THE CARDIOVASCULAR CENTER OF FLORIDA

2025 Cardiovascular Center Of Florida Annual Symposium

Update on the treatment of Hypertension and the adjunct use of Renal Denervation

Dr. Mark Steiner

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Practice:

- Newest private practice cardiology group in Central Florida
- 30 cardiologists in 11 offices throughout Central Florida
- Offer all general, invasive, interventional and electrophysiology cardiac care with a full range of invasive and noninvasive testing

Mark Steiner:

- My training was Washington University in St. Louis (medical school, internship and residency) and Emory University (cardiology and interventional cardiology)
- Been in Orlando since 2001
- Interest in general and interventional cardiology, peripheral vascular disease, and structural including Watchman and Renal Denervation

The Urgency to Act

Hypertension is a major health crisis

50%
of adults
in the U.S.
have high blood pressure[1]

80%
of hypertension patients
do not have their blood pressure under control[2]

#1
leading preventable cause of heart attack, stroke, and death[3]

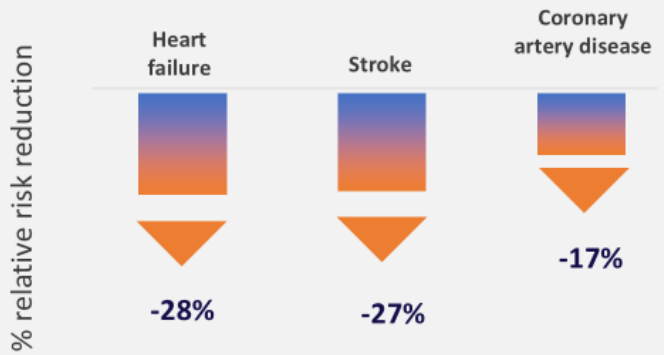
50%
of hypertension patients
become nonadherent to their medication within one year[4]

- [1] U.S. Department of Health and Human Services. The Surgeon General's Call to Action to Control Hypertension. Washington, DC: U.S. Department of Health and Human Services, Office of the Surgeon General; 2020.
- [2] Hypertension fact sheet. World Health Organization. Available at: https://www.who.int/news-room/fact-sheets/detail/hypertension. Accessed August 23, 2023.
- [3] Bundy JD, et al. *JAMA Cardiol*. 2018;3:572–581.
- [4] Jung O, et al. *J Hypertens*. 2013;31:766–774.
- [5] Ettehad D, et al. *Lancet*. 2016;387:957–967.

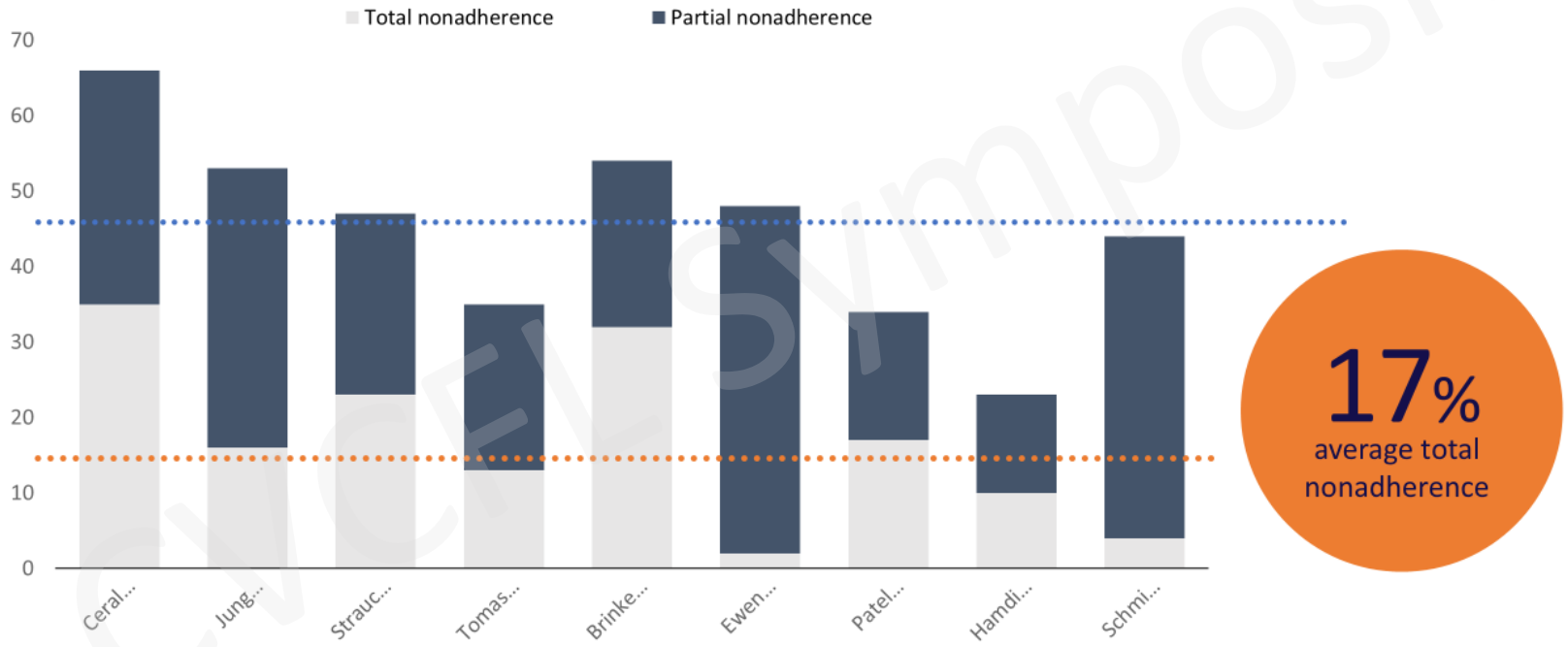
Reducing office systolic blood pressure (SBP) by 10 mmHg leads to clinically meaningful reductions in cardiovascular events[5]

>20% reduction in relative risk of **major cardiovascular events**

>13% reduction in relative risk of **all-cause mortality**



Studies show patients struggle to adhere to their treatment strategy

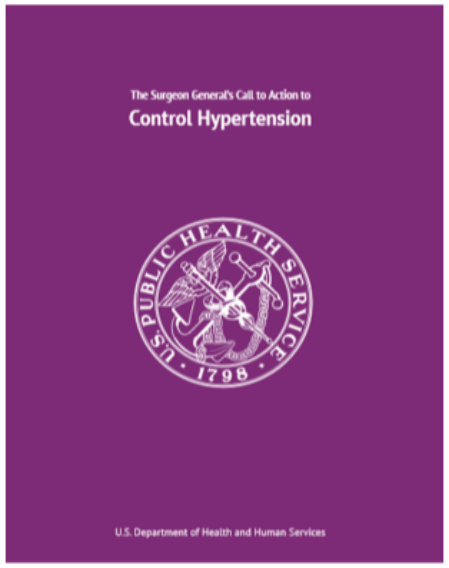


17%
average total nonadherence

- [1] Berra E, et al. *Hypertension*. 2015;68:297–306.

HTN control is not getting better

> Our goal is to improve national hypertension control rates to 80% by 2025
>
> CDC National Hypertension Control Roundtable

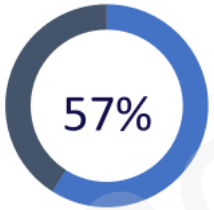


- https://www.cdc.gov/bloodpressure/CTA.htm

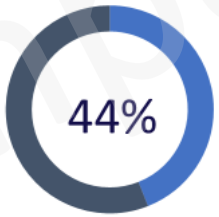
Hypertension differs across race and gender

- African Americans are disproportionately affected by hypertension and less likely to have their blood pressure under control. The excess risks from elevated blood pressure have a dramatic effect on life expectancy for African Americans.[1]
- Nearly half of the eligible Hispanic population don't receive treatment, and of those that do, nearly 60% continue to be uncontrolled. [2]
- Improving awareness and access to hypertension therapies is essential in overcoming disparities in care and improving outcomes for all patients.

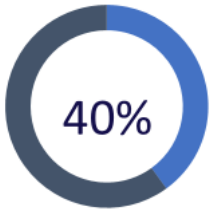
U.S. adults with hypertension[3]



Of Non-Hispanic Black population



Of White and Hispanic population



Of women have hypertension

Communities of color have significantly lower control rates[4]

- [1] Lackland DT. *Am J Med Sci.* 2014;348:138-138..
- [2] *Aggarwal Ret al. Racial/Ethnic Disparities in Hypertension Prevalence, Awareness, Treatment, and Control in the United States, 2013 to 2018. Hypertension. 2021 Dec;78(6):1719-1726.*
- *3 Ostchega Y, et al. NCHS Data Brief. 2020;1-8.*
- *4 Muntner P, et al. JAMA. 2020;324:1190-1200.*

High BP is a global problem and communities of color are disproportionately affected[1]

Hypertension unequally impacts underserved communities

- 1Aggarwal R, et al. Hypertension. 2021;78(6):1719-1726.

Blood pressure control is challenging

- Guideline recommendations focus on lifestyle changes and drug therapy
- Guidelines have increased focus on urgency of establishing and maintaining BP control

[1] Whelton PK, et al. *Hypertension*. 2018;71:e13-e115.

Defining hypertension

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ACC / AHA 2017 HTN Guidelines[1]

Blood Pressure Category	Systolic (mmHg)		Diastolic (mmHg)
Normal	Less than 120	and	Less than 80
Elevated	120-129	and	Less than 80
Hypertension Stage 1	130-139	or	80 – 89
Hypertension Stage 2	140 or higher	or	90 or higher
Hypertensive Crisis	Higher than 180	and/or	Higher than 120

Types of Hypertension[2]

Primary	Also known as essential hypertension; unknown cause of HTN
Secondary	HTN is caused by a different specific disease process
Resistant	BP that continues to remain elevated despite patient prescribed 3 BP medications
Isolated Systolic Hypertension (ISH)	Elevated systolic BP with normal diastolic BP; common in elderly patients
Combined Systolic/Diastolic Hypertension (CH)	Elevated systolic and diastolic BP
Refractory	BP that continues to remain elevated despite patient prescribed ≥ 5 BP medications

[1] American Heart Association. https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings
[2] Jacovic, *Exp Clinical Research* 2016

Table 5. Strategies to Dose Antihypertensive Drugs[a]

Strategy	Description	Details
A	Start one drug, titrate to maximum dose, and then add a second drug	If goal BP is not achieved with the initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add a second drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP
B	Start one drug and then add a second drug before achieving maximum dose of the initial drug	Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended doses of both to achieve goal BP If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP
C	Begin with 2 drugs at the same time, either as 2 separate pills or as a single pill combination	Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination. Some committee members recommend starting therapy with ≥2 drugs when SBP is >160 mm Hg and/or DBP is >100 mm Hg, or if SBP is >20 mm Hg above goal and/or DBP is >10 mm Hg above goal. If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.

Abbreviations: ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

[a]This table is not meant to exclude other agents within the classes of antihypertensive medications that have been recommended but reflects those agents and dosing used in randomized controlled trials that demonstrated improved outcomes.

Important changes in the JNC 8 guideline:

- In patients 60 years or older who do not have diabetes or chronic kidney disease, the goal blood pressure level is now <150/90 mm Hg.

- In patients 18 to 59 years of age without major comorbidities, and in patients 60 years or older who have diabetes, chronic kidney disease (CKD), or both conditions, the new goal blood pressure level is <140/90 mm Hg.

- First-line and later-line treatments should now be limited to 4 classes of medications: thiazide-type diuretics, calcium channel blockers (CCBs), ACE inhibitors, and ARBs.

- Second- and third-line alternatives included higher doses or combinations of ACE inhibitors, ARBs, thiazide-type diuretics, and CCBs. Several medications are now designated as later-line alternatives, including the following: beta-blockers, alphablockers, alpha1/beta-blockers (eg, carvedilol), vasodilating beta-blockers (eg, nebivolol), central alpha2/-adrenergic agonists (eg, clonidine), direct vasodilators (eg, hydralazine), loop diruretics (eg, furosemide), aldosterone antagoinsts (eg, spironolactone), and peripherally acting adrenergic antagonists (eg, reserpine).

Important changes in the JNC 8 guideline:

- When initiating therapy, patients of African descent without CKD should use CCBs and thiazides instead of ACE inhibitors.
- Use of ACE inhibitors and ARBs is recommended in all patients with CKD regardless of ethnic background, either as first-line therapy or in addition to first-line therapy.
- ACE inhibitors and ARBs should not be used in the same patient simultaneously.
- CCBs and thiazide-type diuretics should be used instead of ACE inhibitors and ARBs in patients over the age of 75 years with impaired kidney function due to the risk of hyperkalemia, increased creatinine, and further renal impairment.
- The change to a more lenient systolic blood pressure goal may be confusing to many patients who are accustomed to the lower goals of JNC 7, including the <140/90 mm Hg goal for most patients and <130/80 mm Hg goal for patients with hypertension and major comorbidities.

Guideline Similarities	2017 ACC/AHA	2023 ESH
Accurate Blood Pressure Measurement	Office-based BP measurements and use of validated, cuffed devices and home/ambulatory BP monitoring are recommended prior to diagnosing hypertension.	
Cardiovascular Risk Calculator for Treatment Thresholds	Pooled Cohort Equation and SCORE2/SCORE2-OP provide estimates for 10-year risk of fatal and non-fatal cardiovascular events and should be used to guide treatment decisions.	
Initial Pharmacotherapy Recommendations	Initial therapeutic choices include ACE inhibitors, angiotensin-receptor blockers, thiazide or thiazide-like diuretics, and calcium channel blockers. Single pill combination therapy is a first-line strategy for many patients.	

Guideline Differences	2017 ACC/AHA	2023 ESH
Hypertension Definition	≥ 130/80	≥ 140/90
Normal BP Ranges (mmHg)	Normal: < 120/80 Elevated: 120-129/<80	Optimal: < 120/80 Normal: 120-129/80-84 High-Normal: 130-139/85-89
Hypertensive BP Ranges (mmHg)	Hypertension Stage 1: 130-139/80-89 Hypertension Stage 2: ≥ 140/90	Hypertension Grade 1: 140-159/90-99 Hypertension Grade 2: 160-179/100-109 Hypertension Grade 3: ≥ 180/110
BP Targets for Treatment		
18 – 64 years (mmHg)	< 130/80	< 130/80
65-79 years (mmHg)	< 130/80	< 140/80*
≥ 80 years (mmHg)	< 130/80	140-150/<80
Pharmacotherapy	Initial therapy with beta-blockers reserved for specific conditions including ischemic heart disease or heart failure	Beta blockers included as first-line therapy for hypertension.

** Target < 130/80 if tolerated*

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Renal Denervation

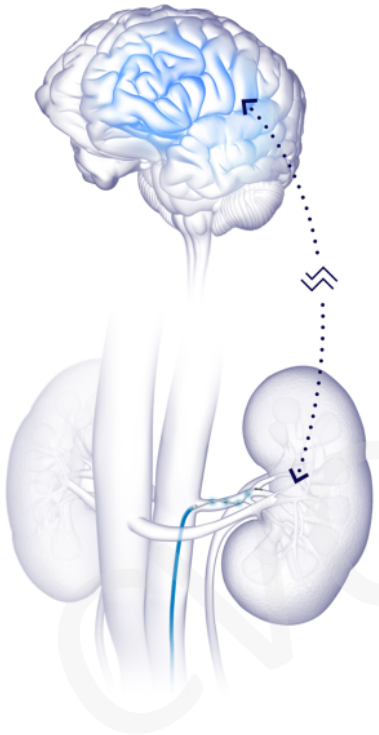
Renal denervation is a complementary option to lifestyle changes and pharmacological therapy[1]

Recommended by cardiovascular experts

The **2023 SCAI position statement** recognizes renal denervation as a promising therapy for treating hypertension. Read the full statement to review recommendations for success, including patient selection, operator competency, procedural training and techniques, and organizational recommendations.

- [1] Symplicity Spryal™ IFU

Complementary approach to treat hypertension[1, 2, 3]



The kidneys modulate the sympathetic tone via the renal nerves to control blood pressure.

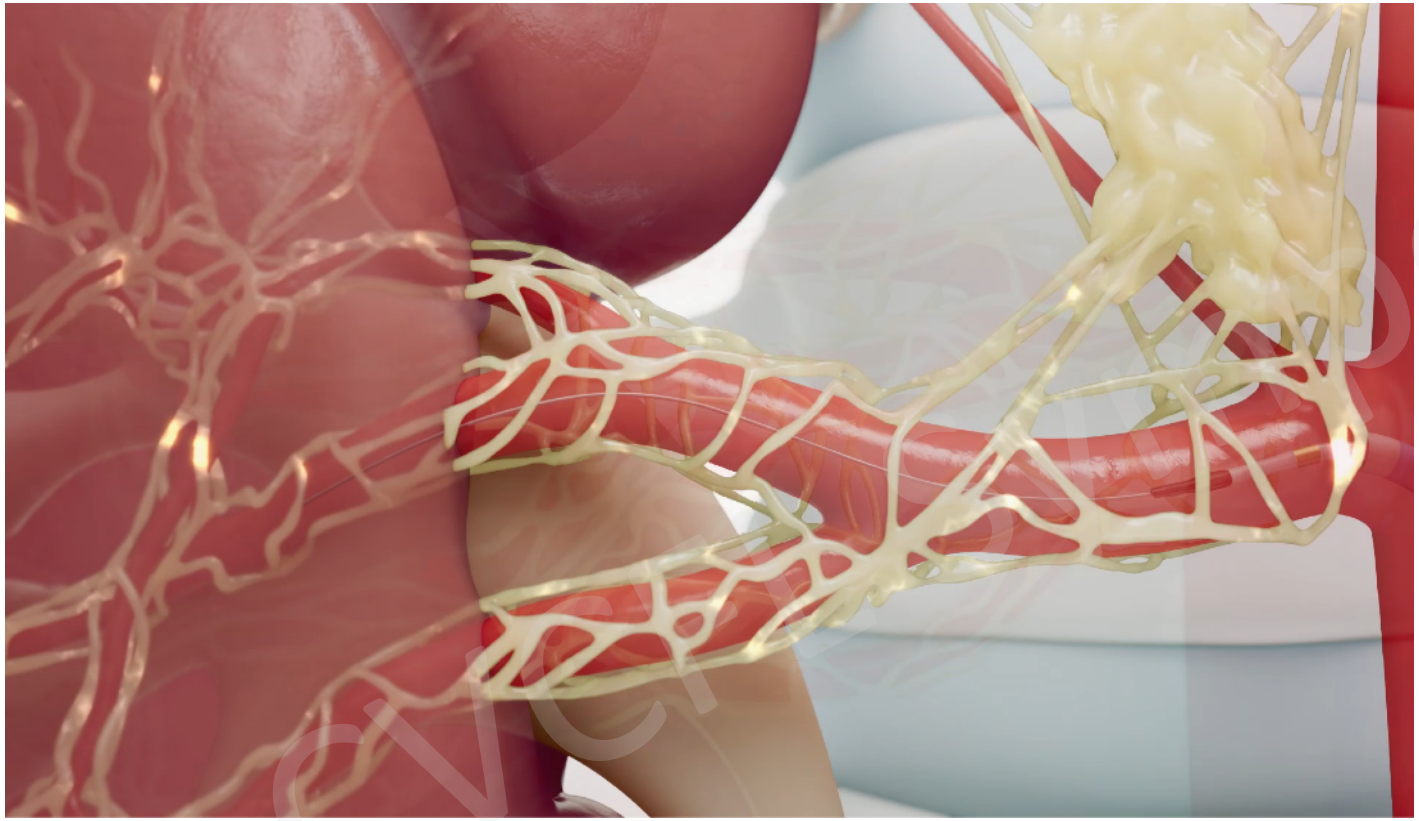
Renal denervation disrupts the overactive sympathetic signaling between kidneys and brain to reduce blood pressure.[4]

RDN systems:

- Supplies precisely controlled and targeted radiofrequency energy to the renal nerves[4]
- Doesn't leave a permanent implant behind
- Is independent of patient adherence[3]

- 1 Symplicity Spyral™ IFU
2 Kandzari D, et al. J Am Coll Cardiol. 2023 Nov 7;82(19):1809-1823
3 Böhm M, et al. Lancet. 2020;395:1444–1451.
4 Coates P, et al. Cardiovasc Revasc Med. 2022;42:171–177.

Nerve bundles around the renal vasculature – target for renal denervation



- One catheter size treats vessels 3–8 mm[1]
- Multi-electrode, helical design covers four quadrants simultaneously for a circumferential ablation[1,2]
- Unique, real-time, and responsive algorithm automatically adjusts power by monitoring temperature and impedance for safe energy distribution[2]

[1] Medtronic Symplicity Spyral Multi-Electrode Renal Denervation Catheter Instructions for Use.
[2] Coates P, et al. *Cardiovasc Revasc Med.* 2022;42:171–177.

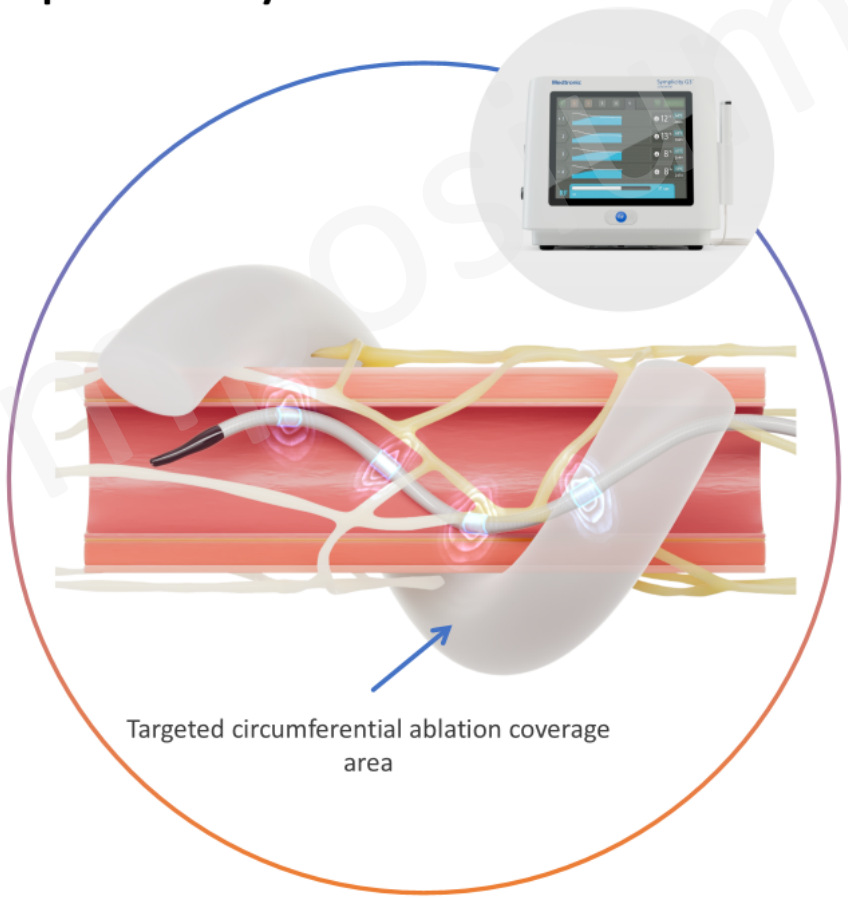
Safe and precise radiofrequency (RF) energy delivery

Responsive algorithm for safe energy distribution

- Automatically adjusts power in real time by monitoring temperature and impedance for safe energy distribution[1]
- Preferentially heats fat tissue where renal nerves are located and avoids nontarget structures[2]

Versatile catheter for a precise ablation

- Multi-electrode, helical design covers four quadrants simultaneously for a circumferential ablation[1,3]
- Allows for denervation with one catheter throughout various vessel sizes in the renal anatomy, including the distal branches[2] where late-arriving nerves are accessible and total nerve density is highest[4,5]



[1] Coates P, et al. *Cardiovasc Revasc Med*. 2022;42:171–177.
[2] Sato Y, et al. *EuroIntervention*. 2023;18:e1120–e1128.
[3] Medtronic Symplicity Spyral multi-electrode renal denervation catheter instructions for use.
[4] García-Touchard A, et al. *Hypertension*. 2020;76:1240–1246.
[5] Struthoff H, et al. *EuroIntervention*. 2023;19:612–620.

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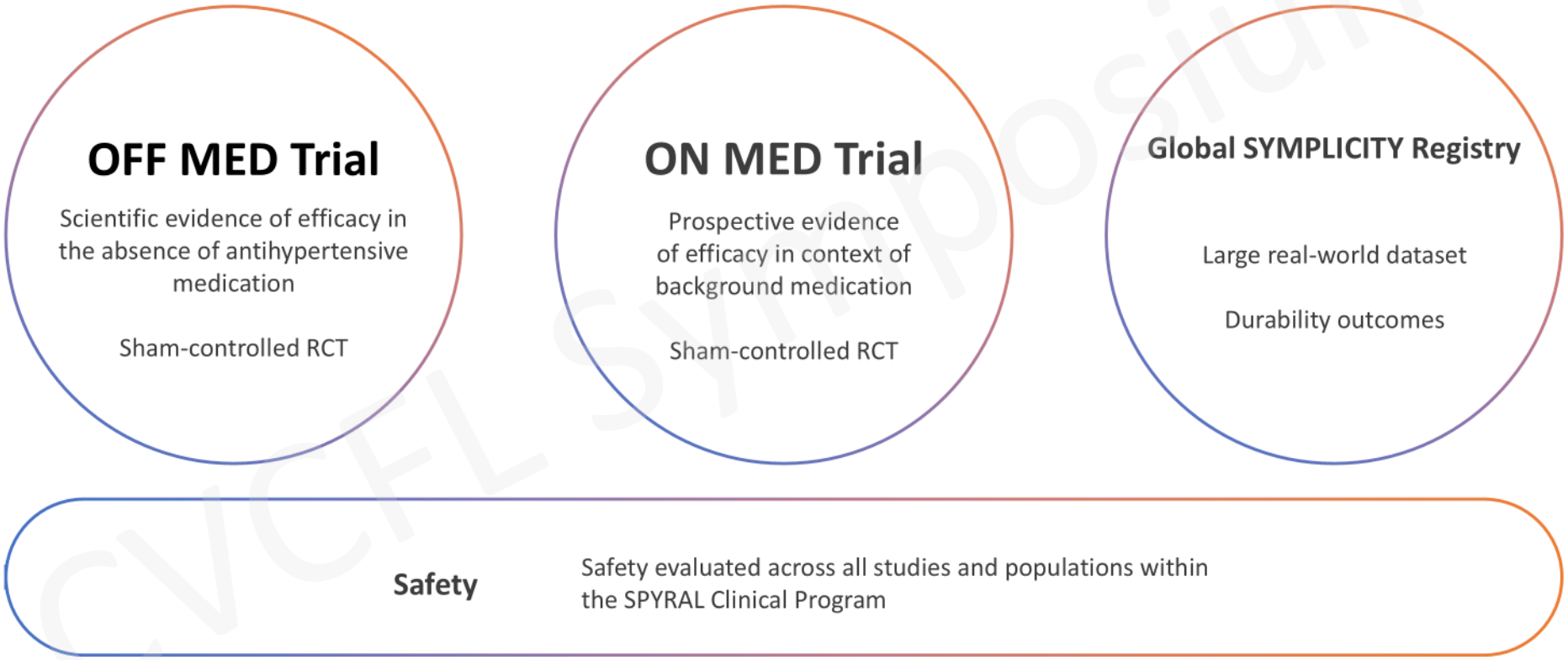
Significant Safe and Sustained Blood Pressure Reductions

SPYRAL Clinical Program



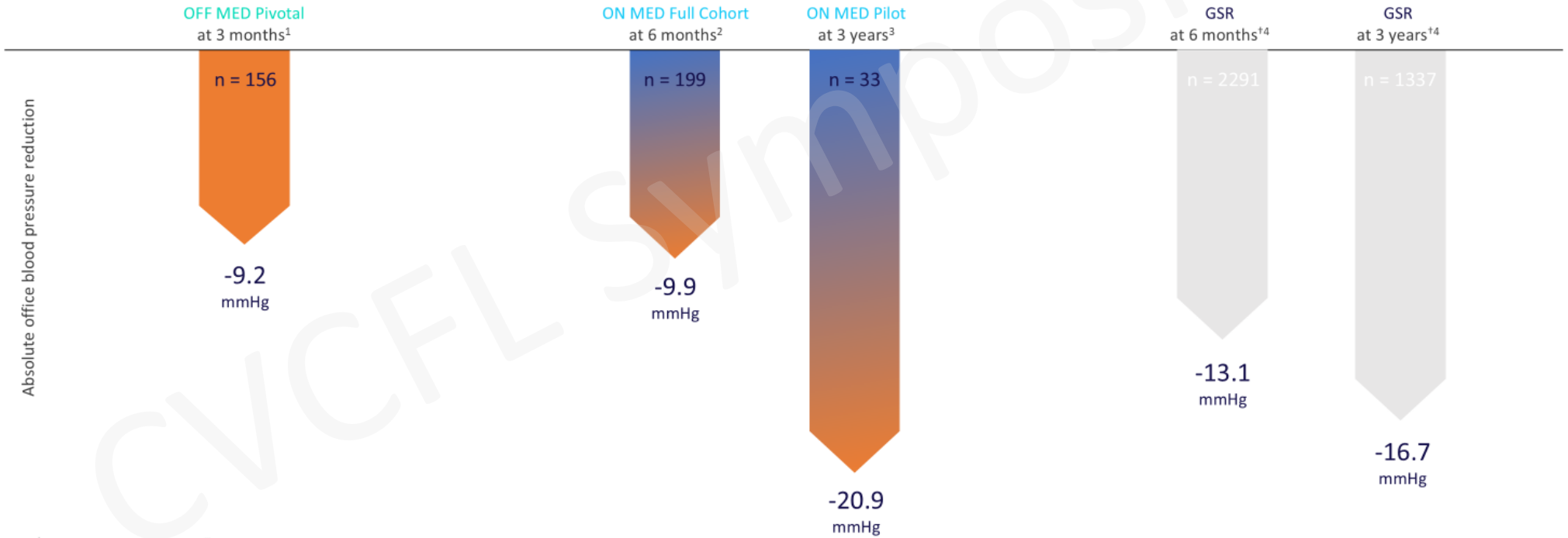
Results may vary

Proven to deliver significant, safe, and sustained blood pressure reductions

OFF MED
Scientific evidence of efficacy without meds

ON MED
Prospective evidence in the presence of meds

GSR†
Large dataset of multiple subgroups in real-world setting



- †Includes the Symplicity Spyral™ and Flex catheters.
- [1] Böhm M, et al. *Lancet*. 2020;395:1444–1451.
  [2] Kandzari D, et al. J Am Coll Cardiol. 2023 Nov 7;82(19):1809-1823
- [3] Mahfoud F, et al. *Lancet*. 2022;399:1401-1410.
- [4] Mahfoud F, et al. Outcomes following radiofrequency renal denervation according to antihypertensive medications: subgroup analysis of the Global SYMPLICITY Registry DEFINE. EuroPCR 2023.

Significant Blood Pressure Reduction

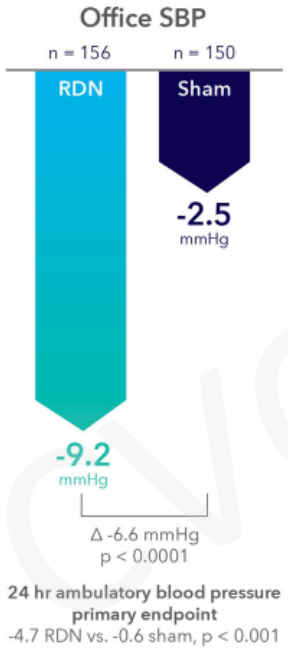
SPYRAL HTN-OFF MED[1]

Pivotal Trial
Significant blood pressure reduction in the **absence of medication** at 3 months

SPYRAL HTN-ON MED[2]

Significant blood pressure reductions with **20% lower medication burden at 6 months** with RDN (2.9 RDN vs. 3.5 sham, p = 0.04)

Average baseline office systolic blood pressure (SBP) for both RDN and Sham arms in both trials = 163 mmHg



24 hr ambulatory blood pressure primary endpoint
-4.7 RDN vs. -0.6 sham, p < 0.001

24 hr ambulatory blood pressure primary endpoint
-6.5 RDN vs. -4.5 sham, p = 0.12

> 9 mmHg
mean reduction in office SBP in patients off and on medications†1,2

Proven to deliver > 9 mmHg office systolic blood pressure (SBP) reduction in patients off and on medications

†Results for each patient may vary.
[1] Böhm M, et al. *Lancet*. 2020;395:1444–1451.
[2] Kandzari D, et al. *J Am Coll Cardiol*. 2023;82:1809–1823.

Safe

Excellent safety profile

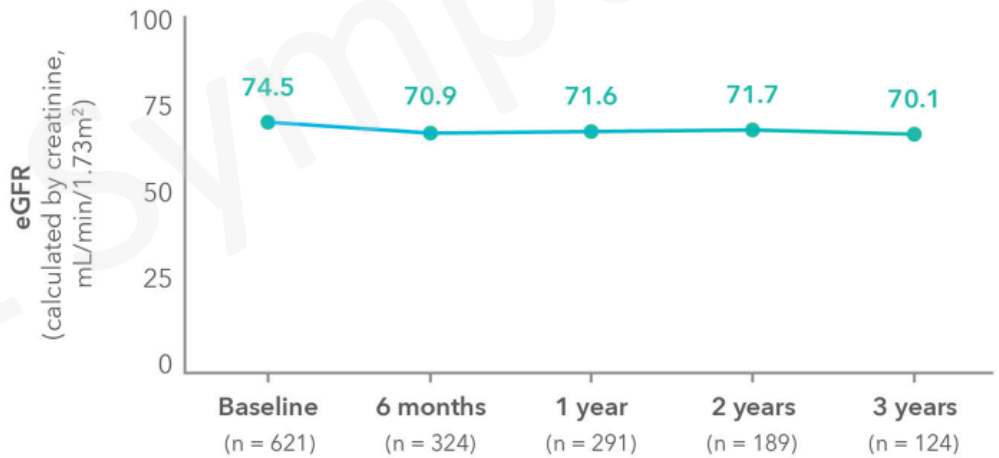
Pooled data from the **SPYRAL HTN-OFF MED** and **SPYRAL HTN-ON MED** trials indicated low incidence of procedural related and clinical adverse events.[1]

0.4 %

major adverse event rate at composite endpoint, including no new incidence of renal artery stenosis (>70%) at 1 month.[1] (N=253)

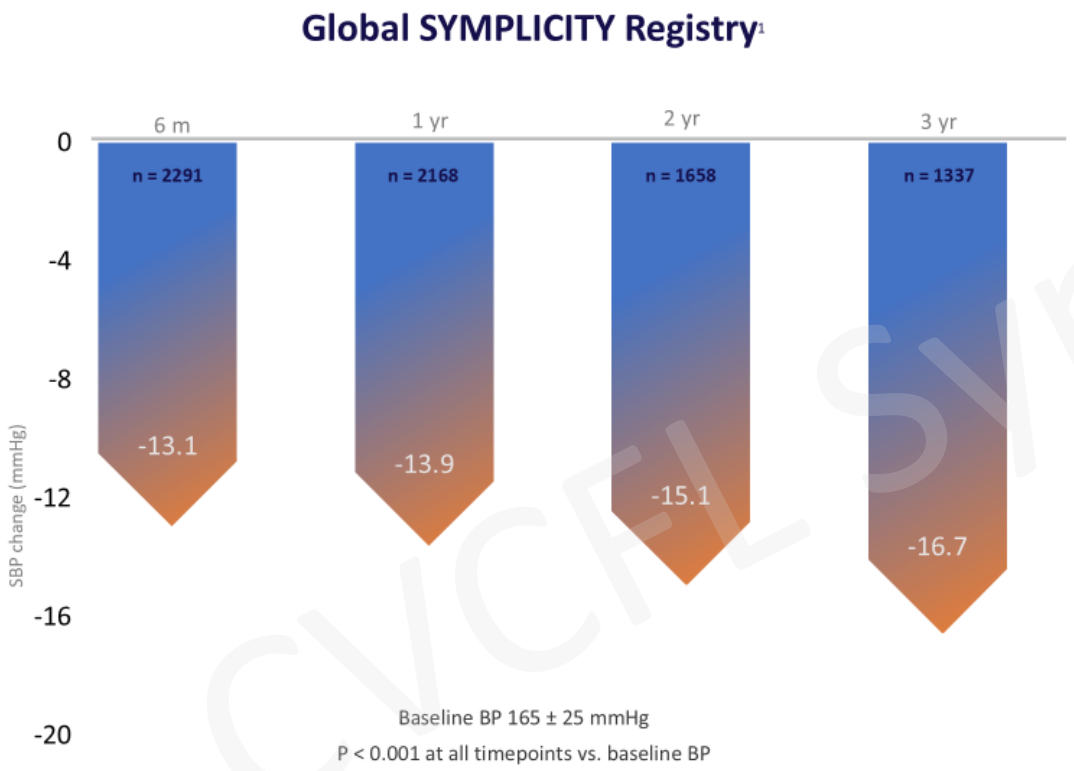
Stable kidney function in real-world patients

The Global SYMPLICITY Registry study showed stable kidney function at three-year follow-up.[2]



[1] Kandzari DE, et al. *J Am Coll Cardiol*. 2023;82:1809–1823.
[2] Schlaich M, et al. Long-term safety and efficacy of renal denervation with the Symplicity Spyral catheter in the Global SYMPLICITY Registry. Presented at American Society of Nephrology Kidney Week, San Diego, CA. November 4–7, 2021.

Sustained Results



- [1] Mahfoud F, et al. Outcomes following radiofrequency renal denervation according to antihyptensive medications: subgroup analysis of the Global SYMPLICITY Registry DEFINE. EuroPCR 2023.
  [2] Medtronic data on file. Global SYMPLICITY Registry clinical data snap, March 2023.

RDN demonstrates an “always on” effect on 24-hour blood pressure reductions

- Baseline (N = 164)
- 3 Months (N=143)
- Difference

The nighttime/early morning period is a “high-risk zone” associated with increased risk for stroke and cardiovascular events[2,3]

- [1] Böhm M, et al. *Lancet*. 2020;395:1444–1451.
- [2] Amodeo C, et al. *Blood Press Monit*. 2014;19:199–202.
- [3] Boggia J, et al. *Lancet*. 2007;370:1219–1229.

Key takeaways

Significant

- Significant BP reductions versus sham in uncontrolled hypertensive patients:
  - In the absence of medications at three months[1]
  - In the presence of medications out to three years[†2]

Safe

Pooled data from the SPYRAL HTN-OFF MED and SPYRAL HTN-ON MED trials indicated low incidence of procedural related and clinical adverse events.[3]

Sustained

RDN has demonstrated sustained blood pressure reductions through three years in real-world patients.[4]

[†]Three-year follow-up of pilot cohort not prospectively powered.
[1] Böhm M, et al. *Lancet*. 2020;395:1444–1451.
[2] Mahfoud et al. *Lancet*. 2022; 399(10333):1401–1410.

[3] Kandzari D, et al. *J Am Coll Cardiol*. 2023;82:1809–1823.
[4] Mahfoud F, et al. Outcomes following radiofrequency renal denervation according to antihyptensive medications: subgroup analysis of the Global SYMPLICITY Registry DEFINE. EuroPCR 2023.

Patient Considerations

Patient selection

Have uncontrolled hypertension

Consider patients where lifestyle modifications and antihypertensive medications haven't adequately controlled blood pressure.

Are willing to undergo an interventional procedure

Consider patients who opt for a renal denervation procedure following shared decision-making and an attempt at lifestyle modifications and medical therapy.

3x

as many patients vs. sham were able to get their **blood pressure under control (< 140 mmHg) at 6 months**[1]

(20% RDN vs. 6% sham, p = 0.001)

30%

of patients

would be willing to consider an interventional approach to manage hypertension versus an additional medication[2]

- 1 Kandzari D, Townsend R, Kario K, et al. Safety and Efficacy of Renal Denervation in Patients Taking Antihypertensive Medications. J Am Coll Cardiol. November 7, 2023;82(19):1809–1823.
- 2 Kandzari DE, Weber MA, Poulos C, et al. Patient Preferences for Pharmaceutical and Device-Based Treatments for Uncontrolled Hypertension: Discrete Choice Experiment. Circ Cardiovasc Qual
- Outcomes. January 2023;16(1):e008997.

Expectations after renal denervation

Patients on one or more antihypertensive medications who underwent the renal denervation procedure as a complementary treatment in SPYRAL HTN-ON MED (N = 199) experienced the following reductions in office systolic blood pressure at six months[1,2] :

61%	51%	37%	24%
of patients	of patients	of patients	of patients
> 5 mmHg	> 10 mmHg	> 15 mmHg	> 20 mmHg

[1] Kandzari DE, et al. *J Am Coll Cardiol*. 2023;82:1809-1823.
[2] Premarket Approval Application (PMA) for Medtronic, Inc.'s Symplicity Spyral Radiofrequency Renal Denervation System. FDA. Available at: https://www.fda.gov/media/171690/download. Accessed December 19, 2023.

Renal Denervation Cases

46-year-old male

Relevant hypertension medical history

- Long standing, malignant hypertension
- Renal insufficiency
  - Cr 1.45
  - Normal renal doppler
- Prior lacunar infarct related to hypertensive urgency

Vital Signs

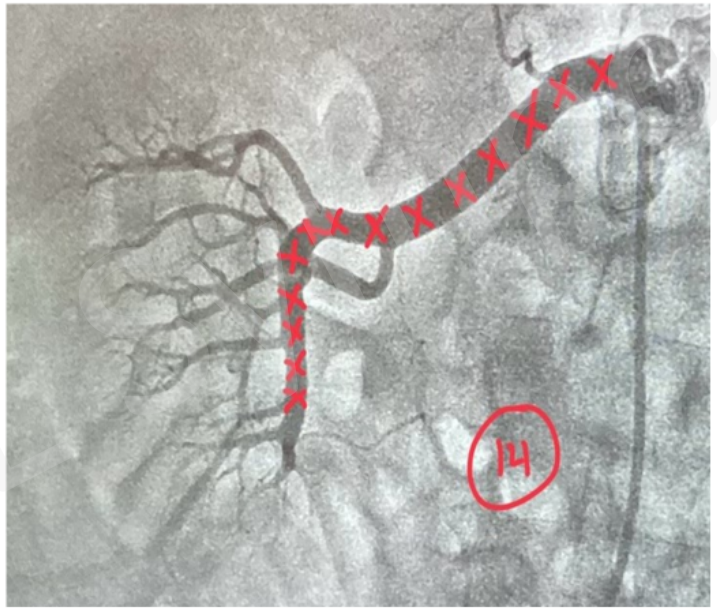
- Office BP 184/98
- HR 54

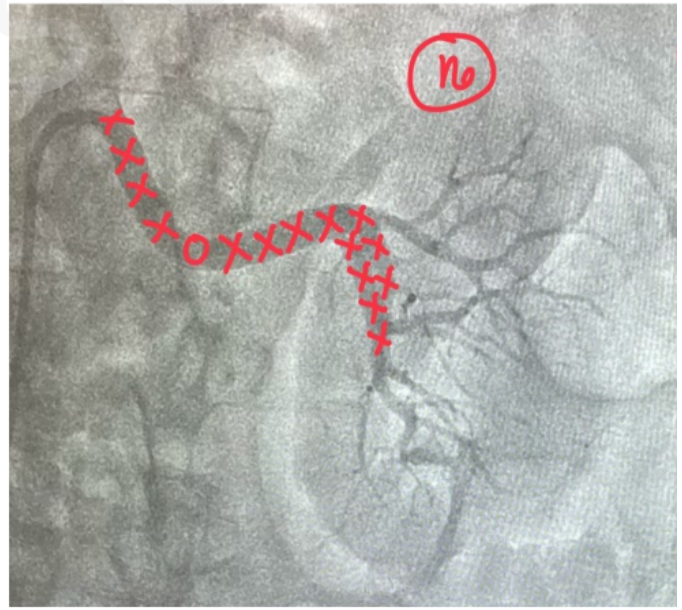
Medications

- Carvedilol 25mg BID
- Olmesartan 40mg daily
- Aldactone 25mg daily
- Hydralazine 100mg TID
- Amlodipine 10mg daily
- Clonidine 0.3mg TID
- Minoxidil 5mg BID

Case Study 1 – Procedure

- Procedure details
- Guide cath: 6Fr IM
- Time: 46 minutes
- Contrast: 30cc
- ACT: 320
- Ablations: 14 right and 11 left





- Labs
  - Cr 1.45 pre-procedure
  - Cr 1.31 two days post-procedure

Case study 1- follow-up

Visit	OBP	HR	eGFR	Was medication changed
3 month	134/82	58	Unchanged	Clonidine and minoxidil discontinued over first three months
6 month	136/83	60	Unchanged	Hydralazine discontinued and amlodipine reduced to 5mg daily in month 4 and 5 respectively

Reduction from 7 meds with persistent hypertension to 4 meds with good BP control

53-year-old female

Relevant hypertension medical history

- Long standing, malignant hypertension
- Coronary artery disease, s/p PCI 2021
- Hyperlipidemia
- Chron's disease
- Normal renal artery on CTA

Vital Signs

- Office BP 177/101
- HR 74

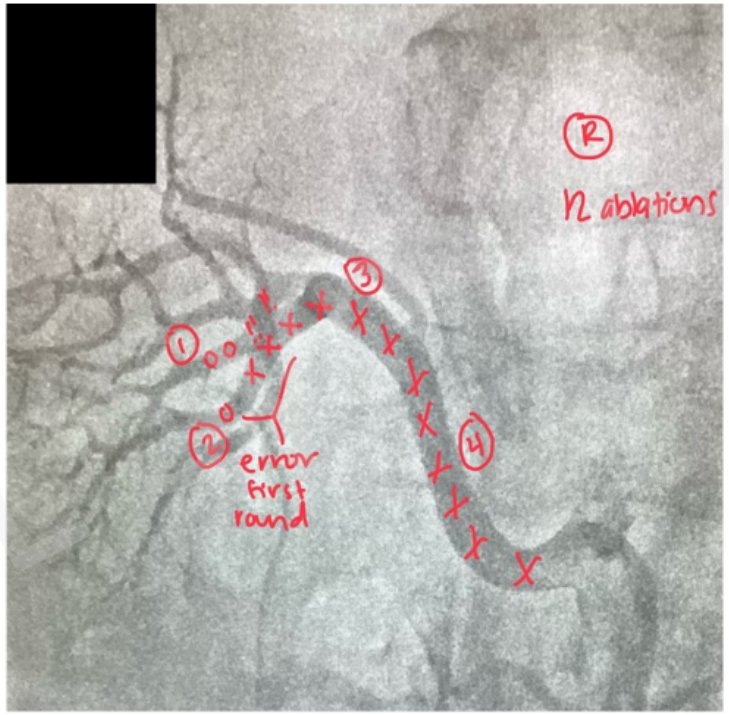
Medications

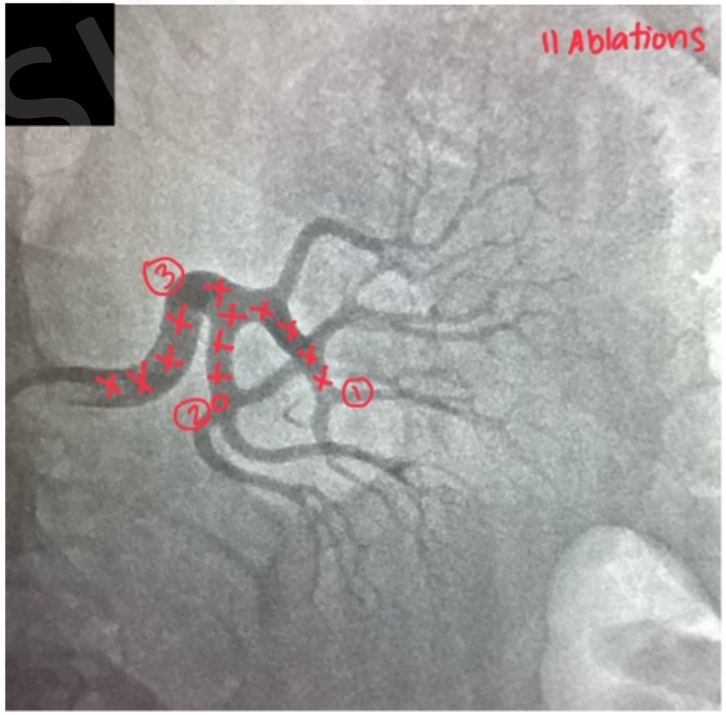
- Carvedilol 25mg BID
- Lisinopril 40mg daily
- Hydralazine 50 TID

- Intolerance to calcium channel blockers, alpha blocker, and minoxidil.
- Refusal to take diuretics.
- Dizziness with higher doses of hydralazine despite normal BP.

Case Study 2 – Procedure

- Procedure details
- Guide cath: 6Fr IM
- Time: 42 minutes
- Contrast: 35cc
- ACT: 360
- Ablations: 12 right and 16 left



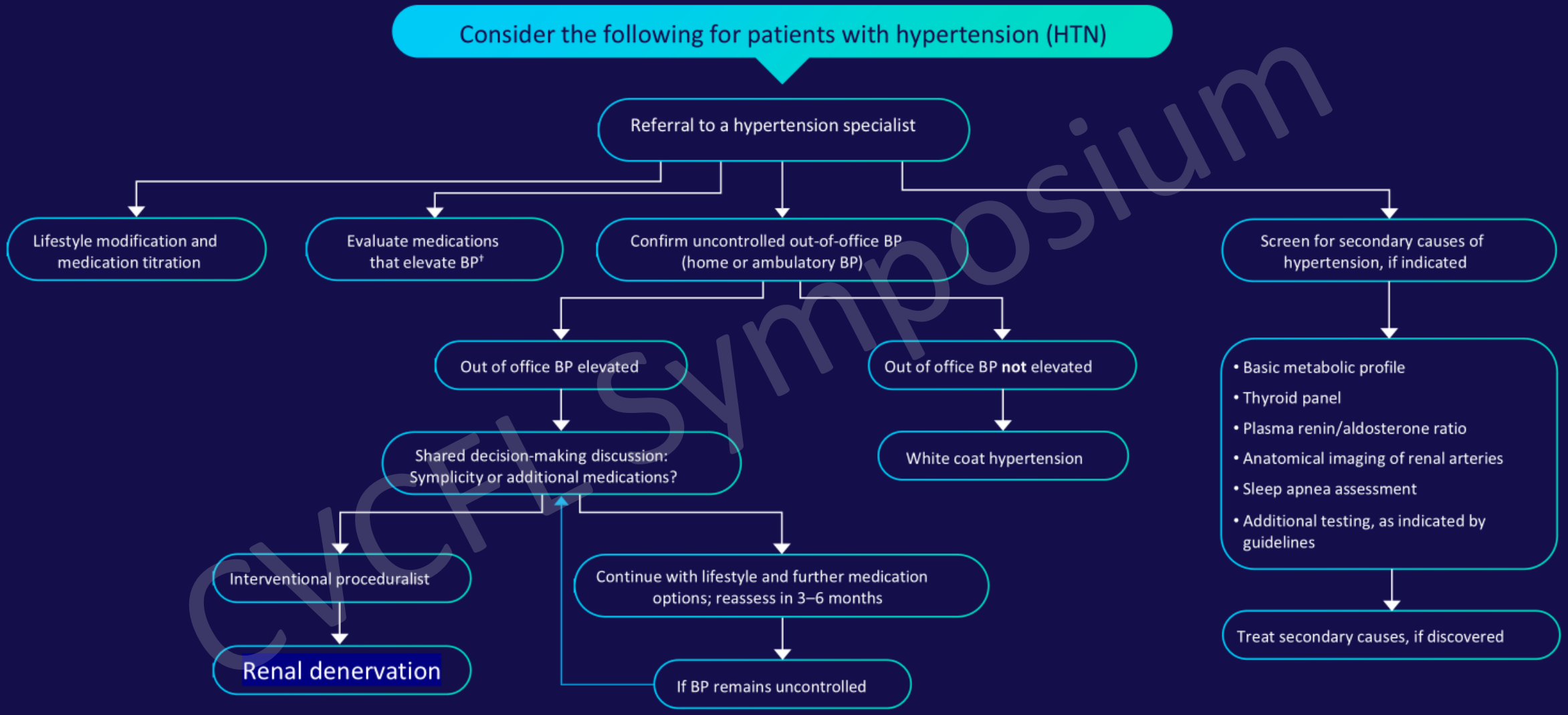


Case study 2- follow-up

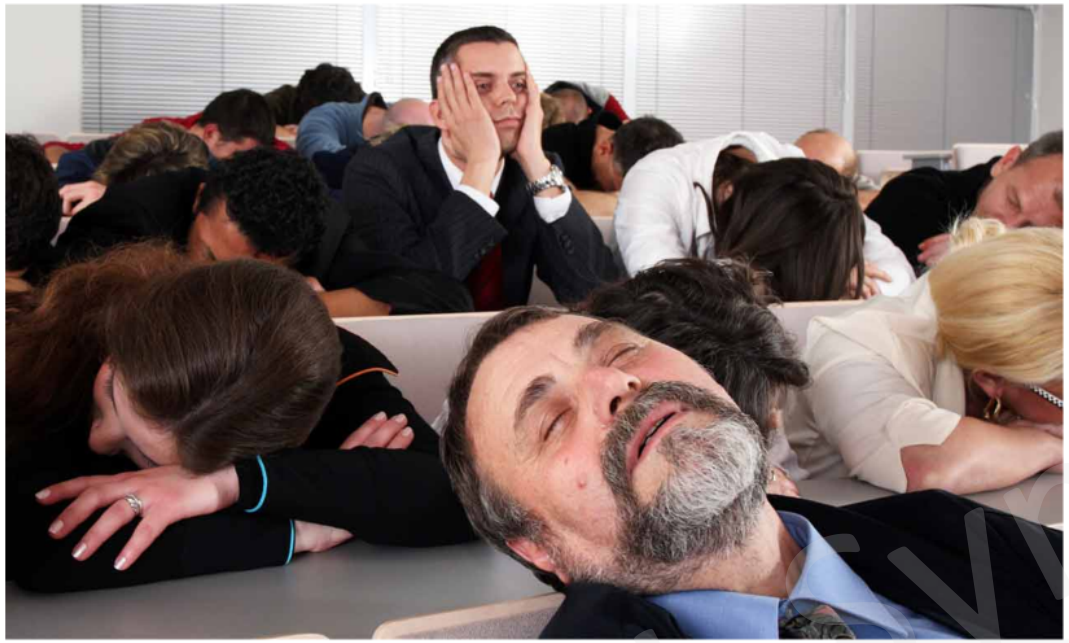
Visit	OBP	HR	eGFR	Was medication changed
3 month	142/78	68	Unchanged	Hydralazine reduced to 25mg TID
6 month	128/67	62	Unchanged	Hydralazine discontinued and coreg reduced to 12.5mg BID

Reduction from 3 meds with persistent hypertension to 2 meds with good BP control

Patient screening flowchart for the Renal Denervation procedure[1–3]



Physician discretion should be used to make a final decision on the screening process and intervention. Refer back to AHA/ACC guidelines for additional information.



Thank you for Listening!