Resistant Hypertension: Practical Tips for the Primary Care Provider

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Disclosures

- None

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Goals

- Review evaluation of resistant hypertension
- Understand pharmacologic and non-pharmacologic strategies for treating resistant hypertension

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Definition of hypertension

TABLE 6 Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

CLINICAL PRACTICE GUIDELINE
2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

Based on an average of ≥2 readings obtained on ≥2 occasions

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Nonpharmacological therapy

- **Weight loss**: in adults who are overweight, aim for at least 1 kg weight loss. Expect about 1mmHg for every 1kg.
- **Heart-healthy diet:** DASH diet, fruits, vegetables, whole grains, low-fat dairy.
- **Sodium reduction**: aim for at least a 1g/day reduction. Ideal total <1.5g/day
- **Increased physical activity**: 90-150 min/week of aerobic activity
- **Limit alcohol**: ≤2 drinks/day for men, ≤1 drinks/day for women
- **High potassium diet**: >120mEq dietary potassium per day

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Medical therapy

- First line agents:
  - Thiazide diuretics
  - Calcium channel blocker (DHP or non-DHP)
  - ACE-I or ARB
  - 2 agents are recommended in stage 2 htn or BP >20/10 mmHg above goal
- Second line agents:
  - Loop diuretic, BB, aldosterone antagonist, alpha-1 blockers, alpha-2 agonist, hydralazine, minoxidil

BP goals

- <130/80 mmHg in adults with known CVD or 10yr risk >10% (class I)
- <130/80 mmHg reasonable in adults without known CVD and without increased CVD risk (class IIb)

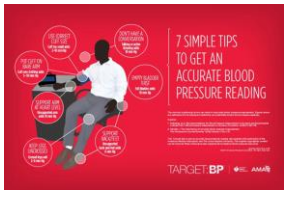
Resistant hypertension

- Uncontrolled resistant hypertension
  - Blood pressure above goal despite concurrent use of 3 antihypertensive agents of different classes, commonly including a long-acting CCB, an ACE-I or ARB, and a diuretic. All agents should be administered at maximum or maximally tolerated doses and at the appropriate dosing frequency
- Apparent treatment resistant hypertension
  - when ≥1 of the following data elements are missing: medication dose, adherence, or out-of-office BP; thus, pseudo-resistance cannot be excluded
  - Pseudo-resistant hypertension is most caused by inaccurate BP measurement, medication non-adherence, under-treatment, white coat effect

Evaluation of resistant hypertension

Confirm diagnosis

- Exclude pseudo-resistance
- Ensure accurate BP measurements
- White coat hypertension
- Assess medication non-adherence



Proper BP measurement

- Relax, sitting in a chair (feet on floor, back supported) for 5 min
- Avoid caffeine, exercise, and smoking for >30 min
- Empty bladder
- No talking
- No clothing under cuff
- Use validated, calibrated device
- Arm supported
- Use correct cuff size

Acute alcohol use:
SBP -24 to +24mmHg

Acute caffeine use:
SBP +3 to +14mmHg

Acute nicotine use:
SBP +3 to +25mmHg

Bladder distension:
SBP +4 to +33mmHg

Legs crossed: SBP
+2 to +15mmHg

Small cuff:
SBP +2 to +11mmHg

No resting period:
SBP +4 to +11mmHg

Talking:
SBP +4 to 19mmHg

Unsupported arm or cuff too low:
SBP +4 to +23mmHg

Kallioinen et al. Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings: a systematic review. Journal of Hypertension 2017; 35:421 -441.

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In office vs out-of-office BP

COR	LOE	RECOMMENDATION
I	A[a]	1. Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension (Table 11) and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions (S4.2.1–S4.2.4).

- Office BP useful for screening for htn
- Out-of-office (HBPM or ABPM) recommended to confirm diagnosis and guide management
- ABPM and HPBM predict long-term CVD risk better than office BPs

TABLE 11 Corresponding Values of SBP/DBP for Clinic, HBPM, Daytime, Nighttime, and 24-Hour ABPM Measurements

Clinic	HBPM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; HBPM, home blood pressure monitoring; and SBP, systolic blood pressure.

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Ambulatory blood pressure monitoring

- BP readings every 15-30min throughout day and every 15-60min at night
- Provides mean estimate of BP
- Assess for normal nocturnal dipping, nocturnal hypertension, morning surge
- Identify symptomatic hypotension
- Accepted as best method for out-of-office BP measurement
- Limited by cost, insurance reimbursement, and practicality

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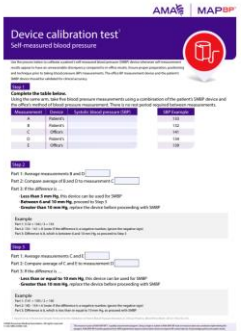

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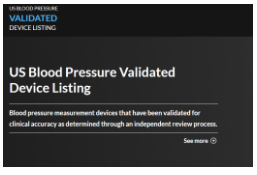
Self-measured blood pressure

Using a wrist cuff* to measure blood pressure



Validatebp.org

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Evaluation of resistant hypertension

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- White coat hypertension
- Assess medication non-adherence

Exacerbating factors
- Obesity, physical inactivity, poor sleep
- Dietary factors: alcohol, high sodium, excessive caffeine
- Interfering medications

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Lifestyle

- Obesity
  - BMI ≥30 kg/m² is independent risk factor for RH
  - Expect about 1 mmHg for every 1 kg weight loss
- Physical inactivity
- Sodium
  - Reduce sodium intake to <2.3 g/day
  - Consider <1.5 g/day
- Sleep quality
  - CPAP use for >4hrs in RH reduces BP by 4mmHg

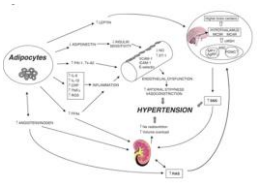

TABLE 15 Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

Nonpharmacological Intervention	Dose	Approximate Impact on SBP: Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	−5 mm Hg	−2/3 mm Hg	(56.2-1)
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	−11 mm Hg	−3 mm Hg	(56.2-6,56.2-7)
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is ~1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	−5/6 mm Hg	−2/3 mm Hg	(56.2-9,56.2-10)
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500-5000 mg/d, preferably by consumption of a diet rich in potassium.	−4/5 mm Hg	−2 mm Hg	(56.2-13)
Physical activity	Aerobic	■ 90-150 min/wk ■ 65%-75% heart rate reserve	−5/8 mm Hg	−2/4 mm Hg	(56.2-18,56.2-22)
	Dynamic resistance	■ 90-150 min/wk ■ 50%-80% 1 rep maximum ■ 6 exercises, 3 sets/exercise, 10 repetitions/set	−4 mm Hg	−2 mm Hg	(56.2-18)
	Isometric resistance	■ 4 × 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk ■ 8-10 wk	−5 mm Hg	−4 mm Hg	(56.2-19,56.2-31)
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol to: ■ Men: ≤2 drinks daily ■ Women: ≤1 drink daily	−4 mm Hg	−3 mm Hg	(56.2-22–56.2-24)

Medication-related hypertension

- NSAIDs
  - ↑ MAP by 2-5mmHg
  - Can inhibit effects of diuretics, ACE/ARB, BB
- Oral contraceptives
  - Estrogen increases angiotensin production
  - Uncommon but can ↑ SBP 3-6mmHg
- Sympathomimetics (decongestants, weight loss drugs, ADHD meds)
- Corticosteroids
- Tyrosine kinase inhibitors, cyclosporine, bevacizumab
- Illicit drugs (cocaine, meth)

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Exacerbating factors
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- Dietary factors: alcohol, high sodium, excessive caffeine
- Interfering medications

Consider secondary causes
- Renovascular
- Primary hyperaldosteronism
- Renal disease
- Endocrine causes: Pheo, Cushing's, thyroid

Secondary causes of hypertension

- Can be sole cause or contributing cause
- Estimated in 5-10% of all hypertension, higher in RH.

Common causes	Uncommon causes
Renal parenchymal disease (CKD, urinary obstruction)	Pheochromocytoma: 0.01-0.6% in all HTN, up to 4% in RH
Renovascular disease (FMD, atherosclerosis): 5% in all HTN, 35% in RH	Cushing's syndrome: <0.1%
Primary hyperaldosteronism: 8% in all hypertension, 20% in RH	Hypo and hyperthyroidism: <1%
OSA: 25-75%	Aortic coarctation: 0.1%
	Hyperparathyroidism, Acromegaly, congenital adrenal hyperplasia: rare

When to consider secondary causes?

- Resistant hypertension
- Abrupt onset hypertension
- Exacerbation of previously controlled hypertension
- Onset of hypertension at <30 yo
- End organ damage disproportionate to htn duration/severity
- Malignant hypertension
- Signs or symptoms suggestive of a specific cause

Pharmacologic treatment of RH

Step 1	Optimize 3 drug regimen (diuretic, ACE/ARB, CCB) • Use combination pills to improve adherence
Step 2	• Consider switching HCTZ to chlorthalidone (↓SBP 7-8 mmHg) • Long acting loop diuretic if low GFR • Consider switching amlodipine to nifedipine • Consider divided dosing or night time dosing
Step 3	Add mineralocorticoid receptor antagonist
Step 4	Add BB or consider clonidine
Step 5	Add hydralazine or alpha-1 blocker

Carey RM et.al. Hypertension. 72:e53-e90 11/2018

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What's new? Renal Denervation!

FDA approval on 11/7/2023
Ultrasound technology

FDA approval on 11/17/2023
Radiofrequency ablation

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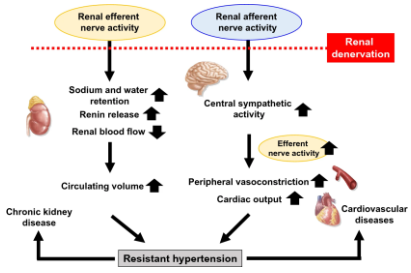

Cardiovascular Intervention and Therapeutics (2022) 37:450–457
https://doi.org/10.1007/s12928-022-00854-2

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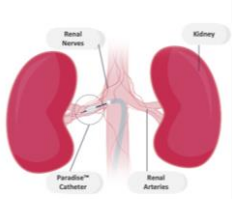

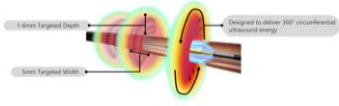

- Who's it for?
  - FDA: "indicated to reduce blood pressure as an adjunctive treatment in hypertension patients in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure"
  - Patients with true resistant hypertension

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Summary

- Exclude pseudo-resistant hypertension
- Address lifestyle factors
- Optimize 3-drug first line regimen
- Consider common secondary causes

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Thank You

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