Verve’s Disruptive Non-vascular Catheter Option in Chronic Kidney Disease

RICHARD R. HEUSER, MD, FACC, FACP, FESC, FSCAI
Chief of Cardiology, St. Luke’s Medical Center,
Phoenix, Arizona
Professor of Medicine Univ. of Arizona,
College of Medicine, Phoenix, Arizona
Presenter Disclosure Information

Name: RICHARD R. HEUSER M.D.

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

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• Spectranetics, Abbott, Medtronic, Bard, Abiomed, Honorarium and
• Medtronic, Abbott, AngioScore, Speaker
• Acist Medical Systems Grant

**Patents** -- RF, Snares, Wires, Balloon Catheters, Covered Stents, Devices for Arterial Venous Connection, Devices for LV and RV Closure
26 million Americans have chronic kidney disease
CKD Patient Hypertension Profile

- Resistant to Drugs RHTN: 30%
- Drug Compliant: 15%
- Stop taking Drugs After 1st Year: 50%
- Untreated: 5%
Kidney Nerve Anatomy

Afferent nerves originate in the collecting system

Rotated view 30 degrees
Arterial Renal Denervation

- Vasoconstriction
- Vascular effects
- Other effects
- Renal afferent nerves
- Renal efferent nerves
- Hypertrophy
- Arrhythmia
- Oxygen Consumption
- Kidney injury / ischaemia
- ↑ Renin Release → RAAS activation
- ↑ Sodium Retention
- ↓ Renal Blood Flow
- ↑ Proteinuria
- ↑ Glomerulosclerosis
Verve’s Tusk Procedure

Diabetes/Sleep apnea

Kidney injury / ischaemia

Renal afferent nerves

Renal efferent nerves

Hypertrophy
Arrhythmia
Oxygen Consumption

↑ Renin Release → RAAS activation
↑ Sodium Retention
↓ Renal Blood Flow
↑ Proteinuria
↑ Glomerulosclerosis

ESRD PATIENTS
DIE FROM HF
Renal nerves in the pathogenesis of hypertension in experimental animals and humans

• These findings suggest that the afferent renal nerves contribute to the pathogenesis of renovascular hypertension by enhancing the activity of the sympathetic nervous system.
• The role of the afferent renal nerves in renovascular hypertension in humans warrants further study
WHAT HAPPENED?
Cardiologist Driven Procedure

Arterial Highway

Ureteral Off-Roading
<table>
<thead>
<tr>
<th>Proximal Renal Artery</th>
<th>Middle Renal Artery</th>
<th>Distal Renal Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>TH (Red) / CGRP (Green) ratio : 16.2±6.8</td>
<td>TH (Red) / CGRP (Green) ratio : 19.2±5.6</td>
<td>TH (Red) / CGRP (Green) ratio : 39.8±27.1</td>
</tr>
</tbody>
</table>

CGRP (Green) = Afferent Nerves = 10 % nerves per bundles
“In contrast to the widespread distribution of Efferent Sympathetic nerve fibers in the kidney, the majority of the Afferent Renal Sensory nerves are located in the renal pelvic area”

Kopp UC, University of Iowa. Neural Control of Renal Function 2011
Controlling Kidney Disease

TUSK

TransUreteral Sympathectomy of the Kidney

a novel device and a 15 minute outpatient procedure
Verve TUSK Procedure

• Minimally invasive “natural orifice” procedure
• Treating Physician - Urologist/ Interventional Nephrologist
• Standard equipment used by the Urologist
  – Monopolar RF generator
  – Cystoscope
  – .035 Guidewire
  – Fluoroscopic Imaging--- Retrograde pyelogram
• Short duration- total procedural time < 15 minutes
• Local or spinal anesthesia
• Outpatient or Office procedure
• Ablation of the afferent nerves located in the renal pelvis
TUSK Device
Procedure and product validation data

Pre-Clinical Animal Studies
50+ acute and chronic up to 90 days follow up

Clinical Trials
Safety Trial- 9 pre-nephrectomy patients
Efficacy Trial-4 resistant hypertensive patients
Efficacy Trial-1 ESRD dialysis patient
Clinical Trial
Clinical Trial
Safety

• Pre-nephrectomy
  9 patients

• Procedure - one month prior to surgery

• After procedure-Explanted kidney
  H&E and Immuno-histochemistry
Pelvis Wall
Pelvis wall, distal to ablation zone (Control)

Kidney explant 2, 63446L

Transitional epithelium
Lamina propria
Renal Pelvic Space

Smooth muscle

BV

Serosa

N

N

N

N
The nerves (N) are located within 1 mm of the pelvic space and adjacent to the treatment area.
Pelvis Wall - Ablation Zone

Renal pelvic space

Transitional epithelium

Lamina propria
Clinical study

Resistant hypertensive patient

Efficacy

• 4 patients resistant hypertension
• 2 or more drugs
• Ave BP 170/94 mmHg
• General Anesthesia
• 1 Mo Follow-up
# India Clinical Trial Results RHTN

## Baseline Systolic Blood Pressure

<table>
<thead>
<tr>
<th>Systolic Blood Pressure</th>
<th>Baseline</th>
<th>1 mo. post-tx.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>172</td>
<td>128</td>
</tr>
</tbody>
</table>

## Baseline Diastolic Blood Pressure

<table>
<thead>
<tr>
<th>Diastolic Blood Pressure</th>
<th>Baseline</th>
<th>1 mo. post-tx.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>94</td>
<td>81</td>
</tr>
</tbody>
</table>

### Significant Changes

- **Systolic Blood Pressure**: Baseline 172 mmHg decreased to 128 mmHg (44 mmHg reduction)
- **Diastolic Blood Pressure**: Baseline 94 mmHg decreased to 81 mmHg (13 mmHg reduction)
<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age</th>
<th>Sex</th>
<th>Procedure</th>
<th>Procedure Date</th>
<th>Nephrectomy Date</th>
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</thead>
<tbody>
<tr>
<td>68135</td>
<td>27</td>
<td>M</td>
<td>Left Ablation</td>
<td>1/21/2015</td>
<td>1/23/2015</td>
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<tr>
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<td>2/26/2015</td>
<td>4/2/2015</td>
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<td>4/1/2015</td>
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<td>F</td>
<td>Right Ablation</td>
<td>2/22/2015</td>
<td>3/25/2015</td>
</tr>
</tbody>
</table>
A 27 year old hypertensive Indian male presented with polycystic kidney disease and a large pelvic stone necessitating nephrectomy
THE SYSTOLIC BP DROPPED 24MMHG WITHIN 20 SECONDS AND WAS MAINTAINED AT THIS LEVEL UNTIL NEPHRECTOMY
• In the early stages of kidney disease, sympathetic activation is detectable being directly proportional to the severity of renal failure
The Double Challenge of Resistant Hypertension and Chronic Kidney Disease

42% of patients with CKD have resistant hypertension
The Renal Patient With Hypertension Falls into the Sweet Spot for Urologic/Nephrologic Medicine
Commercialization Potential

NEPHROLOGY

75% of resistant hypertensive patients are managed by nephrologists...only 12% by cardiologists
Verve TUSK Procedure ESRD Patient

Catholica University Hospital
Santiago, Chile

Patient Details:
Male
51 years old
5’8”
Co-morbidities:
ESRD
BP (mmHg): 174/105

Medications:
5 Drugs
2 Beta Blockers
3 Angiotensin Inhibitors

1. Pre-Pyelogram of Renal Pelvis
2. Catheter Distal Tip within Renal Pelvis
3. Post-Pyelogram of Renal Pelvis
4. Pig-Tail Stent Position within Renal Pelvis
The patient had a 10mmHg immediate BP drop in treating the 1st kidney and then there was some equilibration after treating the 2nd kidney???
AMBULATORY BP AFTER VERVE
BASELINE
2 MONTH

16MM MEAN
SBP DROP

DAY
173
105D
163 S
102D

NIGHT
175S
107D
157S
96D
HR

Baseline Day 69 2 Month Day 63

Night 74 Night 61
The mean ambulatory BP at 2 months dropped 16mmHg from the baseline ambulatory BP...This is very encouraging. More patients are in the queue.
PRE-VERVE TREATMENT

- Losartan
- Enalapril
- Carvedilol
- Cardura
- Concur
POST-VERVE TREATMENT

- Losartan
- Enalapril
- Carvedilol
- Cardura
- Concur
8ml/mm
Impact on Healthcare Cost

Treating and inhibiting the progression of CKD at Stage 3-4 with the TUSK procedure represents over a $33 Billion dollar annual savings to the US healthcare system. Not including Kidney Transplant Surgery.
Verve Clinical Trial Plan

• 14 patients ESRD
  • Status- Approved
  • Start Date- July 2016
  • Anticipated End Date- December 2016
  • Catholica University Hospital, Santiago, Chile

• 15 patients CKD/RHTN
  • Status- Approved ANMAT
  • Anticipated Start date- September 2016
  • Anticipated End Date- March 2016
  • University Hospital
  • University of Buenos Aires, Buenos Aires, Argentina
Renal Denervation in Chronic Kidney Disease: A Non-vascular Approach

**Conclusion**

Why are we different?

**Early Adaptation**
- Nephrologists understanding of the disease
- Urologist needs new procedures

**Technical Feasibility**
- Urologist has been using RF energy > 50 yrs

**Financial Burden**
- Outpatient/ Office setting
- Attractive to third world and developing countries

**CKD**
- Huge burden to the healthcare system with no treatment options
5th Annual Symposium

Cardiovascular Disease Management: A Case-Based Approach

Richard R. Heuser, MD, FACC
Program Director

October 5-6, 2017
Arizona Biltmore, Phoenix, Arizona

Nursing Symposium will take place
October 4, 2017 from 12:00 – 5:00 pm

SAVE THE DATE
For more information, please visit www.promedicacme.com
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