

## MODERN DIAGNOSTICS OF RESISTANT ARTERIAL HYPERTENSION

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**Abstract:** Resistant hypertension is high blood pressure that does not respond well to aggressive medical treatment.

**Key words:** hypertension, resistant, blood pressure, symptoms, patient, intake. Hypertension is considered resistant when all of the following are true:

- Someone is taking three\* different blood pressure medications at their maximally tolerated doses.
- One of the blood pressure medications is a diuretic (removes fluid and salt from the body).
- Blood pressure remains above your goal—(usually 130/80 mmHg, although individual goals should be discussed with your doctor)
- If hypertension requires four or more medications to be controlled it is also called resistant hypertension.

Blood pressure is the force of blood pushing against the artery walls. The force is generated by each heartbeat as blood is pumped from the heart into the blood vessels. The size, tone and elasticity of the arteries walls also affect blood pressure. The kidneys regulate blood pressure as well by regulating the amount of fluid and salt in the body.

**Hypertension** is defined when the average arterial blood pressure during a normal day is 130/80 mmHg or higher. **Hypertension** progressively damages the walls of large arteries (aorta, carotids) as well as smaller ones (cerebral, coronary, renal, retinal) and makes the heart work harder to get blood pumped through the body.

What are the symptoms of resistant hypertension?

You can have hypertension without having any symptoms. The best way to know if you have high blood pressure is to have your blood pressure checked by a health care provider.

However, symptoms may be felt when blood pressure first rises or during a **hypertensive crisis**, when levels are extremely high. These symptoms may include headaches, shortness of breath, chest pain and nosebleeds.

**Dizziness** is usually **not** a symptom of high blood pressure. In fact, dizziness can sometimes be a symptom of *low* blood pressure. Frequent or unexplained dizziness may be a warning sign of a serious condition and should be addressed by your physician.

Recent guidelines have defined resistant hypertension (RHT) as blood pressure (BP) that does not fall below 140/90 mmHg, despite a therapeutic strategy that includes appropriate lifestyle measures, plus a

diuretic and two other antihypertensive drugs belonging to different classes at adequate doses. The definition of RHT has been quite arbitrary, a fact reflected on various definitions of ideal drug dosing (e.g. optimal, appropriate, maximal tolerated), the still office-based BP approach and the inclusion of patients controlled with four drugs (irrespective of dose). Better understanding of the disease in the recent years has led to different reported prevalences of RHT compared to earlier reports. Data from earlier trials documented a prevalence of 15–30 %, but with a more thorough evaluation of treatment resistance, especially with the use of ambulatory BP monitoring, a prevalence of less than 10 % is more realistic, though higher numbers in specialised HT centres may apply.

A patient with RHT represents one of the most complex cases in the field of HT, and referral and management in a specialised HT clinic is considered wise. Accordingly, a thorough clinical history and physical examination can provide significant information, while a proposed set of further tests is presented in . A number of clinical correlates of RHT have been variably documented in post-hoc analysis of clinical trials and large registries. These include older age, obesity, black race, diabetes mellitus, a volume overload state, left ventricular hypertrophy, albuminuria and chronic kidney disease (CKD). A long history of HT and isolated systolic HT are often identified. Proper diagnosis of the condition needs a series of careful checkpoints.

#### **Basic Testing in the Patient with Resistant Hypertension.**

- Ambulatory blood pressure monitoring
- 12-lead electrocardiogram
- Transthoracic echocardiogram
- Complete blood count
- Serum glucose, urea, creatinine, electrolytes, lipids
- Urine analysis (protein, erythrocytes, leukocytes)
- 24-hour urine assessment for aldosterone, sodium and albumin
- Plasma aldosterone concentration and renin
- Thyroid stimulating hormone
- Renal echocardiogram
- Renal artery duplex

#### ***Factors to be Considered in a Patient with Apparent Treatment Resistant Hypertension.***

White-coat Effect

Patient Management Issues

Incorrect blood pressure measurement

Physician inertia

Inappropriate drug regimen

Insufficient drug doses

Adherence Issues

Complicated regimen and dosing

Financial issues

Drug side effects

Lack of disease perception

Insufficient patient education

Secondary Hypertension

Renal parenchymal disease

Renal artery stenosis

Primary hyperaldosteronism

Thyroid disease

Cushing's syndrome

Pheochromocytoma

Aortic coarctation

Conditions Affecting Blood Pressure Control

Obstructive sleep apnoea

Chronic kidney disease

Significant obesity

High salt intake

High alcohol consumption

Drug-induced Resistant Hypertension

Nonsteroidal anti-inflammatory drugs

Oral contraceptives

Corticosteroids

Sympathomimetics (e.g. decongestants)

Erythropoetin

Cancer drugs (e.g. bevacizumab)

Cyclosporin

Cocaine

Licorice

Ephedra

Prevalence of RHT is very high in patients with CKD, which is easily diagnosed with estimation of glomerular filtration rate and urine analysis (protein, erythrocytes, leukocytes). Further data may be gathered with a simple renal ultrasound that can image small or asymmetrical kidneys. Sodium and fluid retention, sympathetic and renin-angiotensin system (RAS) activation and functional vascular changes contribute to treatment resistance.

Renal artery stenosis is by 90 % due to atherosclerotic lesions and should be suspected in patients of an older age, especially when atherosclerotic disease in other sites is present, reaching a prevalence of 70 % among patients undergoing cardiac catheterisation. Flash pulmonary oedemas and deteriorating renal function, especially shortly after application of RAS blockers, should pose suspicion. Imaging with duplex ultrasonography or computed tomography/magnetic resonance will set the diagnosis. The uncommon form of fibromuscular dysplasia of the renal arteries may be effectively treated with balloon angioplasty with or without stent placement. Regarding atherosclerotic stenosis, as a series of randomised controlled trials failed to show a clear benefit of renal artery stenting, management requires a close follow-up of renal function and classic drug treatment. Drugs that block the RAS are not contraindicated unless there are bilateral lesions or a unilateral lesion in a solitary kidney.

A long list of drugs may induce raises in BP or blunt the effects of antihypertensives mostly by promoting vasoconstriction, salt and water retention and improper neurohormonal activation. Oral contraceptives, nonsteroidal anti-inflammatory drugs and aspirin, as well as sympathomimetics, such as some anorectics and locally applied drugs for nasal congestion, should be recorded in the patients' history.

Increased salt intake is a worldwide epidemic and salt intake affects the efficacy of RAS blockers and diuretics. Patients that are traditionally more salt-sensitive are diabetics, the elderly and those with CKD. A total sodium consumption of 2400 mg or 100 mmol/day (6 g or one teaspoon of salt) is advised in current guidelines. In a randomised cross-over study in patients with RHT, extremely low salt intake (2.8 g) compared to high salt intake (14 g) decreased BP by 23/9 mmHg. In clinical practice, salt consumption is preferably assessed via 24-hour urine sodium excretion. Normal salt excretion, indicating normal salt intake is usually defined as 24-hour urine sodium <220 mmol/24 h (5 g/24 h). Higher urine sodium excretion is associated with a need for a greater number of antihypertensive drugs to achieve sufficient BP control.

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