Renal Nerve Denervation

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The majority of patients with resistant hypertension and no secondary cause have elevated SNS activity.

Surgical interventions

- Techniques: radical sympathectomy and splanchnicectomy.
- Employed in 1920-40s for treatment of malignant hypertension (100% 5 year mortality)

Results:

- Improvement in blood pressure
- Survival benefit

Limitations:

- High surgical complexity
- Significant side-effects

Replaced by advent of medical therapy
**SYMPPLICITY HTN-1**

- **6 MONTHS (N=144)**: 
  - Systolic: -22 mmHg
  - Diastolic: -10 mmHg

- **1 YEAR (N=132)**: 
  - Systolic: -27 mmHg
  - Diastolic: -14 mmHg

- **2 YEARS (N=105)**: 
  - Systolic: -29 mmHg
  - Diastolic: -14 mmHg

- **3 YEARS**: 
  - Systolic: -32 mmHg
  - Diastolic: -14 mmHg

**Change in Blood Pressure (mmHg)**

- **Systolic**
- **Diastolic**
SYMPPLICITY HTN-3

Screening Visit 1
- Office SBP ≥160 mm Hg
- Full doses ≥3 meds
- No med changes in past 2 weeks
- No planned med changes for 6 M

Screening Visit 2
- Office SBP ≥160 mm Hg
- 24-h ABPM SBP ≥135 mm Hg
- Documented med adherence

2 weeks
- Home BP & HTN med confirmation

Sham Procedure
- Renal angiogram; Eligible subjects randomized

Renal Denervation
- 1 M
- 3 M
- 6 M
- 12-60 M

Primary endpoint
- Home BP & HTN med confirmation

2 weeks
- Patients, BP assessors, and study personnel all blinded to treatment status
- No changes in medications for 6 M

Primary Efficacy Endpoint

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 Months</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>Denervation</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>180 mm Hg</td>
<td>166 mm Hg</td>
<td>180 mm Hg</td>
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<tr>
<td>Sham</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>180 mm Hg</td>
<td>168 mm Hg</td>
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Δ = -14.1 ± 23.9, P<0.001
Δ = -11.7 ± 25.9, P<0.001
Δ = -2.39 (95% CI, -6.89 to 2.12), P=0.26*

(N=364) (N=353) (N=171) (N=171)

*P value for superiority with a 5 mm Hg margin; bars denote standard deviations

J Am Coll Cardiol. 2015;65(13):1314-1321
WHAT DOES THE FUTURE HOLD FOR RENAL DENERVATION?
• Distal segment lie closer to the lumen
• More nerves in the ventral
• Only 19 patients in SYMPLICITY HTN-3 received ablations in all four quadrants bilaterally
• No of ablations associated with greater BP ↓

22% of patients increased medications between 2 and 5 weeks

One in 4 patients were Afro-Americans

US investigators had no previous experience with the procedure!
1/3 did only 1 RDN!!!

Optimization of Renal Denervation. Mahfoud et al. JACC 6,1 6, 2015, : 1766–75
FUTURE

- RDN Technology
  - Multielectrode catheter (Spyral®, basket, balloon-mounted electrode)
    - Simultaneous, uniform delivery of radiofrequency energy in four quadrants
    - Ablate both distal segments
  - Ethanol-Based Sympathicolysis¹
  - Extracorporeal High Intensity Focused Ultrasound²
- Baroreflex Activation Therapy³
- Study Design⁴

FUTURE: Beyond HTN

• Heart Failure
  • Vascular Stiffness: Aortic augmentation, augmentation index, and mean central aortic BP
  • Systolic Heart Failure
• Arrhythmias
  • Atrial and Ventricular arrhythmias
• Chronic Kidney Disease
• Obstructive Sleep Apnea

Franklin D Roosevelt (1882-1945)

In any moment of decision, the best thing you can do is the right thing, the next best thing if the wrong thing, and the worst thing you can do is nothing.

-Theodore Roosevelt
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