Catheter-Based Renal Sympathetic Denervation in the Management of Resistant Hypertension

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Presenter Disclosure Information

Henry Krum MBBS PhD FRACP

The following relationships exist related to this presentation:

< No relationships to disclose >
Background

- Hypertension is a global public health problem of major magnitude
- Despite the availability of safe and effective pharmacological therapies, only ~50% of patients achieve adequate blood pressure control to guideline targets
- The sympathetic nervous system, in particular renal sympathetic efferent and afferent nerves, is recognized as critical in the hypertension disease process
- Disruption of renal sympathetic nerves has long been considered an attractive therapeutic target for this condition
Anatomical Location of Renal Sympathetic Nerves

- Arise from T10-L1
- Follow the renal artery to the kidney
- Primarily lie within the adventitia
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RF Ablation Approach to Renal Sympathetic Denervation

Syclicity® Catheter System, Ardian, Inc., Palo Alto, CA, USA
Placement of Renal RF Catheter
Treatment by Renal RF Catheter
Renal Sympathetic Denervation First in Man Study

**Study Sites**

- Melbourne, AU (x2)
- Newcastle, AU
- Krakow, Poland
- Frankfurt, Germany
Study Aims

• To perform a first-in-man 12-month evaluation of the safety and blood pressure-lowering efficacy of percutaneous renal sympathetic denervation in patients with refractory hypertension
Inclusion/Exclusion Criteria

**Key Inclusion Criteria**
- Office SBP $\geq 160$ mmHg despite $3+$ anti-hypertensive medications (including diuretic), or confirmed intolerance to medications
- eGFR (MDRD formula) of $\geq 45$ mL/min/1.73m$^2$

**Key Exclusion Criteria**
- Known secondary cause of hypertension
- Type I diabetes mellitus
- Currently taking clonidine, moxonidine, or rilmenidine
- Renovascular abnormalities: significant renal artery stenosis, prior renal stenting or angioplasty, dual renal arteries
Study Endpoints

*Primary Endpoints*

- Peri-procedural and long-term safety
- Office blood pressure levels

*Secondary Endpoints*

- Ambulatory blood pressure monitoring
- Renal norepinephrine spillover rate
- Renal function (eGFR)
Patient Disposition

50 patients enrolled

Treatment eligibility determined by angiographic evaluation of renal artery anatomy

45 patients treated

41 with follow-up available at 1 month
39 with follow-up available at 3 months
26 with follow-up available at 6 months
20 with follow-up available at 9 months
9 with follow-up available at 12 months

5 patients not treated

5 with follow-up available at 1 month
5 with follow-up available at 3 months
5 with follow-up available at 6 months
2 with follow-up available at 9 months

2 lost to follow-up
## 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><strong>Age (years)</strong></td>
<td>58 ± 9</td>
<td>51 ± 8</td>
</tr>
<tr>
<td><strong>Gender (% female)</strong></td>
<td>44</td>
<td>20</td>
</tr>
<tr>
<td><strong>Race (% non-Caucasian)</strong></td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus II (%)</strong></td>
<td>31</td>
<td>40</td>
</tr>
<tr>
<td><strong>CAD (%)</strong></td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td><strong>Heart Rate (bpm)</strong></td>
<td>72 ± 11</td>
<td>79 ± 9</td>
</tr>
<tr>
<td><strong>eGFR (mL/min/1.73m²)</strong></td>
<td>81 ± 23</td>
<td>95 ± 15</td>
</tr>
<tr>
<td><strong>BP (mmHg)</strong></td>
<td>177/101 ± 20/15</td>
<td>173/98 ± 8/9</td>
</tr>
</tbody>
</table>
### Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Patients Undergoing Procedure (N=45)</th>
<th>Patients Anatomically Ineligible for Procedure (N=5)</th>
</tr>
</thead>
<tbody>
<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>
</tr>
</tbody>
</table>
Results

Procedure Characteristics & Safety

- Procedure time: median 38 (IQR 34-48) minutes
- Treatment delivered without complication in 43/45:
  - 1 renal artery dissection during catheter delivery (before RF energy application)
  - 1 femoral pseudoaneurysm, manually reduced without further sequelae
- No long-term vascular complications observed:
  - 18 patients had angiograms at 14-30 days post-
  - 6-months post-: 14 had MRA, 17 had CTA
Results

Office BP: All Treated Patients

Repeated measures ANOVA: P=0.026 for SBP, P=0.027 for DBP
*P<0.001 vs baseline BP

Change in Blood Pressure (mmHg)

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

n=45
Results

Office BP: Untreated Patients

Change in Blood Pressure (mmHg)

<table>
<thead>
<tr>
<th>Time</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>3</td>
<td>-2</td>
</tr>
<tr>
<td>3 months</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6 months</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>9 months</td>
<td>26</td>
<td>17</td>
</tr>
</tbody>
</table>

n=5
Results

Medication Changes

- 4.7 ± 1.5 anti-hypertensive drugs at baseline; unchanged at patients’ latest follow-up visit (p=NS)

- 3 patients required reduction of medications after normalization of BP

- 9 patients had their medications increased:
  - 5 were BP responders: >10mmHg BP reduction prior to medication increase
  - 4 were BP non responders
Results

Office BP: Censoring Medication Increases

Change in Blood Pressure (mmHg)

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<thead>
<tr>
<th>Time</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month (n=41)</td>
<td>-14</td>
<td>-10</td>
</tr>
<tr>
<td>3 months (n=36)</td>
<td>-22</td>
<td>-11</td>
</tr>
<tr>
<td>6 months (n=21)</td>
<td>-22</td>
<td>-10</td>
</tr>
<tr>
<td>9 months (n=16)</td>
<td>-26</td>
<td>-11</td>
</tr>
<tr>
<td>12 months (n=4)</td>
<td>-28</td>
<td>-17</td>
</tr>
</tbody>
</table>

n=36
**Results**

**24-Hr Ambulatory BP**

\[ \Delta \text{ABPM} \text{ vs } \Delta \text{Office BP} \]

\[ r^2 = 0.6216 \]

\[ P < 0.002 \]

**Effect on Dipping**

- **Dippers**
  - Pre-procedure: 33
  - Post-procedure: 67

- **Non- or reverse dippers**
  - Pre-procedure: 67
  - Post-procedure: 33
Results

Norepinephrine Data

% Δ Renal NE Spillover
(n=10)

-47%
Results

Renal Function

eGFR (ml/min/1.73m²)

<table>
<thead>
<tr>
<th>Pre-Procedure</th>
<th>6-Mths Post-Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>83</td>
</tr>
</tbody>
</table>

n=25
Summary

- Therapeutic renal sympathetic denervation involves a brief, simple percutaneous procedure

- No major complications were observed to either the renal artery or the kidney

- Significant and sustained reductions in blood pressure were achieved in patients with resistant hypertension

- Achievement of denervation supported by significant reduction in renal norepinephrine spillover
Conclusions

• Despite the non-randomized nature of this first in man study, percutaneous renal sympathetic denervation represents a novel, simple and effective approach to the management of hypertension in patients refractory to conventional pharmacological therapy.

• Prospective randomized controlled trials are required to definitively determine the role of this therapy in hypertension as well associated disorders.
For More Information

- www.thelancet.com