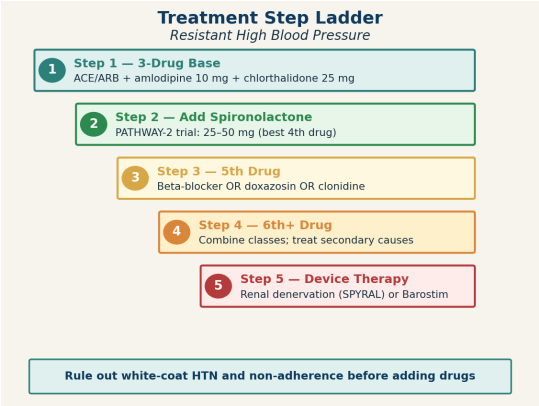
Resistant Hypertension

When Three Medicines Are Not Enough

About 1 in 10 people with high blood pressure cannot control it with three medicines. This guide explains why, and what comes next.



Online: https://go.riasalimd.com/resistant-htn-guide

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Names & Terms You Will Hear

Term	Meaning
Resistant Hypertension	Blood pressure that stays at or above 130/80 on 3 or more medicines, one of which is a water pill (diuretic), all at full doses.
Pseudo-Resistance	Apparent resistant HTN caused by white-coat effect, skipped doses, or poor measuring technique — not true resistance. Must be ruled out first.
Refractory Hypertension	The hardest tier: BP uncontrolled on 5 or more drugs including chlorthalidone and a mineralocorticoid receptor blocker.
ABPM (Ambulatory BP Monitor)	A wrist or arm cuff worn 24 hours that records BP every 15–30 minutes. The gold standard for diagnosing true resistant HTN.
White-Coat HTN	BP that is high in the doctor's office but normal at home or on ABPM. About 30% of 'resistant' patients have this.
Secondary Hypertension	High BP caused by another medical condition — such as sleep apnea, kidney disease, or a hormone tumor. Treating the cause can cure the BP.
Primary Aldosteronism	The adrenal glands make too much aldosterone hormone. The most common secondary cause of resistant HTN (15–20% of cases).
Spironolactone / MRA	Spironolactone (Aldactone) is a mineralocorticoid receptor antagonist (MRA) — it blocks aldosterone. The PATHWAY-2 trial proved it is the best 4th drug for resistant HTN.
Chlorthalidone	A long-acting diuretic (water pill). Preferred over HCTZ in resistant HTN because of its longer half-life and greater BP-lowering effect.
Renal Denervation	A catheter-based procedure that uses radiofrequency or ultrasound energy to reduce nerve activity around the kidney arteries, lowering BP.

Term	Meaning
Barostim (Baroreflex Activation Therapy)	An implanted device that sends signals to the brain's BP-control center via the carotid artery. FDA-cleared for resistant HTN and HF.
STOP-BANG	A short sleep-apnea screening questionnaire. Score 5–8 = high risk of OSA. Ask your care team.

Three questions your doctor must answer first:

1. Are you really taking all three medicines at full dose? (Adherence check — urine drug test if uncertain.)
2. Is the high reading real? (ABPM / 24-hour monitor rules out white-coat effect.)
3. Is a secondary cause driving the BP? (Secondary workup — see the grid on the next section.)

Resistant Hypertension?

- **Resistant HTN** means blood pressure at 130/80 or higher on three medicines. All must be at full dose. One must be a water pill (diuretic). You must also be taking all pills as prescribed.
- **Before calling it resistant**, doctors must rule out *pseudo-resistance.* Fake resistance comes from white-coat effect, missed doses, a wrong cuff size, or medicines at low dose. Up to 30% of 'resistant' patients just have white-coat high BP.
- **True resistant HTN** affects about 10 to 15% of people with high blood pressure. That is roughly 12 to 15 million Americans. It needs specialist care and extra testing.
- **Refractory HTN** is even harder to treat. BP stays high on five or more drugs, including chlorthalidone and spironolactone. This is rare.
- The first step is a **24-hour BP monitor (ABPM)**. You wear a cuff all day and night. It shows your real BP outside the office. If the 24-hour average is under 130/80, white-coat effect is the answer. You do not need more medicine.
- **The key question:** is there a hidden cause pushing BP up? Every person with true resistant HTN should be checked for secondary causes. This is the most important step.

If BP Stays High on 3 Drugs: Screen for These Secondary Causes

Primary Aldosteronism

15–20% of resistant HTN

Test: aldosterone/renin ratio

Treat: surgery or spiro

Sleep Apnea (OSA)

Up to 80% of resistant HTN

Test: STOP-BANG + sleep study

Treat: CPAP drops BP 5–10 mmHg

Renal Artery Stenosis

Older/smokers OR young women

Test: duplex ultrasound / CTA

Treat: stenting or medicine

Pheochromocytoma

Rare but dangerous

Test: plasma metanephrines

Clue: headache + sweating + racing heart

Cushing's Syndrome

Central obesity + stretch marks

Test: 24h urine cortisol

Treat: treat the source

Drug / Medication Cause

NSAIDs, decongestants, OCP, stimulants

Take a full drug history

Remove the offending drug

Six secondary causes to screen for in every resistant HTN patient. Primary aldosteronism is the most common (15–20%). Sleep apnea affects up to 80%. Drug and medication causes are often overlooked. Finding a secondary cause can simplify treatment dramatically. Sources: ACC/AHA Resistant HTN Statement 2018, Endocrine Society Primary Aldosteronism Guidelines 2016.

Why You Need the Secondary Cause Workup

- In 30 to 40% of cases, a hidden cause is driving the BP. Treating that cause is more powerful than adding more pills.
- **Primary aldosteronism** (most common): the adrenal glands make too much aldosterone. Screen with a blood test (aldosterone-to-renin ratio). Treat with surgery or spironolactone.
- **Sleep apnea** (very common, often missed): it affects up to 80% of resistant HTN patients. Screen with STOP-BANG questionnaire and a sleep study. CPAP lowers BP 5 to 10 points on its own.
- **Renal artery stenosis**: a narrowed artery to the kidney. Seen in older smokers and young women. Screen with ultrasound or CT scan of the arteries.
- **Pheochromocytoma** (rare): an adrenaline-producing tumor. Look for episodes of headache, sweating, and fast heart rate. Screen with a plasma metanephrines blood test.
- **Cushing's syndrome**: too much cortisol. Look for belly weight gain, stretch marks, and easy bruising. Screen with 24-hour urine cortisol.
- **Medications**: NSAIDs, cold medicines, birth control pills, stimulants, and licorice all raise BP. Tell your doctor about every drug, vitamin, and supplement you take.

Why It Matters

- **Higher risk of serious events.** True resistant HTN raises the risk of heart attack, stroke, heart failure, and kidney disease. This is true even when BP levels look only slightly high.
- **A secondary cause is often hiding.** In 30 to 40% of cases, a hidden cause is driving the BP. Finding and treating that cause can bring BP down without adding more pills.
- **Primary aldosteronism is the top secondary cause.** It shows up in 15 to 20% of resistant HTN patients. It is often missed. A simple blood test (aldosterone-to-renin ratio) can catch it.
- **Sleep apnea is very common.** Up to 80% of resistant HTN patients have sleep apnea. CPAP treatment alone can lower the top BP number by 5 to 10 points.
- **Spironolactone works very well.** The PATHWAY-2 trial proved it. Adding spironolactone 25 to 50 mg lowered systolic BP by 8.7 points more than the next best drugs. It is now the standard 4th drug.
- **Device therapy is now an option.** Renal denervation is FDA-cleared. It lowers systolic BP by 5 to 7 points in patients on 3 or more drugs. Barostim is cleared for resistant HTN plus heart failure.
- **Sodium matters most in resistant HTN.** Less than 1500 mg of sodium per day makes every drug work better. This is the single best diet step you can take.

Risk Factors

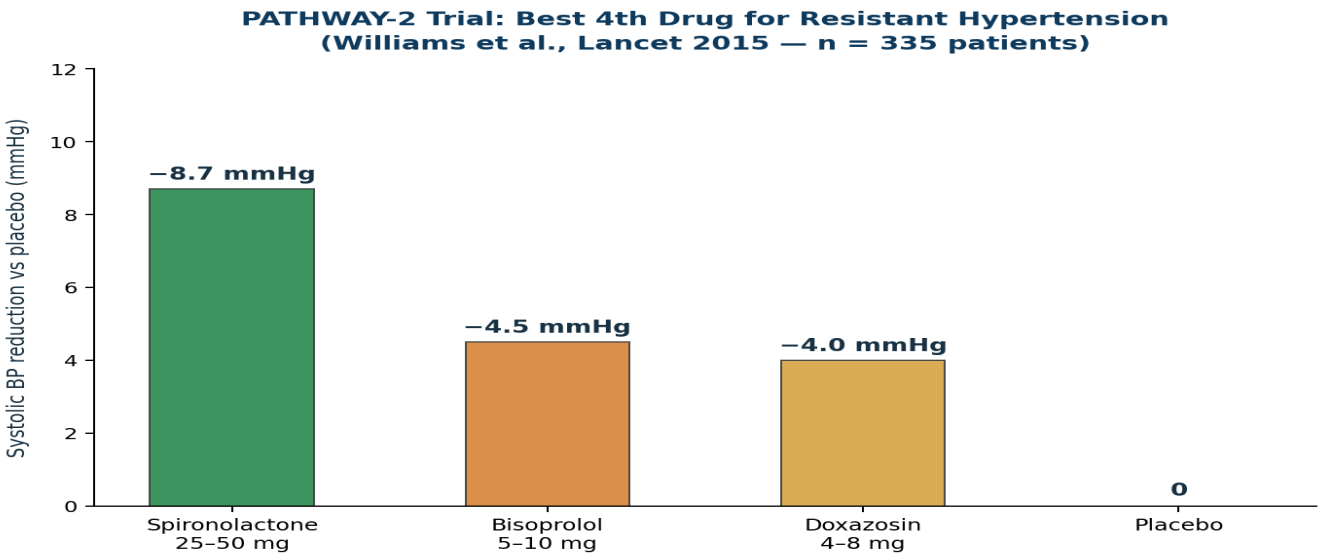
Some patients are more likely to develop this condition. Knowing your risk helps your care team take extra precautions.

Risk Factor	Why It Increases Risk
Chronic kidney disease (CKD)	Damaged kidneys hold on to sodium and fluid. This raises BP. CKD alone can require 4 to 5 drugs.
Obesity (BMI 30 or higher)	Excess weight turns on the stress nervous system and raises aldosterone. Both make BP harder to control. Even 5 to 10 lb of weight loss helps.
Sleep apnea	Low oxygen at night triggers adrenaline surges. This keeps BP high around the clock. CPAP treats it directly.
Primary aldosteronism	Too much aldosterone holds sodium and loses potassium. BP rises hard. It blocks most drug classes.
High sodium diet	Even on diuretics, too much salt blunts the drug effect. Under 1500 mg/day is the goal for resistant HTN.
Arterial stiffness (older age)	Stiff arteries make systolic BP hard to lower. Diastolic may already be low. Isolated high systolic BP is common.
Medications that raise BP	Ibuprofen, naproxen, cold medicines, birth control pills, stimulants, and licorice all raise BP. They work against your medicines.
Skipping doses (non-adherence)	Skipped pills are the top cause of apparent resistant HTN. A urine drug test can confirm whether drugs are being taken.

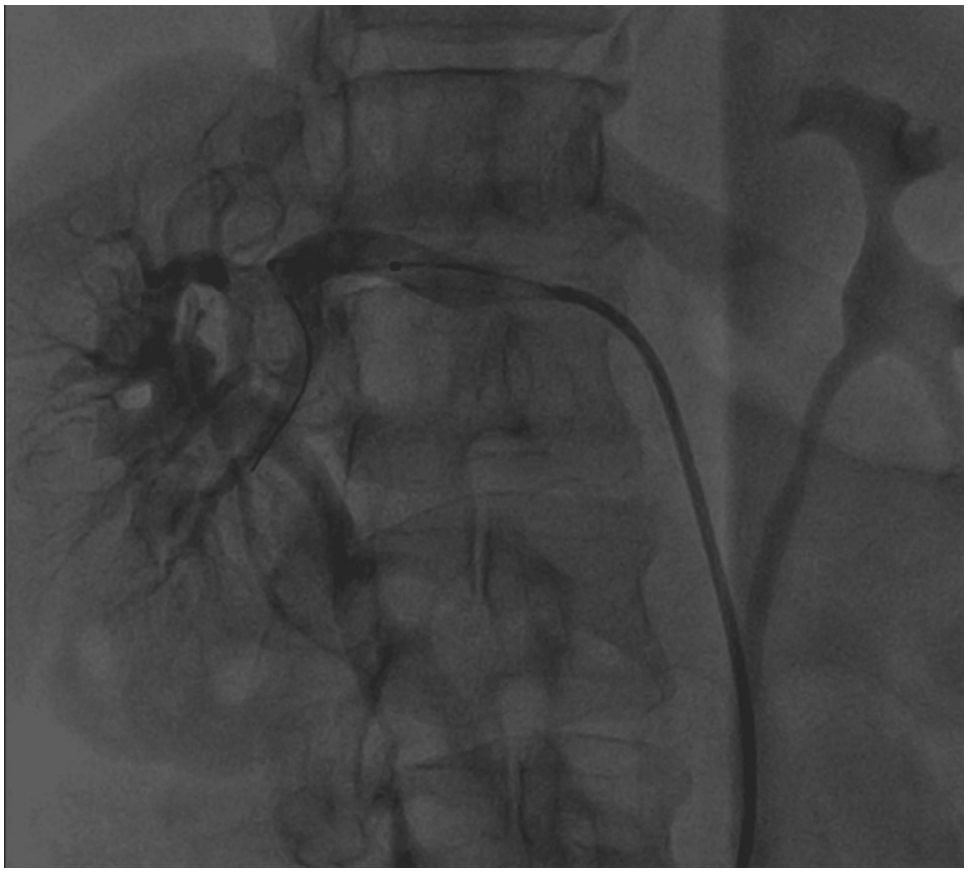
Medication check — ask yourself:
Do you take any of these regularly? **Ibuprofen (Advil), naproxen (Aleve), decongestants (Sudafed), oral contraceptives, licorice candy or supplements, energy drinks, stimulant medicines.**
Any of these can raise BP 5–10+ mmHg and blunt your medicines. Tell your doctor about every pill, supplement, and remedy.

Treatment Options

- **Step 1 — Optimize the 3-drug base.** All three drugs must be at full dose: ACE inhibitor or ARB; amlodipine 10 mg; chlorthalidone 25 mg. Chlorthalidone is preferred over HCTZ. It is stronger and lasts longer. Switch if needed before adding a 4th drug.
- **Step 2 — Add spironolactone 25 to 50 mg.** The PATHWAY-2 trial proved it is the best 4th drug. It lowers the top BP number by 8.7 points more than other options. Check potassium and kidney labs monthly at first.
- **Eplerenone** is an option if spironolactone causes breast tenderness or gynecomastia. It works the same way. Fewer hormonal side effects. Same lab monitoring.
- **Step 3 — Add a 5th drug if needed.** Options: a beta-blocker (bisoprolol 5 to 10 mg); an alpha-blocker doxazosin 4 to 8 mg (also helps the prostate); or clonidine 0.1 to 0.3 mg. Never stop clonidine abruptly. A sudden stop can cause a dangerous BP spike.
- **Step 4 — Device therapy.** Renal denervation is FDA-cleared. A catheter uses energy to calm overactive kidney nerves. It lowers systolic BP by 5 to 7 points. Barostim is cleared for resistant HTN plus heart failure.
- **Treat the secondary cause first** when one is found. Surgery for an aldosterone tumor can cure BP. CPAP for sleep apnea lowers BP by 5 to 10 points on its own.
- **Lifestyle boosts every drug.** Aim for: sodium under 1500 mg/day; DASH or Mediterranean diet; no more than 2 drinks of alcohol per day; 30 min of exercise 5 days a week.
- **Check BP at home.** Use a validated arm cuff. Rest 5 minutes first. Measure in the morning and evening. Write it down. Bring the log to every visit.



PATHWAY-2 trial results (Williams et al., Lancet 2015, n=335). Spironolactone 25–50 mg reduced systolic BP by 8.7 mmHg more than placebo — clearly better than bisoprolol (4.5 mmHg) and doxazosin (4.0 mmHg). This established spironolactone as the standard 4th drug in resistant hypertension, reflected in AHA/ACC and ESH/ESC guidelines.



A real renal denervation procedure. This X-ray angiogram shows the Symplicity Spyral catheter (the coiled wire) threaded into the right renal artery, delivering radiofrequency energy to calm the overactive kidney nerves that drive resistant BP. Image: Rodríguez Acosta et al., Cureus 2026 (CC BY 4.0).

Drug classes in resistant hypertension at a glance

Drug / Class	Dose range	Key side effects	Monitor	Step
Chlorthalidone (diuretic)	12.5–25 mg once daily	Low potassium, increased uric acid	K+, creatinine, uric acid	Step 1
ACE inhibitor or ARB	Maximum labeled dose	Cough (ACEi), rare angioedema	K+, creatinine at 2 weeks	Step 1
Amlodipine (CCB)	5–10 mg once daily	Ankle swelling (up to 15%)	BP; edema — not dangerous	Step 1
Spironolactone (MRA)	25–50 mg once daily	High K+, breast tenderness in men	K+, creatinine monthly × 3 mo, then q3–6 mo	Step 2

Drug / Class	Dose range	Key side effects	Monitor	Step
Eplerenone (MRA)	25–50 mg once daily	High K+ (no hormonal effects)	K+, creatinine	Step 2 alt
Doxazosin (alpha-blocker)	1–8 mg once daily (at bedtime)	First-dose dizziness / fall risk	BP on standing; start low	Step 3
Bisoprolol (beta-blocker)	2.5–10 mg once daily	Fatigue, slow heart rate	Heart rate; avoid if asthma	Step 3
Clonidine (central agent)	0.1–0.3 mg twice daily	Dry mouth, drowsiness; **severe rebound if stopped abruptly**	BP; taper before stopping	Step 3

Spironolactone: The PATHWAY-2 Evidence

- The PATHWAY-2 trial (2015) tested 335 patients with true resistant HTN. Each patient tried 4 add-on drug options. The order was random.
- Spironolactone 25 to 50 mg was the clear winner. It lowered systolic BP by 8.7 points more than placebo. Bisoprolol lowered it by 4.5. Doxazosin lowered it by 4.0.
- Spironolactone works so well because many resistant HTN patients have too much aldosterone. This is true even without a formal diagnosis.
- AHA/ACC (2017) and ESH/ESC (2023) both list it as the standard 4th drug for resistant HTN.
- Do not use spironolactone if potassium is above 5.0 or creatinine is above 2.0. Switch to eplerenone if breast tenderness develops.
- Check potassium and creatinine at 2 weeks, then monthly for 3 months after starting or raising the dose.

Renal Denervation: A New Option

- Renal denervation is a cath-lab procedure. The doctor uses energy (heat or ultrasound) to calm overactive nerves on the surface of the kidney arteries.
- It received FDA clearance in 2023. The SPYRAL trials used a sham control. Patients did not know if they got the real procedure. The 5 to 7 point BP drop was real.
- Best candidates: resistant HTN on 3 or more drugs, no secondary cause found, kidney arteries suitable on imaging.
- The procedure takes 30 to 60 minutes. Most patients go home the same day. Nothing is left inside the body.
- Barostim is a different device. It is implanted near the neck artery. It activates the brain's BP-control reflex. It is cleared for resistant HTN plus weak-pump heart failure.
- Device therapy does not replace pills. It is an add-on for patients who cannot reach goal on drugs alone.

Comfort Measures at Home (No Medication Needed)

These simple steps support healing and ease symptoms. Use them alongside any medication your doctor prescribes.

- Cut sodium to under 1,500 mg/day. Read food labels. The top sources are restaurant food, canned goods, deli meats, and bread. Home cooking is the easiest way to reduce it.
- Eat the DASH or Mediterranean diet. Aim for 4 to 5 servings of fruits and vegetables per day. Add whole grains, low-fat dairy, and lean protein. This lowers systolic BP by 8 to 14 points.
- Limit alcohol. One drink per day for women. Two for men. More than two drinks a day raises BP and blunts medicines.
- Exercise 30 minutes on most days. Brisk walking, swimming, and cycling all count. Aerobic exercise lowers systolic BP by 5 to 8 points.
- Lose weight if BMI is over 25. Even 5 to 10 lbs can lower BP and help medicines work better.
- Avoid ibuprofen and naproxen. Use Tylenol (acetaminophen) for pain instead. NSAIDs raise BP and blunt diuretics.
- Never stop a BP medicine without calling us first. Clonidine must be tapered slowly. A sudden stop can spike BP dangerously.
- Keep a home BP log. Write down morning and evening readings. Bring the log to every visit.

Risks, Benefits, and Alternatives

Every choice has trade-offs. Use this table to start the shared decision conversation.

Option	Risks	Benefits	Alternatives
Spironolactone (MRA) as 4th drug	Elevated potassium (hyperkalemia) — check labs monthly at first. Breast tenderness or enlargement in men (5–10%). Avoid if potassium > 5.0 or creatinine > 2.0.	PATHWAY-2: best 4th drug — 8.7 mmHg more SBP reduction than alternatives. Addresses aldosterone excess common in resistant HTN.	Eplerenone (fewer hormonal effects, same potassium risk). If contraindicated: doxazosin or bisoprolol.
Renal denervation	Catheter procedure (arterial access, 30–60 min). Small risk of access-site bleeding. Renal artery injury is very rare (< 0.5%). Not suitable if renal artery anatomy is unfavorable.	FDA-cleared. SPYRAL trial: ~5–7 mmHg SBP reduction in patients on 3+ drugs. No extra daily pill. Effect sustained at 3 years.	Continue step 3 medicines. Barostim if also have heart failure.
Chlorthalidone vs HCTZ	Chlorthalidone causes more potassium loss than HCTZ. Monitor potassium; supplement if needed.	Chlorthalidone 25 mg is more potent and lasts longer than HCTZ 25 mg. Preferred in resistant HTN guidelines. Fewer patients fail to reach goal.	Indapamide is a second-choice thiazide-like diuretic. Used in European guidelines.

Option	Risks	Benefits	Alternatives
Treating the secondary cause	Workup takes time and may involve specialist referral. Adrenalectomy has surgical risks. Sleep study requires an overnight test.	Treating the cause can normalize BP. Primary aldosteronism surgery can cure HTN in up to 35–40% of patients. CPAP reduces 24-hour BP by 5–10 mmHg.	Medical management (spironolactone for primary aldosteronism) if surgery not possible. CPAP alternatives: positional therapy, weight loss.
Doing nothing (inadequate treatment)	Sustained high BP causes progressive end-organ damage: LVH, kidney failure, retinopathy, stroke, and heart attack over years.	Avoids extra medicines, procedures, and side effects short-term.	Any one drug addition is better than none. Lifestyle alone reduces risk but rarely normalizes BP in true resistant HTN.

Common Misconceptions

Myth	Reality
"My BP is always high — medicines just do not work for me."	Most people do not have true resistant HTN. Before adding more drugs, your doctor should confirm adherence, check ABPM (24-hour monitor), and rule out white-coat effect. Many patients are 'resistant' because of a missed secondary cause like sleep apnea.
"Three medicines is a lot. Adding more is not safe."	Guidelines recommend a step-by-step approach. PATHWAY-2 proved a 4th drug is safe and effective. Combination therapy is standard care, not a last resort.
"HCTZ and chlorthalidone are the same water pill."	They are not. Chlorthalidone lasts 45 to 60 hours. HCTZ lasts only 6 to 12 hours. ACC/AHA guidelines prefer chlorthalidone for resistant HTN.
"I do not need to check my potassium on spironolactone."	You do. Spironolactone raises potassium. High potassium can cause dangerous heart rhythms. Your team checks it monthly at first, then every 3 to 6 months.
"Sleep apnea does not affect blood pressure."	It does. Up to 80% of resistant HTN patients have sleep apnea. Each overnight oxygen dip triggers an adrenaline burst. This keeps BP high all day and night. CPAP alone can lower systolic BP by 5 to 10 points.
"Ibuprofen is safe. It is just an OTC pain reliever."	NSAIDs like ibuprofen block the kidneys from responding to BP drugs. Even a few days of use can raise systolic BP by 5 to 6 points. Use Tylenol for pain instead.
"Renal denervation is experimental."	It received FDA clearance in 2023. The SPYRAL trials used a sham control to confirm the BP reduction is real. It is a valid option for true resistant HTN on 3 or more drugs.

Possible Complications

Knowing what can go wrong helps you spot problems early. Most complications are uncommon, especially with treatment.

Where / What	What Can Happen
Heart	Thickened heart muscle (LVH) from years of high pressure. This leads to poor relaxation, heart failure, and higher risk of sudden cardiac death.
Brain / Stroke	High BP can rupture or block a brain artery. Very high BP can also cause confusion and vision loss (hypertensive encephalopathy). Both need the ER right away.
Kidney	Kidney scarring from sustained high pressure. An early sign is protein in the urine (proteinuria). Over time it can lead to kidney failure and dialysis.
Eyes	Damaged blood vessels in the back of the eye (retinopathy). Your eye doctor grades it on a scale. Severe grades can cause vision loss.
Hypertensive Emergency	BP above 180 systolic or 120 diastolic WITH new symptoms: chest pain, shortness of breath, confusion, or vision change. Call 911. Do not wait.
Aorta	Long-term high BP weakens the wall of the body's main artery. It can balloon (aneurysm) or tear (dissection). Both are life-threatening.

Points to Know

If you remember nothing else, remember these key points.

- Resistant HTN means BP 130/80 or higher on 3 full-dose medicines (including a water pill). Rule out white-coat effect first with a 24-hour BP monitor.
- Search for a secondary cause in every patient. Common ones: sleep apnea, primary aldosteronism, renal artery narrowing, adrenaline tumor, Cushing's, kidney disease, thyroid problems, or a drug that raises BP.
- Chlorthalidone is a better water pill than HCTZ for this condition. It lasts much longer. Switching can lower BP without adding more drugs.
- Spironolactone 25 to 50 mg is the best 4th drug (PATHWAY-2). Check potassium and kidney labs monthly at first.
- CPAP for sleep apnea lowers BP 5 to 10 points on its own. It also helps all other medicines work better.
- Sodium under 1,500 mg/day is the most important diet step. It makes every drug work harder.
- Renal denervation is FDA-cleared for true resistant HTN on 3+ drugs. It is not a cure but lowers systolic BP 5–7 mmHg without an extra daily pill.
- Never stop clonidine abruptly. Missed doses can trigger a dangerous BP rebound spike.

When to Call Us - and When to Call 911

If you are not sure, call. We would rather hear from you twice than miss a real problem.

- **Call 911** for sudden severe headache, chest pain, shortness of breath, confusion, vision change, or weakness on one side. These can be signs of a hypertensive emergency or stroke. Do not drive yourself.
- **Go to the ER** if your home BP is above 180 systolic or above 110 diastolic AND you have any new symptom. If you feel fine and have no new symptoms, call our office first rather than going to the ER.
- **Call our office (727-943-5200)** if potassium symptoms develop on spironolactone: muscle weakness, unusual fatigue, heart palpitations, or muscle cramps. We may need a blood test.
- **Call us** if you stop any BP medicine for any reason. Especially clonidine — stopping it suddenly can cause a dangerous rebound spike.
- **Call us** if you start any new over-the-counter medicine, especially ibuprofen, naproxen, or decongestants. These can raise BP and blunt your medicines within days.
- **Call us** to request a 24-hour ambulatory BP monitor if your readings always seem high only at the office. White-coat HTN is treatable differently from true resistant HTN.
- **See our companion guides:** Hypertension (go.riasalimd.com/htn-guide), Sleep Apnea (osa-guide), and Heart Failure (hfref-guide).

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See also: companion guides.
Hypertension (primary) · Obstructive Sleep Apnea · Heart Failure (HFrEF) · Cardiac Catheterization

Trusted Resources

The links below are the trusted resources Dr. Ali used to write this guide and that he recommends you visit for more information. Each is a clickable link in the digital version and a Short.io tracked URL on the printed version.

- AHA — Resistant Hypertension Patient Page - AHA's plain-language overview of resistant HTN with definition, causes, and management approach.
- Cleveland Clinic — Resistant Hypertension - Practical guide covering diagnosis, secondary causes, and treatment options including device therapy.
- Mayo Clinic — Resistant Hypertension - Mayo Clinic Q&A; on why BP remains high and what to do next.
- ACC/AHA Scientific Statement: Resistant Hypertension (2018) - Comprehensive medical statement on definition, workup, and evidence-based treatment of resistant HTN.
- PATHWAY-2 Trial (Williams 2015, Lancet) - Landmark randomized trial proving spironolactone is the best 4th drug in resistant HTN.
- AHA — Home Blood Pressure Monitoring - Step-by-step guide to accurate home BP measurement with validated devices and correct technique.
- Endocrine Society — Primary Aldosteronism Guidelines (2016) - Guideline for screening and diagnosing primary aldosteronism — the most common secondary cause of resistant HTN.
- AHA STOP-BANG Sleep Apnea Screening - Information on the link between sleep, sleep apnea, and high blood pressure with guidance on CPAP therapy.
- Medtronic Symplicity SPYRAL Renal Denervation (FDA clearance info) - Patient-facing information on renal denervation — how it works, who it is for, and what to expect.
- NIH MedlinePlus — High Blood Pressure - Federal patient resource with basics, measurement guidance, and links to free Spanish-language materials.

Sources Used to Build This Guide

Every recommendation in this guide is grounded in one or more of the studies, guidelines, or trusted resources below. Short links are tracked so Dr. Ali can see which references patients are reading; nothing personally identifying is captured.

- PATHWAY-2 Trial — Williams et al., Lancet 2015 *[Clinical Trial]*
  Landmark crossover RCT (n=335) proving spironolactone is the most effective 4th drug in resistant HTN — 8.7 mmHg SBP reduction vs placebo, better than bisoprolol or doxazosin. Directly cited in PATHWAY-2 chart and subsection.
- SPYRAL-HTN OFF-MED Pivotal Trial 2021 (Böhm et al., Lancet) *[Clinical Trial]*
  Sham-controlled trial confirming 5–7 mmHg SBP reduction with renal denervation. Basis for FDA clearance of renal denervation for resistant HTN. Referenced in Renal Denervation subsection.
- AHA/ACC 2017 High Blood Pressure Clinical Practice Guideline *[Clinical Guideline]*
  Primary guideline defining resistant HTN, recommending chlorthalidone over HCTZ, and listing spironolactone as preferred 4th drug. Used for definition, treatment stepladder, and drug class table.
- ESC/ESH 2023 Guidelines for Hypertension *[Clinical Guideline]*
  European 2023 hypertension guideline confirming resistant HTN definition, secondary workup algorithm, and MRA as preferred 4th drug. Adds ABPM criteria and renal denervation indications.
- ACC/AHA Scientific Statement: Resistant Hypertension 2018 *[Clinical Guideline]*
  Comprehensive 2018 AHA/ACC scientific statement on resistant HTN: definition, workup algorithm, secondary cause prevalence data, chlorthalidone preference, and spironolactone recommendation.
- Endocrine Society — Primary Aldosteronism Clinical Practice Guideline 2016 *[Clinical Guideline]*
  Source for primary aldosteronism prevalence (15–20% of resistant HTN), ARR screening protocol, and treatment (adrenalectomy vs spironolactone). Cited in secondary workup grid.
- Chung et al. — STOP-BANG Questionnaire Validation (Anesthesiology 2016) *[Validation Study]*
  Validation study for STOP-BANG sleep apnea screening tool. Used to support OSA screening recommendation and score interpretation (5–8 = high risk).
- Barostim Pivotal Trial (Swisstom, 2020 — Zile et al., JACC Heart Fail) *[Clinical Trial]*
  Pivotal trial for baroreflex activation therapy (Barostim) showing benefit in heart failure with reduced EF and resistant HTN. Referenced in device therapy subsection and RBA table.
- Cleveland Clinic — Resistant Hypertension *[Patient Education]*
  High-quality patient-facing reference covering definition, secondary causes, and treatment options. Benchmarked for content completeness — this guide adds PATHWAY-2 chart, secondary-cause grid, and device therapy not present in their overview.
- Mayo Clinic — Resistant Hypertension FAQ *[Patient Education]*
  Competitor benchmark. Mayo covers basic definition and lifestyle but lacks PATHWAY-2 evidence, secondary-cause workup depth, and device therapy — gaps this guide fills.
- AHA — Resistant Hypertension Patient Page *[Patient Education]*
  AHA patient-facing overview referenced for trusted-resources section. Provides basic explanation of resistant HTN for the general public.

- AHA — Home Blood Pressure Monitoring *[Patient Education]*
  Authoritative guidance on home BP measurement technique (quiet rest, cuff sizing, both arms, time of day). Used for BP monitoring recommendations in lifestyle and when-to-call sections.
- ABPM Reference: Kario et al., Hypertension 2018 — ABPM in Resistant HTN *[Clinical Study]*
  Reference for ABPM as gold standard in resistant HTN workup. Documents white-coat HTN prevalence (up to 30%) and the 24-hour target < 130/80. Used in definitions and monitoring sections.

About This Guide

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Reviewer note: Reviewed AHA Resistant HTN Scientific Statement 2018, Cleveland Clinic, Mayo Clinic, and ACC/AHA 2017 HTN guideline. This guide adds: the true vs pseudo-resistance distinction; a 6-cause secondary-workup grid; PATHWAY-2 bar chart; device therapy (renal denervation + Barostim); and chlorthalidone vs HCTZ framing — all absent from standard patient pages.

Disclaimer

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