Renal Denervation is a Tool in the Toolbox for Those Who Routinely Manage All Hypertension – The Case for IN

Alexander S. Yevzlin, MD
Associate Prof. of Medicine
Director of Interventional Nephrology
University of Wisconsin

Disclosure of Potential Conflicts
• Cytopherx, Inc.
• Bard Peripheral Vascular

Road Map
• Background
• The lesson from RAS experience
• The Nephrologists’ Perspective
• Conclusion

HYPERTENSION: GLOBAL BURDEN

WHO, Global Health Risks: Mortality and burden of Disease attributable to selected major risks, 2009

HYPERTENSION
THE KIDNEY’S ROLE IS ESSENTIAL

RENAL NERVE DENERVATION
• Historical - sympathectomy
• Anatomical location of nerves allows for endovascular access to achieve RDN.
• Endoluminal ablation techniques:
  – Radiofrequency ablation
  – Ultrasound
  – Injection of neurotoxin

RENAL AFFERENT NERVES
• Renal Injury
• Renal Ischemia

RENAL AFFECTEUR NERVES
• Renin Release
• RAAS activation
• Renal Blood Flow

RENAL EFFERENT NERVES
• Contractility
• Heart rate
• Hypertension, atherosclerosis

Media
Adventitia
Intima
Vasa vasorum
RAS Clinical Trials Failure

Several large randomized controlled trials (RCTs) have evaluated medical therapy versus PTRA.

The results of the STAR study showed no difference in progression of renal failure in patients with impaired renal function.

This has been confirmed by the results of the ASTRAL study.


Clinical Trials Update: CORAL

- Randomly assigned 947 participants who had atherosclerotic renal-artery stenosis and either systolic hypertension while taking two or more antihypertensive drugs or chronic kidney disease to medical therapy plus renal-artery stenting or medical therapy alone
- Followed for the occurrence of adverse cardiovascular and renal events

RAS Clinical Trials Failure

- RAS > 50% ≠ Ischemic Nephropathy (no fibrosis resulting from hemodynamic changes)
- Ischemic Nephropathy ≠ RAS > 50% (small vessel disease)

Clinical Trials Update: CORAL

- Over a median follow-up period of 43 months the rate of the primary composite end point did not differ significantly between participants who underwent stenting in addition to receiving medical therapy and those who received medical therapy alone (35.1% and 35.8%, respectively; hazard ratio with stenting, 0.94; 95% confidence interval [CI], 0.76 to 1.17; P=0.58).
- There were also no significant differences between the treatment groups in the rates of the individual components of the primary end point or in all-cause mortality.
- During follow-up, there was a consistent modest difference in systolic blood pressure favoring the stent group (-2.3 mm Hg; 95% CI, −4.4 to −0.2; P=0.03).
RESISTANT HTN – CLINICAL TRIALS

SYMPLICITY HTN-1
First-in-Man (AU)
Series of Pilot Studies (EU, US & AU)

SYMPLICITY HTN-2
First-in-Man (EU & AU)
Series of Pilot Studies (EU, US & AU)
Global SYMPLICITY Registry (Approved Regions)

SYMPLICITY HTN-3
US Pivotal Trial (US)

SYMPLICITY HTN-4
Pilot Studies in New Indications (Approved Regions)

SYMPLICITY HF
Pilot Studies in New Indications (Approved Regions)

Simplicity Htn-3

A possible explanation for the recent Denervation mess (just like the case of RAS) is that these studies included patients who had little chance to improve anyway

INCLUSION:
1. SBP > 160 mmHg (>150 mmHg in pts with type 2 diabetes)
2. Stable drug regimen with > 3 medications

EXCLUSION:
1. eGFR<45 mL/min/1.73m
2. Renal artery pathology: FMD, RAS or prior RA stenting
3. Renal anatomy: RA diameter<4mm, Accessory RA
4. Type 1 diabetes mellitus
5. MI, stroke or unstable angina within 6 months

The Neprologist’s Perspective

Ca channel blockers, nitrates, vasodilators
Centrally acting meds
Acetazolamide
Ace-i
Ace-i
HCTZ
Loops
K sparing
Ace-I, ARB

Conclusion

A recognized drawback of clinical treatment trials is the intermixture of high-risk and low-risk patients into the “average” of the entire cohort

“Refractory to appropriate HTN therapy” – needs to be rigorously defined

Nephrologists must contribute to the decision making regarding denervation therapy for HTN patients