What Has Anatomy And Pathology Taught Us About Renal Denervation: Where Are The Nerves That Need To Be Destroyed And What Damage Can Radiofrequency Do To The Renal Artery

Renu Virmani, M.D.
CVPath Institute Inc.
Gaithersburg, MD, USA

Disclosures

I have nothing to disclose

Cumulative Distance From Nerves to Lumen

Distance from arterial lumen (mm)

Proposed Diagram of Renal Artery and Circumferential Peri-Arterial Nerve Location

Distribution and Density of Renal Sympathetic Nerves

Distribution of nerves stratified according to treated number (each green dot represents 10 nerves), relative number as percent per segment, and density from the known in previous publications (in green), and from data at location (in purple) prepared using raw data from Sakakura et al. (4), and have raw data provided by M. Joner, of CVPath Inc.
Distribution of Nerves in Accessory Renal Arteries

Mean Number Of Nerves Per Quadrant

<table>
<thead>
<tr>
<th>Nerve Size (µm)</th>
<th>Proximal</th>
<th>Middle</th>
<th>Distal</th>
<th>Post 1</th>
<th>Post 2</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>10</td>
<td>7</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>100-200</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>200-300</td>
<td>7</td>
<td>8</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>300-400</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 400</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Variation in Anatomy Among Human and Pig Renal Arteries

- About 70% of the population have a single renal artery.
- Accessory renal arteries are the most common variant, present in about 1/3 of the population.
- Prehilar (early) branching is a normal variant and present in about 10-20% of the population (32% on right RA, 25% on left RA, and 22% on both sides).

Assessment of Renal Nerves in a Healthy Swine Model

Nerve Size Distribution Along the Renal Artery in a Healthy Swine Model

- Mean nerve size: 85µm
- Number of large nerves (≥100 µm): 13
- Number of large nerves (≥300 µm): 4

The Percentage of Nerves Stratified by Distance from Lumen of Renal Artery

- Any nerves: 38% Proximal, 52% Middle, 62% Distal, 88% Post 1, 88% Post 2
- Any size: 32% Proximal, 58% Middle, 86% Distal, 99% Post 1, 96% Post 2

Mean number of nerves per artery (nerves divided by number of arteries in post bifurcation sections)

- Mean number of nerves (250 µm) within 2 mm per artery:
  - Prox: 4.8, Mid: 5.5, Dist: 6.8, Post 1: 4.0, Post 2: 3.5

The largest proportion of intermediate size nerves are found in the distal main renal artery close to the bifurcation.
Anatomy of Renal Sympathetic Nerves in a Healthy Swine Model

- Nerve size is greater in proximal than distal and post-bifurcation.
- Nerves are located close to the renal artery in distal and post-bifurcation compared to proximal segments.
- Nerves also branch at the site of bifurcation.

Summary

- Maximum number of Nerves are located close to the distal renal artery.
- The size of nerves diminishes from proximal to distal and post-bifurcation renal artery segments.
- Intermediate size nerves (≥50μm) are most frequently located within 2mm of the renal artery lumen in the distal and post-bifurcation segments.
- The maximum number of intermediate sized (>50μm) nerves are located within 2mm are in the distal main renal artery.
- Therefore, renal denervation should be performed in the distal main renal artery, with or without the middle or proximal renal arteries.

Acknowledgments

Funding
CVPath Institute Inc.
CVPath Institute
Kazuyuki Takagi, MD
Funayuki Otsuka, MD, PhD
Kenshi Sakakura, MD
Shana Leitch, MD
Robert Kutz, MS
Rupa Joshi
Ed Acampado, DVM
Youhu Liang, MD
Abebe Atiso, HT
Jinky Beyer
Giselle Magsalin
Hedwig Cipres, HT
Lila Adams, HT
Hengying Ouyang, MD
Frank D Kolodgie, PhD
Emory University - Aloke V. Finn, MD