por enfermedad cardiovascular es mayor que en las mujeres con presión normal a alta.

Un dato esencial faltante es la persistencia de la HSA cuando las mediciones de la PA son repetidas durante períodos de tiempo más prolongados. La variabilidad visita a visita, mayor en la PAS, puede ser relevante en el mantenimiento de la HSA a lo largo del tiempo, y es necesario tener en cuenta el fenómeno de regresión a la media.

### PA aórtica y el concepto de hipertensión espuria

Además de la medición de la PA en la arteria braquial —el método de referencia para el diagnóstico y la clasificación de las condiciones de la PA—, durante los últimos años, la evaluación de la PA central (PAC) ha aumentado, y pareciera ser superior a la PA periférica en cuanto a la correlación con la gravedad de la enfermedad cardiovascular existente y la predicción de eventos posteriores.<sup>19-23</sup> Los valores de la PAC en la raíz aórtica, calculados a partir de la onda de pulso registrada en las arterias periféricas utilizando una función de transferencia, son inferiores a los obtenidos en la arteria braquial. Los valores de la PA aórtica y la presión de pulso central reflejan mejor la PA experimentada por los órganos principales, como el cerebro, el corazón y los riñones, y, por ende, pueden tener una relación más sólida con el riesgo cardiovascular. Lo más probable es que la PAC refleje la presión contra la cual el corazón se contrae durante la sístole y puede cumplir un papel importante en el desarrollo del aumento de la masa ventricular izquierda.

Una evaluación simultánea de la PAC y la periférica identificó un afección denominada pseudohipertensión o hipertensión espuria. Esto lo describió por primera vez O'Rourke<sup>11</sup> en 6 jóvenes, de sexo masculino, de entre 14 y 23 años de edad. Este subtipo de HTN, la hipertensión sistólica espuria, caracterizada por una PAS periférica elevada con PAS central (PASc) normal ha sido atribuida a la exagerada amplificación de la presión de pulso en su travesía desde las arterias centrales hasta la periféricas debido al aumento de la elasticidad vascular, y se alega que probablemente sea un afección benigna. Las diferencias entre la presión de pulso central y periférica —el fenómeno de la amplificación— se debe principalmente a las diferencias en la rigidez de los vasos y el reflejo de la onda, un fenómeno que se observa mucho en personas jóvenes.

En un estudio posterior sobre este concepto, en un subgrupo de sujetos del estudio *Atherosclerosis Risk in Young Adults*, de entre 26 y 31 años de edad, el 16,1% de los hombres y solo 3 mujeres fueron diagnosticadas con hipertensión espuria, en base a la medición de la HSA y PASc en consultorio < 124 mmHg en hombres y < 120 mmHg en mujeres.<sup>24</sup> El riesgo cardiovascular de HSA en sujetos se calculó mediante la escala de riesgo de Framingham y se comparó con los sujetos normoten-



tos y sujetos con HSD. La escala de riesgo, en base a la PAD, no difiere significativamente entre los sujetos con hipertensión espuria y los normotensos, aunque se observa una tendencia hacia un mayor riesgo en sujetos con HSA. A pesar de que existen diferencias cuando se utiliza la PAS para calcular el riesgo, en este grupo etario es más recomendable utilizar la PAD ya que la correlación con el riesgo cardiovascular se da solamente con la PAD.

El valor pronóstico de la PASc en sujetos con HSA ha sido estudiado en un estudio prospectivo.<sup>25</sup> En el seguimiento de 9,5 años, la HTN incidente es más común entre participantes con HSA con PAC alta que en las personas normotensas. En las personas con HSA con PAC baja, la incidencia de HTN es solo levemente superior a la de las personas normotensas. Por lo tanto, los autores llegaron a la conclusión de que la HSA en personas jóvenes a personas de mediana edad implica un riesgo relativamente bajo de desarrollar HTN, sin necesidad de tratamiento cuando la PAC es baja.

La clasificación de la PAC como normal o no es motivo de preocupación debido a que no existen datos fundamentados para definir los valores de referencia.<sup>26</sup> Además de los valores de la PAC, la alta variabilidad del fenómeno de amplificación entre la PAS aórtica y la braquial, a todas las edades,<sup>7</sup> dificulta aún más la interpretación.

### **Monitoreo ambulatorio de la PA y efecto de guardapolvo blanco**

El monitoreo ambulatorio de la PA (MAPA) actualmente es considerado clave en el tratamiento de la hipertensión. El monitoreo ambulatorio de la PA tiene mayor reproducibilidad y ofrece mejor valor pronóstico que las contrapartes de la PA en consultorio.<sup>27</sup> Además, permite la detección de afecciones discordantes con diferente significación pronóstica.<sup>28</sup> Por lo tanto, el MAPA tiene el potencial de mejorar nuestras habilidades diagnósticas, y puede ayudar en la toma de decisiones y el tratamiento. La información respecto del MAPA en HSA en personas jóvenes es prácticamente insignificante, y en qué medida mejora la predicción al incorporar la PA ambulatoria a la PA clínica aún no tiene respuesta.

Se puede obtener información adicional respecto de la HSA si se compara el MAPA con la PA en consultorio y la PASc. Según nuestra experiencia, la mayoría de los jóvenes con HSA con obesidad moderada y PASc normal<sup>29</sup> tienen hipertensión arterial de guardapolvo blanco a diferencia de los sujetos con HSD con PASc normal que en su mayoría tienen HTN sostenida.<sup>6</sup> En el único estudio prospectivo en el que se utilizó el MAPA,<sup>25</sup> la PAS de 24 horas y el efecto de guardapolvo blanco fueron similares en los participantes con HSA y con PAC baja o alta. En este estudio, la necesidad de iniciar un tratamiento antihipertensivo se relaciona con la PASc baja o alta, usando un umbral de 120,5 mmHg, independientemente del promedio del MAPA de 24 horas.

### **Desafío del tratamiento**

Dado que la HSA es el subtipo de hipertensión más prevalente en personas jóvenes, junto con el hecho de tener potencial para la hipertensión espuria, es extremadamente importante

establecer recomendaciones. Pese a eso, las incertidumbres respecto de los mecanismos y la escasez de información de seguimiento a largo plazo no facilitan su tratamiento.<sup>30</sup> Por lo tanto, debería considerarse cierta información antes de tomar decisiones clínicas en esta población.

En primer lugar, la pregunta es si la HSA realmente es hipertensión y conlleva riesgo vascular, o si meramente representa el extremo del patrón normal de la onda de presión en la juventud, donde la amplificación alta entre las arterias centrales y periféricas deriva en valores convencionales sistólicos elevados que exageran los valores de la aorta. El uso de estudios pronósticos en el momento de decidir si la HSA en jóvenes debería tratarse es bastante limitado. En estos estudios, que no diferencian entre HSA y HSD, no es posible determinar el impacto de cada clase de HTN. En estudios en los que se analiza la HSA, el rango etario incluye sujetos de entre 18 y 49 años de edad, un promedio de 34 años en el estudio de Yano et al.,<sup>3</sup> y de entre 30 y 45 años en el estudio de Strandberg,<sup>16</sup> un rango demasiado amplio para considerarlo como información fundamentada para los sujetos jóvenes. De hecho, no se proporciona información respecto del valor pronóstico de segmentos etarios separados. A pesar de que Yano et al.<sup>3</sup> efectuaron análisis específicos por edad –menores o mayores de 40 años– no demostraron interacción significativa. Este grupo etario, no obstante, incluso tiene una edad muy alta para que sus datos sean útiles en sujetos jóvenes. Del mismo modo, no hay a disposición datos con relación al tratamiento antihipertensivo o a la presencia de otros factores de riesgo cardiovascular para el extenso período de seguimiento de >30 años en ambos estudios.

En segundo lugar se encuentra la relevancia de la PASc como marcador de riesgo. El concepto que rodea si la HSA es HTN espuria en base a la PASc no puede atribuirse a todos los sujetos con HSA. Es cuestionable si la PASc es un factor pronóstico mejor que las contrapartes de la PAS en consultorio y la relevancia de la PAC como marcador de riesgo. Aunque la presencia de valores normales de PASc es posible que no sea suficiente para calificar a los sujetos como personas con hipertensión espuria debido a la posible coexistencia de patrones hemodinámicos diferentes, la PASc alta no es considerada un marcador de riesgo que justifique tratamiento. Además, los valores de referencia de la PASc en este grupo etario pueden ser confusos debido a la ausencia de un grupo extenso de sujetos.

En tercer lugar, aunque la mayoría de los resultados adversos ocurren en la adultez, ha quedado claro que la HTN es un problema del ciclo de la vida que puede ponerse en evidencia en la niñez y evolucionar hacia la adolescencia y luego hacia la adultez. Existe una inmensa cantidad de datos epidemiológicos que avalan una correlación entre la PA en la niñez y la adolescencia con la incidencia de hipertensión en la adultez.<sup>31-33</sup> A pesar de que se ha vinculado el aumento del riesgo de desarrollar hipertensión con la PAS en la niñez, no se hace referencia a la HSA en los estudios de Bao et al.<sup>31</sup> y Sun et al.<sup>32</sup> Recientemente, Tirosh et al.<sup>33</sup> han analizado la evolución de adolescentes normotensos a adultos hipertensos en una gran cantidad de sujetos, 26980. El estudio demuestra que la PA en la adolescencia tardía, 17 años de edad, predice en forma

lineal la evolución a hipertensión en la adultez temprana, 42 años de edad. Al mismo nivel de PA, el riesgo es mayor en hombres que en mujeres. Los grupos de riesgo analizados, no obstante, incluyen la combinación PAS y PAD, y la HSA no es analizada por separado.

En cuarto lugar se encuentra la recomendación de las *Scientific Societies*. Las guías actuales proponen el inicio del tratamiento farmacológico conforme a un cálculo de riesgo global.<sup>22</sup> En el caso de jóvenes con HTN primaria, la presencia de daño en órganos es un indicador para el inicio de un tratamiento farmacológico.<sup>34,35</sup> Las decisiones respecto de iniciar un tratamiento conforme al riesgo cardiovascular global se enfrenta con el problema de un riesgo absoluto bajo en jóvenes, incluso, con múltiples factores de riesgo; esto se debe a que el riesgo es evaluado durante los próximos 10 a 20 años en la mayoría de las representaciones gráficas o escalas de riesgo. Otros abordajes como las representaciones gráficas del riesgo relativo,<sup>36</sup> el riesgo de por vida,<sup>37,38</sup> o la Ecuación de estudios de cohortes combinadas<sup>39</sup> son más apropiados para adultos jóvenes, pero no son aplicados porque solo recaban información de personas >35 años de edad. En ausencia de representaciones gráficas adecuadas y de daño prematuro en órganos –la situación más común–, el inicio del tratamiento antihipertensivo no es avalado.

### Conclusiones

Para finalizar, existe evidencia que avala el hecho de evitar el inicio del tratamiento antihipertensivo precipitadamente en jóvenes con HSA. Al detectar el efecto de guardapolvo blanco mediante el MAPA de 24 horas, registrar una PASc normal y verificar la ausencia de daño prematuro en órganos, contamos con argumentos fundamentados respecto de la decisión de no iniciar un tratamiento. Además, en presencia de HSA en el MAPA de 24 horas y PASc alta, no existe evidencia que avale la introducción de un tratamiento antihipertensivo. La decisión también tiene en cuenta que los fármacos antihipertensivos son costosos, producen efectos secundarios, algunos impiden participar en actividades físicas<sup>40</sup> y, por consiguiente, reducen la calidad de vida de las personas. Es aún más importante en los jóvenes, quienes justamente tienen una larga vida por delante.

Considerando la HSA como un fenotipo intermedio con desarrollo impredecible, debería realizarse un seguimiento con recomendaciones sobre cambios en el estilo de vida que ponga atención en los factores de evolución, como la obesidad o la ingesta excesiva de sal. Se deben diseñar estudios adicionales para determinar si la HSA es un afección benigna o no, lo que ayudaría a mejorar su diagnóstico y tratamiento como también a personalizar los tratamientos y restringirlos a aquellos pacientes que pueden beneficiarse de estos. Esto ahorrará costos y esfuerzos considerables, conducirá a beneficios sustanciales a largo plazo y mantendrá a la persona activa y sana por más tiempo.

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### Declaración de conflictos de interés

Ninguna.

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