Catheter-Based Renal Artery Denervation

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Resistant hypertension:

Resistant hypertension is whereby (1) A patient cannot maintain BP values equal to or below 140/90 mmHg, even when taking three or more classes of antihypertensive drugs at their maximum tolerated dosages.[1,2] (2) One of the BP medications is a diuretic (removes fluid and salt from body).
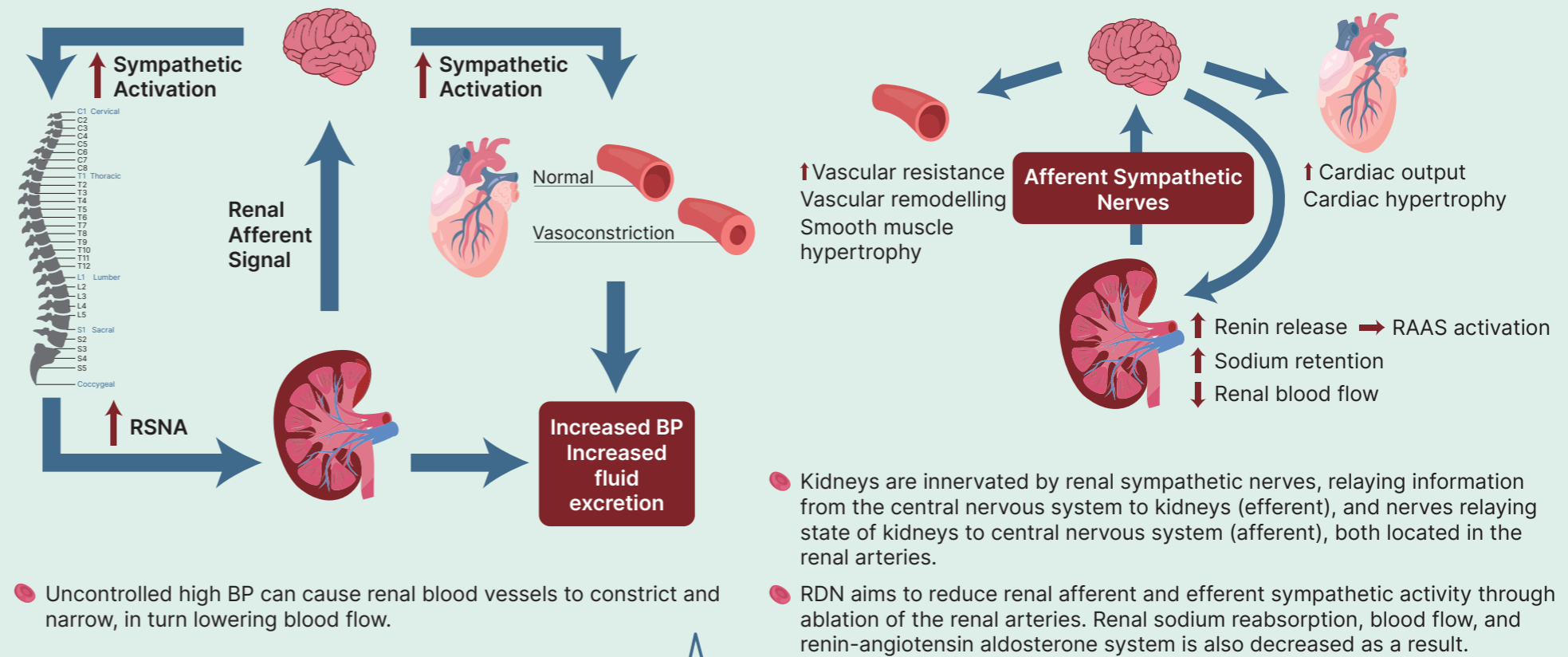
Treatment can be pharmacological, non-pharmacological, or interventional. Examples of common antihypertensive drugs include chlorthalidone, hydrochlorothiazide, and spironolactone.

Examples of interventional procedures include catheter-based RDN, baroreflex activation therapy, and arteriovenous shunts

Relationship between kidneys and hypertension:

↑ **Sympathetic Activation**

C1 Cervical, C2, C3, C4, C5, C6, C7, C8, T1 Thoracic, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12, L1 Lumbar, L2, L3, L4, L5, S1 Sacral, S2, S3, S4, S5, Coccygeal

Renal Afferent Signal

↑ **Sympathetic Activation**

Normal / Vasoconstriction

↑ **RSNA**

Increased BP Increased fluid excretion

↑ Vascular resistance
Vascular remodelling
Smooth muscle hypertrophy

Afferent Sympathetic Nerves

↑ Cardiac output
Cardiac hypertrophy

↑ Renin release ➡ RAAS activation
↑ Sodium retention
↓ Renal blood flow

- Uncontrolled high BP can cause renal blood vessels to constrict and narrow, in turn lowering blood flow.

- Kidneys are innervated by renal sympathetic nerves, relaying information from the central nervous system to kidneys (efferent), and nerves relaying state of kidneys to central nervous system (afferent), both located in the renal arteries.

- RDN aims to reduce renal afferent and efferent sympathetic activity through ablation of the renal arteries. Renal sodium reabsorption, blood flow, and renin-angiotensin aldosterone system is also decreased as a result.

What Is Catheter-Based Renal Artery Denervation? How Does It Work?

How it works:[4]

- Acts to reduce BP by decreasing efferent sympathetic signalling to kidneys, increasing renal blood flow, lowering plasma renin activity, and decreasing renal afferent signalling and central sympathetic activity.

- Small incision is made to the groin and catheter is inserted into the femoral artery.

- Catheter is guided to the renal arteries and the tip is inserted into the artery and rotated in a helical manner. Ultrasound or radiofrequency pulses then intentionally ablate the renal artery nerves.[5]

Advantages:

- ✓ Non-surgical, minimally invasive, and can be performed under local anaesthetic
- ✓ Significantly lowers BP without major adverse events in the long term
- ✓ Makes patients less reliant on antihypertensive drugs, potentially reducing adverse effects of those treatments and improving quality of life
- ✓ Effects seen in several clinical trials (e.g., Symplicity HTN-1 and Symplicity HTN-2)[6,7]

Renal catheter
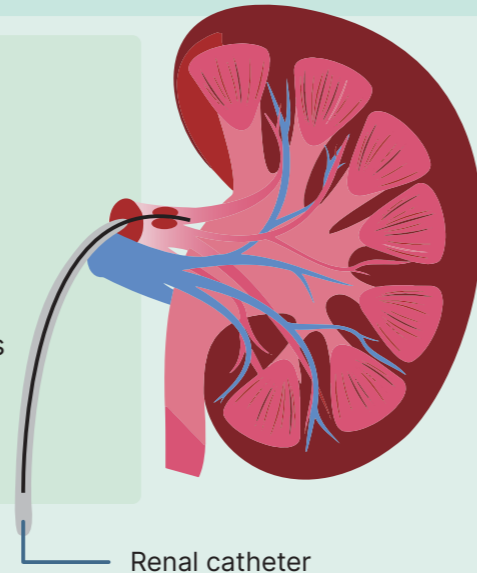
Disadvantages:

- ✗ Limited evidence: further research is needed to support the effectiveness and safety of the procedure
- ✗ Subsequent trials have thrown into question the efficacy of RDN (e.g., SYMPLICITY HTN-3 showed no significant reduction in systolic BP between RDN group and control group from baseline to 6 months). Trials like this have elevated scrutiny of the procedure, trial design, and patient selection
- ✗ Requires surgery, which carries risk (e.g., renal artery spasm, renal artery stenosis, dissection of the renal artery, haematoma in the groin)[8]
- ✗ Still not certain what profile of patient would best benefit from the procedure. Further large-scale, prospective, longitudinal RCTs to further investigate this[7]

The Future of RDN

Improve patient selection criteria: to better identify those that will benefit from the procedure. E.g., biomarkers or genetic profiling to better characterise the underlying mechanisms of hypertension and identify individuals with sympathetic nervous system overactivity

Targeted nerve ablation: to minimise off-target effects

Further research to **explore use of RDN in treating other conditions** caused by sympathetic overactivity, such as heart failure and arrythmias[8]

Resources:
1. British heart foundation (BHF). High blood pressure. 2023. Available at: https://www.bhf.org.uk/informationsupport/risk-factors/high-blood-pressure. Last accessed: 11 March 2024.
2. Johns Hopkins Medicine. Resistant hypertension. Available at: https://www.hopkinsmedicine.org/health/conditions-and-diseases/high-blood-pressure-hypertension/resistant-hypertension. Last accessed: 11 March 2024.
3. Acelajado MC et al. Treatment of resistant and refractory hypertension. Circ Res. 2019;124(7):1061-70.
4. Witowski A et al. Catheter-based renal denervation. E-Journal of Cardiology Practice. 2012;10(22).
5. Penn Medicine. Renal denervation. Available at: https://www.pennmedicine.org/for-patients-and-visitors/find-a-program-or-service/heart-and-vascular/interventional-cardiology/peripheral-interventions/renal-denervation. Last accessed: 11 March 2024.
6. Mountfort K et al. Catheter-based renal sympathetic denervation – long-term simplicity renal denervation clinical evidence, new data and future perspectives. Interv Cardiol. 2013;8(2):118-23.
7. Ionov MV et al. Truth is born in disputes: the pros and cons of renal denervation. E-Journal of Cardiology Practice. 2022;22(1).
8. Olsen LK et al. Renal denervation. Eur J Intern Med. 2015;26(2):95-105.