Treatment Resistant Hypertension:
Treating The Difficult Patient

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Overview

- Definition
- Evaluation of resistant hypertension
- Medical treatment
- Device based interventions

Patient

- A 65 y/o female presents for evaluation of hypertension
- Diagnosed 6 months ago
  - Started initially on amlodipine & lisinopril
  - Chlorthalidone added 3 months ago
- Notes significant daytime somnolence
- Current meds:
  - Amlodipine 10 mg qd, chlorthalidone 50 mg qd, lisinopril 40 mg qd
- Her BP in office is 160/90

Patient

- Which of the following is the most appropriate next step?
    A. Provide reassurance
    B. Return in two weeks for additional BP measurements
    C. Check BP twice daily at home for one week
    D. Change lisinopril to losartan 50 mg qd
    E. Something else?

European Heart Journal (2013) 34, 2159–2219
doi:10.1093/eurheartj/eht151

ESH AND ESC GUIDELINES

2013 ESH/ESC Gu
of arterial hyperte

The Task Force for the m
European Society of Hyp
of Cardiology (ESC)

AHA Scientific Statement

Resistant Hypertension: Detection, Evaluation, and Management

A Scientific Statement From the American Heart Association

Robert M. Carey, MD, FAHA, Chair; David A. Calhoun, MD, FAHA, Vice Chair; George L. Bakris, MD, FAHA; Robert D. Brook, MD, FAHA; Stacie L. Daugherty, MD, MSPH; Cheryl R. Dennison-Himmelfarb, PhD, MSN, FAHA; Brent M. Egan, MD; John M. Flack, MD, MPH, FAHA; Samuel S. Gidding, MD, FAHA; Eric Judd, MD, MS; Daniel T. Lackland, DrPH, FAHA; Cheryl L. Laffer, MD, PhD, FAHA; Christopher Newton-Cheh, MD, MPH, FAHA; Steven M. Smith, PharmD, MPH, BCPS; Sandra J. Taler, MD, FAHA; Stephen C. Textor, MD, FAHA; Tanya N. Turan, MD, FAHA; William B. White, MD, FAHA; on behalf of the American Heart Association Professional/Public Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council

Circulation

Resistant Hypertension: Diagnosis, Evaluation,
From the American Heart Association Professio
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David A. Calhoun, Daniel Jones, Stephen Textor, Da
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pertension in

Clinical Guideline 127

Methods, evidence, and recommendations

August 2011

Commissioned by the National Institute for Health and Clinical Excellence

BHS

Clinical Practice Guidelines for the Management of Hypertension in the Community
A Statement by the American Society of Hypertension and the International Society of Hypertension

Michael A. Weber[a], Ernesto L. Schiffrin[b], William B. White[c], Samuel Mann[d], Lars H. Lindholm[e], John G. Kenerson[f], John M. Flack[g], Barry L. Carter[h], Barry J. Materson[i], C. Venkata S. Ram[j], Debbie L. Cohen[k], Jean-Claude Cadet[l], Roger R. Jean-Charles[m], Sandra Taler[n], David Kountz[o], Raymond Townsend[p], John Chalmers[q], Agustin J. Ramirez[r], George L. Bakris[s], Jiguang Wang[t], Aletta E. Schutte[u], John D. Bisognano[v], Rhian M. Touyz[w], Dominic Sica[x], and Stephen B. Harrap[y]

Resistant Hypertension

- Above-goal elevated blood pressure on 3 antihypertensive drugs from different classes

OR

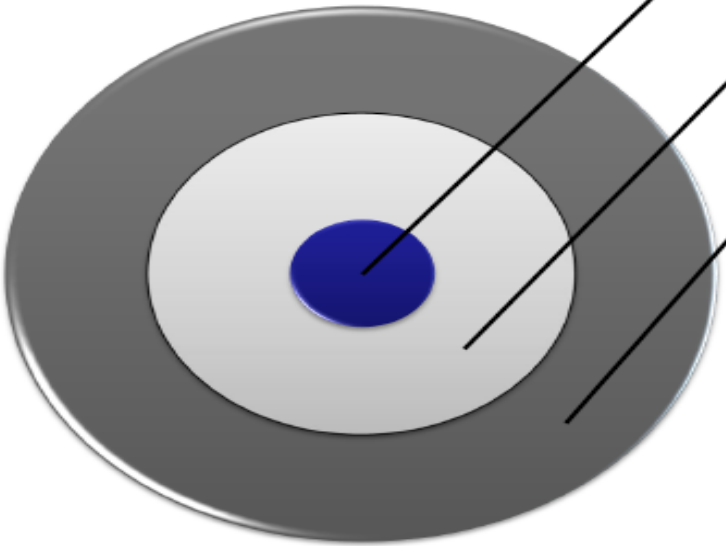
- Treatment with ≥ 4 classes regardless of BP control
- Medications should be prescribed at maximum tolerated doses
- Ideally one drug should be a diuretic
- Assurance of antihypertensive medication adherence
- Exclusion of the “white-coat effect”

Journal of Human Hypertension (2011) 25, 137–140

www.nature.com/jhh

RESEARCH LETTER

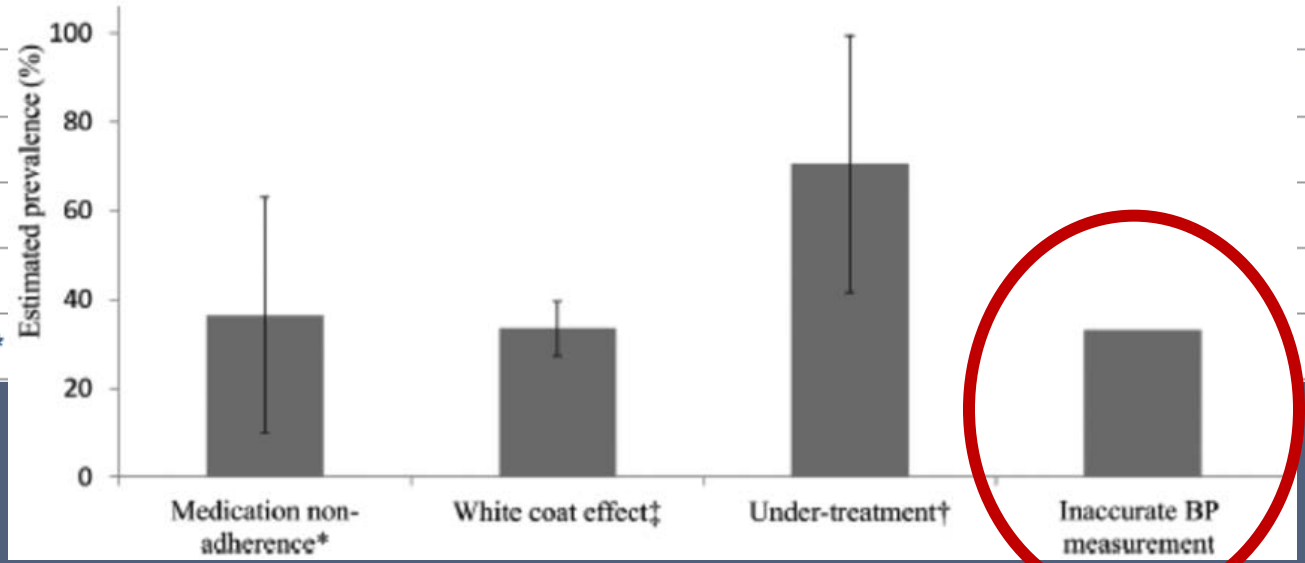
How common is true resistant hypertension?



Persell SD, Hypertension 2011; de la Sierra, Hypertension 2011

Apparent Treatment Resistant Hypertension

Population Based	Time Period	n	Uncontrolled With ≥3 BP Medications, %	Controlled With ≥4 BP Medications, %	aTRH, %
NHANES[13]					9.4
NHANES[13]					11.7
NHANES[14]					12.8
NHANES[13]					14.5
REGARDS[15]					14.1
REGARDS[16] (CKD)*					28.1



Hypertension. 2018;72:e53-e90.

Accurate Measurement of BP in the Office

COR	LOE	Recommendation for Accurate Measurement of
I	C	

Checklist for Accurate Measurement of BP

Key Steps for Proper BP Measurements
Step 1: Properly prepare the patient.
Step 2: Use proper technique for BP measurements.
Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/hypertension.
Step 4: Properly document accurate BP readings.
Step 5: Average the readings.
Step 6: Provide BP readings to patient.

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American Heart Association.
life is why

Co-morbidities associated with resistant hypertension

Co-morbidities	Odds ratio (95% CI)
Coronary artery disease	1,3 (1,1-1,5)
Peripheral vascular disease	1,3 (1,1-1,5)
Cerebrovascular disease	1,3 (1,1-1,5)
Congestive heart failure	2,9 (2,4-3,4)
Atrial fibrillation	3,5 (2,0-6,2)
Left ventricular hypertrophy	2,1 (1.2-4,6)
Chronic kidney disease	2,1(1,8-2,5)
Albuminuria	2,4 (1,7-3,5)

Adapted from Rimoldi S et al, EHJ 2015; 36:2586-2695

Konradi, ACC.16

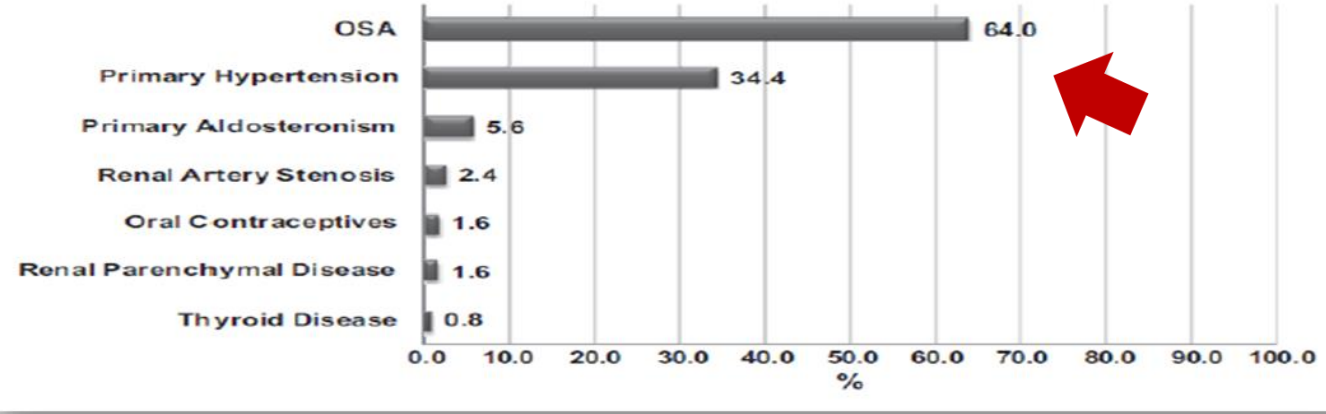
Evaluation of Resistant Hypertension

Confirm Treatment Resistance

Obstructive Sleep Apnea

The Most Common Secondary Cause of Hypertension Associated With Resistant Hypertension

Rodrigo P. Pedrosa, Luciano F. Drager, Carolina C. Gonzaga, Marcio G. Sousa, Lílian K.G. de Paula, Aline C.S. Amaro, Celso Amodeo, Luiz A. Bortolotto, Eduardo M. Krieger, T. Douglas Bradley, Geraldo Lorenzi-Filho



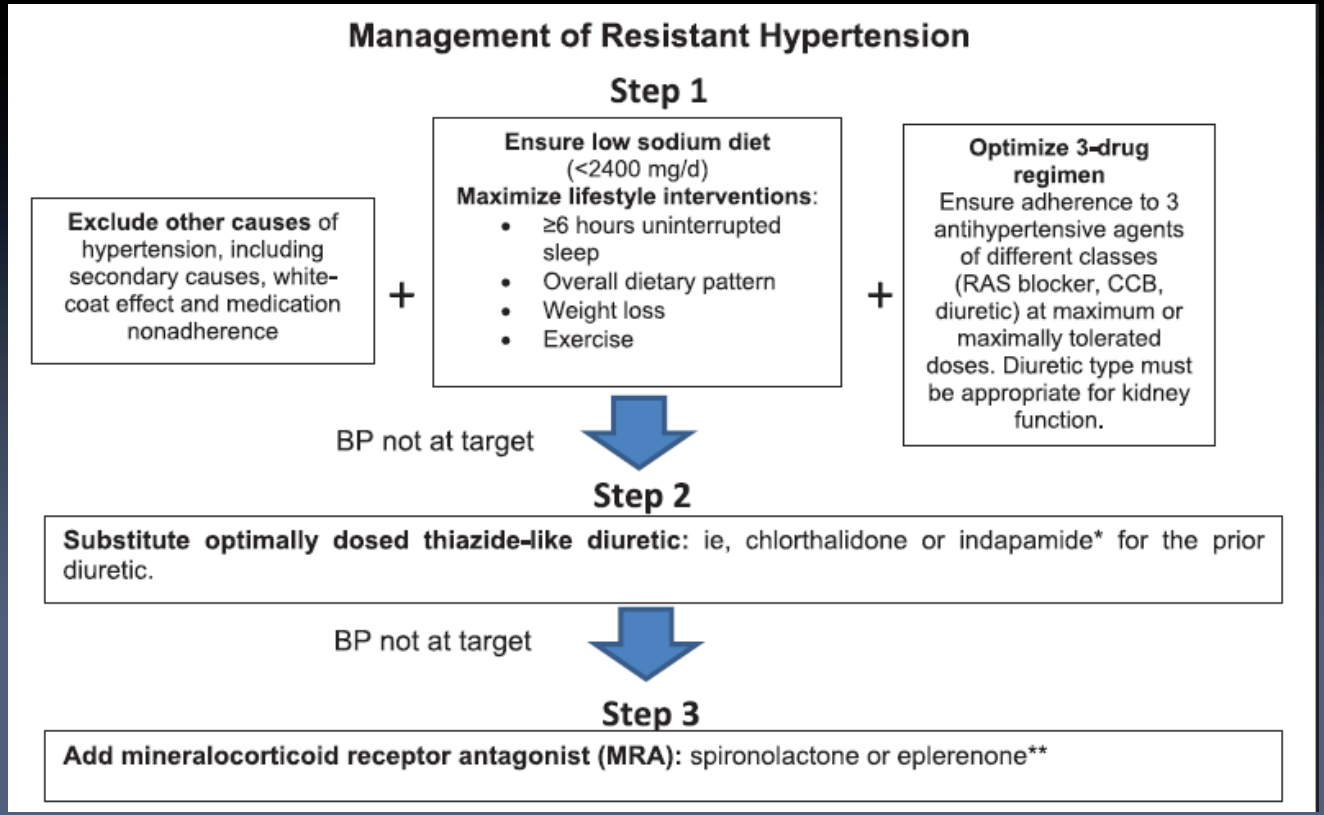
Hypertension 2011

Cardiac: left ventricular hypertrophy, coronary artery disease
Renal: proteinuria, reduced glomerular filtration rate
Peripheral arterial disease: ankle/brachial index

Hypertension. 2018;72:e53-e90

Medications That Can Interfere With BP Control

- NSAIDs/COX-2 inhibitors
- Oral contraceptives (estrogen predominant)
- Sympathomimetic agents
  - Decongestants
  - Diet Pills
  - Cocaine
- Stimulants (amphetamines)
- Alcohol
- Anti-depressants
  - TCAs and SSRIs
- Cyclosporine
- Erythropoietin
- Natural licorice
- Herbal compounds
- VEGF Inhibitors



Hypertension. 2018;72:e53-e90

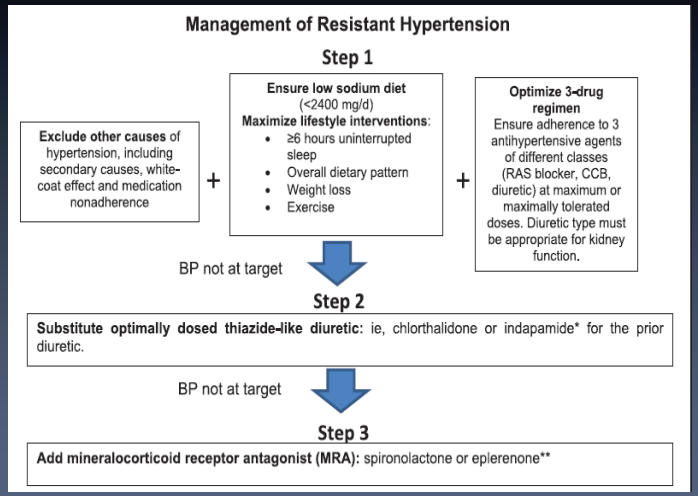
Optimizing Diuretic Therapy

- Further increase in diuretic dose
- Switching from HCTZ to chlorthalidone/indapamide
- GFR <30 ?
  - Replace thiazides/chlorthalidone with loop diuretic
- Combine diuretics with different mechanisms of action
  - Spironolactone 12.5-25 mg daily
  - Eplerenone 50 mg once daily
  - Amiloride 5-10 mg daily

J Hypertens 2013, 31:1281–1357

Patient continued

- You have patient check BP twice daily at home and refer for sleep evaluation - BP measurements confirm office measurements.
- You have added spironolactone 25 mg qd
- BP two weeks later is 150/80
- Which of the following is the most appropriate next step?
  A. Start losartan
  B. Start hydralazine
  C. Start metoprolol
  D. Refer to hypertension specialist



BP still not at target

Note: Steps 4-6 are suggestions on the basis of expert opinion only and these steps should be individualized.

Step 4

Check heart rate: unless <70 beats/min, **add β-blocker** (eg, metoprolol succinate, bisoprolol) or combined α-β-blocker (eg, labetalol, carvedilol). If β-blocker is contraindicated, consider central α-agonist (ie, clonidine patch weekly or guanfacine at bedtime). If these are not tolerated, consider once-daily diltiazem.

BP still not at target

Step 5

Add hydralazine*** 25 mg three times daily and titrate upward to max dose; in patients with congestive heart failure with reduced ejection fraction, hydralazine should be administered on background isosorbide mononitrate 30 mg daily (max dose 90 mg daily).

BP still not at target

Step 6

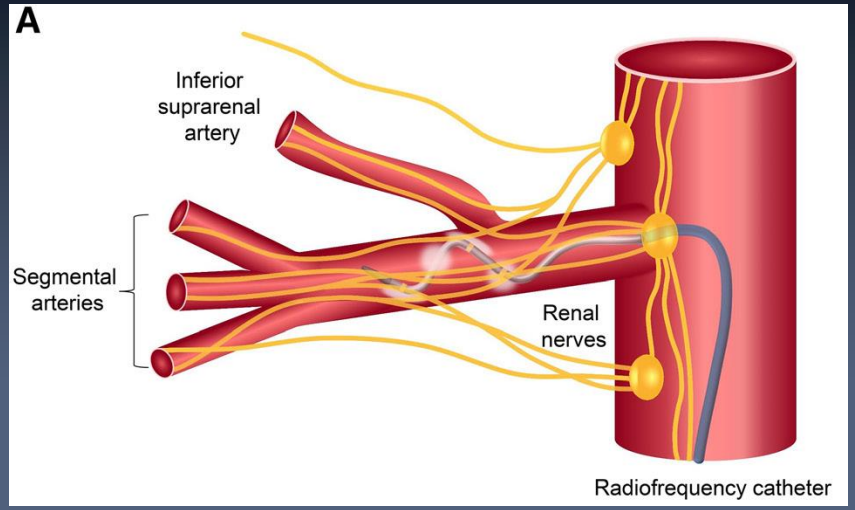
Substitute minoxidil**** 2.5 mg two to three times daily for hydralazine and titrate upward. If BP still not at target, consider referral to a hypertension specialist and/or for ongoing experimental studies—www.clinicaltrials.gov.

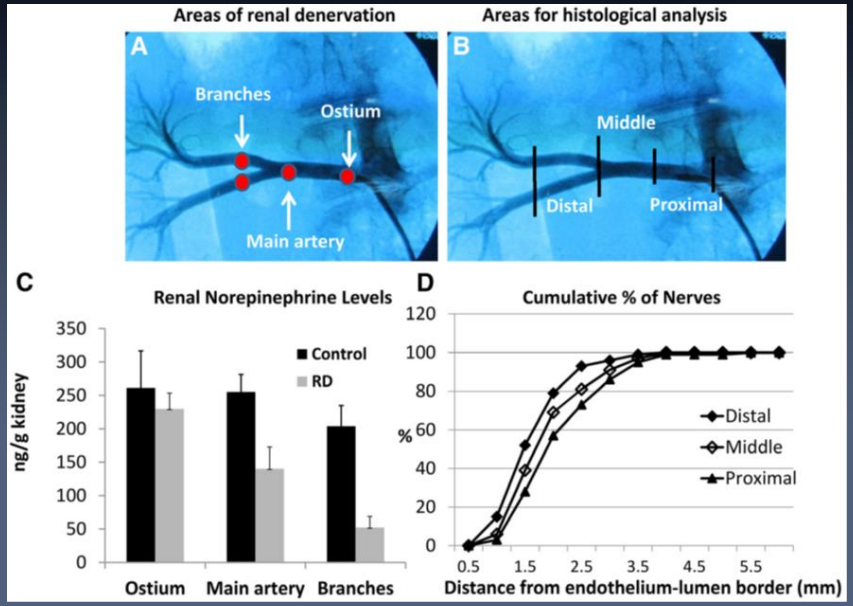
Hypertension. 2018;72:e53-e90

Interventional Treatments

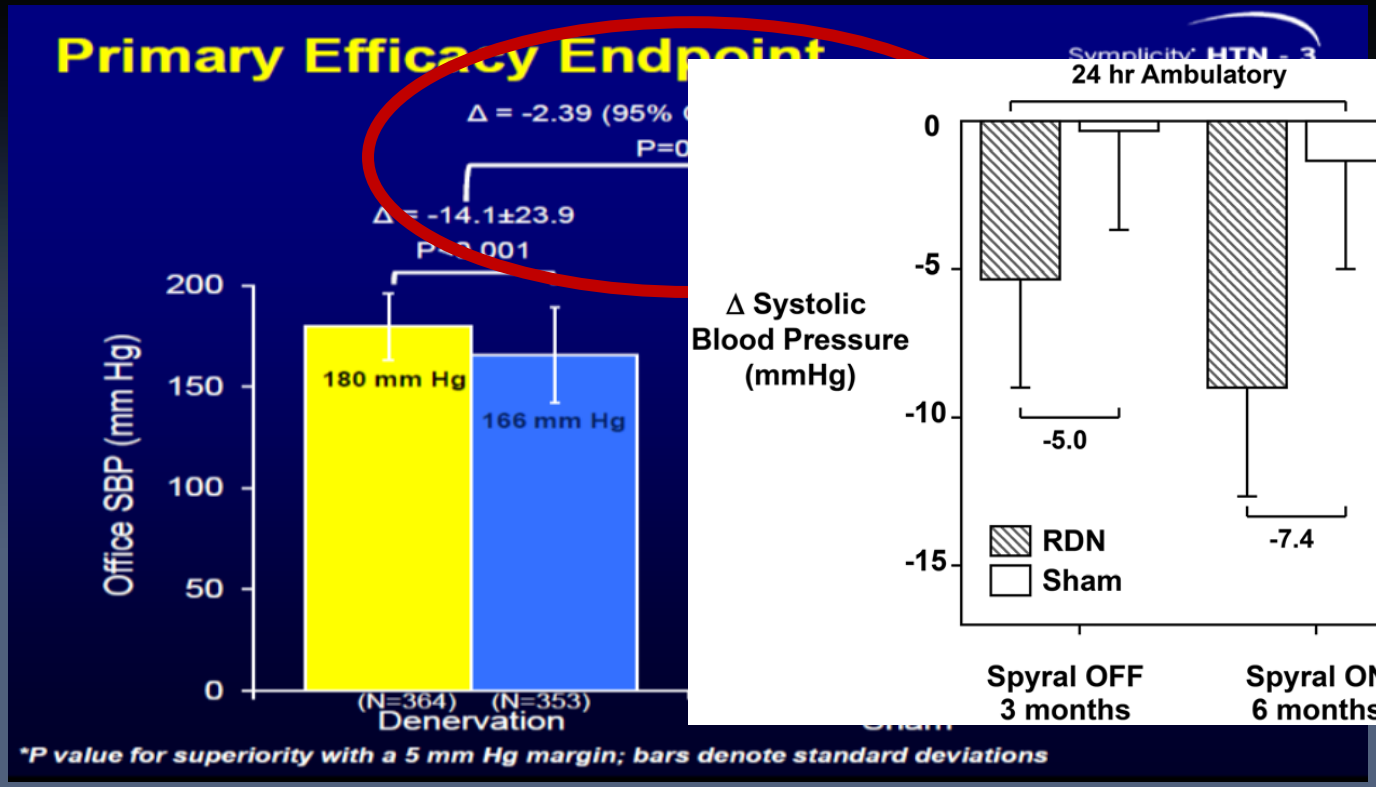
- Renal denervation
- Baroreflex activation therapy
- Noninvasive renal denervation
- Central arteriovenous fistula
- Renal artery revascularization/renal artery stenting

Renal Denervation





Circ Res. 2019;124:1071-1093.



Circ Res. 2019;124:1071-1093.

Baroreflex Activation Therapy

3. Brain

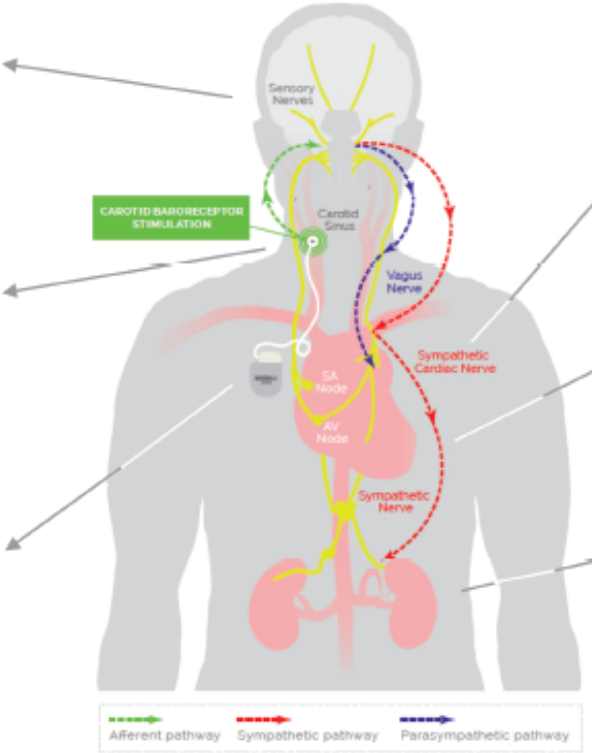
- Control board for autonomic nervous system.
- Achieves autonomic balance by reducing sympathetic activity while increasing parasympathetic activity.

2. Baroreceptors

- Sensors that provide information to the central nervous system, which are used in autonomic reflexes and act as part of the baroreflex.
- Are stimulated by BAROSTIM THERAPY™.

1. BAROSTIM NEO™

- A single electrode, powered by one of the most powerful implantable batteries in the world.
- Activates the baroreflex.



In resistant hypertension:

4. Heart

↓ HR ↓Remodeling

- Reduces myocardial work
- Reduces LV hypertrophy

5. Blood Vessels

↑Vasodilation ↑ Venous capacitance

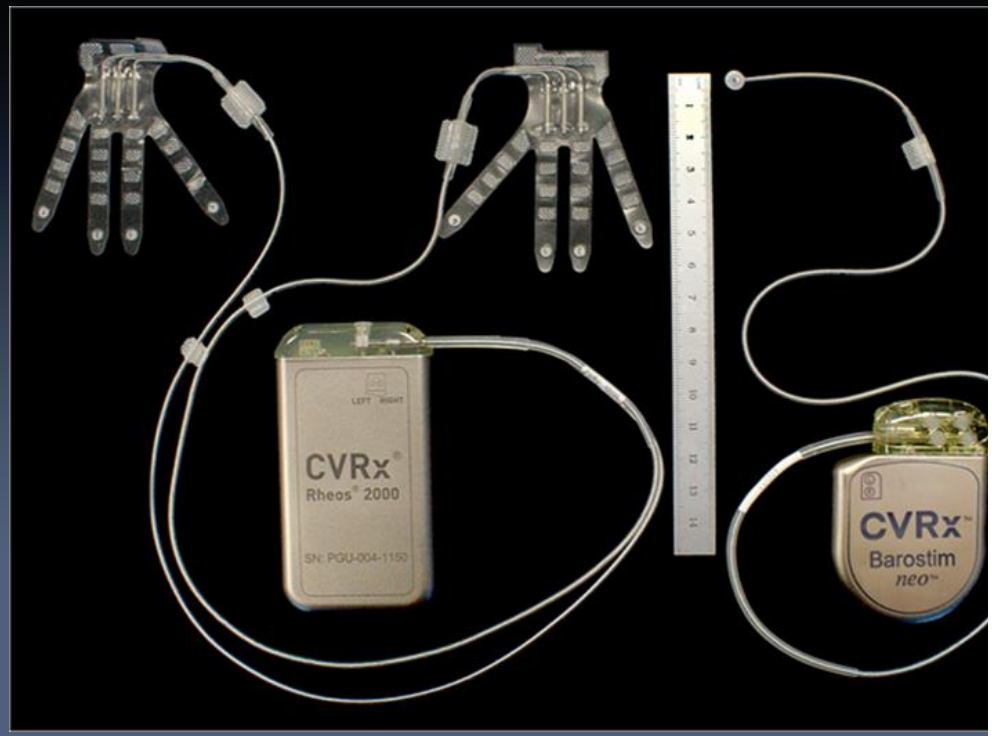
- Reduces arterial pressure
- Reduces pulse pressure

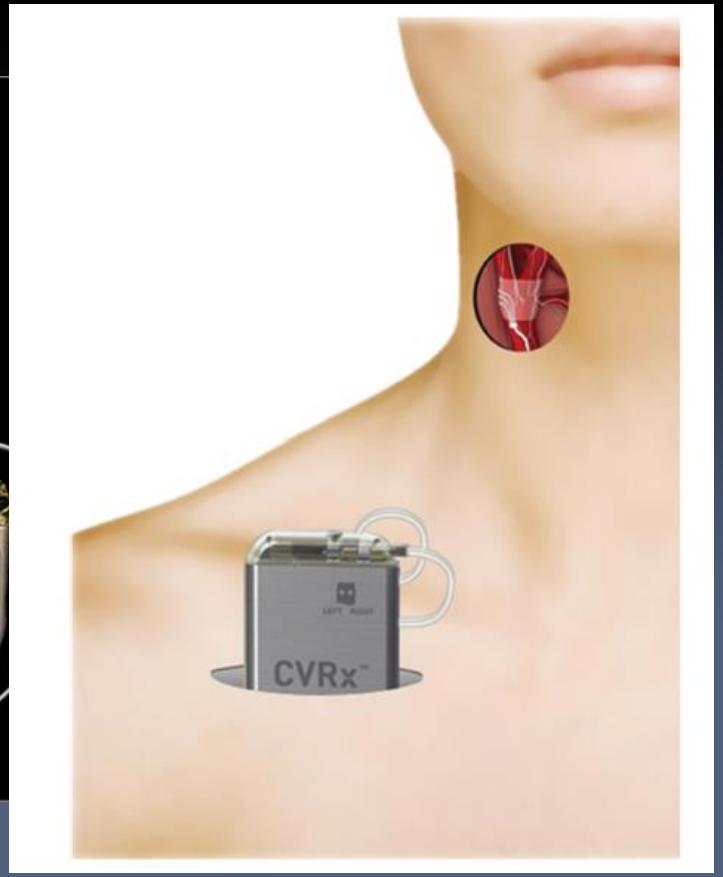
6. Kidneys

↑ Diuresis ↓ Renin secretion

- Reduces arterial pressure
- Reduces pulse pressure

American Journal of Hypertension 29(12) December 2016





American Journal of Hypertension 29(12) December 2016

Summary

- Confirm definition criteria
- Evaluate for apparent resistant hypertension
- Ensure adequate treatment
- Diuretic options and beyond
- Refer to specialist for treatment