



## Renal denervation in South Africa

**To the Editor:** Renal denervation (RD) is a minimally invasive therapy aimed primarily at hypertension.<sup>[1]</sup> The procedure involves modification of the renal sympathetic nerve supply, which courses around the renal arteries. Access to the renal arteries is obtained via peripheral vessels (femoral, radial or brachial artery), and radiofrequency energy is applied to the arterial wall.<sup>[2]</sup> After proof-of-concept studies in animals and humans, the SYMPPLICITY HTN-2 trial demonstrated a significant blood pressure reduction in patients with resistant hypertension, compared with pharmacological management.<sup>[3]</sup> Surprisingly, RD was not found to be more effective than a sham procedure for resistant hypertension in the SYMPPLICITY HTN-3 trial.<sup>[4]</sup> This trial, however, was subject to significant limitations, including the inability to monitor treatment adherence and changes of pharmacotherapy during the trial, as well as variation in the extent of RD performed in individual patients. Three sham-controlled trials have been published since, addressing many of the shortcomings of SYMPPLICITY HTN-3. The SPYRAL-HTN-OFF MED trial<sup>[5]</sup> was designed to control for differences in between-group pharmacotherapy, and blood pressure at 3 months' follow-up was significantly lower in the RD group than in the sham procedure group. In the SPYRAL-HTN-ON MED trial,<sup>[6]</sup> pharmacotherapy was continued, and blood pressure control was also improved in RD recipients. In the endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO) trial,<sup>[7]</sup> RD was more effective in decreasing blood pressure than a sham procedure.

The latter three trials have provided compelling new evidence for RD efficacy, with few major complications. By correcting for the confounders of the SYMPPLICITY-HTN-3 trial, the SPYRAL-HTN-OFF MED, SPYRAL HTN-ON MED and RADIANCE-HTN SOLO trials have provided substantial evidence in favour of RD, expanding its scope to patients who do not suffer from resistant hypertension. In preclinical and clinical models, RD has demonstrated benefits beyond blood pressure reduction, e.g. attenuation of adverse left ventricular remodelling and improvement in left ventricular systolic function, which have led to the investigation of RD for applications other than hypertension treatment, e.g. the prevention of atrial fibrillation.<sup>[8]</sup>

RD has not become widespread as a treatment option for hypertension in South Africa (SA). All RD therapy is currently provided in the private sector. The South African Heart Association and the Southern African Hypertension Society released a consensus statement regarding RD in 2014,<sup>[9]</sup> which recommends that it only be performed as part of prospective studies or registries. Although these recommendations were written before the SPYRAL-HTN-OFF MED, SPYRAL HTN-ON MED and RADIANCE-HTN SOLO trials were published, they allow for patients with resistant hypertension to be referred to centres of expertise for possible inclusion in a

trial or a clinical registry. In a recent study of more than 10 000 individuals in sub-Saharan Africa,<sup>[10]</sup> SA had the highest prevalence of hypertension, with a high degree of uncontrolled blood pressure (55.4% women, 68.1% men) in the study sites. Given the substantial healthcare burden of hypertension in SA and the latest evidence base, the time has come to review the local recommendations and allow RD technology to penetrate the SA healthcare system. This will only be achieved by a co-ordinated effort between healthcare providers, funders and regulators.

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1. Heradien M, Mahfoud F, Hettrick D, Brink P. Renal denervation: Dark past, bright future? *Cardiovasc J Afr* 2019;30(5):290-296. <https://doi.org/10.5830/CVJA-2019-045>
2. Heradien MJ, Augustyn J, Saaman A, Brink PA. First reported cases: Renal denervation with second-generation multi-electrode catheter via brachial and radial access. *Cardiovasc J Afr* 2016;27(1):53-55. <https://doi.org/10.5830/CVJA-2015-089>
3. Esler MD, Krum H, Sobotka PA, Schlaich MP, Schmieder RE, Böhm M. Renal sympathetic denervation in patients with treatment-resistant hypertension (the Symplicity HTN-2 Trial): A randomised controlled trial. *Lancet* 2010;376(9756):1903-1909. [https://doi.org/10.1016/S0140-6736\(10\)62039-9](https://doi.org/10.1016/S0140-6736(10)62039-9)
4. Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med* 2014;370(15):1393-1401. <https://doi.org/10.1056/NEJMoa1402670>
5. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): A randomised, sham-controlled, proof-of-concept trial. *Lancet* 2017;390(10108):2160-2170. [https://doi.org/10.1016/S0140-6736\(17\)32281-X](https://doi.org/10.1016/S0140-6736(17)32281-X)
6. Kandzari DE, Böhm M, Mahfoud F, 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* 2018;391(10137):2346-2355. [https://doi.org/10.1016/S0140-6736\(18\)30951-6](https://doi.org/10.1016/S0140-6736(18)30951-6)
7. Azzizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): A multicentre, international, single-blind, randomised, sham-controlled trial. *Lancet* 2018;391(10137):2335-2345. [https://doi.org/10.1016/S0140-6736\(18\)31082-1](https://doi.org/10.1016/S0140-6736(18)31082-1)
8. Heradien MJ, Mahfoud F, Greying CJ, et al. Renal denervation prevents atrial fibrillation and reduces cardiovascular death in patients with hypertensive heart disease. Presented at EuroPCR 2019, Paris, France, 21 - 24 May 2019. <https://www.pconline.com/Cases-resources-images/Resources/Course-videos-slides/2019/Innovative-First-in-Man-trials-and-early-phase-studies> (accessed 5 January 2020).
9. Seedat YK, Rayner BL, Veriava Y. South African hypertension practice guideline 2014. *Cardiovasc J Afr* 2014;25(6):288-294. <https://doi.org/10.5830/CVJA-2014-062>
10. Gomez-Olive FX, Ali SA, Made F, et al. Regional and sex differences in the prevalence and awareness of hypertension: An H3Africa AWI-Gen study across 6 sites in sub-Saharan Africa. *Glob Heart* 2017;12(2):81-90. <https://doi.org/10.1016/j.gheart.2017.01.007>

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