BIHS Statement on Renal Denervation (RDN) following publication of the NICE Interventional Procedures Guidance IPG754: Percutaneous transluminal renal sympathetic denervation for resistant hypertension. 1st March 2023.
www.nice.org.uk/guidance/ipg754

Dr Wayne Sunman, Professor Peter Sever, Professor Adrian Brady, Professor Neil Poulter, Dr Philip Lewis, Dr Sarah Partridge, Dr Luca Faconti, Dr Spoorthy Kulkarni, and Professor Ian Wilkinson, on behalf of the British and Irish Hypertension Society Guidelines Standing Committee.

10th May 2023

The NICE Interventional Procedures Guidance IPG754 recommends that "*percutaneous transluminal renal sympathetic denervation for resistant hypertension should only be used with special arrangements for clinical governance, consent and audit or research*".

The BIHS supports the NICE guidance IPG754 in that RDN may have a role in the management of resistant hypertension when all other therapeutic avenues have been exhausted and the patient fully understands the limitations of the procedure and the unpredictability of the effect on blood pressure lowering. However, the BIHS wishes to draw attention to the following issues: first, the evidence for the use of RDN is weak and inconsistent; second, at best, RDN produces a small reduction in blood pressure (on average about 5mmHg systolic); third the long-term effects of the procedure are unclear; fourth there is minimal evidence comparing the efficacy of different techniques and devices.

The BIHS notes that the NICE recommendations are based on the expert review of a small body of evidence including 1 Cochrane review, 1 meta-analysis, 3 randomised controlled trials, 1 three-arm randomised trial, 4 case series (registries) and confidential documentation provided by a company. It is the view of the BIHS that unpublished data from a party with a vested interest should be viewed with caution due to the high risk of bias. Second, the BIHS notes that only 3 randomised trials were of sufficient quality to evaluate efficacy, and when considered together the results are not conclusive (Azizi 2022, Bhatt 2022, Kario 2022). The available evidence suggests RDN is safe in the short term, with renal artery damage (>50% diameter stenosis and dissection) being reported in 0.45% of patients within 6 months (Townsend 2020). The view of the BIHS is that the benefits of RDN have not yet been reliably demonstrated and well-designed trials to determine long term outcomes are essential. Furthermore, the BIHS recommends that all RDN procedures are registered to enable long term follow-up of patients, procedures and outcomes.

The NICE guidance notes that there are different techniques to achieve RDN, including radiofrequency and ultrasound, and acknowledge that different devices may have different efficacy and safety profiles.

The BIHS wish to draw attention to one 3-way randomised trial comparing radiofrequency ablation of the main artery only, the main and branch arteries and ultrasound ablation (Fengler 2019). In this trial, ultrasound was associated with the greatest reduction in blood pressure. However, this single trial serves to highlight the minimal evidence comparing

different devices and techniques used to achieve RDN which is compounded by the market dominance of the radiofrequency ablation device companies. It is the view of the BIHS that further work in this area is needed.

NICE recommends that for individuals with resistant hypertension, additional medications and device-based antihypertensive therapies (including RDN and carotid baroreceptor stimulation) may be considered. NICE defines resistant hypertension as blood pressure that is not controlled after treatment with at least 3 antihypertensive medications from different classes.

It is the view of the BIHS that due to the limited evidence for the benefit of RDN more stringent criteria should be used to define resistant hypertension in an individual that is being considered for RDN, to avoid diagnostic error. The BIHS recommend that patients being considered for RDN should meet all of the following criteria:

1. Blood Pressure above target.
2. Evidence for exclusion of secondary causes of hypertension, including hyperaldosteronism.
3. Treatment with at least 3 antihypertensive agents at maximum tolerated doses, from different therapeutic classes, one of which should be a thiazide-like diuretic. Spironolactone should be considered as a 4th line agent (PATHWAY-2).
4. Evidence of medication concordance by urinary analysis or direct observation.
5. Evaluation of current and previous blood pressure management by an independent hypertension specialist to ensure all therapeutic options have been considered.

References

Azizi M, Mahfoud F, Weber MA, et al. Effects of Renal Denervation vs Sham in Resistant Hypertension After Medication Escalation: Prespecified Analysis at 6 Months of the RADIANCE-HTN TRIO Randomized Clinical Trial. JAMA Cardiol. 2022;7(12):1244–1252. doi:10.1001/jamacardio.2022.3904

Bhatt DL, Vaduganathan M, Kandzari DE, Leon MB, Rocha-Singh K, Townsend RR, Katzen BT, Oparil S, Brar S, DeBruin V, Fahy M, Bakris GL; SYMPLICITY HTN-3 Steering Committee Investigators. Long-term outcomes after catheter-based renal artery denervation for resistant hypertension: final follow-up of the randomised SYMPLICITY HTN-3 Trial. Lancet. 2022 Oct 22;400(10361):1405-1416. doi: 10.1016/S0140-6736(22)01787-1. Epub 2022 Sep 18. PMID: 36130612.

Kario K, Yokoi Y, Okamura K, Fujihara M, Ogoyama Y, Yamamoto E, Urata H, Cho JM, Kim CJ, Choi SH, Shinohara K, Mukai Y, Ikemoto T, Nakamura M, Seki S, Matoba S, Shibata Y, Sugawara S, Yumoto K, Tamura K, Yoshihara F, Nakamura S, Kang WC, Shibasaki T, Dote K, Yokoi H, Matsuo A, Fujita H, Takahashi T, Kang HJ, Sakata Y, Horie K, Inoue N, Sasaki KI, Ueno T, Tomita H, Morino Y, Nojima Y, Kim CJ, Matsumoto T, Kai H, Nanto S. Catheter-based ultrasound renal denervation in patients with resistant hypertension: the randomized,

controlled REQUIRE trial. Hypertens Res. 2022 Feb;45(2):221-231. doi: 10.1038/s41440-021-00754-7. Epub 2021 Oct 15. PMID: 34654905; PMCID: PMC8766280.

Townsend RR, Walton A, Hettrick DA, Hickey GL, Weil J, Sharp ASP, Blankestijn PJ, Böhm M, Mancia G. Review and meta-analysis of renal artery damage following percutaneous renal denervation with radiofrequency renal artery ablation. EuroIntervention. 2020 May 20;16(1):89-96. doi: 10.4244/EIJ-D-19-00902. PMID: 32038027.

Fengler K, Rommel KP, Blazek S, Besler C, Hartung P, von Roeder M, Petzold M, Winkler S, Höllriegel R, Desch S, Thiele H, Lurz P. A Three-Arm Randomized Trial of Different Renal Denervation Devices and Techniques in Patients With Resistant Hypertension (RADIOSOUND-HTN). Circulation. 2019 Jan 29;139(5):590-600. doi: 10.1161/CIRCULATIONAHA.118.037654. PMID: 30586691.

Williams B, MacDonald TM, Morant S, Webb DJ, Sever P, McInnes G, Ford I, Cruickshank JK, Caulfield MJ, Salsbury J, Mackenzie I, Padmanabhan S, Brown MJ; British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet. 2015 Nov 21;386(10008):2059-2068. doi: 10.1016/S0140-6736(15)00257-3. Epub 2015 Sep 20. PMID: 26414968; PMCID: PMC4655321.