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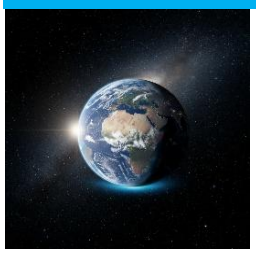

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Isolated Systolic Hypertension in Young Adults: a Narrative Review of Epidemiology, Pathophysiology and Clinical Management

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I. Abstract

Background: Isolated systolic hypertension in young adults is a problem of rising importance. Although it has been considered a benign condition caused by a hemodynamic phenomenon in a specific patient group, current population-based studies challenge this view. These data suggest increased cardiovascular risk and possible progression to sustained hypertension.

Aim: The aim of this narrative review is to summarize current evidence on isolated systolic hypertension in young adults and to compare recent findings with previous studies and the concept of spurious systolic hypertension.

Materials and methods: A systematic literature search using PubMed and Google Scholar online databases was conducted. Authors included and analyzed 30 studies published between 2000 and 2025 focusing on epidemiology, pathophysiology, hypertension progression, cardiovascular risk and therapeutic management of isolated systolic hypertension.

Results: The prevalence of isolated systolic hypertension appears to be increasing, affecting a considerable proportion of the young adults population, especially men. Hemodynamic findings suggest heterogeneity of pathophysiological mechanisms underlying this condition, including high arterial pulse pressure amplification, elevated stroke volume and aortic stiffness. Evidence indicates possible progression to sustained hypertension and increased cardiovascular disease and mortality risk. Data regarding therapeutic management is limited with current guidelines recommending a non-pharmacological approach.

Conclusions: Isolated systolic hypertension in young adults is a heterogeneous condition requiring further research to optimize its clinical management.

Key words: isolated systolic hypertension; young adults; cardiovascular risk; physiopathology; treatment

II. Introduction

Isolated systolic hypertension (ISH) is a subtype of hypertension defined by systolic blood pressure (SBP) value ≥140 mmHg and diastolic blood pressure (DBP) value <90 mmHg.[1] ISH is highly prevalent in older patients, constituting for >80% of cases in untreated, hypertensive patients aged >60 years, which makes it the most common type in this group.[2,3] Despite being typically associated with older adults, isolated systolic hypertension is increasingly observed in young adults, a condition referred to as isolated systolic hypertension of the young (ISHY).[4–6] Given the rising prevalence of ISHY and the complexity of its pathophysiological background, this narrative review aims to provide a comprehensive overview of current evidence concerning its epidemiology, pathophysiology, possible progression, cardiovascular risk and therapeutic strategies.

III. Methods

This review provides a narrative overview of the current literature on isolated systolic hypertension in young adults, focusing on its epidemiology, pathophysiology, cardiovascular risk and therapeutic strategies. A systematic literature search using the PubMed and Google Scholar online databases was conducted to determine relevant studies published between 2000 and 2025. One historical study, published in 1971, was included for context to illustrate early observations related to the subject. The following keywords were used: “isolated systolic

hypertension", "ISH", "ISHY", "systolic hypertension", "young adults", "young", "spurious hypertension", "central blood pressure", "cardiovascular risk", "pharmacotherapy" and their combinations with Boolean operators (AND, OR). Open access studies examining isolated systolic hypertension in young adults (aged 18 to 40 years) were included particularly addressing epidemiological data, pathophysiological and hemodynamic mechanisms, disease progression, cardiovascular risk and current therapeutic approaches. Case reports and studies not available in English were excluded. Data from selected studies were extracted and summarized narratively by the authors.

IV. Epidemiology

Accumulating epidemiological evidence shows that an increasing number of young adults are affected by ISHY. According to the HELIUS Study (2018), conducted in a multi-ethnic cohort of 3,744 participants under 40 years of age, the overall prevalence of ISH was 2.7%, with 5.2% in men and 1.0% in women.[5] This prevalence is notably higher than that previously reported by the US National Health and Nutrition Examination Survey (NHANES), which also documented an increase in overall ISH prevalence among individuals under 40 years of age, from 0.7% (1988–1994) to 1.57% (1999–2004)[6] with no further statistically significant change observed up to 2010.[7]

The Hypertension and Ambulatory Recording (HARVEST) study concluded that ISHY prevalence was initially higher in men, up to 37 years of age, and reached comparable levels between men and women at 38–41 years (as cited in [8]). Some studies have reported anthropometric differences in individuals with ISHY, particularly greater height[5,9–12] and increased body mass index (BMI).[4,6,12,13] Positive associations with smoking[6,13,14], low educational level[6] and Black ethnicity[14] have also been observed.

V. Pathophysiology

The pathophysiological causes of ISH in older persons has been connected to dysfunction of the endothelium, remodeling of the blood vessels and fibrosis, which as a result present in elevated arterial stiffness, occurring in large elastic arteries. This process leads to subsequent rise of SBP and, observed later, decrease of DBP.[1,15] However, the underlying mechanisms of ISH in younger individuals remain a subject of debate. The hypothesis of spurious systolic hypertension (SSH) was first proposed by O'Rourke et al. in 2000.[11] The

basic premise of this concept is that, in some individuals, elevated brachial SBP is not equivalent to elevated central SBP (cSBP) and therefore should not be diagnosed as hypertension. The suggested mechanism underlying this phenomenon is an unusually high amplification of the arterial pressure pulse as it is transmitted from the more elastic central aorta to stiffer peripheral arteries. As a result SBP in the upper limb arteries exceeds that in the ascending aorta, indicating that this finding represents a hemodynamic phenotype rather than hypertension per se.[10,11] Later studies showed that this clinical presentation is predominantly observed in young, tall men[10,16] which corresponds to the group with high risk of developing ISHY.

On the contrary, other studies suggest that amplification of the arterial pressure pulse is a highly improbable cause of ISHY. An alternative hypothesis proposes that ISHY represents an early, neurogenically mediated stage of hypertension. Intensified sympathetic activity and co-occurring reduced parasympathetic modulation results in increased cardiac output and heart rate, which is consistent with early stages of hypertension.[17] The ENIGMA cohort study, involving 1,008 participants aged 17–27 years, investigated the hemodynamic determinants of ISHY. The main conclusion from this research is that in young adults, essential hypertension (EH) characterised by SBP ≥140 and DBP ≥90 or DBP only, has a different hemodynamic pattern from ISHY. Compared to the normotensive group, EH was characterised by increased peripheral vascular resistance, whereas subjects with ISHY had increased stroke volume and/or aortic stiffness. However, no significant difference in pulse pressure amplification was observed between the two groups mentioned above.[18]

An intriguing aspect of ISHY pathophysiology is the potential hemodynamic mechanism contributing to elevated SBP in physically active individuals and athletes. Regular training, especially endurance training, lowers the heart rate resulting in training-induced bradycardia. Bradycardia increases stroke volume and peripheral pulse pressure amplification, leading to elevated brachial SBP in athletes. The hemodynamic implications for central blood pressure, however, appear to be variable.[8]

VI. Risk of developing sustained hypertension

The potential for progression from ISHY to hypertension remains a clinically relevant issue. A prospective study based on the HARVEST database investigated risk of future development of clinic hypertension in individuals with ISHY. Clinic hypertension was defined by average SBP exceeding ≥140 and/or DBP ≥90 on two consecutive visits, assessed at least

six months after implementing lifestyle modifications. The results indicate that ISHY is associated with a smaller risk of evolving into clinic hypertension than systolic-diastolic hypertension (SDH) or isolated diastolic hypertension (IDH).[19] Consistently, a study by Kanegae et al. concluded that the risk of developing hypertension in the population of people younger than 50 years is more correlated to elevated DBP than SBP.[20]

Central blood pressure (cBP) has also been proposed as a potential marker for identifying individuals with ISHY at increased risk of progression to sustained hypertension. Saladini et al. investigated risk of developing hypertension needing treatment in participants with ISHY based on cBP non-invasive measurements. This data shows that individuals with ISHY and lower cBP showed a hypertension risk similar, or slightly higher, to that of normotensive participants.[21] A 12-month observational study on a sample of children with increased brachial SBP and normal cSBP evaluated risk of progression into true hypertension, characterized by elevation of both parameters. The test group received only non-pharmacological treatment. The results show that 23% of the sample developed true hypertension.[22]

VII. Cardiovascular disease risk

The risk of developing cardiovascular disease (CVD) in adults with ISHY is still a matter of debate. The concept of spurious systolic hypertension questions the estimation of cardiovascular risk in ISHY cases based solely on peripheral blood pressure measurements, particularly SBP. In a study by Hulsen et al., the 20-year risk of coronary heart disease was estimated. The research found that, based on brachial SBP, the group with ISHY had a significantly higher risk compared to the normotensive group. However calculations made with brachial DBP indicated a reduction in risk that was no longer statistically significant.[16]

In contrast, several later studies have reported an increased cardiovascular risk among individuals with ISHY.[9,13,23,24] Lee et al. examined cardiovascular risk on a large cohort of 6 424 090 adults from a South Korean database. The findings prove that ISHY corresponds with significantly higher risk for CVD events such as myocardial infarction, stroke, heart failure, and CVD-related death. The increased risk was found to be present in both stage 1 and stage 2 ISHY population, although in stage 2 the risk was greater.[23] Similarly, MONICA/KORA study analyzed cardiovascular mortality risk in a cohort of 5 597 young adults, demonstrating a significantly increased risk in the ISHY group compared with normotensive individuals, as reflected by a hazard ratio of 1.89. The results also indicate a statistically significant difference

depending on gender, reporting that cardiovascular mortality was nearly twofold higher in men with ISHY than in women.[9] Elevated CVD risk and mortality was also confirmed by Yano et al.[13] and Bo et al.[24]

These latest findings align with earlier evidence of long-term CVD risk of elevated SBP. For example, a research from 1971 by Paffenbarger and Wing demonstrated high SBP level in young adults was associated with increased incidence of non-fatal stroke in later life.[25]

VIII. Treatment

There is strong evidence to demonstrate that decreasing elevated blood pressure (BP) notably reduces CVD risk in a wide range of patient populations. A meta-analysis published in The Lancet in 2016 confirmed that antihypertensive therapy significantly decreases risk of major CVD events and mortality.[26] Consistently with this data, in MONICA/KORA study authors observed protective effects of antihypertensive treatment, which lowered the risk of CVD mortality by 54%.[9] These findings provide strong evidence supporting pharmacotherapy, in the ongoing discussion regarding ISHY treatment management.

The 2023 guidelines of the European Society of Hypertension (ESH) emphasise the importance of lifestyle interventions in individuals diagnosed with ISHY, particularly smoking cessation, limiting sodium intake and body weight reduction in case of increased BMI.[1] Dietary modifications represent an important component of treatment in patients diagnosed with hypertension. The Dietary Approaches to Stop Hypertension (DASH) diet is one of the most extensively studied nutritional strategies for blood pressure control, emphasising increased consumption of fibre-rich foods, while limiting intake of sodium, red and processed meat and sugar-sweetened beverages. This approach results in high consumption of potassium, magnesium and calcium, which overall contributes to improved vascular function and blood pressure regulation. Evidence indicates that adherence to the DASH diet significantly reduces both SBP and DBP in normotensive individuals and hypertensive patients.[27]

In patients without major additional risk factors, non-pharmacological modification of lifestyle and observation may be applied for the first 3-6 months. Anti-hypertensive medication use may be introduced if BP fails to normalize after this period, however this decision should be individualised according to the patient's hypertension stage, race, gender and co-occurring conditions.[28] More detailed recommendations on ISHY therapeutic strategies are presented in 2024 guidelines for the management of hypertension in Poland by the Polish Society of Hypertension.[29] The experts emphasize the importance of non-pharmacological treatment in

ISHY, especially in patients with SBP of 140-159 mm Hg and no hypertension-mediated organ damage or other cardiovascular risk factors. In this group, an initial period of lifestyle modification accompanied by clinical observation is recommended for 6-12 months. In patients with higher SBP (≥160 mm Hg) or additional markers of cardiovascular risk, initiation of antihypertensive pharmacotherapy is advised.[29]

IX. Discussion

The findings presented in this review highlight the heterogeneity of ISHY, underscoring the need to interpret epidemiological, hemodynamic and prognostic data circumspectly. Current epidemiological evidence suggests that ISHY represents a common and potentially still increasing problem among young adults, affecting especially men.[5,6] The concept of ISHY as a benign phenomenon of "tall men with elastic arteries", introduced by O'Rourke,[11] has been widely discussed in subsequent studies. The MONICA/KORA study reported that patients with ISHY were taller than those with other hypertensive phenotypes, however there was no significant height difference compared to the normotensive sample.[9] These findings question whether this condition should be generalized to this specific anthropometric type.

Furthermore the nonuniformity of the patient population was identified in a scoping review on the subject of ISHY, which distinguished between two subpopulations. One was associated with unfavorable modifiable and non-modifiable factors, such as increased BMI, decreased physical activity, smoking and lower socioeconomic status, whereas the other represented patients with low-risk phenotype regarding these aspects. The coexistence of those highly contrasting subgroups in the ISHY population clearly suggests at least two different pathophysiological mechanisms that underlie this condition.[30] Considering an increasing problem of obesity in young adults,[31] the low-risk subpopulation of ISHY patients might be underrepresented in large cohort studies and meta-analyses. To further explore this subject, future studies should focus on careful selection of study groups, targeting individuals with no additional CVD risks.

ISHY carries a risk of progression to sustained hypertension, however that risk is lower than in other hypertension subtypes and DBP may be a stronger predictor of future hypertension in young adults.[20] Measuring cBP may serve as a valuable additional tool for assessing the risk of hypertension progression.[21]

The spurious systolic hypertension hypothesis raised some questions about whether this condition should be treated. Lurbe et. al highlight several unresolved issues regarding

management of ISHY, particularly the limited prognostic evidence specific to this population and the lack of validated risk assessment tools for young adults. Consequently, they argue against the premature initiation of anti-hypertensive medication in young adults with ISHY.[32] On the contrary, McEniery et al. draw attention to the potential long-term cardiovascular implications of untreated ISHY and propose that early mechanism-targeted intervention may modify disease progression and ultimately reduce cardiovascular risk.[17] In light of recent evidence showing an increased cardiovascular risk in patients with ISHY[9,13,23,24] the view of it being a benign condition is challenged. Further research is needed to develop risk assessment tools in this patient population. From a clinical perspective, these findings support a more thorough diagnostic evaluation of young individuals presenting with high SBP.

Despite the growing recognition of ISHY and its clinical significance, the literature provides limited guidance of pharmacological management. The lack of studies comparing efficiency of different anti-hypertensive medication groups and overall pharmacological treatment highlights the need for prospective studies to determine optimal strategies in the ISHY population.

In summary, further research contributing to deeper understanding of ISHY and its therapeutic management could have far-reaching implications for cardiovascular prevention in the growing population of young adults affected by this condition.

X. Conclusions

Isolated systolic hypertension in young adults is increasing in prevalence, affecting particularly men. Epidemiological and hemodynamic studies highlight the heterogeneity of this condition, with populations differing in hemodynamic phenotypes, anthropometric characteristics and cardiovascular risk factors. The risk of progression to sustained hypertension is lower than in other hypertension subtypes, however recent studies underscore increased cardiovascular and mortality risk in this population. The literature on therapeutic management of ISHY is scarce with guidelines recommending non-pharmacological intervention. The lack of studies specifically evaluating pharmacological therapy in this population represents a significant gap in current findings. Further research is needed to develop risk assessment tools and evaluate optimal diagnostic and therapeutic approaches in young adults with ISHY, ultimately aiming to reduce cardiovascular risk.

XI. Disclosures

All authors have read and agreed with the published version of the manuscript.

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