Hypertension is one of the most prevalent diseases in the world and represents a major cardiovascular risk factor. About 30-40% of the adult population suffers from hypertension in developed countries.

Sympathetic nerves of the renal arteries play an important role in the development of high blood pressure. Both afferent and efferent nerves are responsible for stimuli that through different mechanisms result in an increase of sympathetic tone.

Renal Sympathetic Activation: Afferent Nerves

Kidney as Origin of Central Sympathetic Drive

- Vasoconstriction
- Atherosclerosis
- Hypertrophy
- Arrhythmia
- Oxygen Consumption
- Sleep Disturbances
- Insulin Resistance
- Renin Release → RAAS activation
- Sodium Retention
- Renal Blood Flow

Renal Nerve Anatomy

- Nerves arise from T10-L2
- The nerves arborize around the artery and primarily lie within the adventitia

Disclosures

- PATENTS IN BOLTON AND ST GEORGE
Renal Sympathetic Activation: Efferent Nerves

Kidney as Recipient of Sympathetic Signals

- Renal Efferent Nerves
  - Renin Release → RAAS activation
  - Sodium Retention
  - Renal Blood Flow

Resistant Hypertension

- Resistant hypertension has been defined as a failure to reach blood pressure targets despite a combination of three to four antihypertensive drugs from different drug classes (including a diuretic) at optimal dosages. The goal blood pressure is defined as < 140/90 mm Hg for the general population and < 130/80 mm Hg for those with diabetes mellitus or chronic kidney disease.

- The publication of data from the Symplicity HTN-1 trial in 2009 was a landmark event for patients with resistant hypertension. The trial reported on the first experience using the Symplicity renal denervation system (Medtronic, Inc., Minneapolis, MN).

- The 3-year results from the Symplicity HTN-1 clinical trial demonstrated that the significant decrease of systolic and diastolic pressures after renal denervation persisted after three years.

- The number of nerves increased along the length of the artery, with a total of 216 in the proximal section, 323 in the middle section, and 417 in the distal section. The increasing nerve counts along the length of the artery likely reflect an arborization pattern of the nerves according to one anatomic study.

- Recent results of the Symplicity III trial showed no significant difference between renal denervation and a sham operation.

Resistant Hypertension
Sympathetic Nerves

- The renal sympathetic nervous system was a therapeutic target for antihypertensive treatment decades ago, when surgical sympathectomy was the only option for patients with blood pressure that was difficult to control.
- Although effective, surgical targeting of renal sympathetic nerves lacked precision and resulted in collateral nerve damage, which led to orthostasis, bowel and bladder incontinence, and sexual dysfunction. This technique was abandoned.

Resistant Hypertension

- Prospective, randomized, multicenter study. Centers in Argentina and Brazil were included.
- Population: Resistant Hypertension in patients subjected to AAA repair or ABF bypass.
- Informed consent and authorization from the Ethical Committee of the Hospital.
- No Obese, Low risk patients, with resistant Hypertension with or without diabetes.

Sympathectomy: An Early Surgical Precedent

- Dr. Reginald H. Smithwick
- Photo of Dr. Smithwick reproduced with permission from JAMA.

Surgical Protocol

- 24 hrs ambulatory pressureometry before the procedure and after 3, 6, 9 and 12 months.
- Glucose tolerance test before the procedure and after 3, 6, 9 and 12 months.
- Na+ excretion in urine for 24 hrs before the procedure and after 3, 6, 9 and 12 months.
- After finishing the primary procedure, heparin was reversed and the initial 3 cm of both renal arteries were denuded resecting the tissue around the artery and the adventitia.
- Specimen were sent to pathology to study the presence of sympathetic nerves.
- Sympathetic nerves were found up to 1 cm from the adventitia.
Results:

- Nine patients with resistant hypertension reached 12 months after the treatment, five received surgical denervation and four were controls.
- Two patients were subjected to aorto-bifemoral bypass and seven AAA repair.
- Specimens of denervation showed nerves up to 1 cm of the adventitia.

ARROWS ARE NERVES
CROSSES ARE VESSELS
Results:

- Volume of urine produced during the initial 24 hrs varied between 6.4 liters and 10.2 liters in patients with renal denervation.
- Sodium excretion in urine in the initial 24 hrs increased in all denervated patients.
- Blood pressure decreased significantly in all denervated patients.
- Blood pressure didn’t change in the control group.
- All patients in the denervated group had the blood pressure controlled, three needed one drug.
- Glucose tolerance test improved in three of the five patients who had denervation.

Results:

- At 9 months, two denervated patients needed to increase the number and dose of drugs to control hypertension.
- At 12 months 100% of patients returned to the pre-operative status of uncontrollable hypertension with three or more drugs.

Conclusions:

- In this small observational group of patients with uncontrollable hypertension subjected to open renal denervation initial encouraged results lasted less than 12 months.
- Re-innervation could be an explanation.
- Small number of patients represents a limitation of this conclusion.