Can Renal Denervation Still Be An Effective Treatment For Resistant Hypertension: Results With The Spyral-HTN Device (Medtronic) In A Sham Controlled RCT Suggest It Can: What About Other Endovascular Treatments

Horst Sievert,
Ilona Hofmann, Laura Vaskelyte, Sameer Gafoor, Stefan Bertog, Predrag Matić, Markus Reinartz, Bojan Jovanovic, Kolja Sievert, Iris Grunwald, Nalan Schnelle

CardioVascular Center Frankfurt - CVC,
Frankfurt, Germany

Disclosures

<table>
<thead>
<tr>
<th>Physician name</th>
<th>Company</th>
<th>Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horst Sievert</td>
<td>4 tech Cardio, Abbott, Ablative Solutions, Ancora Heart, Bavaria Medizin Technologie GmbH, Bioventrix, Boston Scientific, Carag, Cardiac Dimensions, Celonova, Comed B.V., Contego, CVRx, Edwards, Endologix, Hemotek, Lifetech, Maquet Getinge Group, Medtronic, Mitralign, Nuuanuo Medtech, Mekko, Occlutech, pfm Medical, Recor, Renal Guard, Rex Medical, Terumo, Vascular Dynamics, Veno, Vivaure Medical</td>
<td>Consulting fees, Travel expenses, Study honoraria to institution</td>
</tr>
</tbody>
</table>

You know the story!

Renal denervation
... was almost destroyed by The Earthquake
Jan 9, 2014

MEDTRONIC ANNOUNCES U.S. RENAL DENERVATION PIVOTAL TRIAL FAILS TO MEET PRIMARY EFFICACY ENDPOINT

What has been achieved since the earthquake?
- Better technique with old devices
- Positive trials with old devices
- New devices
- Positive trials with new devices

Better technique with old devices
- "More is better"
  - Total number of ablations is important
  - Circumferential ablation is important
- "Go distal"
  - In distal vessel segments the nerves are closer to the vessel wall
New trials with new devices:

- SPYRAL HTN-OFF MED
- SPYRAL HTN-ON MED
- REDUCE HTN
- RADIANCE HTN SOLO
- RADIOSOUND-HTN
- Peregrine PMS - TARGET BP OFF-MED

New devices

- Symplicity Spyral™ Catheter
- Vessix™ Renal Denervation System
- Paradise™ Ultrasound Balloon
- Peregrine - Chemical denervation
Key Patient Eligibility Criteria

- In Japan, patients could be prescribed less than 50% of maximum manufacturer’s recommended dosage of a thiazide-type diuretic per standard of care.


INCLUSION

- 1. Ineligible renal artery anatomy (accessory arteries allowed)
- 2. eGFR < 45 mL/min/1.73m²
- 3. Type 1 diabetes mellitus or type 2 diabetes mellitus with HbA1C > 8.0%
- 4. Secondary causes of hypertension

EXCLUSION

- 1. Patients on 1-3 anti-hypertensive medications:
  - Thiazide diuretic
  - Calcium channel blocker
  - ACE-I / ARB
  - Beta-Blocker
  - Prescribed at minimum 50% of maximum recommended dosage*
  - Stable regimen for ≥6 weeks
- 2. Office SBP ≥ 150 and < 180 mm Hg
- 3. Office DBP ≥ 90 mm Hg
- 4. Systolic 24-hour mean ABPM ≥ 140 and < 170 mm Hg

Safety Results at 6 Months

- TI MI definition: intracranial hemorrhage, ≥ 5 g/dl decrease in hemoglobin concentration, a ≥ 15% absolute decrease in hematocrit, or death due to bleeding within 7 days of the procedure

New trials with new devices:

- SPYRAL HTN-OFF MED
- SPYRAL HTN-ON MED
- REDUCE HTN
- RADIANCE HTN SOLO
- RADIOSOUND-HTN
- Peregrine PMS - TARGET BP OFF-MED

Vessix™ Renal Denervation System

- Radiofrequency
- Balloon-based technology
- Helical pattern of bipolar RF electrodes
- All electrodes are activated simultaneously
- 30 second treatment time
- Temperature-control algorithm for energy delivery at 68°C
- One-button operation
- 7F compatible
REDUCE HTN: REINFORCE --- Vessix™ Renal Denervation System (N up to 100, ≤20 US Sites)

Primary Follow-up Period – No Meds (unless rescue)
Primary Endpoint: ASBP at 8 weeks

Washout Period (4 weeks)

Final Eligibility Assessment

Primary Endpoint: Difference in reduction of 24h ambulatory systolic BP between intervention group and sham control at 8 weeks

The trial was stopped early due to slow enrolment and because it was determined that the trial could not achieve its primary endpoint at 8 weeks

But:

Over 6 months, systolic BP continued to decrease in the Vessix group, with a lesser decrease in the control group

At 6 months, there was a significantly greater proportion of Vessix patients with office systolic BP <140 mmHg vs Control

New trials with new devices:
- SPYRAL HTN-OFF MED
- SPYRAL HTN-ON MED
- REDUCE HTN
- RADIANCE HTN SOLO
- RADIOSOUND-HTN
- Peregrine PMS - TARGET BP OFF-MED

Paradise™ Ultrasound Based Renal Denervation
- Balloon technique
- Ring of ablative energy (depth of 1-6 mm)
- Endothelial cooling by water circulating through balloon
- 2-3 ablations delivered to each main renal artery
### Individual Patient Response at 2 Months:

**Change in Daytime Ambulatory Systolic BP at 2 Months (ITT Population)**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>% Patients with ≥ 5 mm Hg Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Denervation (N=74)</td>
<td>66%</td>
</tr>
<tr>
<td>Sham Procedure (N=72)</td>
<td>33%</td>
</tr>
</tbody>
</table>

*P<0.001*

### New trials with new devices:

- SPYRAL HTN-OFF MED
- SPYRAL HTN-ON MED
- REDUCE HTN
- RADIANCE HTN SOLO
- RADIO SOUND-HTN
- Peregrine PMS - TARGET BP OFF-MED

---

### Radiosound HTN - Objective

To compare the effects of renal denervation applying:

1. Radiofrequency main renal artery ablation
2. Radiofrequency main and branch renal artery ablation
3. Ultrasound main renal artery ablation

in patients with resistant hypertension.

Philipp Lurz, TCT 2018

### Primary Endpoint

**Group Difference of Change in Daytime Ambulatory Systolic BP at 3 Months**

- **Radiofrequency main artery** vs. **ultrasound**:
  - p=0.002

- **Radiofrequency main artery** + **branches** vs. **ultrasound**:
  - p<0.001

Embolic ultrasound based renal denervation was superior to radiofrequency ablation of the main renal arteries.

Philipp Lurz, TCT 2018

---

### New trials with new devices:

- SPYRAL HTN-OFF MED
- SPYRAL HTN-ON MED
- REDUCE HTN
- RADIANCE HTN SOLO
- RADIO SOUND-HTN
- Peregrine PMS - TARGET BP OFF-MED

---

### Peregrine - Ablative Solutions

**PeriVascular Renal Denervation (PVRD)**

Reagents or other agents.
1, 3, 6 and 12 Months Blood Pressure Reduction (Systolic)*
(Post-Market Peregrine Study)

Responders: 79%                70%                   69%                   75%                         66%                  58%                   65%                    60%

* 24-hour data From CL, OBP Data: site reported and not yet monitored; as of 4/24/18

Data as of 24 Apr 2018

So now we have ...

• ... multiple randomized blinded renal denervation trials (OFF and ON meds) ...
• ... which are clearly positive
• The decrease of blood pressure is without any question clinically relevant
• But it is smaller than expected and hoped
• Everybody is asking “does this justify an invasive procedure?”
  - So better not to do it?
• At the same time, no major adverse events occurred!
  - So why not to do it?
• Everybody agrees that more research is needed

Other device based approaches

• Baroreceptor stimulation                           not catheter-based
• Carotid bulb expansion (Mobius)                   covered in this session
• Carotid body ablation                             stopped
• Pacemaker                                         not catheter-based
• Median nerve stimulation                          not catheter-based
• AV fistula (Rox Coupler)                          covered in this session

Thank you!

www.CSI-Congress.org