Effects of renal sympathetic denervation on noradrenaline spillover and systemic blood pressure in patients with resistant hypertension

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Disclosures

- This study was sponsored by ARDIAN Inc., Palo Alto, CA, USA.

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Sympathetic Nervous System Activation - A major Player in CV disease
SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Smithwick, M.D.
and
Jesse E. Thompson, M.D., Boston
Selective Renal Denervation

- Disrupt sympathetic nerve traffic to and from the kidneys
- Disable the renal nerves via RF ablation
- A 40-minute catheter-based procedure
The Renal Nerves

Nerves
Lumen
Endothelium
Media
Adventitia
Fat

3 mm

...follow the renal artery to the kidney

...primarily within the adventitia
Treatment by Renal RF Catheter
Selective Renal Denervation:
Symplicity® Catheter System, Ardian, Inc., Palo Alto, CA, USA

Focal ablations spaced along vessel

Multiple focal ablations ↑ circumferential coverage
# Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patients Undergoing Procedure (N=45)</th>
<th>Patients Anatomically Ineligible for Procedure (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58 ± 9</td>
<td>51 ± 8</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>44</td>
<td>20</td>
</tr>
<tr>
<td>Race (% non-Caucasian)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes Mellitus II (%)</td>
<td>31</td>
<td>40</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>72 ± 11</td>
<td>79 ± 9</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>81 ± 23</td>
<td>95 ± 15</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>177/101 ± 20/15</td>
<td>173/98 ± 8/9</td>
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## Baseline Patient Characteristics

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<tr>
<td>Number of anti-HTN meds (mean)</td>
<td>4.7 ± 1.5</td>
<td>4.6 ± 0.5</td>
</tr>
<tr>
<td>ACE/ARB (%)</td>
<td>96</td>
<td>80</td>
</tr>
<tr>
<td>Beta-blocker (%)</td>
<td>76</td>
<td>100</td>
</tr>
<tr>
<td>Calcium channel blocker (%)</td>
<td>69</td>
<td>100</td>
</tr>
<tr>
<td>Vasodilator (%)</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Diuretic (%)</td>
<td>96</td>
<td>60</td>
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Office BP: All Treated Patients

Change in Blood Pressure (mmHg)

-14 -10  -21 -10  -22 -11  -24 -11  -27 -17

1 month (n=41)  3 months (n=39)  6 months (n=26)  9 months (n=20)  12 months (n=9)

n=45
Evidence for denervation

-47% for Renal NE Spillover (n=10)

-85% for Total Kidney NE Content (pigs n=70)
Effects of renal denervation on renal and total body NE spillover

Mean office blood pressure

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<th>161/107</th>
<th>141/90</th>
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</table>

- **Renal Norepinephrine Spillover (ng/min)**
  - Baseline
  - 30 days after bilateral denervation

- **Total Body Norepinephrine Spillover (ng/min)**
  - Baseline
  - 30 days after bilateral denervation
Effects of renal denervation on MSNA

Baseline | 1 month FU | 12 months FU

- **ECG**
- **BP**
- **MSNA**

56 bursts/min | 41 bursts/min | 19 bursts/min

10 sec
Conclusions

Selective renal sympathetic denervation via a catheter based approach using RF ablation

• appears to be a safe procedure

• effectively reduces efferent sympathetic nerve activity (NA spillover ↓)

• appears to inhibit afferent signaling via renal sensory nerves (MSNA ↓)

• is associated with a substantial and sustained reduction in blood pressure

• may represent a treatment option for other conditions characterized by heightened sympathetic drive
# Acknowledgements

<table>
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<tr>
<th>Location</th>
<th>Contributors</th>
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| Alfred Hospital, Melbourne, AU: | Cardiology Team  
    Prof Murray Esler  
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| St Vincent’s Hospital, Melbourne, AU: | Cardiology Team  
    A/Prof Rob Whitbourn |
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| Jagiellonian University, Krakau, Poland: | Cardiology Team  
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    Dr Krzysztof Bartus  
    Dr Boguslav Kapelak |
| Ohio State University, Columbus, Ohio, USA: | Prof William Abraham  
    Prof Paul Sobotka |
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Other interesting aspects and open questions

- Predictors of response (age, sex, PMHx, BP, HR, GFR…?)
  (6 patients had BP reduction <10mmHg = non-responders)

- Dipping pattern in responders (n=12)

- Glucose control and insulin sensitivity
- Long term effects (re-innervation?…)
- Relevance in other patients cohorts (CHF, CRF, ESRD….)?