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REVIEW ARTICLE

Diagnostic and Therapeutic Approach to Different Hypertensive Phenotypes According to the 2023 ESH Guidelines

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Abstract

The European Society of Hypertension (ESH) in the guidelines document issued in 2023 made specific recommendations regarding the diagnostic and therapeutic approach for the different hypertensive phenotypes detectable in current clinical practice. The present paper will offer a critical review of these recommendations.The clinical hypertensive phenotypes of most frequent detection in current clinical practice, namely white-coat hypertension, masked hypertension, nocturnal hypertension and isolated systolic hypertension of the elderly will be reviewed. Other less common phenotypes will be also addressed. Recommendations for each clinical phenotype are made, emphasizing the need for an accurate diagnosis and treatment for specific clinical conditions, i.e. when target organ damage and/or high cardiovascular risk is detected. Areas of uncertainty related to clinical phenotypes in which pathophysiological and prognostic information are still lacking will be discussed. Future studies will allow to refine the guidelines recommendations, particularly for the clinical conditions for which pathophysiological and prognostic information are at present scanty.

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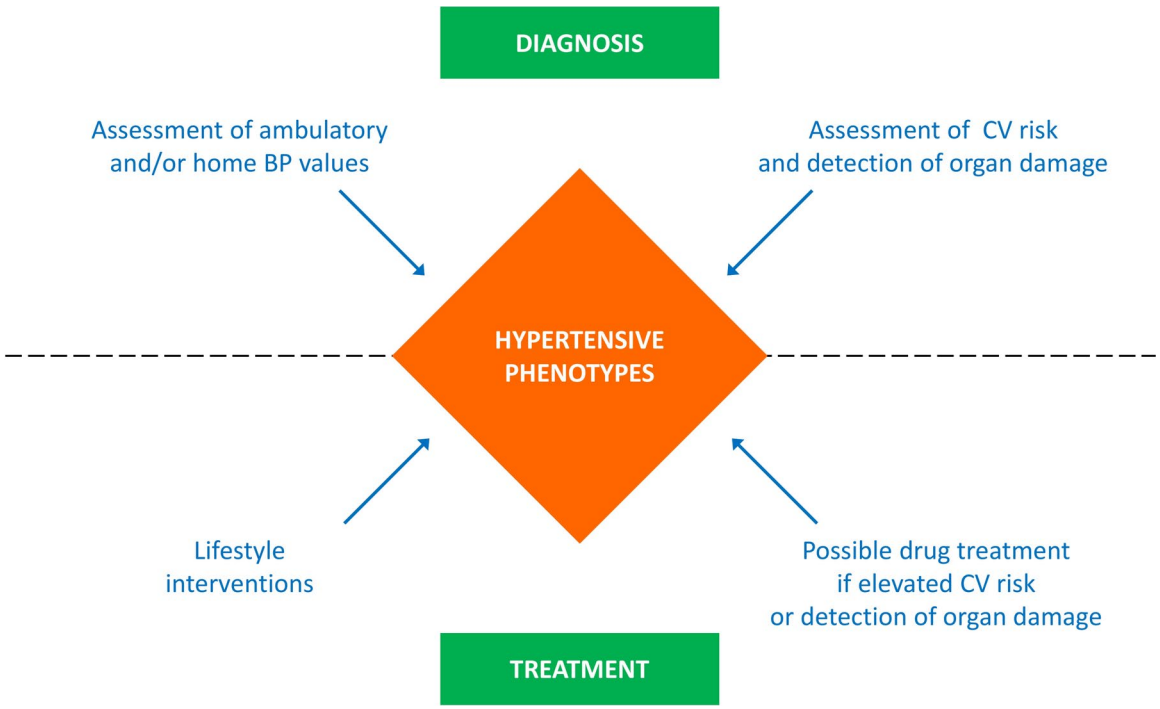
Graphical Abstract



Keywords Guidelines · Antihypertensive treatment · White-coat hypertension · Nocturnal hypertension · Isolated systolic hypertension · Hypertensive phenotypes

1 Introduction

The 2023 guidelines on hypertension diagnosis and treatment issued by the European Society of Hypertension (ESH) devoted, for the first time in the history of the document, a main section on the high blood pressure (BP) phenotypes, i.e. the clinical conditions characterized by selective increases of systolic or diastolic BP as well as by only office, out-of-office or nighttime BP elevation (Table 1) [1]. Description has been made of their prevalence, which in many cases is elevated, of the associated cardiovascular (CV) risk, which usually is increased, as well as of the diagnostic and treatment approaches.

The present paper will review the main information included in the 2023 ESH guidelines document regarding the prognosis, the diagnostic assessment as well as the therapeutic approach to the different hypertensive phenotypes. It should be emphasized that a limitation of these recommendations, which is also properly recognized by the guidelines document [1], refers to the fact that, with very few exceptions (see isolated systolic hypertension of the elderly, ISHE), they are mainly based on observational data, in absence of results of "ad-hoc" multicenter randomized clinical trials. The present paper will focus in sequence on the four most common phenotypes, namely white-coat hypertension (WCH), masked hypertension (MH), nocturnal hypertension (NH) and ISHE. It will also discuss in the second part of the review the other less frequent phenotypes listed in Table 1. As a general recommendation, which applies to all the different hypertensive phenotypes, but particularly to the ones characterized by selective increases of office and out-of-office BP (i.e. WCH and MH), guidelines emphasize the need to achieve their identification by repeated BP measurements, given the recent evidence of their limited reproducibility [2].

2 White-Coat Hypertension

It has been repeatedly reported that office BP assessed by the physician may not accurately reflect BP levels outside medical environment [1, 3], due to the occurrence of an alerting reaction with a resulting BP elevation. WCH defines the subjects whose BP is high (i.e. ≥140 mmHg and/or 90 mmHg) in the medical setting, but normal when detected away from doctor's office by 24-hour ambulatory blood pressue monitoring (ABPM) and/or home BP measurement [1, 3]. Since the first report of this clinical condition by Pickering and coworkers [4], several studies documented that WCH

Table 1 Specific Hypertension Phenotypes

Sustained hypertension and true normotension
White coat hypertension (WCH)
Masked hypertension MH)
White-coat uncontrolled hypertension (WUCH) and masked uncontrolled hypertension (MUCH)
Isolated systolic hypertension of the young (ISHY)
Isolated systolic hypertension in older persons (ISHE)
Isolated diastolic hypertension (IDH)
Nighttime hypertension (NH) and dipping
Orthostatic hypertension (OH) and hypotension

may account for a consistent fraction of the hypertensive population.

2.1 Prevalence

It has been reported, indeed, that WCH can be not infrequently detected in the general population and it is relatively common in the hypertensive one. Its prevalence may vary according the methods used to assess BP values (home BP or 24-hour ABPM) and the definition of out-of-office BP values normality. WCH can be detected in about 20-25% of the hypertensive population displaying a mild-to-moderate BP increase. According to normal cutoffs of clinic BP <140/90 mmHg and daytime ambulatory BP values <135/85 mmHg, WCH prevalence may range from 15 to 45% [5]. Among 1637 untreated subjects belonging to the Pressioni Monitorate e Loro Associazioni (PAMELA) study, i.e. an observational investigation carried out in the area around Milan (Italy), coordinated by our group and initiated in 1991 with a follow-up lasting more than 25 years, WCH prevalence ranged from 9% to 12%, depending on whether the definition of normal out-of-office BP was based on ABPM or home BP values [6]. More recently, spanish investigators [7] evaluated the prevalence and reproducibility of the different high BP phenotypes defined by clinic and ambulatory BP measurements in untreated patients recruited in the Spanish BP Monitoring Registry. The proportion of true normotensives and WCHs at first 24-hour BP monitoring amounted to 17% and 24%, respectively. In the majority of the published studies, WCH was established taking into account only one ambulatory BP recording. Although more reproducible than clinical BP measurement, ABPM values during the 24-hour period have an intrinsic variability from one recording session to another one, depending on physical activity, environmental stimuli, duration and quality of sleep of each patient [8]. This suggests that WCH cannot be regarded as a stable hypertensive clinical phenotype [1].

2.2 Target organ damage and CV risk

2023 ESH guidelines document emphasizes that information on the impact of WCH on target organ damage and CV risk are frequently not uniform and still matter of debate. Cross-sectional studies evaluating the potential link between WCH and target organ damage have provided conflicting results. Some studies reported an independent association between WCH and different markers of organ damage, including left ventricular hypertrophy, left ventricular diastolic dysfunction, renal damage and micro- as well as macro-vascular alterations [9, 10]. Other reports documented the similarity of the cardiac, renal and vascular organ damage profiles in WCH individuals and in normotensive subjects, even after data adjustments for confounders. In general, reports underline that if there is a difference between groups, this can be detected only when data collected in WCH are compared to those found in age- and sex-matched sustained hypertensives [11, 12, 13]. A meta-analysis of the studies published during the past 20 years and aimed at defining the main features of the different cardiac organ damage occuring in WCH has documented that: a) left ventricular mass index undergoes a progressive increase from the normotensive state to WCH and to sustained hypertension, b) left atrial diameter value is higher in WCH as compared to the one detected in the pure normotensive state, and c) in WCH subjects, office BP shows a direct, significant relationship with left ventricular mass index, quantified by the echocardiographic technique. Compared with the true normotensive state, WCH has also been shown to be characterized by an elevated sympathetic cardiovascular drive to the heart and the peripheral circulation [14], and a greater prevalence of metabolic risk factors [6]. In the already mentioned PAMELA study, we found that detection of renal (microalbuminuria and reduction in estimated glomerular filtration rate), cardiac (increase in left ventricular mass index) and vascular (increase in carotid wall thickness) asymptomatic target organ damage occurs in about 30%-35% of the patients with WCH as compared to 10% in pure normotensive subjects [15]. Recently, we also found that alterations in left ventricular mass seen in WCH are accompanied by an increase in arterial stiffness, as quantified by the cardio-ankle vascular index measurements [16]. Taken together these findings strongly support the notion that WCH represents a risk factor for the development and progression of the subclinical cardiac and vascular organ damage.

Although many studies have investigated the prognostic outcome of WCH, the impact of this hypertensive phenotype on the CV risk profile remains uncertain. In recent meta-analyses, the incidence of fatal and non fatal CV events in WCH individuals has been reported to be either similar as in normotensive subjects or intermediate

between normotensive and hypertensive patients [17]. The differences in CV risk reported in the different studies may depend on the behavior of central aortic BP. Indeed when this hemodynamic variable displays normal or low normal values the prognostic impact of WCH appears to be more benign [1]. Finally, in the above mentioned PAMELA study WCH subjects displayed, compared to normotensive individuals, a greater long-term risk of developing diabetes mellitus and an established hypertensive state, with a resulting increase in fatal CV events [15, 18].

2.3 Therapeutic approach (Fig. 1, left upper box)

According to 2023 ESH guidelines recommendations [1], the therapeutic approach to WCH should be based on 1) lifestyle modifications capable to to reduce CV risk profile and 2) careful follow-up compared with what is usually done in true normotensive individuals. It remains uncertain, however, whether WCH subjects should undergo antihypertensive drug treatment. This is because, although WCH patients have been a considerable proportion of virtually all randomized clinical trials proving the benefits of antihypertensive treatment [19], no specific outcome-based trial has been performed. Antihypertensive pharmacological treatment may be taken into account in WCH subjects who display target organ damage and show a high CV risk profile [1].

3 Masked Hypertension

In the early 2000s Pickering and coworkers [20] defined as MH the BP elevation identified throughout ABPM or home BP but not office BP measurement. In the following years cross-sectional and longitudinal studies reported that this BP phenotype is associated with the detection of multiple target organ damages and with an increased risk of CV events [1]. Out-of-office BP, indeed, either monitored at home or in

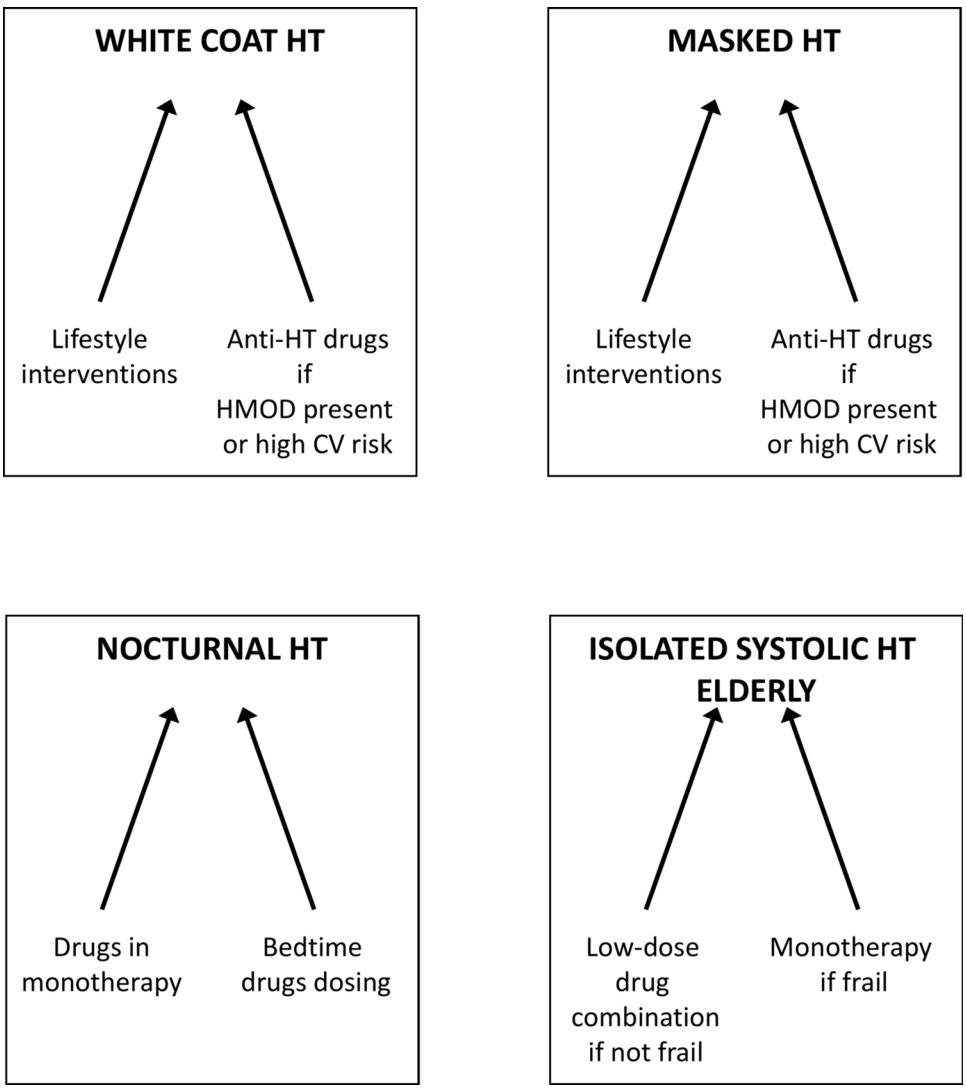


Fig. 1 Scheme illustrating the recommendations made by the 2023 European Society of Hypertension guidelines for the diagnosis and treatment of the hypertensive clinical phenotypes of most frequent detection. HT: hypertension, HMOD: hypertension-mediated organ damage, CV: cardiovascular.

ambulatory conditions over the 24 hours, has been shown to have a greater prognostic value than clinical BP readings. Several aspects concerning MH are still largely undefined. This particularly is true for the identification of the best methodology to be employed for the detection of this specific phenotype in current clinical practice. Specifically, it remains largely debated which is the BP measurement method (i.e. home versus ABPM) capable to more reliably identify subjects with an elevated BP in the out-of-the office environment. Additional uncertainty concerns the prevalence of MH in the general population, its clinical correlates and reproducibility over time [21, 22].

3.1 Prevalence

MH has been estimated to be present in about 10–25% of the individuals, depending, as previously mentioned, on the methods and diagnostic approaches used to detect this condition. A further confounder refers to the clinical characteristics of study samples (i.e. general population, subjects with suspected hypertension, diabetes, chronic renal disease, obesity, sleep apnoea syndrome). A number of reports evaluated the magnitude of MH phenomenon in the general population. In the japanese population of the Osahama study, 10% of subjects with normal BP values displayed mildly elevated average 24-hour ABPM. A fraction of these subjects, approximately 3%, showed 24-hour ABPM values equal or even greater than 145/86 mmHg [23]. In the PAMELA study, the only investigation published so far defining MH via home self-measured BP or ABPM, this condition is detectable in 9% to 12% of the population sample of untreated adult and elderly individuals. This prevalence variability depends on whether MH is defined by ambulatory or home BP, diastolic or systolic BP values [6]. Findings from the Jackson Heart Study, an African American population-based cohort including about one thousand participants, provided new information on the association of MH and prehypertension, i.e the condition defined by office systolic BP values between 120 to 139 mmHg and diastolic between 80 to 89 mmHg [24]. The prognostic value of MH for development of stable hypertension has been comfirmed recently [25]. Clinical factors associated with MH have not been fully elucidated, so far. Some studies have identified male gender, older age, high normal office BP, low physical activity, obesity, current smoking and habitual alcohol drinking as the main variables differentiating MH individuals from true normotensives [1]. Additional factors include an active role of neuroadrenergic mechanisms, the resulting sympathetic activation playing a central role in the MH development [1].

One major criticism of the studies assessing the main features of MH is the limited evidence about the reproducibility of this hypertensive phenotype. In the vast majority of cases, indeed, diagnosis of MH was based on the data collected by a single ABPM or home BP monitoring. Results of the above mentioned spanish ABPM registry have shown that in MH development of sustained hypertension involves about 30% of the patients during an average observation period lasting 3 months [7]. Overall, these findings are in line with the hypothesis that MH represents a transient hypertensive condition in a large fraction of the population [1].

3.2 Target organ damage and CV risk

MH phenotype has been frequently reported to be associated with subclinical damage detectable in different organs. Years ago our group [6] documented that in the PAMELA population prevalence of cardiac hypertrophy in MH subjects (14%) was similar to the one detected in WCH subjects (15%), lower than in sustained hypertensives (26%), but much greater than in the individuals displaying office and out-of-office normal BP values (4%). In subsequent years a number of studies evaluated the association between MH and organ damage in different clinical settings. A recent meta-analysis performed by our group provides a further contribution on MH and CV organ damage, as assessed by cardiac and carotid ultrasonography. From the analysis of the data collected in 12 studies including a total of about 2500 normotensive, 800 MH and 1700 sustained hypertensive subjects identified by ABPM, we found that left ventricular mass index shows a progressive increase from the normotensive state to MH and to overt hypertension [26]. Prevalence rates of LVH in normotensive controls, MH and sustained hypertensive subjects amounted to 3.7%, 14.1% and 11.3%, respectively. Results of the meta-analysis show that common carotid intima-media thickness progressively increased from the normotensives, to MH and sustained hypertensives [26]. As previously mentioned for WCH, also MH is characterized by an increase in arterial stiffness, based on the assessment of pulse wave velocity [16].

Data collected during the years provide almost conclusive evidence that MH is a BP phenotype with an important association with an increased risk of CV events as compared to the pure normotensive state [1]. In the PAMELA population, the incidence of CV deaths showed a gradual increase from true normotension to WCH, MH and sustained hypertension, independently of major CV risk factors [1]. The different impact on CV mortality detected in the four BP phenotypes was independent on whether these conditions were detected by office versus ambulatory or office versus home BP. Altogether these findings support the view that out-of-office BP is a powerful predictor of CV events.

3.3 Therapeutic approach (Fig. 1, right upper box)

The 2023 ESH guidelines on the diagnosis and treatment of hypertension strongly recommend that the therapeutic interventions of MH should be based on lifestyle modifications of several CV risk factors [1]. Whether the BP lowering drug treatment should be used in MH remains still an unsolved issue, but it can be considered in patients with subclinical organ damage and an elevated CV risk. The decision on the therapeutic approach of MH can be guided by the subclassification of MH in isolated daytime or nocturnal MH. Indeed, in isolated daytime MH morning administration of relatively short-acting antihypertensive drugs would be recommended. On the other hand, in nocturnal MH a chronotherapeutic intervention with bedtime administration of BP lowering drugs is indicated by ESH guidelines as a recommended choice [1].

4 Nocturnal Hypertension

As properly recognized by the 2023 ESH guidelines [1], ABPM represents the technique allowing a precise assessment of day-night BP variability. This technique has consistently documented that nighttime BP values are 10-20% lower than daytime values in the vast majority of healthy subjects. The drop in nighttime BP has as pathophysiologic background a reduction in sympathetic CV drive and an increased cardiac vagal tone during nocturnal bed rest period. These autonomic modidifications are in turn responsible for a sustained decrease in heart rate, cardiac output, and peripheral vascular resistance occurring during nighttime [27].The magnitude of the 24-hour BP variations in active subjects is related to a variety of factors such as age, level of physical activity, cigarette smoking habits, emotional state, duration and quality of sleep. The mechanism(s) of the impaired circadian BP pattern is multifactorial. A blunted BP fall at night in hypertensive patients has been shown to be highly prevalent in various clinical conditions including secondary hypertension, chronic kidney diseases, types 1 and 2 diabetes mellitus, sleep apnoea, autonomic nervous system dysfunction and preeclampsia [1]. As a consequence, the detection of a blunted decline in the neuroadrenergic cardiovascular influence and in the renin-angiotensin-aldosterone activity, the discovery of an endothelial dysfunction, of an impaired baroreflex sensitivity, and of a reduced renal sodium excretion capacity has been found to be linked to elevated nighttime BP values [28]. Clinical evidence supporting the key role of sodium in circadian BP rhythm is provided by the reversal of non-dipping status and NH after salt restriction or administration of thiazide diuretics [1]. It should also be emphasized that subclinical vascular damage itself might attenuate the vasodepressor influence of sleep, thus contributing to maintenance of NH.

4.1 Prevalence

Prevalence rates of NH, as defined according to 2023 ESH guidelines (i.e., nighttime. systolic BP > 120 mm Hg or diastolic BP > 70 mmHg), largely vary across studies, depending on demographic, clinical, and ethnical factors [29, 30]. In the PAMELA population, about 1/3 of participants was found to fulfill the ABPM diagnostic criteria for NH [31]. Patients with NH were characterized by older age, greater prevalence of diabetes, higher levels of serum creatinine, cystatin C, calcium, uric acid, and homocysteine than nocturnal normotensive patients. Although available information on NH prevalence across different clinical settings remain scanty, this condition appears highly prevalent in the hypertensive population. Genetic, demographic, and lifestyle factors appear to be responsible for the nighttime BP differences across studies [31–33]. Of note, scarce are the information on the NH patterns in the very elderly, and no age-adjusted specific criteria for defining NH are provided by current guidelines [1]. Few studies investigated the reproducibility of NH phenotype. A study carried out in Italy examined NH prevalence, correlates, and reproducibility in a cohort of 658 untreated hypertensives [34]. About 75% of the study cohort displayed NH in both ABPM sessions, and about 10% showed normal nighttime BP in both ABPMs.

4.2 Target organ damage and CV risk

Similarly to what has been discussed for asymptomatic target organ damage, a limited number of cross-sectional observations performed in the general population and in the hypertensive cohorts suggests that NH combined to daytime BP elevation is associated with more advanced structural and functional CV alterations [31–33]. Furthermore, a relationship between isolated NH (a clinical hypertensive phenotype displaying a BP elevation restricted to the nighttime period) and target organ damage has been documented in recent years [34]. These findings are in line with the concept that average nighttime BP values are superior to the daytime ones in predicting subclinical cardiac and extra-cardiac organ damage and, more importantly, the risk of fatal and non-fatal CV events [35, 36].

4.3 Therapeutic Approach (Fig. 1, left lower box)

The above findings explain why 2023 ESH guidelines suggest that restoring a normal circadian BP rhythm in hypertensive patients is regarded as an effective therapeutic

intervention designed to counteract the development and/or the progression of target organ damage and to improve CV prognosis [1]. Growing evidence on the different therapeutic approaches to nighttime BP abnormalities, and particularly on the bedtime administration of antihypertensive drugs, supports this therapeutic scheme as one of the more effective against CV risk related to NH [1, 37]. In a practical perspective, targeting NH by correcting associated risk factors and implementing a chrono-therapeutic approach may have important implications for public health [37].

5 Isolated Systolic Hypertension of the Elderly

Ageing is characterized by an increase in arterial stiffness, which depends on the sympathetic activation, the endothelial dysfunction, the vascular remodelling and the changes in the extracellular matrix reported in the elderly population [38]. The development of ISHE is also associated with an age-related increase in sodium sensitivity and phenotypic changes of aortic smooth muscle cells of arterial distensibility through structural and functional changes in the large arteries [38, 39].

5.1 Prevalence

The clinical relevance of ISHE is growing, since in people aged 60 years and older, ISHE is by far the most common phenotype of clinical hypertension. At the age of 70 years or more, about 70% of patients display ISHE, and in those older than 80 years, the prevalence is above 90% [39].

5.2 Target Organ Damage and CV Risk

Although ISHE has been regarded for many years as a benign condition, several studies over the past decades reported an increased CV morbidity and mortality in older persons with ISHE [36]. Data from large-scale studies demonstrated several complications of ISHE, which can be properly predicted by office BP, home BP and ABPM measurements [1, 40]. The use of ABPM is highly recommended, because elderly hypertensive patients are at higher risk not only for hypertension but also for cardiac arrhythmias, the most common being atrial fibrillation [41].

The Framingham Heart Study provided conclusive evidence that ISHE is associated not only with increased CV mortality and morbidity. This is documented by the finding that the risk of stroke and myocardial infarction was increased three and two times, respectively, in presence of ISHE [36, 41]. Other age-related complications include cognitive dysfunction, heart failure and heart attack. Furthermore the ageing process is associated with a decreased renal function, a factor contributing to the increased CV risk of ISHE [41, 42].

5.3 Therapeutic Approach (Fig. 1, Right Lower Box)

Randomized controlled clinical trials have provided conclusive evidence on the benefits related to ISHE treatment, leading to a clearcut reduction in all cause mortality (8-13%), CV mortality (-18%) and composite CV outcomes (-26%) [1, 42]. Results of these clinical studies have also indicated calcium-channel blockers and thiazide diuretics as drugs of choice for the management of ISHE, angiotensin converting enzyme (ACE)-inhibitors and angiotensin receptors antagonists being shown to be less effective [1, 42]. 2023 ESH guidelines strongly recommend also in the treatment of this phenotype to initiate the therapeutic approach with a low-dose dual drug combination, if patients are not frail and treatment is well tolerated [1]. Although largely debated during the last years, target BP to be achieved during treatment is located for the systolic component between 140 and 150 mmHg, greater reduction of BP values being not recommended because associated with unfavorable clinical outcomes [1, 42].

6 Other Less Common Phenotypes

In the following paragraphs we will recall the main diagnostic and therapeutic recommendations included in the ESH document related to other BP phenotypes (Table 1), which appear to be of less frequent detection in current clinical practice.

6.1 White-Coat and Masked Uncontrolled Hypertension (WUCH and MUCH)

WUCH refers to the clinical condition in which BP control by treatment is detectable during the 24 hour period but not by office BP measurements, while MUCH to the detection of a BP controlled by treatment is in-office but not outside the office [1, 2]. Both these two phenotypes are of recent detection and data on prevalence, impact on CV risk not yet conclusively established. According to the data collected in the SPRINT trial, MUCH appears to be of larger detection than WUCH (35% vs 10%) and associated with a worse metabolic profile, increased sympathetic overdrive, enhanced hypertension-mediated organ damage and greater CV risk as compared to the WUCH phenotype [43]. The greater risk of CV events detectable in MUCH appears to be independent on the type of out-of-office measurements

(ambulatory or home BP) the diagnosis of the phenotype was based on.

As far as treatment is concerned, 2023 ESH guidelines recommend to perform both in WUCH and in MUCH an uptitration of antihypertensive drugs used in order to achieve a better BP control [1] (Fig. 2, left upper box). This approach is particularly indicated in MUCH, given it worse impact on the CV risk profile.

6.2 Isolated Systolic Hypertension of the Young (ISHY)

This phenotype appears to be detectable in young individuals, more frequently found in men and also in children and adolescents, in which is frequently associated with hemodynamic abnormalities, such as elevated heart rate, increased cardiac output, and anthropometric alterations, such as an overweight or an obese state [1]. However, in about ¼ of the patients all the above mentioned abnormalities are not detectable, indicating an heterogeneity of the main pathopysiological features of this hypertensive phenotype. Heterogeneous also appear to be the results of the studies designed to define the CV risk proflile and the associated target organ damage of this hypertensive phenotype [44]. Given the limited prognostic data available, suggestion is made by 2023 ESH guidelines to adopt lifestyle modifications, particularly aimed at loosing weight, if an obese or an overweight state is detected and to start drug treatment in the patients who display target organ damage or an elevated CV risk [1, 45] (Figure 2, right upper box). Control of elevated heart rate and blood pressure values should be the main targets of the therapeutic intervention [1]. In future, more clear indications regarding prognosis and treatment may be obtained from the data collected by assessing in these patients central BP values, i.e. the pressure in the ascending aorta, which may represent, if elevated, markers of an increased CV risk more sensitive than traditional office BP [1].

6.3 Isolated Diastolic Hypertension (IDH)

This hypertensive phenotype, which is characterized by diastolic BP >90 mmHg, with a systolic value within the normal range, may be detected in about 3-8% of the general population. IDH has been reported to be associated with an increased CV risk, particularly in the patients aged less than 50 years [46]. This association may allow to recommend life style inteventions as well as standard antihypertensive drug treatment in this group of younger individuals [1, 46] (Figure 2, left lower box). It should be mentioned, however, that in the few clinical intervention trials performed on this specific phenotype during the years, although diastolic BP was the main target of the therapeutic approach, both systolic and diastolic BPs were favorably affected by the therapeutic intervention. This prevented to establish whether a selective control of the altered hemodynamic variable. i.e. elevated diastolic BP, allows in these patients to provide protective effects on CV risk.

6.4 Orthostatic Hypertension and Hypotension

Abnormal responses of BP to assumption of the upright posture (BP reductions or increases of magnitude greater than 20 mmHg for systolic BP or 10 mmHg for diastolic BP) are associated with an increased cardiovascular risk [1, 47]. In young inviduals detection of an exaggerated BP repsonse to othostasis may represent a marker of future hypertensive state [47]. Diagnosis of orthostatic hypertension should be based on BP measurements performed in the supine position and during upright active position, with evaluation of BP and heart rate after 1, 3 and 5 minute of the standing position time. To avoid the potential limited reproducibility of the approach, the manoeuvre should be repeated twice.Treatment of orthostatic hypertension is based on prescription of antihypertensive therapies according to ESH hypertension guidelines [1] (Figure 2, right lower box), being no evidence that patients with orthostatic hypertension benefit from a particular drug class in terms of CV risk protection. According to some authors, diuretic treatmnet should probably be avoided, given the possibility that these pharmacological compounds may exacerbate the neurohumoral activation reported in these patients [47].

The therapeutic approach of the opposite clinical condition, i.e. orthostatic hypotension, is challenging and based on the treatment of the underlying cause of the disease, such as the baroreflex dysfunction, which appears to be of very common detection in this clinical condition [1].

7 Conclusions

As mentioned in the Introduction, ESH guidelines in the document published in 2023 for the first time systematically address the reader's attention to the diagnostic and treatment approach to specific clinical hypertensive phenotypes [1]. This emphasizes the pivotal position of these clinical conditions in current practice, with particular focus on an accurate diagnosis and a tailored treatment. Future studies will allow to refine the guidelines recommendations, particularly for the clinical conditions for which pathophysiological and prognostic information remain at present scanty.

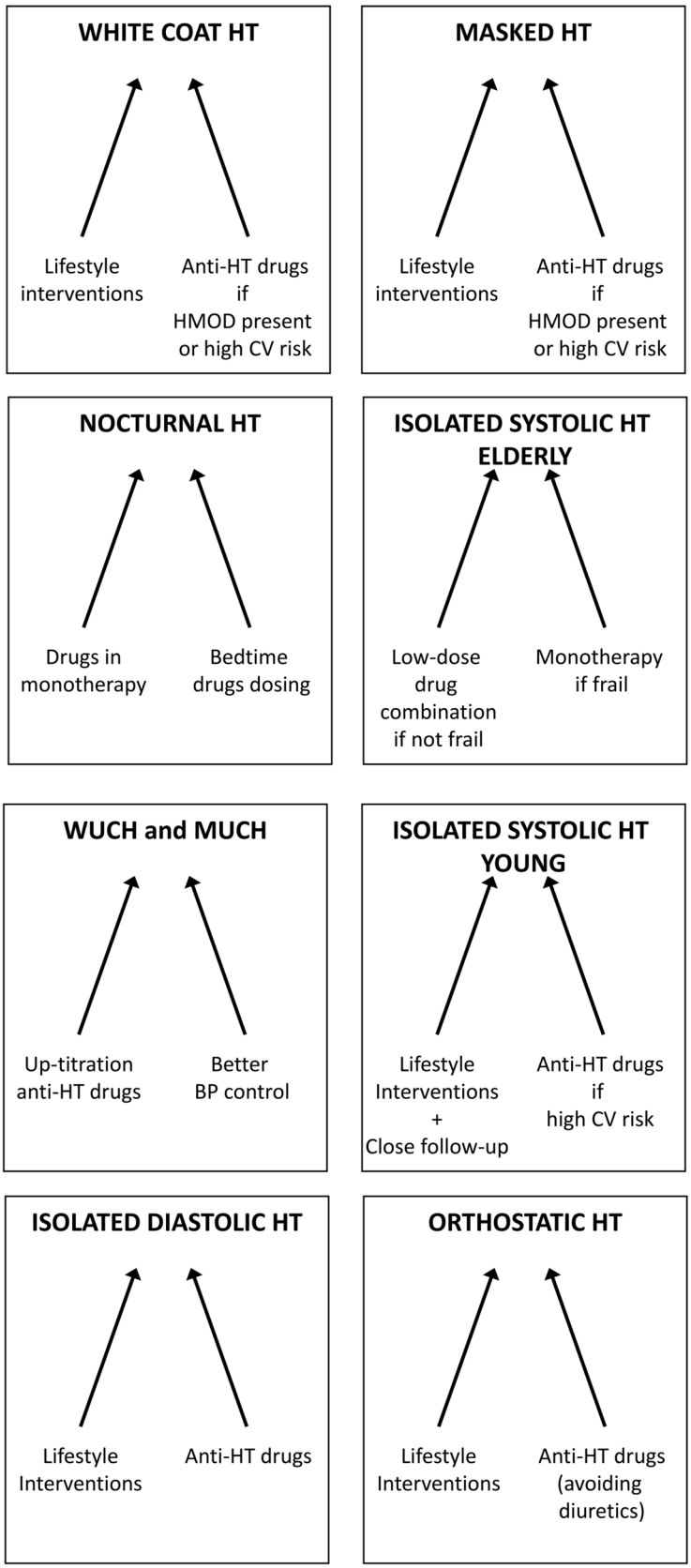


Fig. 2 Scheme illustrating the recommendations made by the 2023 European Society of Hypertension guidelines for the diagnosis and treatment of the hypertensive clinical phenotypes of less frequent detection. WUCH: white-coat uncontrolled hypertension, MUCH: masked uncontrolled hypertension, BP: blood pressure. Other abbreviations as in Fig. 1.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

References

1. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH guidelines for the management of arterial hypertension. J Hypertens. 2023;41:1874–2071.
2. Mancia G, Facchetti R, Cuspidi C, Bombelli M, Corrao G, Grassi G. Limited reproducibility of MUCH and WUCH: evidence from the ELSA study. Eur Heart J. 2020;41:1565–71.
3. Muntner P, Shimbo D, Carey RM, et al. Measurement of blood pressure in humans. A scientific statement from the American Heart Association. Hypertension. 2019;73:e35–66.
4. Pickering TG, James GD, Boddie G, Harshfield GA, Blank S, Laragh JH. How common is white-coat hypertension? JAMA. 1988;259:225–8.
5. Dolan E, Stanton A, Atkins N. Determinants of white-coat hypertension. Blood Press Monit. 2004;9:307–9.
6. Grassi G, Bombelli M, Sega R, et al. The PAMELA (Pressioni Arteriose Monitorate E Loro Associazioni) Study. High Blood Press Cardiovasc Prev. 2007;14:83–8.
7. de la Sierra A, Vinyoles E, Banegas J, et al. Short-term and long-term reproducibility of hypertension phenotypes obtained by office and ambulatory blood pressure measurements. J Clin Hypertens. 2016;18:927–33.
8. Redon J. The importance of 24-hour ambualtory blood pressure monitoring in patients at risk of cardiovascular events. High Blood Press Cardiovasc Prev. 2013;20:13–8.
9. Palatini P, Mormino P, Santonastaso M, et al. Target-organ damage in stage I hypertensive subjects with white-coat and sustained hypertension: results from the Harvest study. Hypertension. 1998;31:57–63.
10. Muldoon ME, Nazzaro P, Sutton-Tyrrell K, Manuck SB. White-coat hypertension and carotid artery atherosclerosis: matching study. Arch Intern Med. 2000;160:1507–12.
11. Cavallini MC, Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB. Is white-coat hypertension associated with arterial disease or left ventricular hypertrophy? Hypertension. 1995;26:413–9.
12. Cuspidi C, Marabini M, Lonati L, et al. Cardiac and carotid structure in patients with established hypertension and white-coat hypertension. J Hypertens. 1995;13:1707–11.
13. Cuspidi C, Rescaldani M, Tadic M, Sala C, Grassi G, Mancia G. White-coat hypertension, as defined by ambulatory blood pressure monitoring, and subclinical cardiac organ damage: a meta-analysis. J Hypertens. 2015;33:24–32.
14. Grassi G, Pisano A, Bolignano D, et al. Sympathetic nerve traffic activation in essential hypertension and its correlates: systematic reviews and meta-analyses. Hypertension. 2018;72:483–91.
15. Mancia G, Facchetti R, Vanoli J, Dell'Oro R, Seravalle G, Grassi G. White-coat hypertension without organ damage: impact on long-term mortality, new hypertension, and new organ damage. Hypertension. 2022;79:1057–66.
16. Cuspidi C, Facchetti R, Gherbesi E, et al. Ambulatory blood pressure phenotypes, arterial stiffness, and cardiac remodeling. Am J Hypertens. 2024;37:978–86.
17. Briasoulis A, Androulakis E, Palla M, Papageorgiou N, Tousoulis D. White-coat hypertension and cardiovascular events: a meta-analysis. J Hypertens. 2016;34:593–9.
18. Mancia G, Facchetti R, Bombelli M, Cuspidi C, Grassi G. White-coat hypertension: pathophysiological and clinical aspects: excellence award for hypertension research 2020. Hypertension. 2021;78:1677–88.
19. Townsend RR, Cohen JB. White-coat hypertension & cardiovascular outcomes. Curr Hypert Rep. 2024;26:399–407.
20. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. Hypertension. 2002;40:795–6.
21. Cuspidi C, Facchetti R, Gherbesi E, et al. Increased arterial stiffness and left ventricular remodelling as markers of masked hypertension: findings from the PAMELA population. J Hypertens. 2025;43:781.
22. Trudel X, Milot A, Brisson C. Persistence and progression of masked hypertension: a-5 year prospective study. Int J Hypertens. 2013;2013:836387.
23. Imai Y, Tsuji I, Nagai K, et al. Ambulatory blood pressure monitoring in evaluating the prevalence of hypertension in adults in Ohasama, a rural Japanese community. Hypertens Res. 1996;19:207–12.
24. Redmond N, Booth JN, Tanner RM, et al. Prevalence of masked hypertension and its association with subclinical cardiovascular disease in African Americans: results from the Jackson Heart Study. JAHA. 2016;5: e002284.
25. Cesario V, Presta V, Figliuzzi I, et al. Epidemiological impact and clinical consequences of masked hypertension a narrative review. High Blood Press Cardiovasc Prev. 2020;27:195–201.
26. Cuspidi C, Sala C, Tadic M, Rescaldani M, Grassi G, Mancia G. Untreated masked hypertension and subclinical cardiac damage: a systematic review and meta-analysis. Am J Hypertens. 2015;28:806–13.
27. Sherwood A, Steffen PR, Blumenthal JA, Kuhn C, Hinderliter AL. Nighttime blood pressure dipping: the role of the sympathetic nervous system. Am J Hypertens. 2002;15:111–8.
28. Grassi G, Seravalle G, Quarti-Trevano F, et al. Adrenergic, metabolic, and reflex abnormalities in reverse and extreme dipper hypertensives. Hypertension. 2008;52:925–31.
29. Kario K. Nocturnal hypertension: new technology and evidence. Hypertension. 2018;71:997–1009.
30. Kario K. Sleep and nocturnal hypertension: genes, environment and individual profiles. J Clin Hypertens. 2022;24:1263–5.
31. Grassi G, Quarti Trevano F, Dell'Oro R, Cuspidi C, Mancia G. The PAMELA research project: a 25-year long journey. Panminerva Med. 2021;63:430–5.

32. Kokubo A, Kuwabara M, Tomitani N, Yamashita S, Shiga T, Kario K. Nocturnal blood pressure surge in seconds is associated with arterial stiffness independently of conventional nocturnal blood pressure variability in suspected obstructive sleep apnea patients. J Clin Hypertens. 2023;25:388–92.
33. Kim HS, Shin C, Kim S, et al. Prevalence of isolated nocturnal hypertension and development of arterial stiffness, left ventricular hypertrophy, and silent cerebrovascular lesions: the KoGES (Korean Genome and Epidemiology Study). JAHA. 2022;11: e025641.
34. Hansen TW, Li Y, Boggia J, Thijs L, Richart T, Staessen JA. Predictive role of the nighttime blood pressure. Hypertension. 2011;57:3–10.
35. Mohammed AAS, Lin X, Yangyang Y, et al. The asociation of morning surge and night-time dipping blood pressure with significant and complex coronary artery lesions. High Blood Press Cardiovasc Prev. 2012;28:467–74.
36. Kario K, Hoshide S, Mizuno H, et al. Nighttime blood pressure phenotype and cardiovascular prognosis: practitioner-based nationwide JAMP study. Circulation. 2020;142:1810–20.
37. Hoshide S, Mogi M, Kario K. How do we tackle nighttime blood pressure? Hypertens Res. 2023;46:2262–3.
38. AlGhatrif M, Lakatta EG. The conundrum of arterial stiffness, elevated blood pressure, and aging. Curr Hypertens Rep. 2015;17:12.
39. Liu X, Rodriguez CJ, Wang K. Prevalence and trends of isolated systolic hypertension among untreated adults in the United States. J Am Soc Hypertens. 2015;9:197–205.
40. Battistoni A, Michielon A, Marino G, Savoia C. Vascular aging and central aortic blood pressure: from pathophysiology to treatment. High Blood Press Cardiovasc Prev. 2020;27:299–308.
41. Chobanian AV. Clinical practice Isolated systolic hypertension in the elderly. N Engl J Med. 2007;357:789–96.
42. Ferri C, Ferri L, Desideri G. Management of hypertension in the elderly and frail elderly. High Blood Press Cardiovasc Prev. 2017;24:1–11.
43. Ghazi L, Cohen LP, Muntner P, Shimbo D, Drawz PE. Effect of intensive versus standard office-based hypertension treatment strategy on white-coat effect and masked uncontrolled hypertension: from the SPRINT ABPM ancellary study. Hypertension. 2020;76:1090–6.
44. Saladini F, Palatini P. Isolated systolic hypertension in young individuals: pathophysiological mechanisms, prognostic significance, and clinical implications. High Blood Press Cardiovasc Prev. 2017;24:133–9.
45. Palatini P, Rosei EA, Avolio A, et al. Isolated systolic hypertension in the young a position paper endorsed by the European Society of Hypertension. J Hypertens. 2018;36:1222–6.
46. Yano Y, Kim HC, Lee H, et al. Isolated diastolic hypertension and risk of cardiovascular disease: controversies in hypertension-Pro side of the argument. Hypertension. 2022;79:1563–70.
47. Jordan J, Biaggioni I, Kotsis V, et al. Consensus statement on the definition of orthostatic hypertension endorsed by the American Autonomic Society and the Japanese Society of Hypertension. Clin Auton Res. 2023;33:69–73.