Selection of Patients with Resistant Hypertension for Renal Denervation Procedures

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Patient Selection for Renal Denervation Procedure

Clinical criteria

Anatomical Suitability

Other considerations

Patient selection for Renal Denervation: clinical consideration

Patient Selection for Renal Denervation Procedure

Clinical inclusion / exclusion

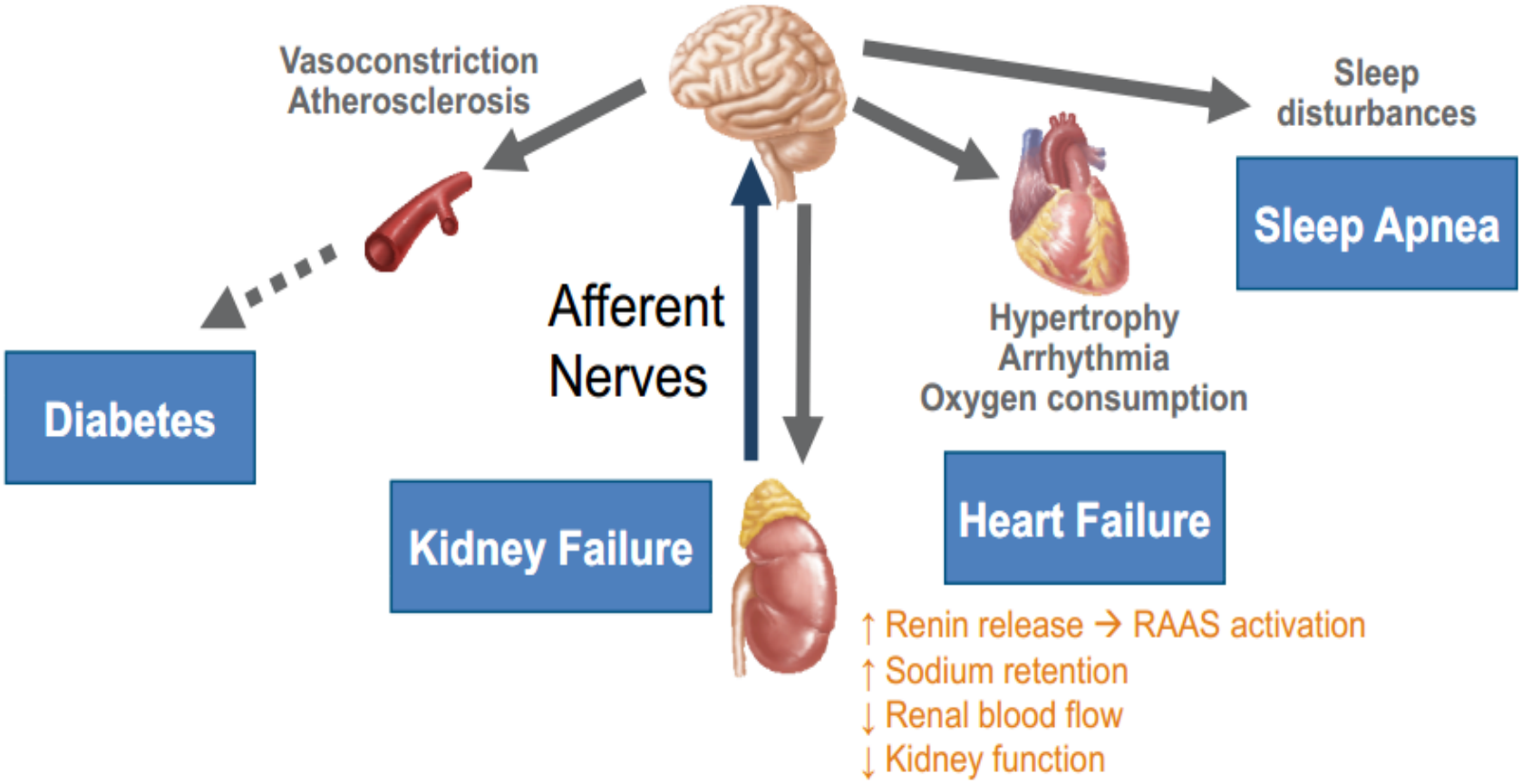
Established indication(s)

1. **Resistant hypertension with normal renal function**

Investigational indications

1. **Resistant hypertension with abnormal renal function**
2. **OSA**
3. **DM; impaired glucose tolerance**
4. **Heart failure**
5. **Kidney failure +/- hypertension**

- Chronic activation of renal nerves is common in multiple conditions/disease states[1,2]
- Future research may be warranted in disease states characterized by hyperactive afferent and efferent renal nerves



Resistant Hypertension Patient Selection for Renal Denervation Procedure

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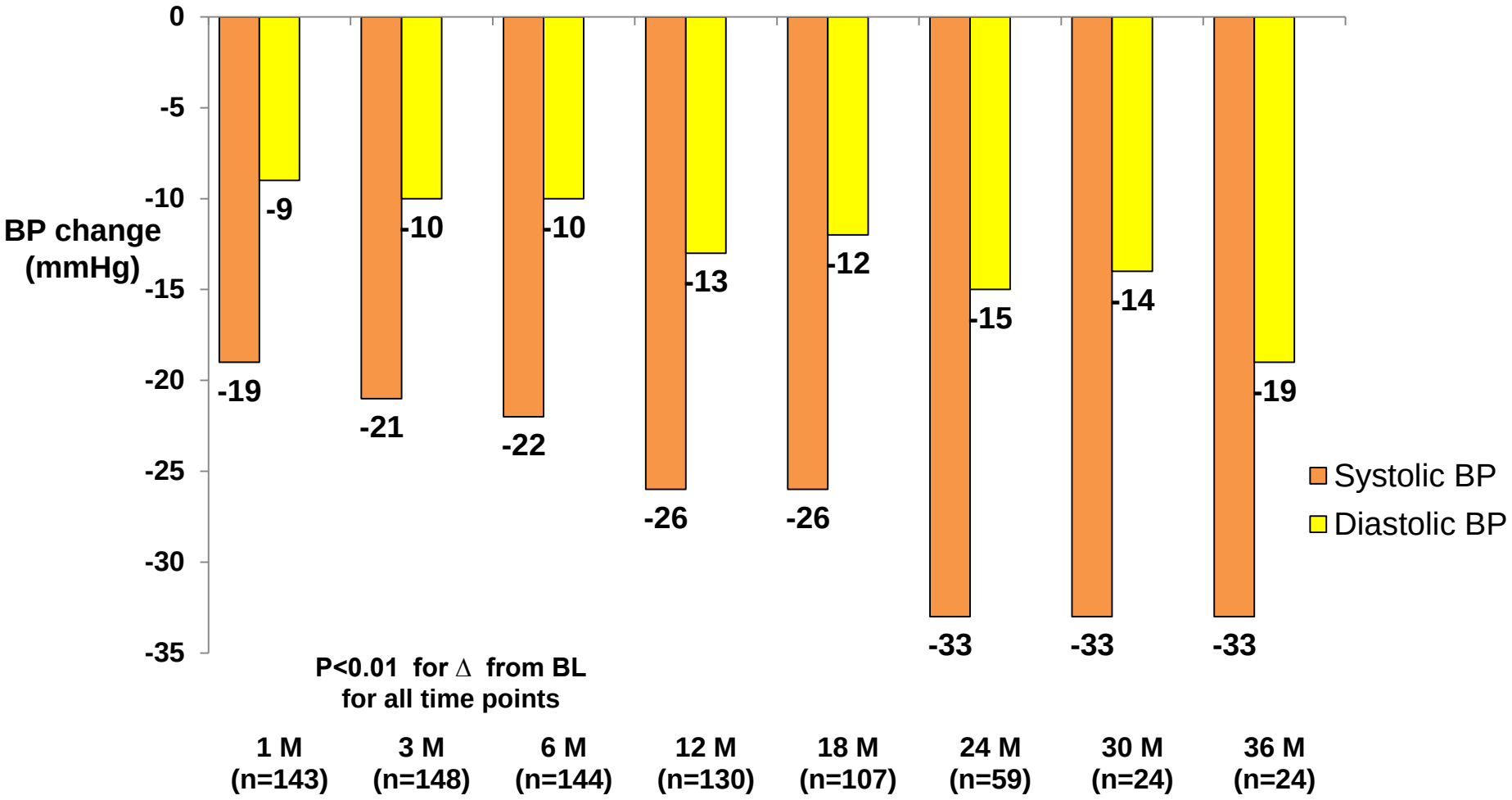
Symplicity HTN-1:
BP Reductions through 3 years



*Expanded results presented at the *American College of Cardiology Annual Meeting 2012* (Krum, H.)

Symplicity HTN-1


THE LANCET

Volume 373 · Number 9671 · Pages 1223-1310 · April 11-17, 2009 www.thelancet.com

Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study

Henry Krum, Markus Schlaich, Rob Whitbourn, Paul A Sobotka, Jerzy Sadowski, Krzysztof Bartus, Bogusław Kapelak, Anthony Walton, Horst Sievert, Suku Thambar, William T Abraham, Murray Esler

Lancet. 2009;373:1275-1281


Hypertension

Celebrating 30 Years: 1979 to 2009

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension

Durability of Blood Pressure Reduction Out to 24 Months

Symplicity HTN-1 Investigators*

Hypertension. 2011;57:911-917.

Initial Cohort – Reported in the *Lancet*, 2009:

-First-in-man, non-randomized

-Cohort of 45 patients with **resistant HTN (SBP ≥160 mmHg on ≥3 anti-HTN drugs, including a diuretic; eGFR ≥ 45 mL/min)**

- 12-month data

\

Expanded Cohort* – This Report (Symplicity HTN-1):

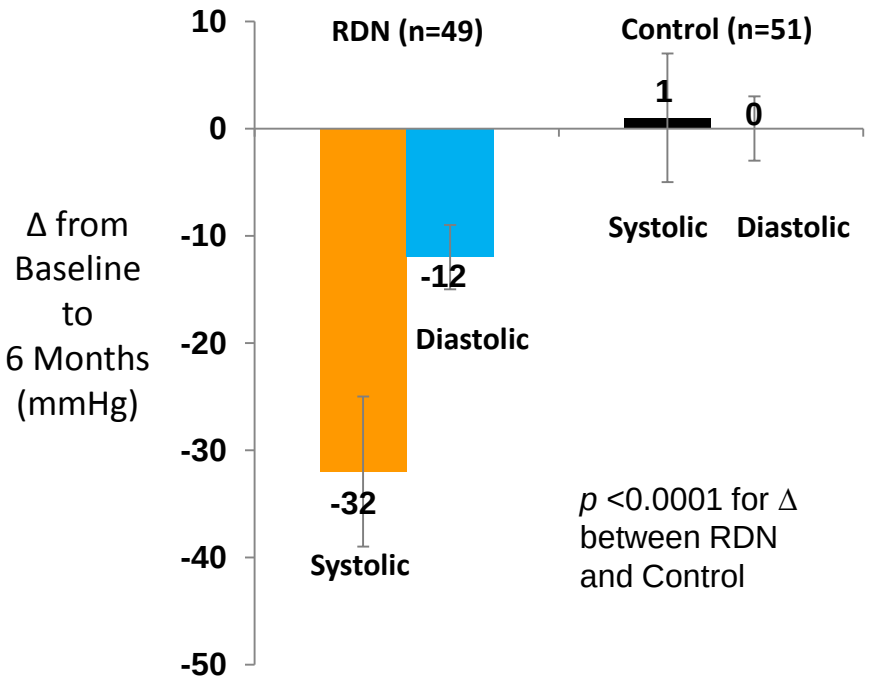
-Expanded cohort of patients (n=153)

-36-month follow-up

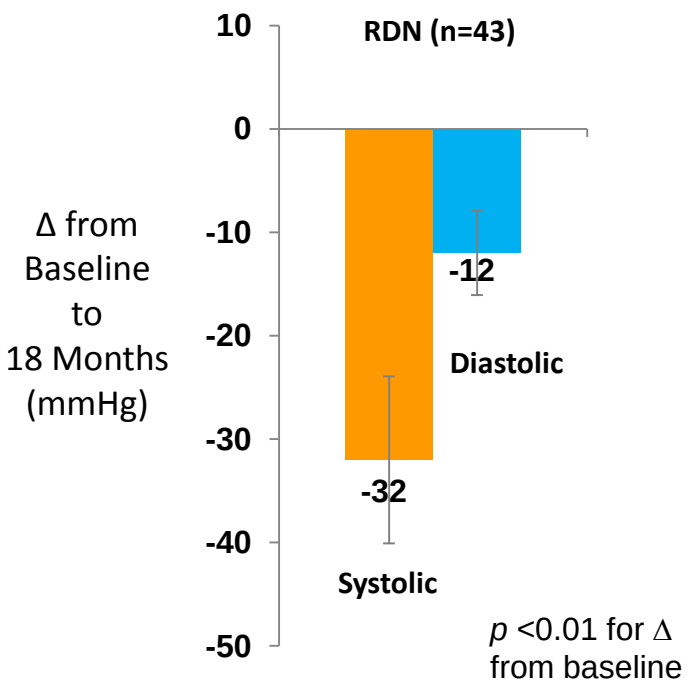
*Expanded results presented at the *American College of Cardiology Annual Meeting* 2012 (Krum, H.)

Symplicity HTN-2: RDN Superior to Medical Management, Reductions Sustained to 18M

Primary Endpoint (6M post Randomisation)



Latest Follow-up (18M post Randomisation)



Primary Endpoint:

- >80% of RDN patients had ≥10 mmHg reduction in SBP
- 5 patients had ≤ 5mmHG reduction in SBP

Symplicity HTN-2 Trial

- Treatment-resistant HTN population
- BL OBP 178/97 mmHg
- 49 RDN, 51 Control
- Age 58 years
- BMI 31 kg/m^2
- 40% with Diabetes
- eGFR 77*
- Avg # meds 5.2
- RDN and Control groups generally well-matched

Inclusion Criteria:

- **Office SBP ≥ 160 mmHg (≥ 150 mmHg with type II diabetes mellitus)**
- **Stable drug regimen of 3+ more anti-HTN medications**
- Age 18-85 years

Exclusion Criteria:

- Hemodynamically or anatomically **significant renal artery abnormalities or prior renal artery intervention**
- **eGFR < 45 mL/min/1.73m^2** (MDRD formula)
- Type 1 diabetes mellitus
- Contraindication to MRI
- Stenotic valvular heart disease for which reduction of BP would be hazardous
- MI, unstable angina, or CVA in the prior 6 months

*MDRD, ml/min/1.73m^2

Symplicity HTN-2 Investigators. *Lancet*. 2010;376:1903-1909.

Resistant Hypertension – Diagnosis and Treatment

1

Confirm Treatment Resistance

Office blood pressure >140/90 or 130/80 mm Hg in patients with diabetes or chronic kidney disease

and

Patient prescribed 3 or more antihypertensive medications at optimal doses, including if possible a diuretic

or

Office blood pressure at goal but patient requiring 4 or more antihypertensive medications

2

Exclude Pseudoresistance

Is patient adherent with prescribed regimen?

Obtain home, work, or ambulatory blood pressure readings to exclude white coat effect

Calhoun DA et al. Hypertension 2008: 51: 1403-1419

Resistant Hypertension – Diagnosis and Treatment

3

Identify and Reverse Contributing Lifestyle Factors

Obesity
Physical inactivity
Excessive alcohol ingestion
High salt, low fiber diet

4

Discontinue or Minimize Interfering Substances

Non-steroidal anti-inflammatory agents
Sympathomimetics (diet pills, decongestants)
Stimulants
Oral contraceptives
Licorice
Ephedra

Calhoun DA et al. Hypertension 2008: 51: 1403-1419

Resistant Hypertension – Diagnosis and Treatment

5

Screen for Secondary Causes of Hypertension

Obstructive sleep apnea (snoring, witnessed apnea, excessive daytime sleepiness)

Primary aldosteronism (elevated aldosterone/renin ratio)

Chronic kidney disease (creatinine clearance <30 ml/min)

Renal artery stenosis (young female, known atherosclerotic disease, worsening renal function)

Pheochromocytoma (episodic hypertension, palpitations, diaphoresis, head ache)

Cushing's syndrome (moon facies, central obesity, abdominal striae, inter-scapular fat deposition)

Aortic coarctation (differential in brachial or femoral pulses, systolic bruit)

Calhoun DA et al. Hypertension 2008: 51: 1403-1419

Resistant Hypertension – Diagnosis and Treatment

6

Pharmacologic Treatment

Maximize diuretic therapy, including possible addition of mineralocorticoid receptor antagonist

Combine agents with different mechanisms of action

Use of loop diuretics in patients with chronic kidney disease and/or patients receiving potent vasodilators (e.g., minoxidil)

Consider Renal Denervation Therapy

7

Refer to Specialist

Refer to appropriate specialist for known or suspected secondary cause(s) of hypertension

Refer to hypertension specialist if blood pressure remains uncontrolled after 6 months of treatment

Calhoun DA et al. Hypertension 2008: 51: 1403-1419

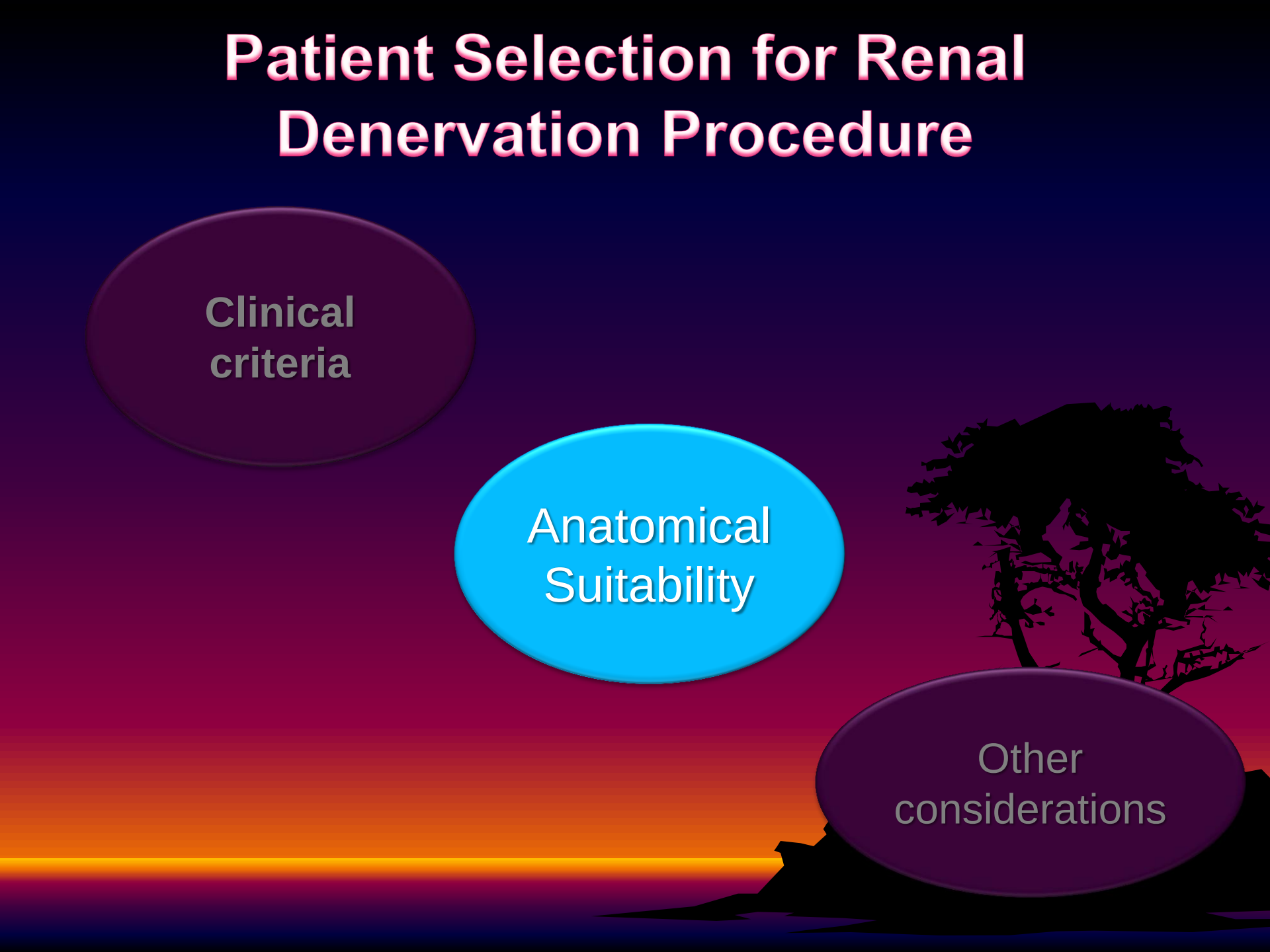
Patient selection for Renal Denervation: anatomical consideration

Patient Selection for Renal Denervation Procedure

Clinical criteria

Anatomical Suitability

Other considerations



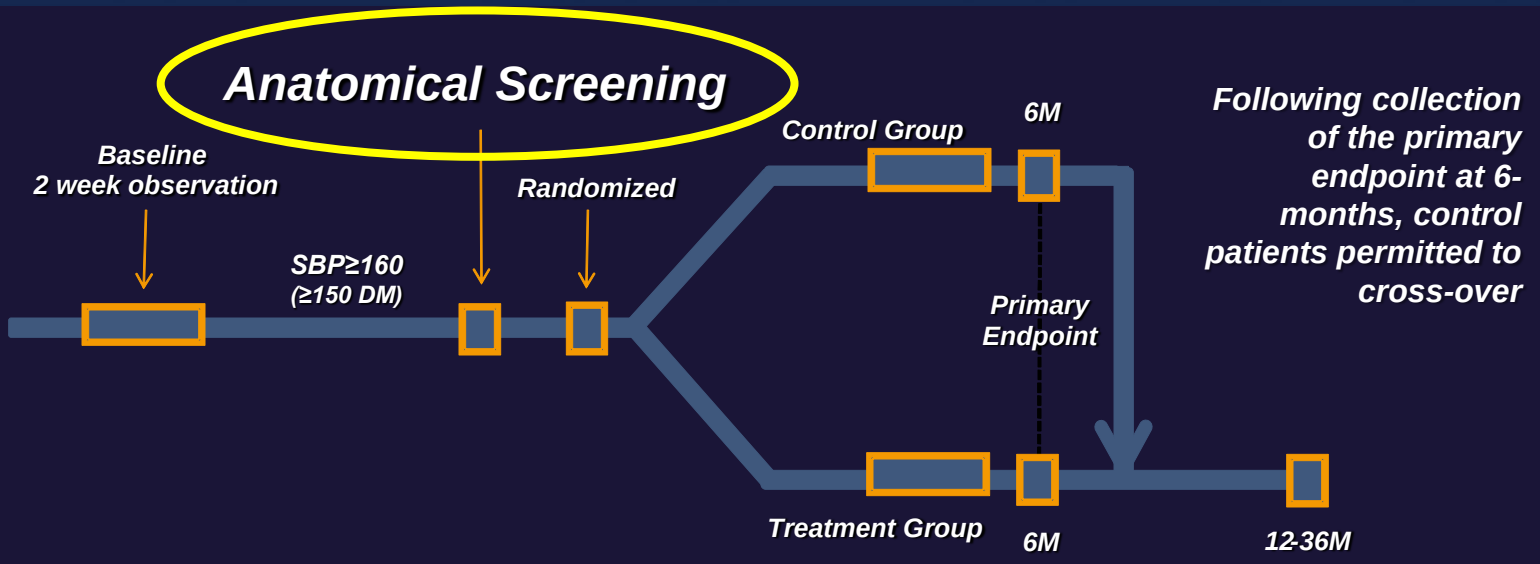
Symplicity HTN-2: Study Design

Primary Endpoint:

- Change in Office SBP from baseline to 6 months without changes in medications

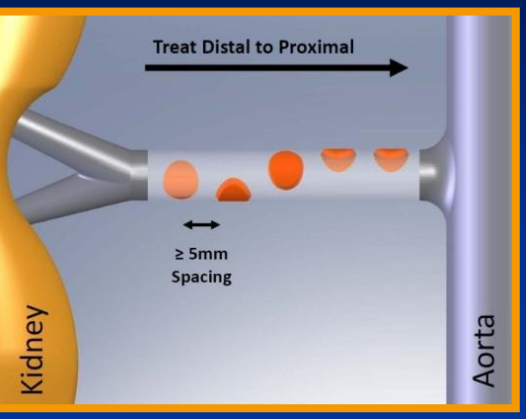
Secondary Endpoints:

- Safety: Procedural and 6-month (renovascular & kidney function)
- Composite CV endpoint
- Other measures of BP reduction (e.g. ABPM, % at target, % with 10mmHg response)
- LV function (cardiac MRI to assess LV mass)



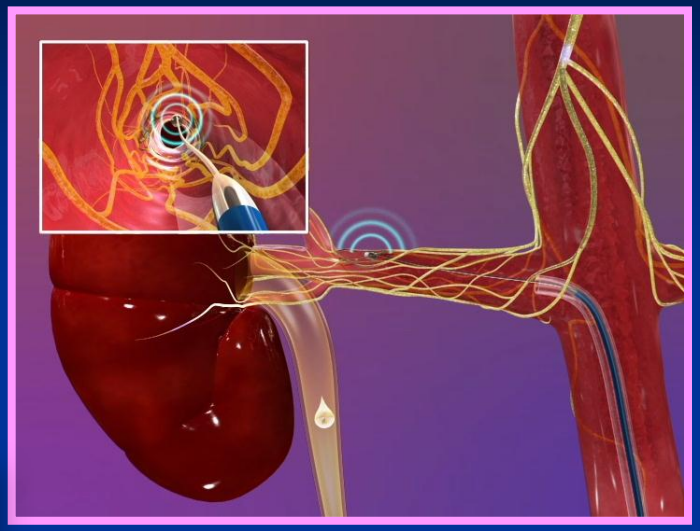
Symplicity HTN-2 Investigators. *Lancet.* 2010;376:1903-1909

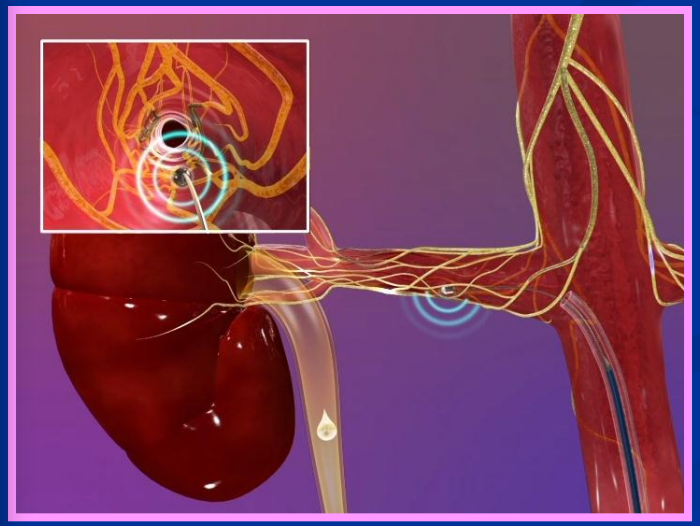
Treatment by Renal RF Catheter



Radiofrequency ablations

- 4-6 focal 2-minute ablations (5-8W bursts) along each renal artery.
- Temperature limited.
- Rotationally and longitudinally dispersed.

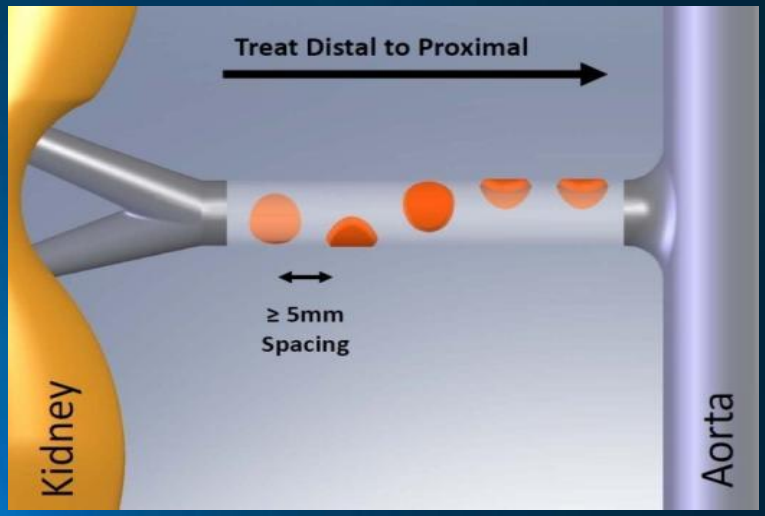




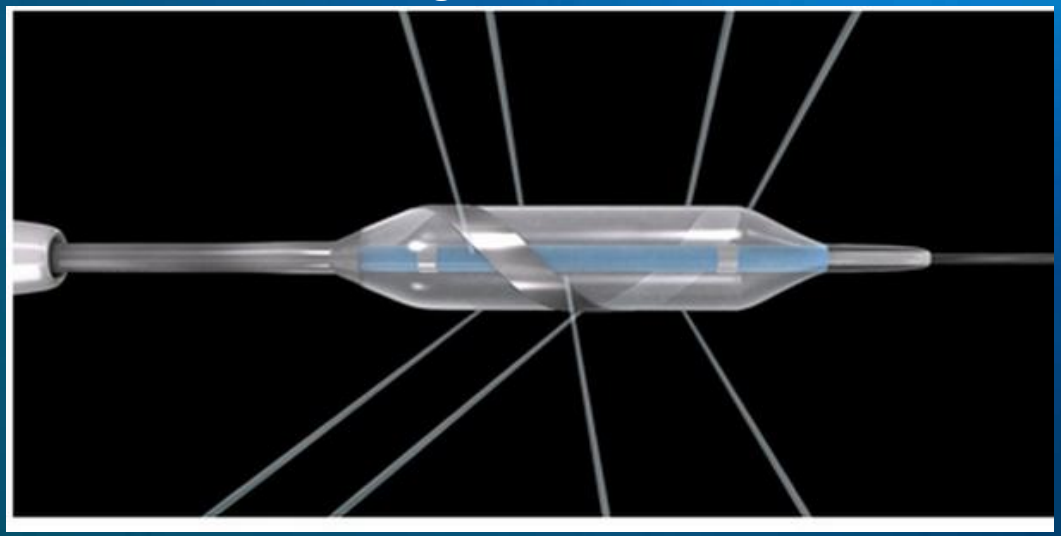
Updates on RDN devices

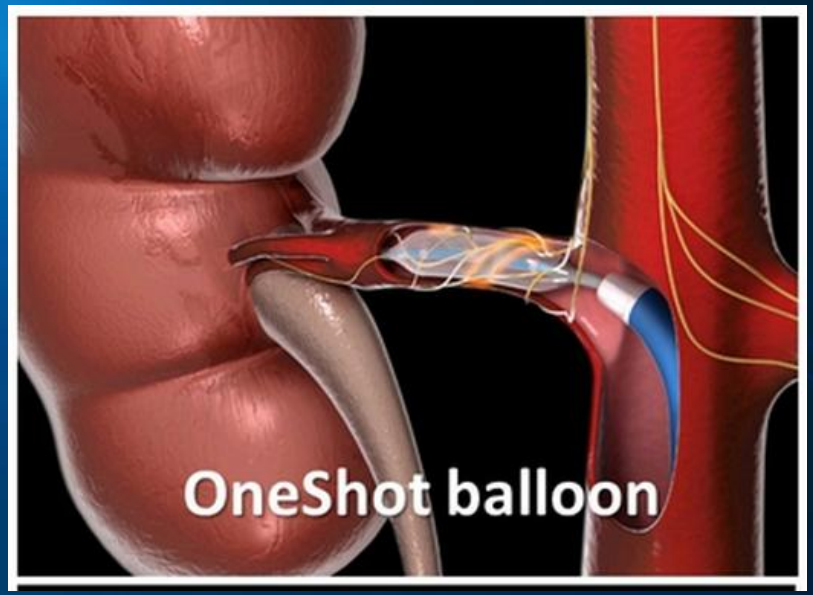
EnligHTN Renal Denervation System

Symplicity Point-by-point System



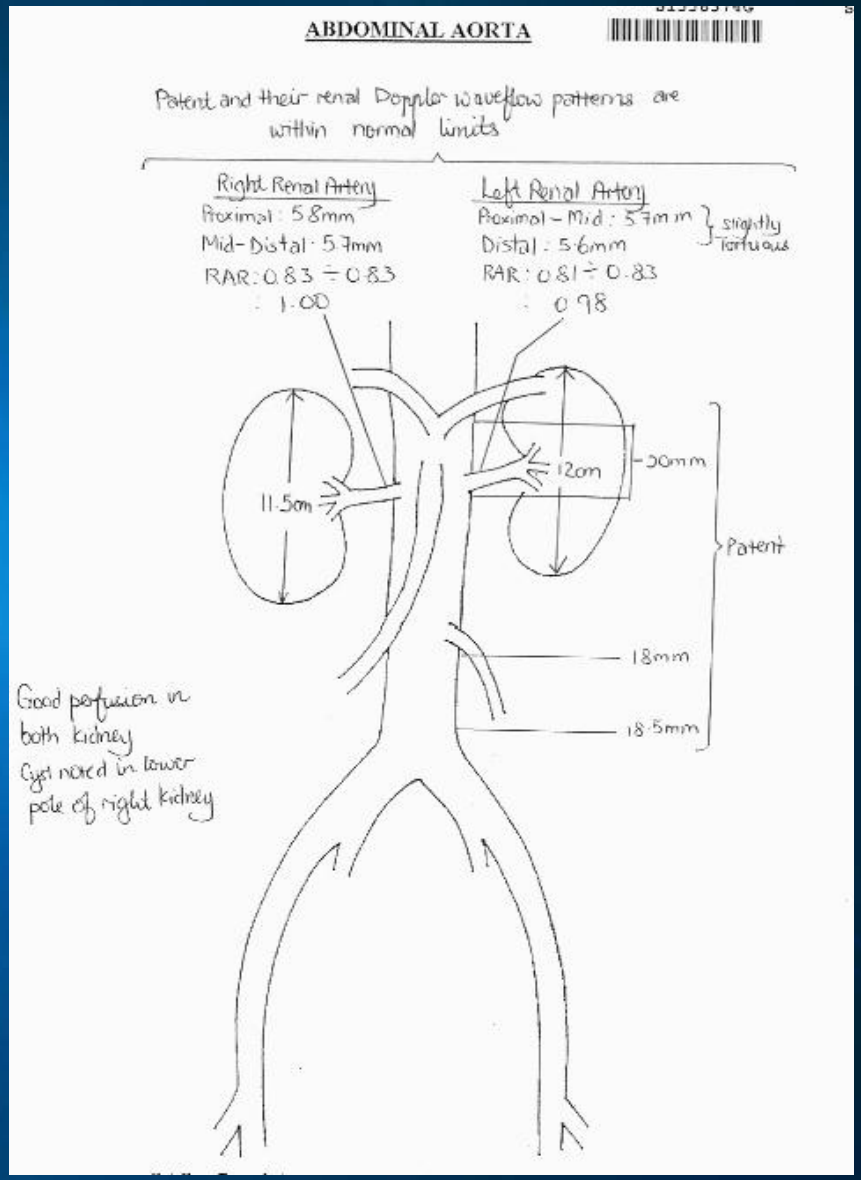
OneShot RF Irrigation Balloon Catheter

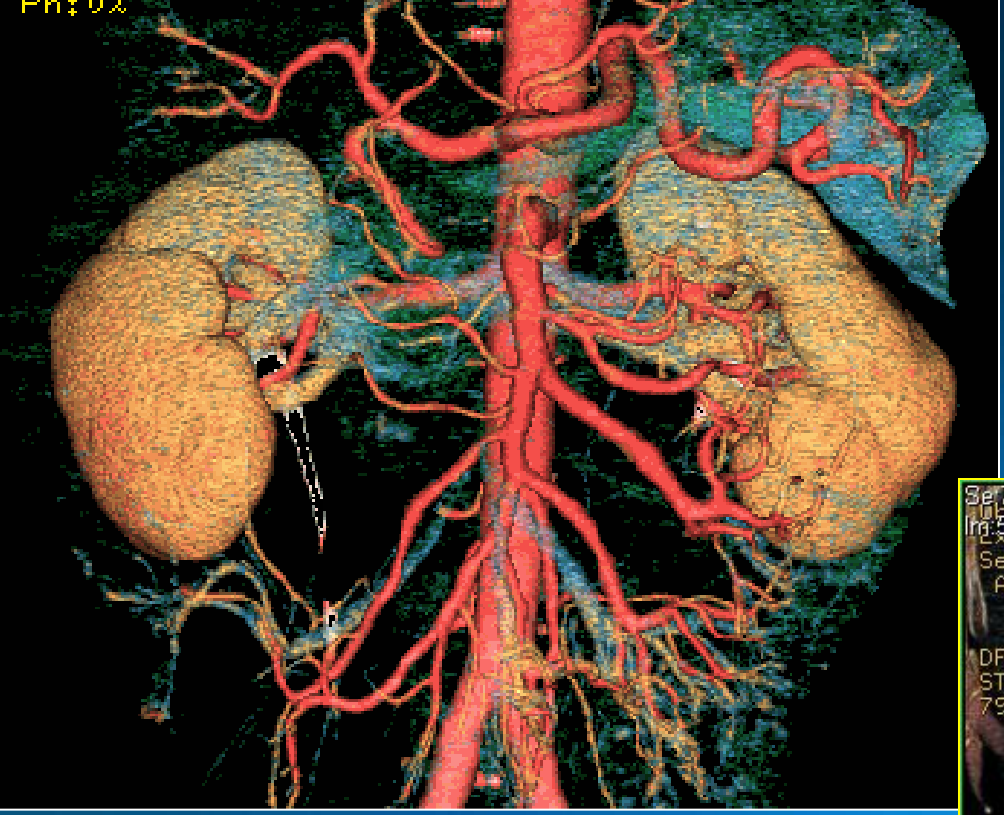


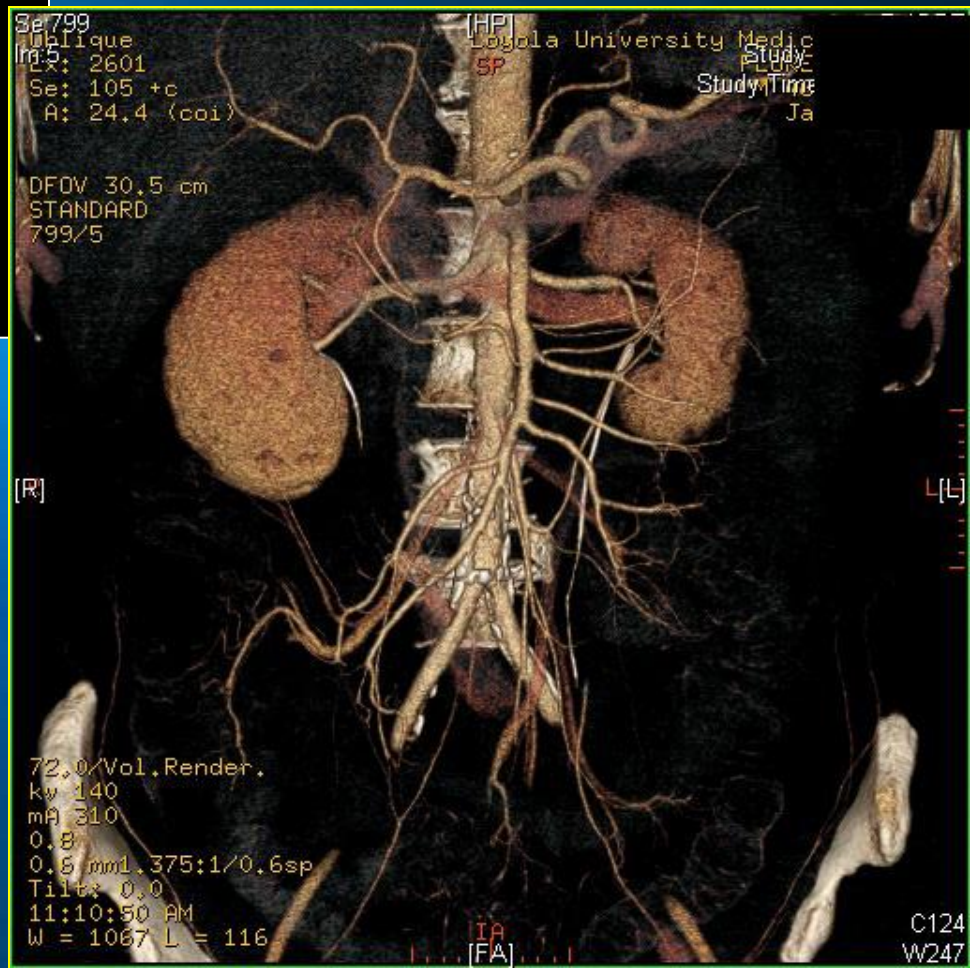


Renal Arteries Anatomy

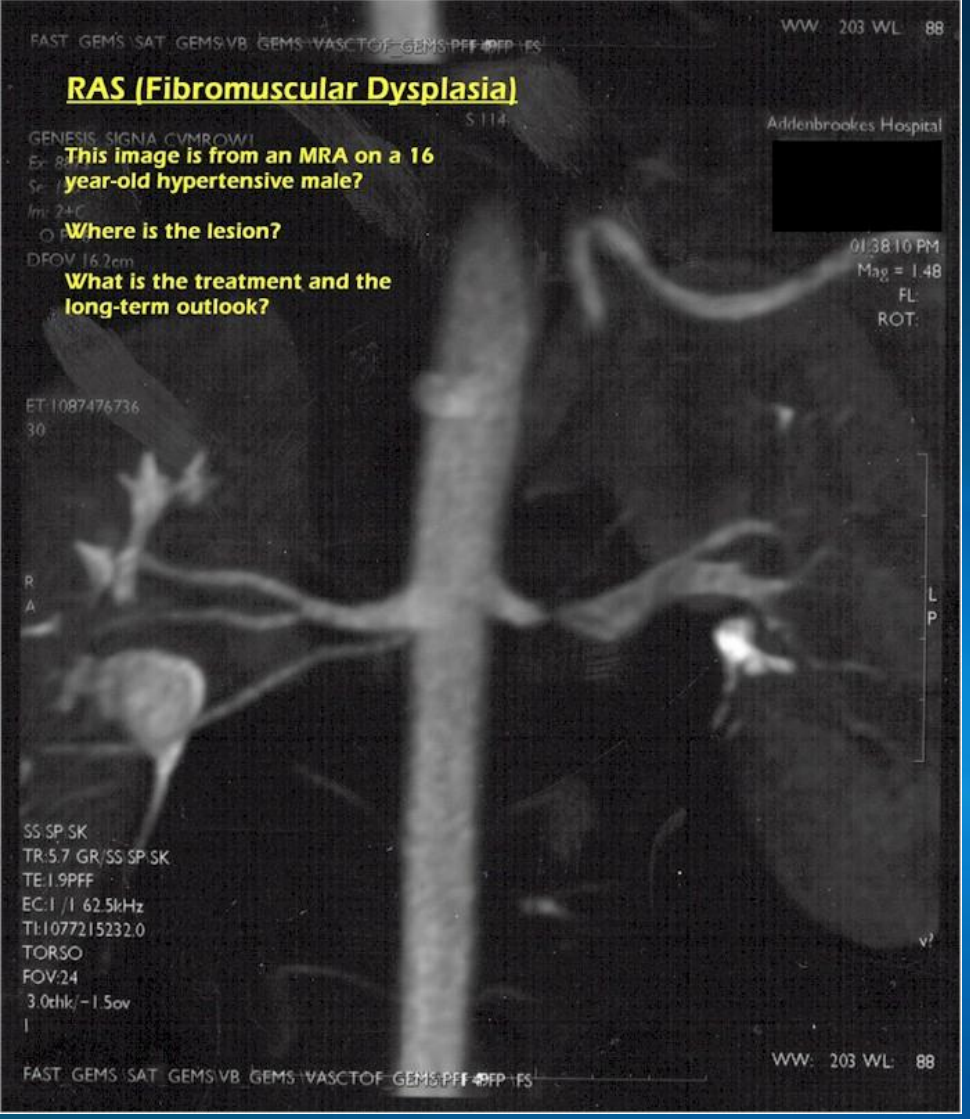
- Main renal arteries
  - ≥ **4 mm** in diameter
  - ≥ **20 mm** in length
- Renal artery stenosis
- Previous renal artery stenting
- (?) multiple main / accessory renal arteries
- Severe tortousity ; calcification

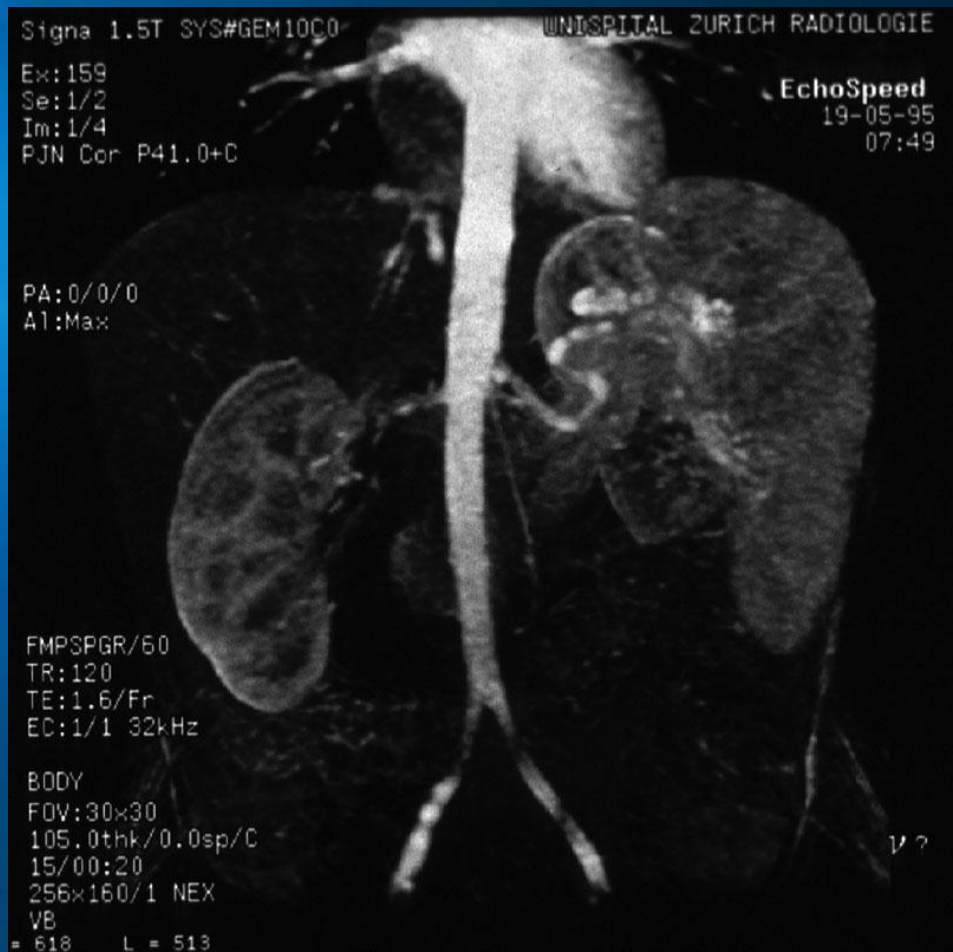






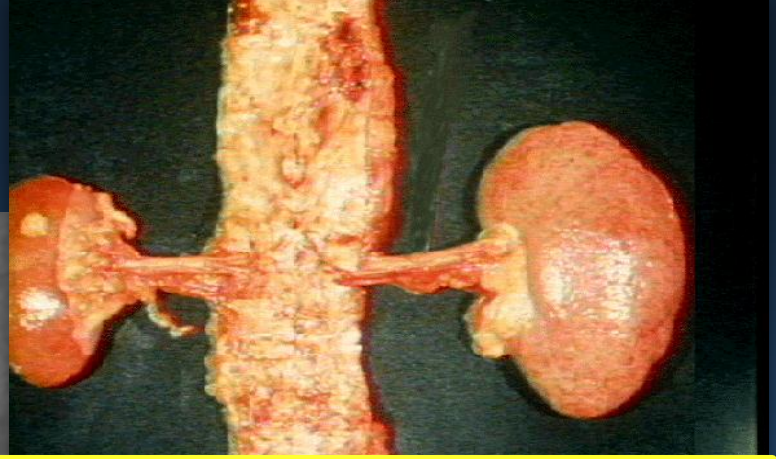
CT Angiography





MR Angiography

Renal Artery Stenosis



Right Renal Artery

Proximal : 70% (2.1mm) L=1cm

mid : 5.6mm } Patent.

Distal : 5.6mm }

RAR : 2.88 ÷ 0.79 = 3.64

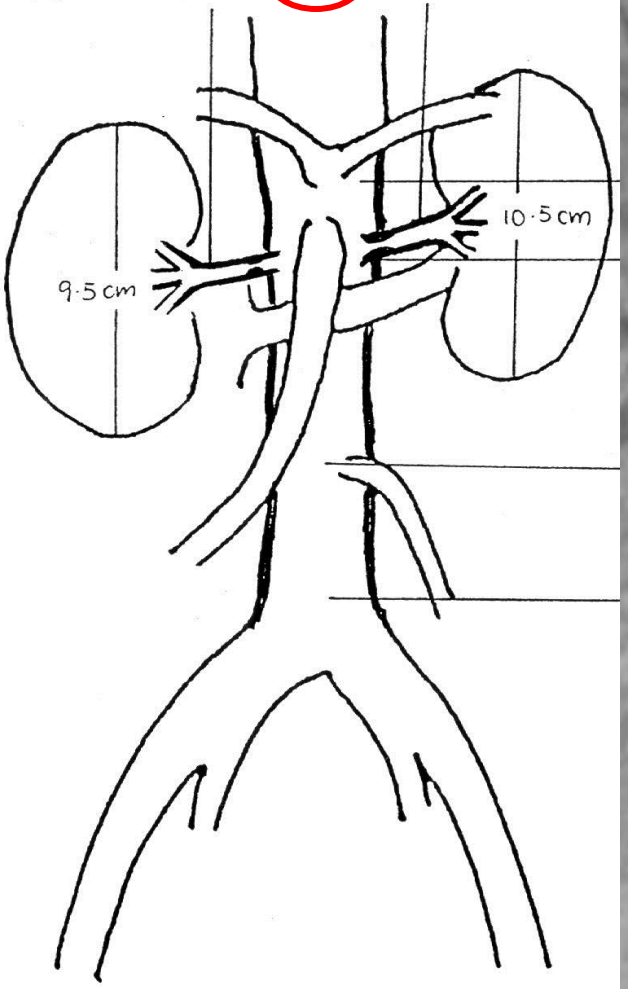
Left Renal Arter

Proximal : 45%

mid : 4.1mm

Distal : 5.1mm

RAR : 1.06 ÷



ABDOMINAL AORTA

Patent.

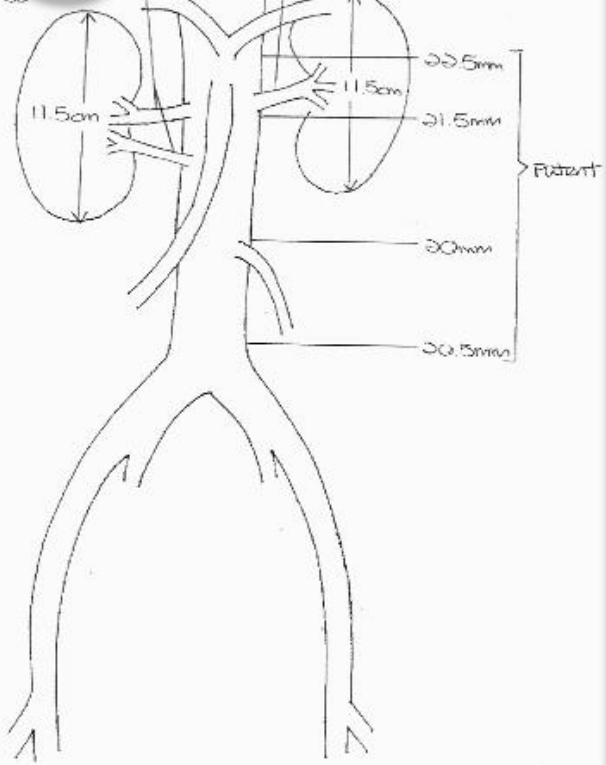
Doppler waveform patterns are within normal limits.

Right Renal Artery (RRA)

1st RRA
Proximal-Mid: 5.3mm
Distal: 5.[illegible]mm
RAR = 0.8[illegible] / 0.86 = 1.0[illegible]

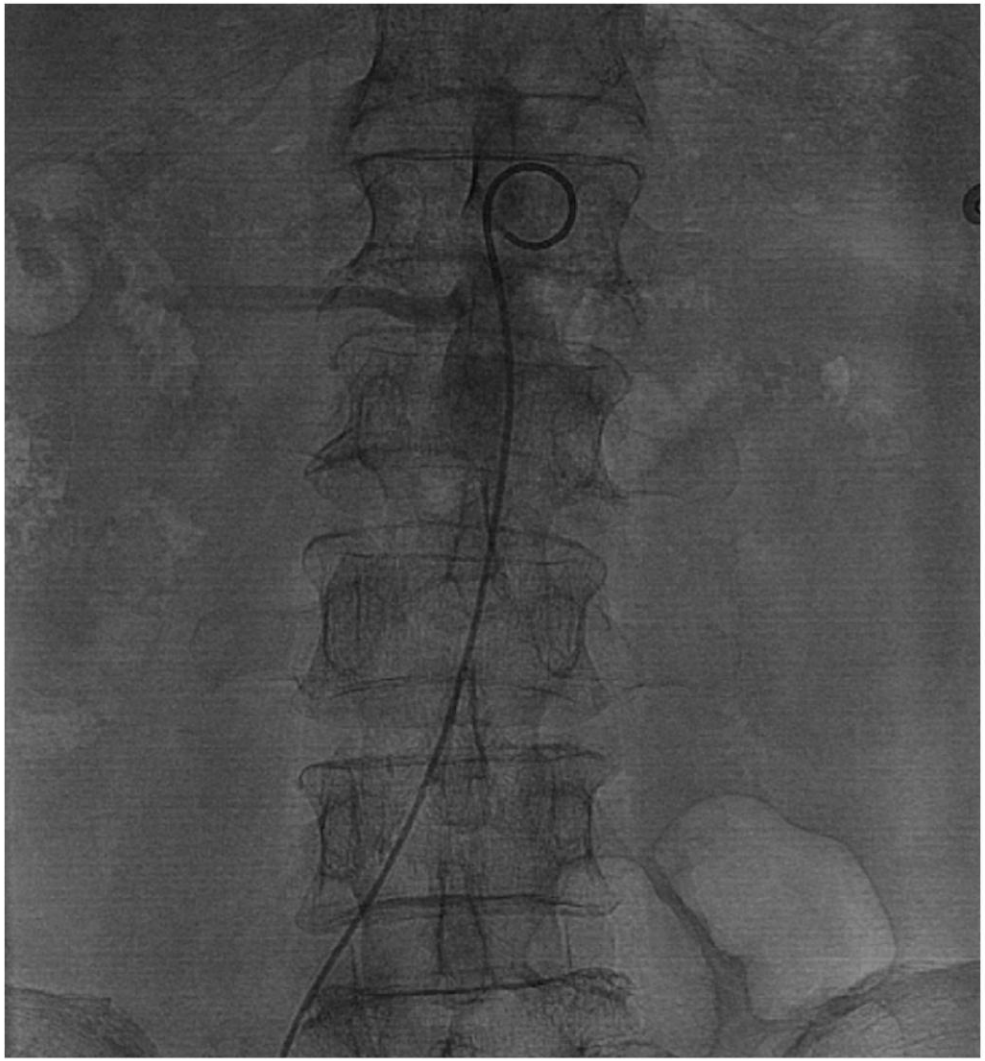
2nd RRA
Proximal-Mid: 5.1mm
Distal: 5.[illegible]mm
RAR = 0.8[illegible] / 0.86 = 0.9[illegible]

Left Renal Artery
Proximal-Mid: 5.8mm
Distal: 5.[illegible]mm
RAR = 0.73 / 0.86 = 0.85



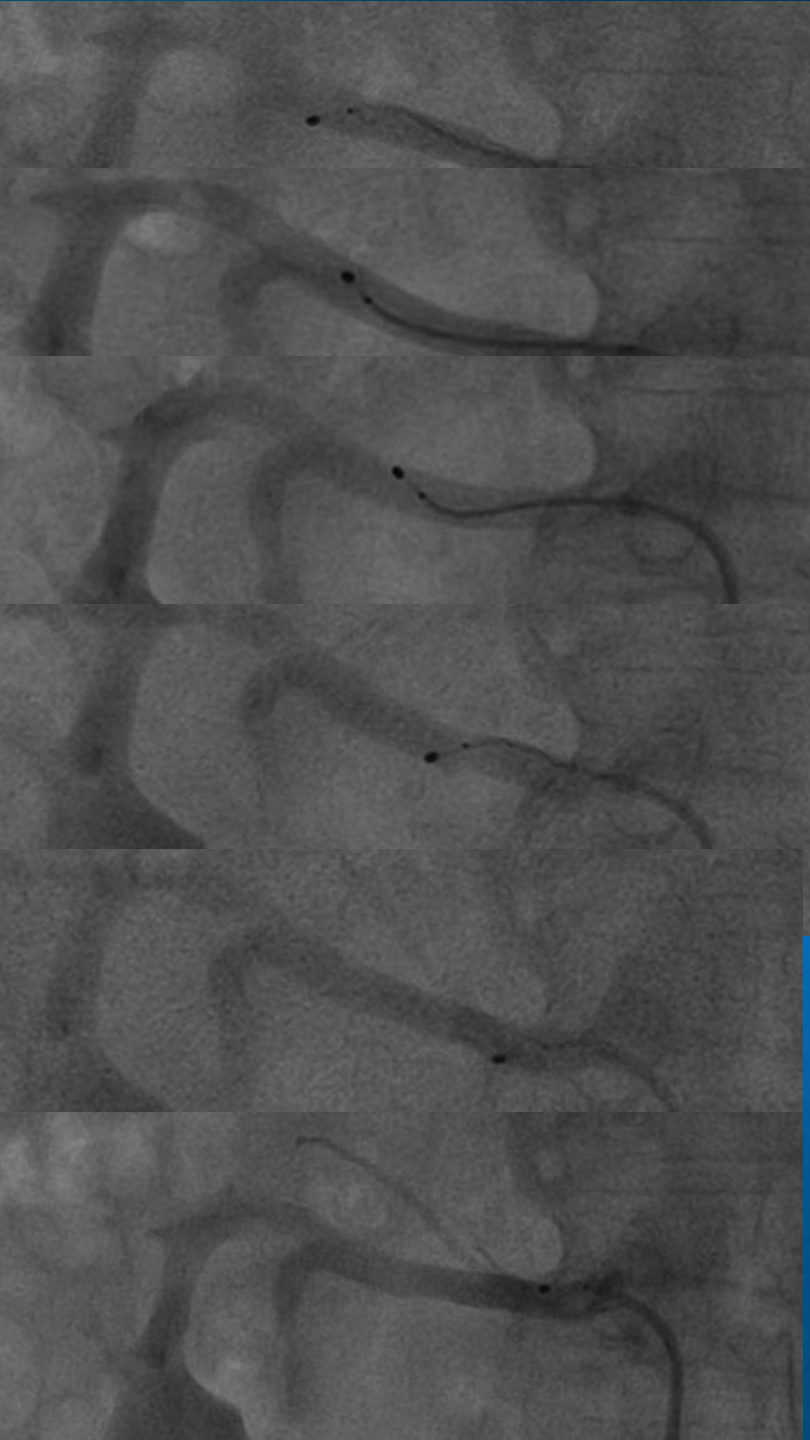
Good perfusion noted in both kidneys.

RAR = Renal Artery to Aorta Systolic Velocity Ratio



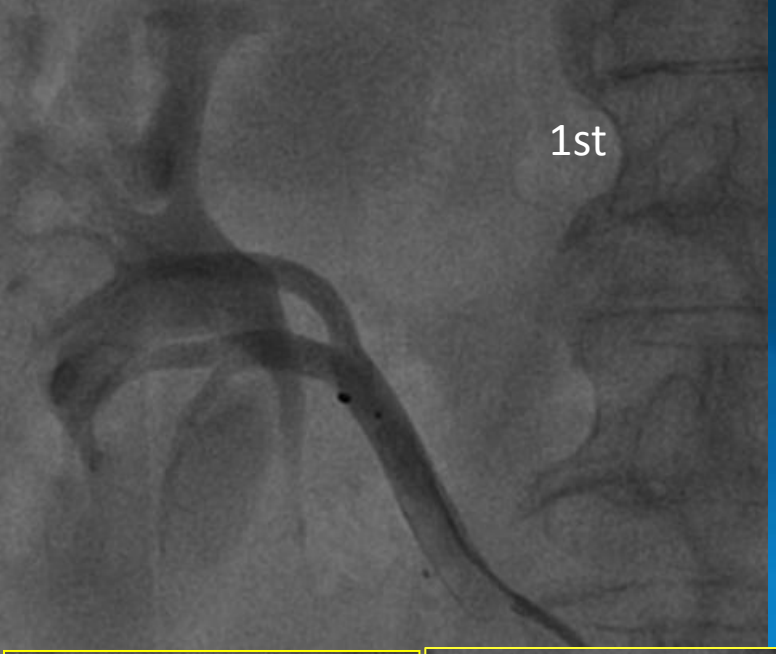
RIGHT UPPER RENAL ARTERY

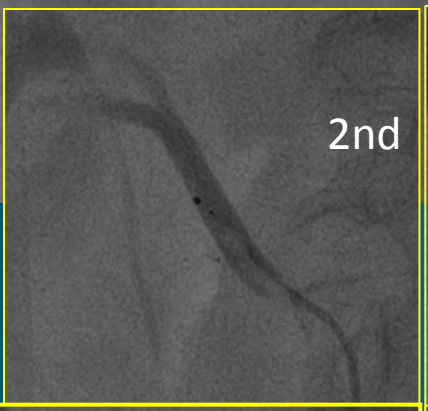
6 RF ablations

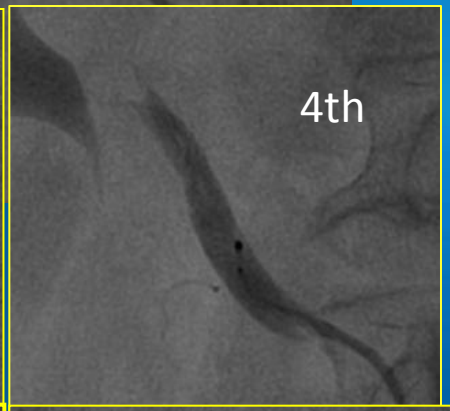


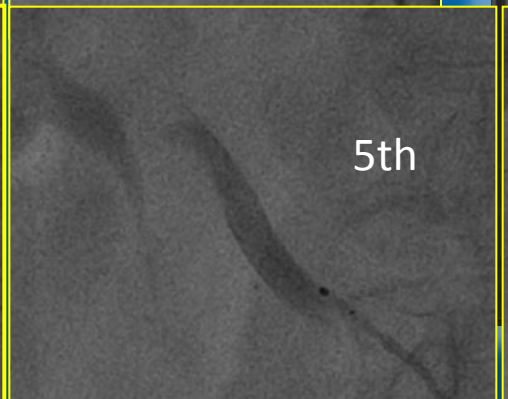
RIGHT LOWER RENAL ARTERY

6 RF ablations









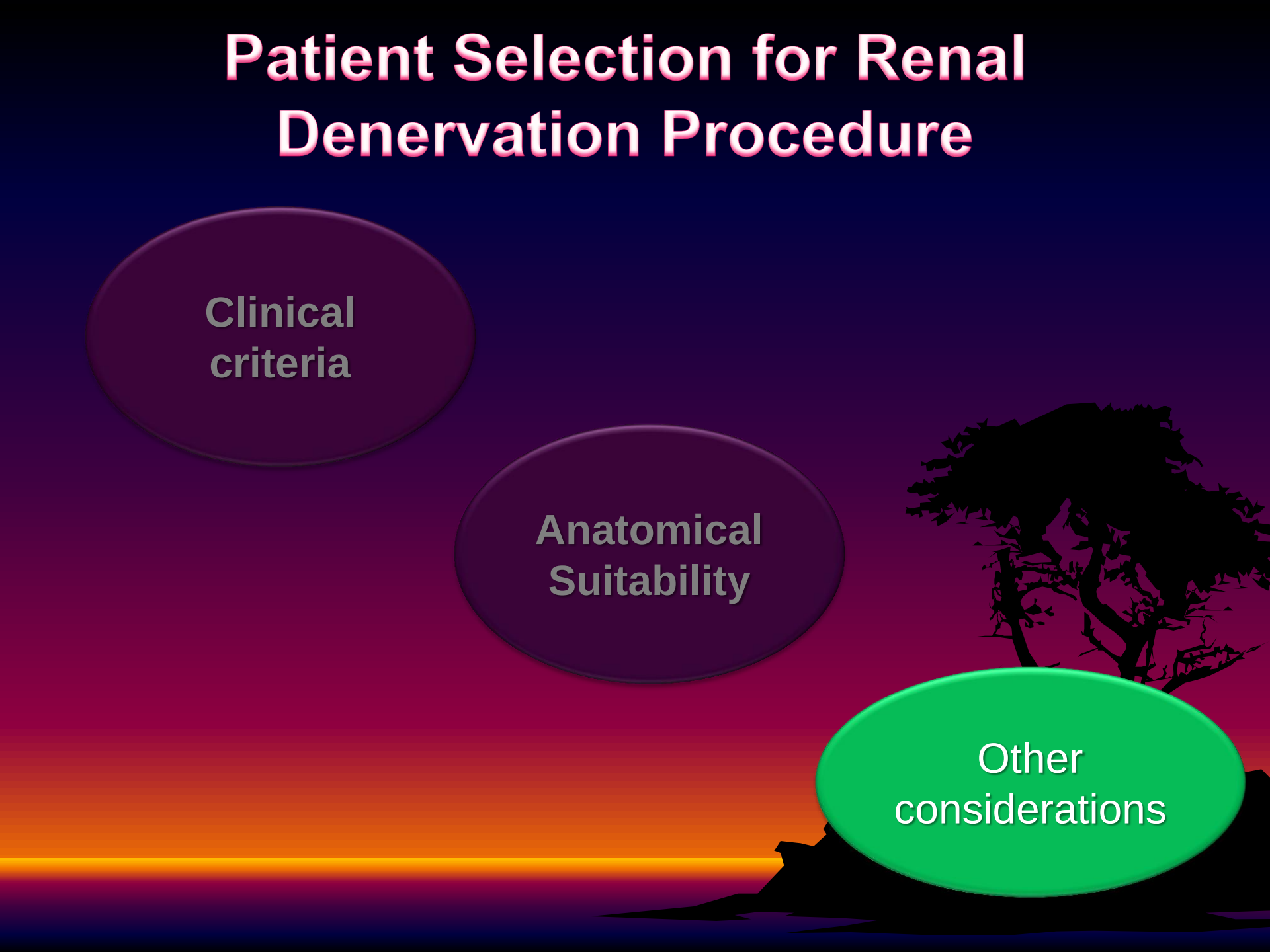
Patient selection for Renal Denervation: other consideration

Patient Selection for Renal Denervation Procedure

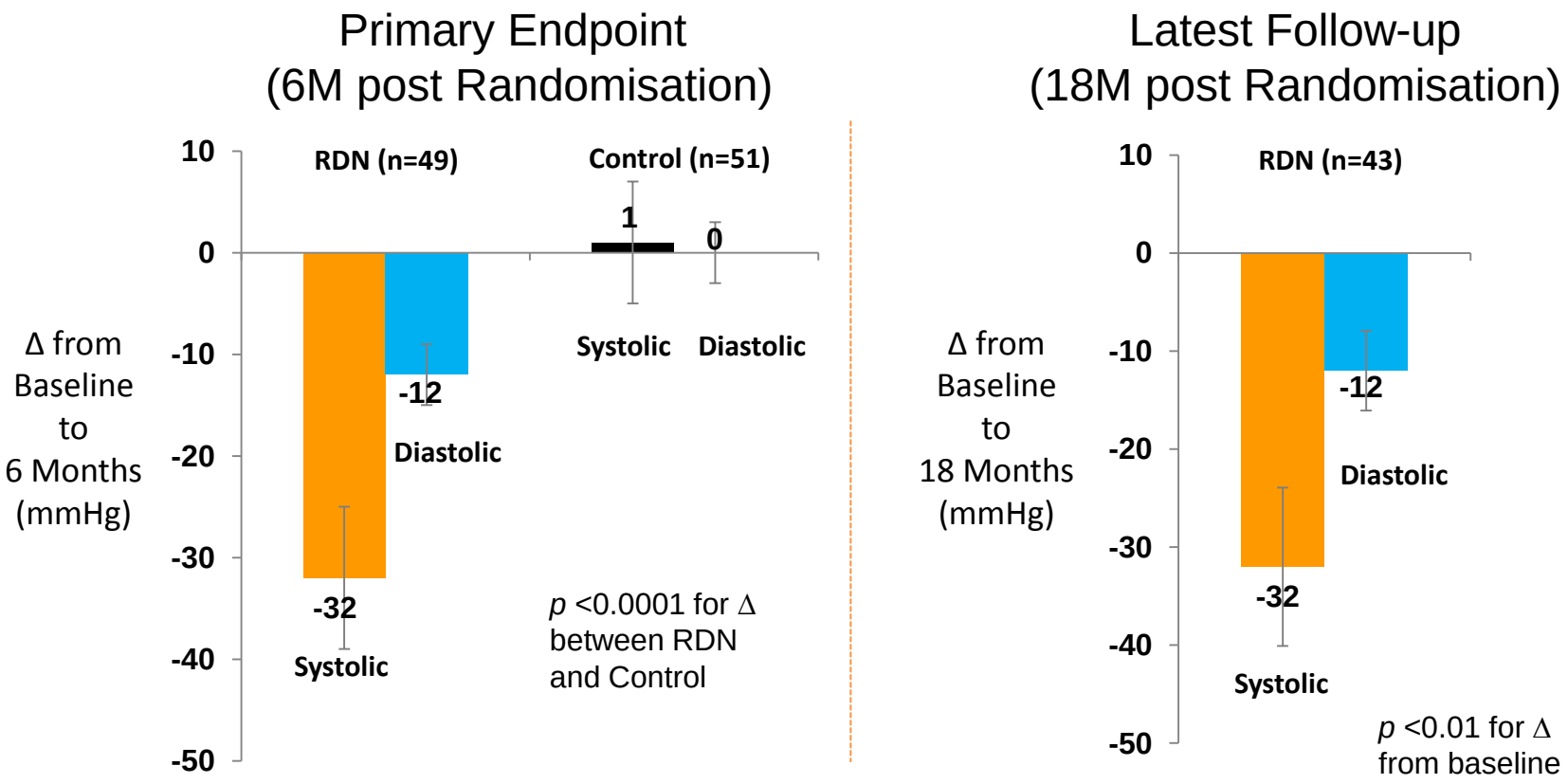
Clinical criteria

Anatomical Suitability

Other considerations

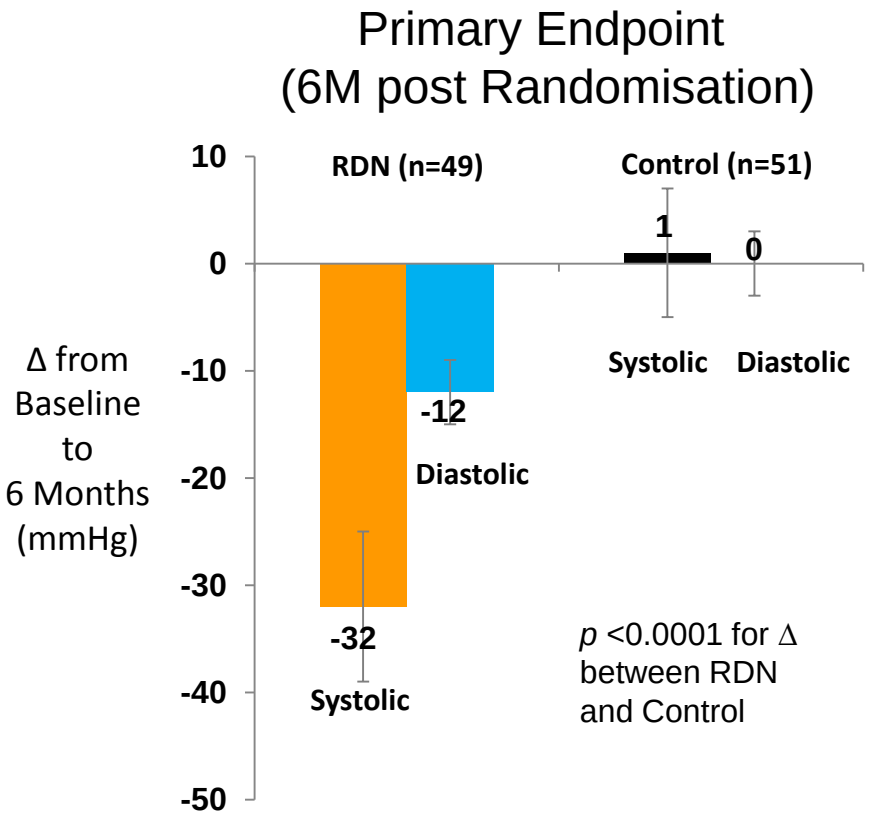


Symplicity HTN-2



- **>80% of RDN patients had ≥10 mmHg reduction in SBP**
- **5 patients had ≤ 5mmHG reduction in SBP**

Symplicity HTN-2

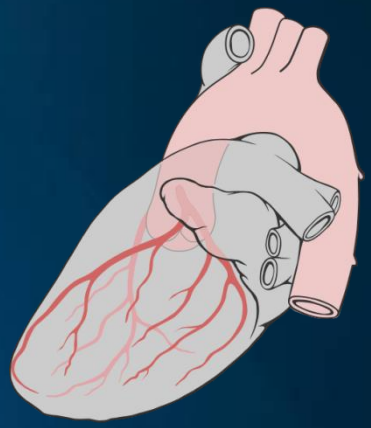


3 Groups of patients:

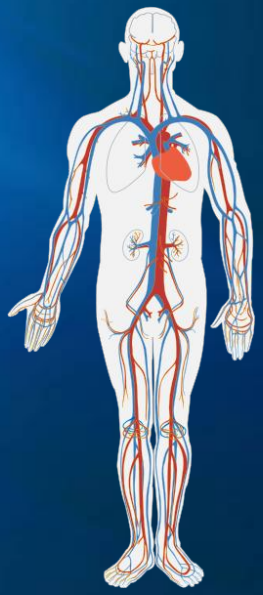
1. **Non-responders**
   - ~ 10%
2. **Excellent-responders**
   - ~ 40%
   - sBP < 140 mmHg
3. **Moderate responders**
   - ~ 50%
   - Some response with BP drop of at least 10 mmHg

- >80% of RDN patients had ≥10 mmHg reduction in SBP
- 5 patients had ≤ 5mmHG reduction in SBP

Patient selection for RDN



- **Predictor of response**
  - ? high baseline sympathetic tone
  - *high baseline BP*
  - *DM*
  - ? response to centrally-acting sympatholytic drug (e.g clonidine, moxonidine)
  - ??? others



The future of renal denervation rests on selecting the right patient

Monday, 03 Sep 2012 10:26

Pierre-Fracois Plouin, Thomas Zeller and Felix Mahfoud

"We need to be very careful not to kill a promising technology with incorrect patient selection," Pierre-François Plouin, Paris, France, warned delegates at the EuroPCR Great Debate 2012 on renal denervation. In the debate, Plouin and four other experts in interventional cardiology, interventional radiology and nephrology agreed that identifying the right group of patients is key for the future of the technique. The group also discussed patient compliance to medical therapy, clinical data associated with the procedure and the balance between risk and benefit.

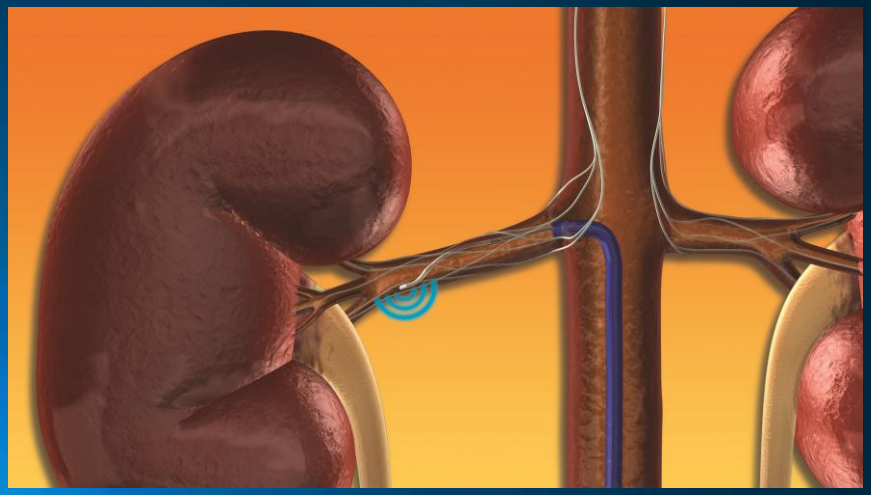
Patient Selection for Renal Denervation Procedure

Clinical criteria

Anatomical Suitability

Other considerations

Conclusion



- Renal denervation is a very promising new technology
- At this stage, careful patient selection is mandatory
  - invasive, with $$$$ involved
  - still limited data, in a small number of patients
  - many unanswered questions
- Best current indication: resistant hypertension without renal impairment


THANK
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