# Resistant hypertension – a review of the 2023 guidelines

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Resistant hypertension is defined as the official values of blood pressure (BP) >140/90 mmHg despite lifestyle changes and treatment with optimal or best tolerated doses of three or more antihypertensives (one of which is thiazide/diuretic like thiazide) and after the exclusion of pseudoresistance, secondary hypertension and hypertension caused by drugs. The inadequate BP control should be confirmed by out-of-office BP measurement showing an uncontrolled 24-hours BP (≥ 130 mmHg systolic or ≥ 80 mmHg diastolic) values. If confirmation of true resistant hypertension by ambulatory blood pressure monitoring is not feasible, home blood pressure monitoring may be used.[1] The prevalence of true resistant hypertension is about 5%. But in patients with comorbidities the prevalence increases to 22.9% with chronic kidney disease, 56.0% with renal transplant and 12.3% with aging.[2] These patients are at higher risk of complications including cardiovascular disease, stroke, kidney failure, and death. Effective treatment should combine lifestyle changes such as reduction of sodium and alcohol intake, implementation of regular physical activity and weight loss in overweight or obese patients, discontinuation of interfering substances, rationalization of current treatment and the sequential addition of antihypertensive drugs to the existing triple therapy. Considering the pathophysiological mechanism, an interplay between multiple neurohumoral factors such as increased levels of aldosterone, endothelin-1, vasopressin and increased sympathetic activity which contribute to volume and sodium overload, increase in peripheral vascular resistance, arterial stiffness the fourth lines of treatment are antagonists of mineralocorticoid receptors.[1] The PATHWAY-2 trial demonstrated that spironolactone was superior in reducing BP compared with bisoprolol (a beta-blocker), doxazosin (an alpha-blocker), or placebo as add-on therapy in patients with resistant hypertension on three blood pressure medications.[3] This drug should be used with caution in chronic kidney disease because of hyperkalemia. The use of newer potassium binders such as patiromer or sodium zirconium cyclosilicate can reduce the risk of hyperkalemia. If gynecomastia becomes intolerable, spironolactone can be switched to eplerenone, a selective aldosterone receptor antagonist that has minimal interaction with sex hormone steroid receptors. The type of diuretic needs to be adapted to renal function. In patients with preserved glomerular filtration rate, the preferred first-line diuretic is either chlorthalidone or indapamide because of their longer half-life and more potent antihypertensive effect compared with hydrochlorothiazide. Chlortalidone (12.5 mg or 25 mg once daily) may be used with or without loop diuretic if eGFR <30mL/min/1.73m$^2$. Loop diuretics are preferred in patients with an estimated glomerular filtration rate less than 30 mL/min/1.73 m$^2$. Torsemide can be used once a day, but shorter-acting loop diuretics such as furosemide or bumetanide must be dosed at least twice a day. Finally, new more selective nonsteroidal MRAs such as finerenone (approved for the treatment in diabetic kidney disease), esaxerenone (approved for the treatment of hypertension in Japan), and ocedurenone (KBP-5074, in development for resistant hypertension in CKD) might provide future alternatives to spironolactone. Renal denervation, a promising new treatment method, should be considered as an additional therapeutic option if the appropriate criteria are met in patients with eGFR >40 ml/min.[1]

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## LITERATURE

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