

2008 American Heart Association Statement on diagnosis, evaluation, and treatment of resistant hypertension: what should we remember in everyday practice?

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Resistant hypertension is a common clinical problem faced by both primary care clinicians and specialists. While the exact prevalence of resistant hypertension is unknown, clinical trials suggest that it affects approximately 20% of study participants. As older age and obesity are 2 of the strongest risk factors for poorly controlled hypertension, the incidence of resistant hypertension will likely increase as populations become older and heavier [1].

Data from the National Health and Nutrition Examination Survey indicate that among hypertensive patients, only 53% were controlled to <140/90 mmHg [2]. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, at the study's completion, 27% of participants were on 3 or more medications. Overall, 49% of participants were uncontrolled on 1 or 2 medications, meaning that approximately 50% needed 3 or more blood pressure medications [3].

The prognosis of patients with resistant hypertension compared with other hypertensive patients is probably impaired as the former typically present with a long-standing history of poorly controlled hypertension and commonly have associated cardiovascular risk factors such as diabetes, obstructive sleep apnea, left ventricular hypertrophy, and chronic kidney disease (CKD) [1].

The recently released American Heart Association Scientific Statement specifies that uncontrolled hypertension is not synonymous with resistant hypertension. Resistant hypertension is defined as blood pressure that remains above goal in spite of concurrent use of 3 antihypertensive agents of different classes. Ideally, one of the 3 agents should be a diuretic and all agents should be prescribed at optimal dose amounts. Causes of pseudoresistance must be excluded, including blood

pressure technique, lack of medication adherence, and white-coat resistant hypertension [1].

Lifestyle factors contribute importantly to development of resistant hypertension and should be reversed as possible including obesity and heavy alcohol intake. Dietary salt restriction, ideally to <100 mEq of sodium/24 h is recommended [1].

Several classes of pharmacological agents can contribute to treatment resistance, with the most common being non-steroidal anti-inflammatory agents, including aspirin and selective COX-2 inhibitors [1].

Secondary causes of hypertension are common in patients with resistant hypertension. The likelihood of a secondary cause of hypertension is greater in older patients because of a greater prevalence of sleep apnea, renal parenchymal disease, renal artery stenosis, and possibly hyperaldosteronism [1].

Untreated obstructive sleep apnea is strongly associated with hypertension. It is particularly common in patients with resistant hypertension with a reported prevalence of more than 80% of patients. Treatment with continuous positive airway pressure likely improves blood pressure control [1].

Primary aldosteronism is common in patients with resistant hypertension with a prevalence of approximately 20%. As reported by our clinic, the high prevalence of primary aldosteronism is true of both African American and white patients [1,4].

Renovascular disease is a common finding in hypertensive patients undergoing cardiac catheterization. Unknown, however, is the role such lesions play in causing hypertension and the long-term benefit of percutaneous revascularization. Available evidence does not support a relative advantage of either medical treatment or revascularization procedures. However, if the blood pressure remains poorly controlled in spite of optimal medical therapy, revascularization is recommended, recognizing that significant blood pressure response is not assured [1,5].

Biochemical evaluation should include a routine metabolic profile; urinalysis; and a paired, morning plasma aldosterone and plasma renin activity to screen for primary aldosteronism. A high ratio, generally 20–30, is suggestive of prima-

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ry aldosteronism, but further evaluation is necessary to confirm the diagnosis. A 24-hour urine collected during ingestion of the patient's routine diet is recommended as part of the routine evaluation in order to estimate dietary sodium intake, calculate creatinine clearance, and measure aldosterone excretion. Noninvasive renal imaging should be reserved for patients in whom there is increased level of suspicion for renal artery stenosis. Likewise, adrenal imaging should be done only after biochemical confirmation of hormonal excess suggestive of adrenal tumors [1].

Use of effective diuretic therapy is essential to maximize pharmacologic therapy. Previous studies indicate that chlorthalidone 25 mg daily provides greater 24-hour ambulatory blood pressure reduction than hydrochlorothiazide 50 mg, therefore, the former is recommended. In patients with underlying advanced CKD (creatinine clearance <30 ml/min), loop diuretics may be necessary for effective volume and blood pressure control [1,6].

Beyond studies of 2-drug combinations, there is little data assessing the efficacy of specific combinations of 3 or more drugs. A triple drug regimen of an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker, calcium channel blocker, and a thiazide diuretic is effective and generally well tolerated. Although β -antagonists are indicated in the setting of coronary heart disease and/or congestive heart failure, combined α - β -antagonists, because their dual combination of action, may be more effective antihypertensives [1].

Consistent with reports of a high prevalence of primary aldosteronism in patients with resistant hypertension have been studies demonstrating that mineralocorticoid receptor antagonists provide significant antihypertensive benefit when added to existing multi-drug regimens [1,7]. Spironolactone can provide significant additional antihypertensive benefit. Hyperkalemia, while uncommon, can occur, particularly in patients with CKD.

The 2008 American Heart Association Scientific Statement on resistant hypertension provides extensive recommendations for the evaluation and treatment of patients with resistant hypertension. However, studies of clinical outcomes indicate that patients with resistant hypertension do benefit from referral to a hypertension specialist. If a specific secondary cause of hypertension is suspected, referral to the appropriate specialist is recommended. In the absence of suspected secondary causes of hypertension, referral to a hypertension specialist is recommended if the blood pressure remains elevated in spite of 6 months of treatment [1].

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