HYPERTENSION

Renewed hopes for renal denervation in hypertension

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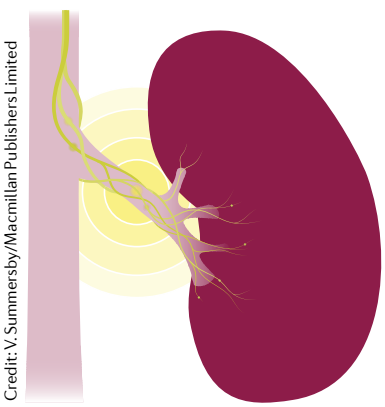
Two new clinical trials on catheter-based renal denervation targeting the sympathetic nervous system show that this approach significantly reduces systolic blood pressure (BP) among patients with uncontrolled hypertension taking antihypertensive medication and also among those not taking antihypertensive drugs. These randomized, sham-controlled trials tested different devices and ablation techniques in different patient populations. "These trials finally provide biological proof of principle of the BP-lowering effect of renal denervation in the absence but also in the presence of antihypertensive medication," remarks Felix Mahfoud, who was involved in both trials. The SPYRAL HTN-ON MED and RADIANCE SOLO trials were presented at EuroPCR 2018 in Paris, France, and published simultaneously in *The Lancet*.

The proof-of-principle SPYRAL HTN-ON MED study was designed to assess the effect of renal denervation in the presence of antihypertensive drugs. Patients with moderate, uncontrolled hypertension (office systolic BP 150–180 mmHg and diastolic BP ≥90 mmHg; 24-h ambulatory systolic BP 140–170 mmHg) who were taking one to three antihypertensive drugs were randomly assigned to undergo renal denervation ($n = 38$) or a sham control procedure ($n = 42$). Renal denervation was performed with radiofrequency ablation applied to the main renal arteries and branches. At 6 months, patients treated with renal denervation had significantly greater reductions from baseline in office and 24-h ambulatory systolic and diastolic BP (the primary end point) compared with patients in the sham group (office systolic BP difference −6.8 mmHg, office diastolic BP difference −3.5 mmHg, 24-h systolic BP difference −7.4 mmHg, and 24-h diastolic BP difference −4.1 mmHg). The BP reduction with renal denervation was progressive over the 6 months of follow-up, and the BP reductions were consistent throughout the day.



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The SPYRAL HTN-ON MED study included assessment of medication adherence, revealing that medication nonadherence was common among the study cohort. "Half of patients become nonadherent to the treatment in the first year after initiation of medications, and about 20% are completely nonadherent to medication," explains Mahfoud. "Device-based clinical trials have reinforced previous findings showing that adherence gets worse with increasing number of antihypertensive medications a patient is taking," he points out.

The RADIANCE SOLO study assessed the BP-lowering effect of renal denervation with a new, ultrasound catheter in the absence of antihypertensive medications. Patients with systolic–diastolic hypertension (off-medication daytime ambulatory systolic BP 135–170 mmHg and diastolic BP 85–105 mmHg) were randomly assigned to renal denervation ($n = 74$) or a sham procedure ($n = 72$) after a 4-week discontinuation of antihypertensive medication. All patients remained off antihypertensive medications throughout the study follow-up. At 2 months, the renal denervation group had a greater reduction in daytime ambulatory systolic BP (the primary efficacy end point) than the sham control group (−8.5 mmHg versus −2.2 mmHg).

No major adverse events were reported in any group in either of the trials. The finding of these studies confirm the results of the previous SPYRAL HTN-OFF MED trial, showing that catheter-based renal denervation with ultrasound or radiofrequency ablation is safe and is associated with BP lowering both in the presence and in the absence of antihypertensive medication. "These data are very important for the field and significantly enhance our understanding of renal denervation," says Mahfoud. "Follow-up, pivotal studies are currently ongoing," he explains, "until then, renal denervation in hypertension remains investigational."

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ORIGINAL ARTICLES Kandzari, D. E. et al. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. *Lancet* https://doi.org/10.1016/S0140-6736(18)30951-6 (2018) | Azizi, M. et al. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomised, sham-controlled trial. *Lancet* https://doi.org/10.1016/S0140-6736(18)31082-1 (2018)
FURTHER READING Gulati, R. et al. The rise, fall, and possible resurrection of renal denervation. *Nat. Rev. Cardiol.* **13**, 238–244 (2016)