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# Resistant Hypertension and Its Correlated Disease

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***Abstract:*** **Resistant hypertension is defined as blood pressure above the patient's goal despite the use of 3 or more antihypertensive agents from different classes at optimal doses, one of which should ideally be a diuretic .Evaluating patients with resistive hypertension should first confirm that they have genuine resistant hypertension through elimination or correction of pseude resistence factors such as white coat hypertension, suboptimal blood pressure measurement technique, poor medication compliance, inappropriate antihypertensive dosage or combinaison, and white coat effects and clinical inertia.Resistant hypertension therapy includes improved compliance with the use of drugs, secondary hypertension detection and treatment, use of lifestyle measures and treatment of obesity, and other comorbidities. switching to a long-acting diuretic type of thiazide like chlorthalidone could improve the BP from the patients taking hydrochlorothiazide. However, clinical trials of OSAHS have heterogeneous outcomes, surrogate outcomes, subjective outcomes, composite outcomes, and a lack of endpoints or patient perspectives. The diagnosis is confirmed by a sleep study. The main treatment for OSAS is the use of continuous positive airway pressure (CPAP) at night via a nasal or oronasal mask, which usually results in rapid improvement of symptoms. Patients who cannot tolerate CPAP therapy can be successfully treated with a mandibular advancement device. Supportive measures include regular and sufficiently long sleep periods, refraining from smoking and alcohol consumption in the evening, and weight reduction in overweight patients.**

***Keywords:*** **Hypertension, Resistant hypertension, Obstructive sleep apnea.**

## I. INTRODUCTION

Hypertension is the predominant driver of cardiovascular disease the leading cause of morbidity and mortality worldwide [1] and patients with resistant hypertension are at particularly high risk of cardiovascular complications [2]. True resistant hypertension refers to a diagnosis of essential hypertension with exclusion of all other potential causes of uncontrolled blood pressure, including secondary hypertension, pseudo- resistance due to poor adherence to antihypertensive therapy or the white- coat effect[3].The independent and continuous relationship of hypertension with incident cardiovascular events along with its prevalence at 25–30 % of the adult population, render high blood pressure (BP) the most important modifiable cardiovascular risk factor [4] and therefore a major issue of public health.

Although awareness and treatment of hypertension have improved over the years, the rates of control in the general hypertensive population remain unacceptably low, i.e., below 20–30%in many Western countries, with few exceptions in countries that implemented targeted public health programs aiming at improving hypertension care . while Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common, chronic sleep disorder in which respiratory arrest and hypoventilation frequently occur during sleep[5]. This syndrome is associated with a characteristic clinical presentation and specific abnormalities on examination. In OSAHS, there is repetitive upper airway collapse, which may be partial or complete, resulting in hypopnea or apnea; during sleep, this occurs more than five times per hour (apnea-hypopnea index (AHI) [6].

There is also clinical evidence that OSAHS may contribute to the development of hypertension, cardiovascular disease, and abnormalities in glucose metabolism [3, 4]. Apnea refers to a pause in breathing of more than 10 seconds and occurs in both central sleep apnea (CSA) and obstructive sleep apnea (OSA). They are distinguished by a lack of respiratory effort in CSA as opposed to a sustained but ineffective respiratory effort in OSA. Hypopnea is defined as a reduction in ventilation of at least 50%, resulting in a reduction in arterial saturation of 4% or more due to partial airway obstruction [5]. Early detection and appropriate therapy are the main options to treat the disease [7]. Overnight polysomnogram is the standard test for diagnosing OSAHS [8].

## II. EPIDEMIOLOGY AND PREVALENCE OF RHF

As the definition suggests, determining the true prevalence of resistant hypertension is extremely difficult. Patients who take two or fewer antihypertensive medications may have resistant hypertension, but they are not classified as such because they do not strictly meet the definition of requiring four or more drugs to control their blood pressure. Prevalent aTRH occurs in a higher percentage of the population-and clinic-based samples when an at-risk group is identified, for example, patients with treated hypertension and chronic kidney disease (CKD) [9], [10] .

The increased prevalence of aTRH among treated hypertensive adults in clinical trials (34% –39%) is probably due to the selection of patients with demographic and comorbidity characteristics that place them at high risk for the fatal and nonfatal CVD outcomes of interest[9]. Furthermore, in population-and clinic-based studies, some RH cases may go unrecognized because patients are not prescribed ≥3 drugs at maximal doses despite uncontrolled BP. In contrast, clinical trials usually include forced titration schemes that unmask RH by reducing the prevalence of suboptimal treatment[10]. OSAS is the second most common condition in terms of frequency among the various respiratory diseases, surpassed only by asthma. The syndrome can affect any age group and is estimated to affect 2-4% of the adult population, with a higher incidence in middle-aged men. One in five adults suffers from moderate OSAS and one in 15 from moderate to severe OSAS [11].

The syndrome is characterized by tense breathing, decreased blood oxygen levels, and agitation that disrupts normal sleep. In some cases, there is a high health risk, and patients may suffer from excessive daytime sleepiness, early morning headaches, difficulty concentrating, social problems, and systemic disorders 12].

Prevalence estimates for OSAS vary from study to study depending on research design and sampling criteria. The American Academy of Sleep Medicine (AASM) defines OSAS as AHI C 5 plus the presence of two or more symptoms, such as daytime sleepiness or snoring [13]. Many researchers hypothesize that a large proportion of the general population suffers from increased AHI but has no associated symptoms [14]. For example, in a representative sample of US men, the prevalence of OSAS (defined by AHI 10 and the presence of symptoms during the day) was 3.3%, whereas the prevalence of AHI [15] was 17%, suggesting that many people suffer from respiratory symptoms but may not experience or report symptoms of OSAS. Similarly, 9% of women and 24% of men were found to have a AHI of C 5 but had no symptoms of OSAS. Thus, current prevalence estimates for OSAS do not capture all people who have sleep-disordered breathing. In a representative sample, one in four adults in the United States was found to be at high risk for OSAS [16].

**White coat effect**

white-coat HTN is defined as patients whose BP is elevated in the clinic but normal or controlled when monitored outside of the clinic.[17] White-coat HTN is a complicating factor that falsely elevates BP and complicates the determination of HTN.Other signs include repetitive symptoms of overtreatment such as orthostatic hypotension and persistent fatigue as well as absence of target organ damage including left ventricular hypertrophy, retinopathy, and chronic kidney disease [18]. According to the Jackson Heart Study (JHS), the prevalence of white-coat hypertension is 25.4% among non-antihypertensive participants and 34.6% among antihypertensive participants.Moreover, white-coat HTN is more common with increasing age, in women, and in non-smokers [19].

The white-coat effect can be easily identified by 24-hour ABPM. However, ABPM is not readily available in all countries and, because of limitations in insurance reimbursement, is not even commonly used in the United States [20]. Oscillometric digital devices that can automatically record 3 to 6 BP measurements without a clinician in the examination room are now available for clinical use, a process called automated office BP. BP measurement by automated office BP attenuates the white-coat effect. Self-measured home BPs (with appropriate instruction in the BP measurement technique) correlate with

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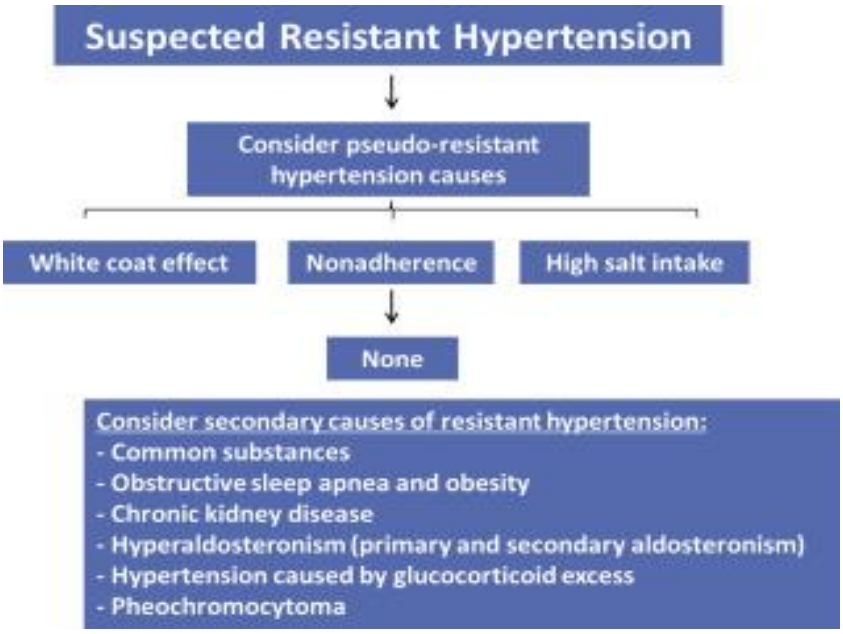
average daytime BPs measured by 24-hour ABPM and can be used to identify the white-coat effect [21]. However, it is important to consider that individuals may alter their BP logs or under report high or low BP values.

**Concomitant Conditions**

Obesity is associated with resistant hypertension. Obese patients have increased sympathetic activity, higher cardiac output, and a rise in peripheral vascular resistance due to reduced endothelium dependent vasodilation. Plasma aldosterone and endothelin are also increased, while excessive surrounding adipose tissue results in increased intrarenal pressures and changes in renal architecture [22]. As the body mass index increases, progressively higher doses of antihypertensive drugs are required to control blood pressure [23]. Weight loss has been found to reduce both systolic and diastolic blood pressure [24, 25]. Another common concomitant condition in hypertensive patients is diabetes. Insulin resistance increases sympathetic nervous activity, vascular smooth muscle cell proliferation, and sodium retention leading to elevated blood pressure resistant to treatment [26]. The common comorbidities of obesity, hypertension, and diabetes induce renal dysfunction, further hindering blood pressure treatment figure1.




**Nonpharmacologic Approaches to Management**

The potential causes of resistant hypertension must be examined before deciding if a treatment for resistant hypertension is appropriate. To rule out pseudoresistance, we must first assess drug adherence, BP procedure, and the risk of white-coat hypertension.In addition, evidence of contribution to the manifestation of resistance to high blood pressure such as heavy alcohol use, obesity and high salt intake is conflicting,[27] However, most clinical guidelines suggest encouraging patients Weight loss, a diet rich in fruits, vegetables, and low-fat dairy products with less saturated and total fat, smoking cessation, regular aerobic physical activity, avoidance of excessive alcohol intake, avoidance of excessive caffeine, and avoidance of drugs which can raise blood pressure, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids, are all recommended. [28,29].

## III. CONCLUSION

Once a diagnosis of resistant hypertension is confirmed,optimization of drug treatment remains the cornerstone of its management.Therapy of resistant hypertension includes improving compliance with use of medication, detection, and treatment of secondary hypertension, use of lifestyle measures, and treatment of obesity and other comorbidities.Switching the patient from hydrochlorothiazide to a longer acting thiazidetype diuretic such as chlorthalidone may improve blood pressure control.If a fourth antihypertensive drug is needed to control blood pressure in persons treated with adequate doses of antihypertensive drugs from different classes including a thiazide-type diuretic, a mineralocorticoid receptor antagonist should be added to the therapeutic regimen.

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