

- **SPECIFIC HYPERTENSION PHENOTYPES**

1 Sustained hypertension and true normotension

Use of out-of-office BP m. by HBPM and/or ABPM allows identifying BP phenotypes.

One phenotype is termed sustained hypertension and consists of an elevation of both office and out-of-office BP.

Another is true normotension, which is characterized by office and out-of-office BP normality.

White-coat hypertension

WCH refers to the **untreated condition** in which BP is elevated in the office but is normal when measured by ABPM, HBPM or both

which is believed to mainly reflect the **pressor response** to an alerting reaction elicited by office BP measurements by a physician or a nurse

WCH can account for about 30% of people attending hypertension clinics

It is more common with increasing age (>50% in the very old patients), in women and in nonsmokers.

A significant white-coat effect can be seen at all grades of hypertension (including resistant hypertension), while the **prevalence** of WCH is the **greatest** in grade 1 hypertension

HMOD is less prevalent in WCH than in sustained hypertension,

However, compared with true normotensives, patients with WCH have **increased adrenergic activity**, a greater prevalence of **metabolic risk factors** and a more frequent **asymptomatic HMOD**].

Furthermore, **compared to normotensive** individuals, white-coat hypertensive individuals have shown a greater long-term risk of **new-onset diabetes**, progression to **sustained hypertension** and **CV mortality**
nocturnal hypertension

The **increased CV risk and mortality** have been reported with diagnostic use of both HBPM and ABPM, in the absence of HMOD at baseline and in ISH, older patients and other conditions

diagnosis of WCH should be confirmed by repeated office and out-of-office BP measurements.

Ideally, out-of-office BP measurements should include **both ABPM and HBPM** because the two values can give discrepant results, i.e. one value can be normal and the other elevated or vice versa,

and the CV risk appears to be lower (and close to sustained normotension) in white-coat hypertensive individuals in whom ABPM and HBPM **are both normal**

Thorough assessment of CV risk factors and HMOD are recommended.

Treatment should consider lifestyle changes to reduce CV risk and a closer FU compared with true normotensive individuals.

Whether or not patients with WCH should receive *antihypertensive drugs is still unresolved*,
no specific outcome-based trial has been performed.

Drug treatment may be considered in patients with HMOD and a high CV risk.

Out-of-office BP measurement by ABPM and/or HBPM should be done when WCH is suspected, particularly in people with grade 1 hypertension

In patients with WCH, assessment of CV risk factors and HMOD is recommended

Out-of-office BP measurements should be done by ABPM and/or HBPM and repeated during follow up to timely identify sustained hypertension or new HMOD.

In patients with WCH, lifestyle interventions to reduce CV risk and close follow are recommended

Whether antihypertensive drugs should be used is still unresolved,

but it can be considered in patients with HMOD and high CV risk.

3 Masked hypertension

MH refers to untreated patients in whom the BP is normal in the office but elevated when measured by HBPM or ABPM .About 10–20% of patients

Screening all individuals with nonelevated office BP for MH is impractical.

An office BP in the high-normal BP range is associated with a higher likelihood of MH.

The prevalence is greater in younger people, men, smokers and

those with higher levels of physical activity, alcohol consumption, anxiety and job stress

Obesity, diabetes, low HDL-cholesterol, CKD, family history of hypertension, are also associated with

An exaggerated BP response to exercise and to the orthostatic posture have also been found to be predictors of MH

A CV risk-based approach, limiting the use of out-of-clinic BP measurement to those individuals *with multiple risk factors* for MH, has been proposed

]. MH has been associated with HMOD such as impaired kidney function, LVH, carotid intima–media thickness and large artery stiffness

People with MH have an increased risk of developing metabolic abnormalities and diabetes as well as sustained hypertension and have increased sympathetic activity

the risk of CV events is substantially greater in MH compared with normotension, and intermediate risk or even close to the risk of sustained hypertension

Out-of-office BP measurement by ABPM and/or HBPM should be done in people with high normal blood pressure to identify MH.

In patients with MH, lifestyle interventions and close follow up are recommended to reduce CV risk and to timely identify sustained hypertension and new HMOD.

ISHY,

ISHY, defined as an SBP $140 >$ mmHg and a DBP < 90 mmHg, is present

not only in older persons but also in young and very young individuals (ISHY), more commonly in **male** individuals

ISHY may be present also in children and adolescents and is often associated with overweight and obesity.

. Increased cardiac output, heart rate and stroke volume are the predominant hemodynamic abnormalities in ISHY

and may explain why peripheral pulse pressure is higher and ISHY is more **common in athletes** than sedentary people

obesity, male sex, high salt intake and smoking

Close follow-up *and* lifestyle interventions

and

out-of-office BP measurement is recommended.

n individuals with *high out-of-office BP* or high central BP,
particularly with *other CV risk factors or HMOD*,

BP lowering drug treatment can be considered.

14.6 Isolated systolic hypertension in older persons

, aging is accompanied by a steady increase in SBP while a plateau of DBP occurs at the age of 50–60 years, followed by a decrease

The increased arterial load due to the high SBP *promotes vascular atherosclerosis and LVH, ultimately leading to CAD, cerebrovascular disease and HF.*

ISH, defined as SBP 140 mmHg and DBP <90 mmHg, becomes the most common form of hypertension after 50 years of age and is present in most patients with hypertension who are >70 years of age

ISH is also more common in women and overweight people
that SBP has a **greater impact on outcomes than DBP after 50 years** of age and that ISH, either assessed with office BP or by ABPM is associated with a high risk of CV outcomes and mortality.

metaanalysis of older patients with ISH showed that active treatment reduced all-cause mortality by 13%, CV mortality by 18 %, and all CV outcomes by 26%

This meta-analysis also showed that DBP was inversely associated with total mortality, highlighting the role of **pulse pressure as a risk factor**

that **early** versus late initiation of treatment after the detection of ISH led to a persistently **greater CV protection** at all ages.

Based on the data, **CCBs and Thiazide-like diuretics** emerged as the drugs of **choice** for the management of ISH

, whereas ACEis/ARBs showed less efficacy, suggesting that they should be used as first-line agents when there are compelling indications such as HF, coronary artery disease, CKD, metabolic syndrome and diabetes [865,871].

Because the rate of BP control with monotherapy is low in patients with ISH, the general recommendation to start with **dual combination therapy** applies also in older patients with ISH, if they are not frail.

antihypertensive treatment that **lowered SBP <140 mmHg** was associated with asignificant outcome reduction

a marked decrease in DBP should be avoided

7 Isolated diastolic hypertension

Isolated diastolic hypertension (IDH) is a hypertension phenotype characterized by an SBP <140 mmHg and a DBP >90 mmHg.

a peak between **30 and 39** years, a decrease in the fifth and sixth decades (<15%) and

almost **no case above 70** years of age [882].

IDH has a greater prevalence in men than in women

Some reports have shown that **awareness and treatment** of hypertension are **very low** among IDH patients

IDH is associated with **a greater CV risk** compared with normotensive individuals

More frequent in **central obesity**, and is linked with other components of the **metabolic syndrome**

When compared with other hypertension phenotypes, IDH patients are generally **younger**, of **male** sex, consume more **alcohol and tobacco**, and are more frequently **diabetic** patients

Periodic BP evaluation and lifestyle interventions
are recommended for all patients with IDH.

, it is recommended that the BP lowering **drug treatment** should follow the **general treatment strategy**

Baroreflex failure and efferent autonomic failure

Arterial baroreceptors sense changes in vascular stretch resulting from BP fluctuations. The information is conveyed through afferent nerves to the **brainstem** and elicits counter-regulatory adjustments in sympathetic and parasympathetic efferent activity, thereby stabilizing BP

Clinically, baroreflex failure is characterized by **extreme BP variability** with dramatic hypertensive surges, hypotensive episodes and orthostatic hypotension in some but not all patients

Given the importance of the baroreflex in BP control, damage to the afferent portion, the integrating brainstem centers and/or the efferent portion of the baroreflex results in severe BP abnormalities.

Causes of baroreflex failure include **neck dissection** or **radiation** therapy, bilateral resection of carotid body paragangliomas, **familial dysautonomia** (hereditary sensory and autonomic neuropathy type 3), and, very rarely, **brainstem lesions**

The clinical presentation of autonomic failure is characterized by a variety of manifestations of loss of autonomic BP control, including posture-related BP abnormalities with orthostatic hypotension and, in many patients, supine hypertension

. Because **hypertensive** episodes in patients with baroreflex failure are mediated through unrestrained sympathetic activation, which are exacerbated by psychological and physiological stress,

long-acting central sympatholytic agents are the mainstay of therapy [917].

Vasodilators and diuretics can dramatically lower BP in patients with baroreflex failure and should be avoided whenever possible.

Hypotensive episodes are usually managed using **nonpharmacological** means.

Bradycardia through unrestrained cardiac parasympathetic activation **may require pacemaker**

The clinical presentation of autonomic failure is characterized by a variety of manifestations of **loss of autonomic BP control**, including posture-related BP abnormalities with orthostatic hypotension and, in many patients, supine hypertension

The diagnosis of (afferent) baroreflex failure should be considered in patients with highly volatile hypertension that is exacerbated by psychological and physiological stress, particularly in those with predisposing conditions (e.g., following neck dissection or radiation therapy).

The diagnosis of (afferent) baroreflex failure should be confirmed by baroreflex testing preferably in specialized centers

Long-acting sympatholytic drugs can be prescribed to attenuate hypertensive episodes in patients with (afferent) baroreflex failure.

In patients with (efferent) autonomic failure, the underlying causes should be sought for to identify potentially treatable conditions and to gauge prognosis.

For patients with (efferent) autonomic failure and symptomatic orthostatic hypotension, non-pharmacological treatments such as increased sodium ingestion, sufficient water ingestion, and venous compression garments should be instituted first. Medications worsening orthostatic hypotension (e.g., diuretics, alpha-1 blockers, vasodilators) should be discontinued whenever possible.

Anti-hypotensive medications (e.g., alpha-adrenoreceptor agonists) may be considered for patients with (efferent) autonomic failure who remain symptomatic on non-pharmacological treatments, however, the treatment can worsen hypertension in the supine position.

In patients with (efferent) autonomic failure and hypertension in the supine position, sleeping with the head of the bed tilted up can improve BP. Pharmacological therapy of supine hypertension can be considered in selected patient after individual risk-benefit consideration weighing potential benefits on cardiovascular risk against risk of fall and overall prognosis of the underlying disease.