REVIEW ARTICLE

# Modern Device-based Renal Denervation Approach for the Management of Uncontrolled Hypertension

Arun Gopi[1], Sarita Rao[2*], Nakul Sinha[3], Nihar Mehta[4], Milind Nadkar[5], Mangesh Tiwaskar[6]

*Received:* 07 February 2025; *Accepted:* 24 November 2025

## Abstract

Uncontrolled hypertension can result from untreated high blood pressure (BP) or the inefficacy of established antihypertensive therapeutic regimens. Renal denervation (RDN) is a nonpharmacologic catheter-based intervention that achieves targeted renal sympathetic nerve ablation to modulate sympathetic activation. RDN is suitable for those with uncontrolled primary hypertension, resistant to therapy or intolerant to drugs, and who have a favorable renal artery anatomy. Long-term data demonstrate RDN's efficacy in significantly reducing elevated BP. RDN procedures have shown a good safety profile, and no significant difference in adverse events has been reported between RDN-treated and control groups in most clinical trials. Thus, RDN offers an effective and safe approach for sustained BP control.

*Journal of The Association of Physicians of India* (2026): 10.59556/japi.74.1468

## Introduction

Hypertension [systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg] is a leading cause of premature mortality. Hypertension prevalence has doubled from 1990 to 2019.[1] Hypertension management involves a combination of pharmacologic and nonpharmacologic approaches tailored to individual patient needs. In 2019, less than half of the individuals diagnosed with hypertension received treatment, and less than half of those who underwent pharmacological treatment achieved control of hypertension, translating to global control rates equal to 23% in women and 18% in men.[1] The main reasons for such poor control are low patient adherence to treatment and lack of proactive clinical management by healthcare providers.[2] Hypertension can be termed uncontrolled when the current treatment plan is ineffective, i.e., when the brachial SBP/DBP remains above the target values (140/90 mm Hg) even with the use of at least three different antihypertensive drugs (including diuretics).[3] Uncontrolled and untreated hypertension is of concern, as it leads to cardiovascular (CV) morbidity and mortality due to the occurrence of peripheral arterial disease, ischemic heart disease, stroke, congestive heart failure, renal disease, and aortic aneurysm.[4]

While pharmacological treatments are essential for managing hypertension, modern device-based approaches offer complementary dimensions to address the challenges in controlling elevated blood pressure (BP) effectively. In essential hypertension, sympathetic nervous system activity varies in terms of severity and complications. Research indicates that overactivation of the sympathetic nervous system occurs in all stages of hypertension.[5] Renal denervation (or RDN) is a nonpharmacologic catheter-based intervention that modulates the activity of the sympathetic nervous system by ablating renal sympathetic nerves in a targeted fashion. RDN can benefit patients with uncontrolled hypertension undergoing pharmacologic and nonpharmacologic antihypertensive therapy. A meta-analysis demonstrated significant reductions in office and/or ambulatory SBP in those ($N$ = 1368) with resistant/untreated hypertension managed by RDN.[6] Recent data on the long-term safety and efficacy of RDN have shown that it successfully decreases BP and may lower the risk of CV and/or renal events for up to 36 months after the intervention.[7]

While RDN is a promising antihypertensive therapy, uncertainties remain about optimal patient selection and its long-term effectiveness. This review aims to collate evidence on RDN, addressing its long-term outcomes, safety profile, and criteria for patient selection in the management of uncontrolled hypertension.

## Mechanism of Renal Denervation

Renal arteries have dense innervation with afferent and efferent sympathetic nerve fibers. Activation of afferent fibers increases central sympathetic activity and norepinephrine spillover, while overactivity of efferent fibers promotes sodium reabsorption, increases renin release, and decreases renal blood flow, thus raising BP. RDN helps control BP by reducing efferent signaling, norepinephrine spillover, and plasma renin activity; restoring natriuresis; and decreasing afferent signaling.[8] Figure 1 illustrates the mechanism of RDN, highlighting the afferent and efferent renal nerves and ablation targets.

### Preprocedural Evaluation and Patient Selection

Preprocedural evaluation typically involves a comprehensive assessment, including baseline BP, renal function [estimated glomerular filtration rate (eGFR)], renal artery anatomy, and secondary hypertension to ensure that the patient meets the eligibility criteria for the procedure. Since sympathetic nervous system activity increases with age, age is also a factor during patient selection.[9]

Evidence indicates that RDN may benefit patients with severe primary hypertension, irrespective of medication, though the characteristics of an ideal candidate are still being explored.[10] The data suggest that the reduction in BP following RDN is more significant for those with higher baseline SBPs.[10,11]

Renal artery anatomy, including size, tortuosity, and branching, is critical for RDN success and is assessed using imaging modalities such as renal or computed tomography angiography

[1]Director, Cath Lab and Senior Consultant Interventional Cardiologist and Electrophysiologist, Metromed International Cardiac Centre, Kozhikode, Kerala; [2]Interventional Cardiologist, Apollo Hospital, Indore, Madhya Pradesh; [3]Interventional Cardiologist, Sahara Hospital, Lucknow, Uttar Pradesh; [4]Interventional Cardiologist, Jaslok Hospital; [5]Professor and Head, Department of Medicine, KEM Hospital and Seth GS Medical College; [6]Consultant Physician and Diabetologist, Shilpa Medical Research Centre, Mumbai, Maharashtra, India; *Corresponding Author

**How to cite this article:** Gopi A, Rao S, Sinha N, *et al.* Modern Device-based Renal Denervation Approach for the Management of Uncontrolled Hypertension. J Assoc Physicians India 2026;74(4):96–102.

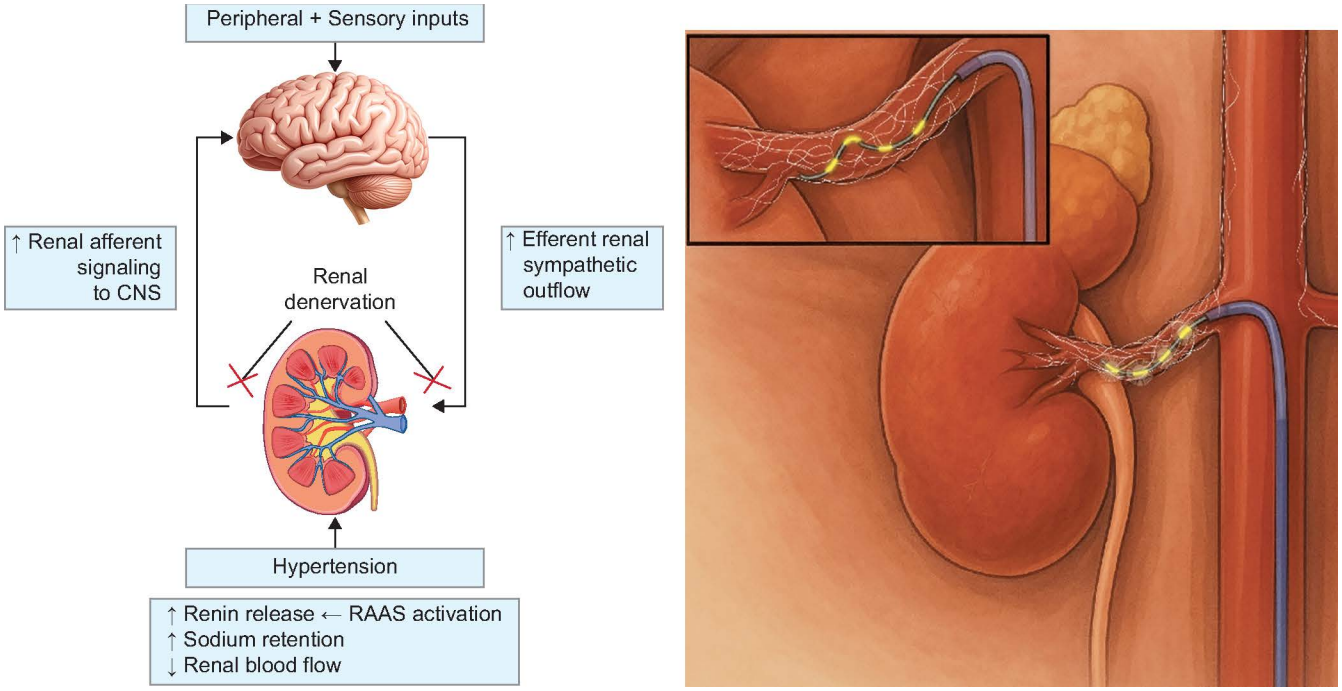


**Fig. 1:** Representation of the mechanism of action of RDN (CNS, central nervous system; RAAS, renin–angiotensin–aldosterone system)

during preevaluation.[12] Clinical trials for RDN require patients to have a renal artery diameter of 3.0–8.0 mm (with or without accessory arteries). However, studies suggest that accessory renal arteries may have more renal nerve fibers than the main artery; therefore, targeting them during RDN could enhance the procedure's effectiveness.[13,14]

### *Patient Selection*

Renal denervation is primarily opted for patients with (1) inability/difficulty in controlling BP despite using multiple antihypertensive medications, (2) decreased adherence to treatment as the number of medications increases, and (3) low motivation, which is shaped by the perceived risks of hypertension, adverse medication effects, and intolerance to antihypertensive drugs.[3,15,16] Figure 2 presents the patient selection criteria provided by guidelines and relevant medical societies.[3,17–19]

### *Procedural Considerations and Optimization*

Procedural optimization techniques include ablation of the main and accessory renal arteries and their branches, circumferential ablation, and an appropriate number of total ablations.[18] The primary efficacy goal of RDN is to maximize nerve destruction for lowering BP while ensuring arterial integrity, avoiding collateral damage, and minimizing procedure time and contrast volume.[20] Factors to be considered during the optimization of RDN, in addition to factors specific to the use of radiofrequency, have been discussed below and in Figure 2.

*Number of Ablations*: Analysis of the SIMPLICITY HTN-3 trial data (*post hoc*; *N* = 340) showed that those receiving 12–13 ablations of the renal artery with energy delivery in a pattern with four-quadrants were associated with higher and more consistent reductions in measures such as office/ambulatory SBP and heart rate than those receiving <8 ablations.[21]

*Ablation Pattern*: The ablation pattern in RDN refers to the distribution of thermal/radiofrequency energy applied to the renal sympathetic nerves during the procedure. The goal of ablation is to disrupt the sympathetic nerves within the renal arteries' adventitia, mostly in the adipose tissue surrounding the artery, while minimizing damage to the proximal endoluminal surface and external elastic lamina.

*Ablation of the Distal Branch*: Since renal sympathetic nerves are nearer the renal artery lumen, distal denervation is likely to disrupt more sympathetic nerves than proximal denervation, ensuring a consistent treatment effect.[22] A single-center, double-blind study (*N* = 51) found RDN more effective in reducing office and 24-hour ambulatory BP (ABP) when distal segmental branches were ablated than when the trunk of the renal artery was targeted.[23]

*Ablation of Accessory Arteries*: A comprehensive RDN approach involves denervation of the main and branch/accessory renal arteries to ensure thorough disruption of sympathetic nerve activity and improve BP management.

## Postprocedure Assessment

### *Assessment of BP at Follow-up*

The time taken for an apparent BP response could vary from a few days to several weeks. Unlike antihypertensive medications, RDN produces an "always on" effect, suggesting the relevance of measuring BP over 24 hours.[24] However, combinations of ABP measurements, such as baseline nighttime SBP and its variability, should be considered, given that variations in the levels of physical activity and sleep duration may impact ABP readings.[25] To assess early RDN response, a 3–6 months follow-up for office BP and ABP is needed, and annual ABP and home and office BP measurements should be monitored for long-term response.[18] The SIMPLICITY HTN-3 and SPYRAL HTN-ON trials demonstrated that after RDN, reductions in office BP at 6 months and 24-hour ABP at 36 months were significant.[13,26]

### *Assessment of Renal Function*

Renal denervation may lead to decreased kidney function or a transient drop in the eGFR due to hemodynamic changes from rapid BP reduction. However, a meta-analysis using mean follow-up data at 9.1 months demonstrated no significant changes in

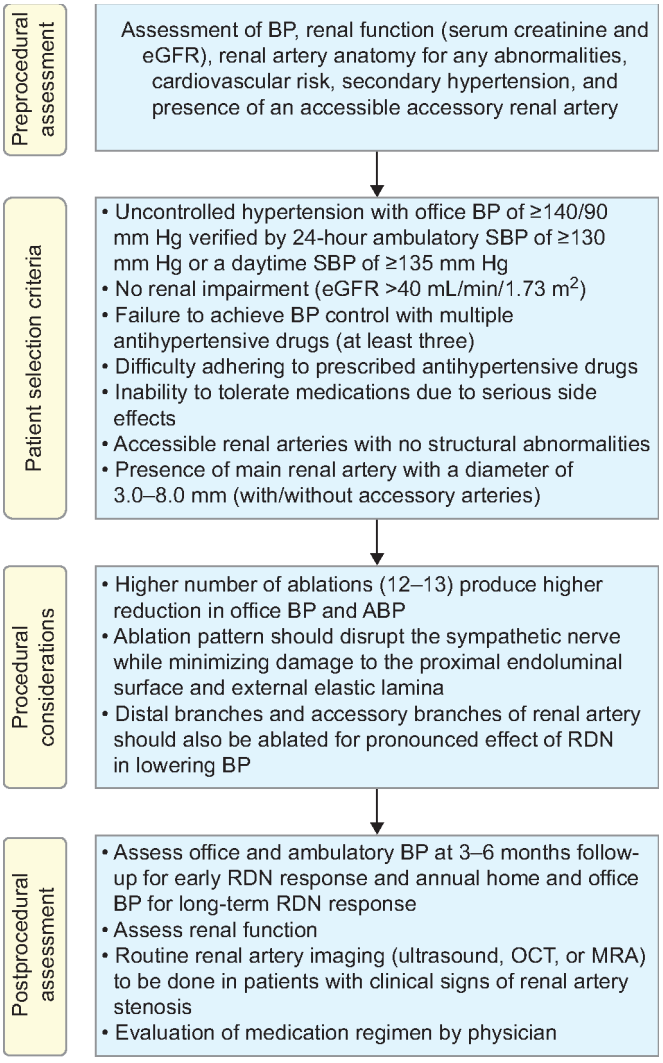


**Fig. 2:** Flowchart depicting the preprocedural assessment, patient selection criteria, procedural considerations, and postprocedural assessment to be considered for RDN treatment. (MRA, magnetic resonance angiography; OCT, optical coherence tomography; RDN, renal denervation.)

renal function parameters (eGFRs and serum creatinine levels).[27]

### *Renal Artery Imaging*

Renal artery injury, leading to stenosis, dissection, or access site complications, is possible. Routine imaging (ultrasound, optical coherence tomography, or magnetic resonance angiography) should only be done if clinical signs of renal artery stenosis, such as worsening hypertension or renal function, are present.[18]

## Clinical Evidence on Renal Denervation

### Efficacy

So far, five randomized and sham-controlled studies, namely the SYMPLICITY HTN-3 trial,[28] RADIANCE-HTN SOLO trial,[29] proof-of-concept SPYRAL HTN-ON MED trial,[13] SPYRAL HTN-OFF MED pivotal trial,[30] and RADIANCE-HTN TRIO trial,[31] have assessed the utility of RDN in lowering BP (Table 1). Some studies reported significantly higher reductions in BP after RDN (compared with those in sham control groups) at follow-ups of 2–36 months, while others reported nonsignificant results at 3–6 months. The follow-up data (36 months) from the SPYRAL HTN-ON MED trial have demonstrated that RDN can reduce ambulatory SBP by 18.7 mm Hg compared with 8.6 mm Hg.[33]

The SYMPLICITY HTN-3 trial data on the long-term effects of RDN demonstrated that RDN can significantly reduce office SBP (by 26.4 mm Hg, as compared to the 5.7 mm Hg reduction with a sham control) at the 36-month follow-up.[26] Three-year data from the Global SIMPLICITY Registry (GSR) demonstrated that in-office SBP was lowered by 16.5 mm Hg from baseline after RDN.[34] A study of the 10-year outcomes of RDN in those with resistant hypertension ($N = 107$) showed that the reductions in 24-hour SBP readings (–16.2 mm Hg) were maintained for as long as 10 years after the intervention.[35]

Renal denervation also reduces incidences of major adverse cardiovascular events (MACE). A study based on GSR data ($N = 3,077$ as of March 2022) reported that a 10% increase in the time within therapeutic range for 6 months after RDN was associated with significant reductions in MACE (15%, $p < 0.001$), CV death (11%, $p = 0.010$), stroke (23%, $p < 0.001$), and myocardial infarction (15%, $p = 0.023$) from 6 to 36 months.[36] Overall, RDN is effective in controlling BP, with positive outcomes observed across both radiofrequency and ultrasound-based designs. These findings highlight the robustness of RDN as a therapeutic approach, regardless of the specific technology used in reducing office BP and ABP.

### Safety

Most clinical trials demonstrated no significant differences in the occurrence of AEs between RDN and control groups (Table 2). The GSR study reported relatively lower rates of myocardial infarction (2.3% for RDN vs 2.5% for the whole cohort) and CV-related deaths (2.8% for RDN vs. 2.9% for the whole cohort) 3 years after RDN treatment in the resistant hypertension group.[38]

After RDN, the occurrence of renal artery stenosis requiring an intervention is rare.[39] A meta-analysis using 14 randomized controlled trials (RCTs; $N = 511$) showed that in 0.2% of the patients, at a median follow-up of 11 months, renal artery stenosis occurred after RDN.[40] The SIMPLICITY HTN-3 trial, however, showed that renal function did not worsen significantly; instead, the serum creatinine level increased by >50% in 1.4% of those in the RDN group compared with 0.6% of those in the sham group.[28] Furthermore, the composite safety endpoint rate over 48 months was 15% in the RDN group; this was comparable to that in the other intervention groups in the study.[28] Real-world studies by Panchavinnin *et al.* and Vogt *et al.* have reported that no AEs occurred at 10 and 9 years after RDN treatment, respectively.[41,42]

Overall, RDN procedures have demonstrated a good safety profile, and AEs associated with RDN are generally manageable; however, continuous monitoring and adherence to safety protocols in RDN procedures must be maintained.

## Clinical Efficacy in High-risk Patients with Hypertension

Analysis of data from the GSR for patients with uncontrolled hypertension ($N = 2,652$) showed significant ($p < 0.0001$) reductions in office SBP at 3 years in all subgroups of

**Table 1:** Clinical evidence from RCTs on the efficacy of RDN

| *Study, year* | *Study design* | *Sample size* | *Age* | *Comorbidities* | *Follow-up period* | *Office BP reduction from baseline (SBP)* | *Office BP reduction from baseline (DBP)* | *Interpretation* |
|---|---|---|---|---|---|---|---|---|
| Radiofrequency-based RDN* | | | | | | | | |
| SPYRAL HTN-OFF MED pivotal trial, 2020[30] | Single-blind, randomized, sham-controlled trial | RDN: 166, Sham: 165 | 52.4–52.6 years | Type 2 diabetes, coronary artery disease, obstructive sleep apnea, stroke, transient ischemic attack | 3 months | RDN: −9.2 mm Hg, Sham: −2.5 mm Hg | RDN: −5.1 mm Hg, Sham: −1.0 mm Hg | The RDN group had a significantly greater reduction in office BP at 3 months than the sham control group. |
| SPYRAL HTN-ON MED proof-of-concept trial, 2018[13] | Single-blind, randomized, proof-of-concept sham-controlled trial | RDN: 38, Sham: 42 | 53.0–53.9 years | Type 1 and type 2 diabetes, coronary artery disease, obstructive sleep apnea, stroke, transient ischemic attack | 6 months | RDN: −9.4 mm Hg, Sham: −2.6 mm Hg | RDN: −5.2 mm Hg, Sham: −1.7 mm Hg | The RDN group had a significantly greater reduction in office BP at 6 months than the sham control group. |
| SYMPLICITY HTN-3 trial, 2014[28] | Single-blind, randomized, sham-controlled trial | RDN: 364, Sham: 171 | 56.2–57.9 years | Type 2 diabetes, obstructive sleep apnea, coronary artery disease, stroke, myocardial infarction, transient ischemic attack, peripheral artery disease, hyperlipidemia | 6 months | RDN: −14.1 mm Hg, Sham: −11.7 mm Hg | NR | Compared with the sham control group, the RDN group did not show significant reduction in office BP at 6 months. |
| SYMPLICITY HTN-3 trial, 2022[26] | Single-blind, randomized, sham-controlled trial | RDN: 364, Sham: 171 | 56.2–57.9 years | Type 2 diabetes, obstructive sleep apnea, coronary artery disease, stroke, myocardial infarction, transient ischemic attack, peripheral artery disease, hyperlipidemia | 36 months | RDN: −26.4 mm Hg, Sham: −5.7 mm Hg | NR | The RDN group had a significantly greater reduction in office BP at 36 months than the sham control group. |
| SPYRAL HTN-ON MED, 2022[33] | Single-blind, randomized, sham-controlled trial | RDN: 38, Sham: 42 | 51.0–55.1 years | Type 1 and type 2 diabetes, coronary artery disease, obstructive sleep apnea, stroke, and transient ischemic attack | 36 months | RDN: −21.3 mm Hg, Sham: −12.2 mm Hg | NR | Compared with the sham control group, the RDN group did not show significant reduction in office BP at 36 months. |
| Ultrasound-based RDN** | | | | | | | | |
| RADIANCE-HTN TRIO, 2021[31] | Single-blind, randomized, sham-controlled trial | RDN: 69, Sham: 67 | 18–75 years | Type 2 diabetes, obstructive sleep apnea, heart failure, prior history of hospitalization for hypertension | 2 months | RDN: −9.0 mm Hg, Sham: −4.0 mm Hg | RDN: −5.0 mm Hg, Sham: −1.0 mm Hg | The RDN group had a significantly greater reduction in office SBP at 2 months than the sham control group. However, no significant reduction in DBP was observed in the RDN group compared with the sham control group. |
| RADIANCE-HTN SOLO, 2018[29] | Single-blind, randomized, sham-controlled trial | RDN: 74, Sham: 72 | 54.1 years | Type 2 diabetes, obstructive sleep apnea | 2 months | RDN: −10.8 mm Hg, Sham: −3.9 mm Hg | RDN: −5.5 mm Hg, Sham: −1.2 mm Hg | The RDN group had a significantly greater reduction in office BP at 2 months than the sham control group. |

NR, not reported; *Radiofrequency RDN uses alternating electrical current to create lesions through direct heating at the catheter tip and passive heat transfer to deeper tissues; **Ultrasound RDN uses ultrasound energy to thermally ablate and disrupt the renal efferent and afferent sympathetic nerves to achieve a reduction in systemic arterial blood pressure

**Table 2:** Clinical evidence from RCTs on the safety of RDN

| *Sl. no.* | *Study, year* | *Study design* | *Sample size* | *Total adverse events* | *Type of adverse events: Procedure-related* | *Type of adverse events: Device-related* | *Type of adverse events: Other* | *Inference* |
|---|---|---|---|---|---|---|---|---|
| 1 | SYMPLICITY HTN-3 trial, 2014[28] | Single-blind, randomized, sham-controlled trial | RDN: 364, Sham: 171 | RDN: 11.8%, Sham: 11.6% | None | None | RDN: Death (0.6%), myocardial infarction (1.7%), increase in serum creatinine level >50% (1.4%), end-organ damage (0.3%), vascular complications (0.3%), hypertensive crisis (2.6%), stroke (1.1%), heart failure (2.6%), atrial fibrillation (1.4%), new renal stenosis >70% (0.3%); Sham: Death (0.6%), myocardial infarction (1.8%), increase in serum creatinine level >50% (0.6%), hypertensive crisis (5.3%), stroke (1.2%), heart failure (1.8%), atrial fibrillation (0.6%) | No significant differences in safety outcomes between the RDN and sham groups. |
| 2 | SPYRAL HTN-OFF MED Pivotal, 2020[30] | Single-blind, randomized, sham-controlled trial | RDN: 166, Sham: 165 | RDN: 0.6%, Sham: 0.6% | None | None | RDN: Hypertensive crisis (0.6%); Sham: Stroke (0.6%) | No differences in safety outcomes between the RDN and sham groups. |
| 3 | SPYRAL HTN-ON MED proof-of-concept trial, 2018[13] | Single-blind, randomized, proof-of-concept, sham-controlled trial | RDN: 38, Sham: 42 | None | None | None | None | No adverse events were reported in the RDN and sham groups. |
| 4 | SPYRAL HTN-ON MED, 2023[32] | Assessor-blinded, randomized, sham-controlled trial | RDN: 206, Sham: 131 | RDN: 0% | None | None | None | Major adverse events related to the procedure and device were not reported in the RDN and sham control groups. |
| 5 | RADIANCE-HTN TRIO, 2021[31] | Single-blind, sham-controlled trial | RDN: 69, Sham: 67 | RDN: 23.2%, Sham: 16.4% | RDN: Access site complication (1%), pain for >2 days (17%); Sham: Pain for >2 days (15%) | None | RDN: All-cause mortality (1%), acute renal injury (1%), acute myocardial infarction (1%); Sham: Coronary revascularization (1%) | No differences in safety outcomes between the RDN and sham groups. |
| 6 | RADIANCE-HTN SOLO, 2018[29] | Single-blind, randomized, sham-controlled trial | RDN: 74, Sham: 72 | RDN: 11%, Sham: 11% | RDN: Pain for >2 days (11%); Sham: Pain for >2 days (11%) | None | None | No differences in safety outcomes between the RDN and sham groups. |

patients with high-risk profiles, such as those with type 2 diabetes mellitus (–16.4 ± 26.8; *n* = 465), chronic kidney disease (CKD) (–11.6 ± 29.6; *n* = 254), isolated systolic hypertension (ISH) (–15.9 ± 23.7; *n* = 477), and atrial fibrillation (–17.6 ± 27.4; *n* = 144), and those older than 65 years (–18.4 ± 28.3 mm Hg; *n* = 472).[43]

Chronic sympathetic overactivation is a hallmark of aging, and RDN has demonstrated clinical feasibility in managing aging-related hypertension.[44] Therefore, its effectiveness in elderly patients should not be discounted.[43] Pooled evidence from the SIMPLICITY HTN-3 trial and GSR data suggests that RDN has a less pronounced effect in patients with ISH than in those with combined systolic–diastolic hypertension.[45,46] However, assessments of arterial stiffness could identify ISH patients who might benefit from RDN.[47] While RDN achieved significant reductions in office and ambulatory SBP after 1 month in CKD patients, there is a lack of strong evidence to support the use of RDN in these patients.[48]

### Moving from Evidence to Clinical Practice

Transitioning from evidence to clinical practice in the use of RDN for treating hypertension involves integrating the findings from rigorous clinical studies into routine patient care. Patients with hypertension may have different perspectives on RDN than physicians.[15] A study found that 40% of those not on medications would opt for a one-time procedure, such as catheter-based RDN, over medication, and nearly 30% of those taking medications would choose RDN, with many having high expectations for BP reduction.[49]

Different devices are used for RDN, but the lack of standardized protocols and technical expertise may contribute to the variability in efficacy and safety outcomes across clinical studies. The European Society of Cardiology Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions recommend RDN as an evidence-based treatment for a broad range of patients.[19,50]

Key obstacles to the clinical applicability of RDN include the lack of standardized criteria for identifying responsive patients and the absence of a feedback mechanism to determine sympathetic nerve location and extent of ablation in the renal artery.[50–52] The cost of RDN is another practical challenge, limiting its wide applicability.[18] However, a Markov modeling analysis of RDN's cost-effectiveness in the UK, using a willingness-to-pay threshold of €35,000/quality adjusted life year, found it to be cost-effective with 95% probability for men and women up to 78 and 76 years, respectively. Additionally, RDN may be considered cost-effective for patients with medication-resistant hypertension.[53]

## Conclusion

Renal denervation is an effective and safe adjunctive therapy for achieving sustained control of BP and reducing the risk of adverse CV events. Adopting a patient-centered approach by considering comorbidities, responses to previous treatments, and overall CV risk profile is crucial for the successful use of RDN in the management of hypertension. RDN could prove to be cost-effective when considered early in the management of hypertension.

## Source of Support

None.

## Conflict of Interest

None.

## Author Contributions

All authors have contributed equally to the conception, design, drafting, review and finalization of the manuscript.

## Acknowledgments

The authors of the manuscript would like to thank BioQuest Solutions for the editorial assistance.

## Orcid

*Nakul Sinha* https://orcid.org/0000-0001-8347-4356

*Mangesh Tiwaskar* https://orcid.org/0000-0003-4024-0095

## References

1. Zhou B, Carrillo-Larco RM, Danaei G, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: A pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021;398:957–980.
2. Parati G, Lombardi C, Pengo M, et al. Current challenges for hypertension management: From better hypertension diagnosis to improved patients' adherence and blood pressure control. Int J Cardiol 2021;331:262–269.
3. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J Hypertens 2023;41:1874–2071.
4. Yugar-Toledo JC, Brunelli V, Vilela-Martin JF, et al. Controlled versus uncontrolled resistant hypertension: Are they in the same bag? Curr Hypertens Rep 2018;20:26.
5. Zhou H, Xu Y, Chen W, et al. Present evidence of determinants to predict the efficacy of renal denervation. Int J Hypertens 2022;2022:e5694127.
6. Ahmad Y, Francis DP, Bhatt DL, et al. Renal denervation for hypertension: A systematic review and meta-analysis of randomized, blinded, placebo-controlled trials. JACC Cardiovasc Interv 2021;14:2614–2624.
7. Dimitriadis K, Schmieder RE, Iliakis P, et al. Long-term efficacy and safety of renal denervation: An update from registries and randomised trials. Blood Press 2023;32:2266664.
8. Wilson AL, Gandhi J, Suh Y, et al. Renal innervation in resistant hypertension: A review of pathophysiology and renal denervation as potential treatment. CHYR 2020;16:115–127.
9. Giunta S, Xia S, Pelliccioni G, et al. Autonomic nervous system imbalance during aging contributes to impair endogenous anti-inflammaging strategies. Geroscience 2024;46:113–127.
10. Li S, Phillips JK. Patient selection for renal denervation in hypertensive patients: What makes a good candidate? Vasc Health Risk Manag 2022;18:375–386.
11. Schmieder RE, Mahfoud F, Mancia G, et al. Higher baseline systolic blood pressure is associated with greater blood pressure reductions following radiofrequency renal denervation in a pooled cohort of over 3900 patients. J Hypertens 2024;42:e137.
12. Myat A, Redwood SR, Qureshi AC, et al. Renal sympathetic denervation therapy for resistant hypertension. Cir Cardiovas Interv 2013;6(2):184–197.
13. 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;391:2346–2355.
14. 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;390:2160–2170.
15. Schmieder RE, Kandzari DE, Wang TD, et al. Differences in patient and physician perspectives on pharmaceutical therapy and renal denervation for the management of hypertension. J Hypertens 2021;39:162.
16. Schmieder RE, Mahfoud F, Azizi M, et al. European Society of Hypertension position paper on renal denervation 2018. J Hypertens 2018;36:2042–2048.
17. Zeijen VJM, Kroon AA, van den Born BH, et al. The position of renal denervation in treatment of hypertension: an expert consensus statement. Neth Heart J 2023;31:3–11.
18. Roubsanthisuk W, Kunanon S, Chattranukulchai P, et al. 2022 Renal denervation therapy for the treatment of hypertension: a statement from the Thai Hypertension Society. Hypertens Res 2023;46:898–912.
19. Barbato E, Azizi M, Schmieder RE, et al. Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2023;44:1313–1330.
20. Coates P, Tunev S, Trudel J, et al. Time, temperature, power, and impedance considerations for radiofrequency catheter renal denervation. Cardiovasc Revasc Med 2022;42:171–177.
21. Kandzari DE, Bhatt DL, Brar S, et al. Predictors of blood pressure response in the SYMPLICITY HTN-3 trial. Eur Heart J 2015;36:219–227.
22. Beeftink MMA, Spiering W, De Jong MR, et al. Renal denervation beyond the bifurcation: The effect of distal ablation placement on safety and blood pressure. J Clin Hypertens 2017;19:371–378.
23. Pekarskiy SE, Baev AE, Mordovin VF, et al. Denervation of the distal renal arterial branches vs conventional main renal artery treatment: a randomized controlled trial for treatment of resistant hypertension. J Hypertens 2017;35:369–375.
24. Fengler K. Renal denervation for resistant hypertension: A concise update on treatment options and the latest clinical evidence. Cardiol Ther 2022;11:385–392.
25. Gosse P, Cremer A, Kirtane AJ, et al. Ambulatory blood pressure monitoring to predict response to renal denervation. Hypertension 2021;77:529–536.
26. Bhatt DL, Vaduganathan M, Kandzari DE, et al. Long-term outcomes after catheter-based renal artery denervation for resistant hypertension: Final follow-up of the randomised SYMPLICITY HTN-3 trial. Lancet 2022;400:1405–1416.
27. Sanders MF, Reitsma JB, Morpey M, et al. Renal safety of catheter-based renal denervation: systematic review and meta-analysis. Nephrol Dial Transplant 2017;32:1440–1447.
28. Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. N Engl J Med 2014;370:1393–1401.
29. Azizi 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;391:2335–2345.
30. Böhm M, Kario K, Kandzari DE, et al. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED pivotal): A multicentre, randomised, sham-controlled trial. Lancet 2020;395:1444–1451.
31. Azizi M, Sanghvi K, Saxena M, et al. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): A randomised,

multicentre, single-blind, sham-controlled trial. Lancet 2021;397:2476–2486.
32. Kario K, Mahfoud F, Kandzari DE, et al. Long-term reduction in morning and nighttime blood pressure after renal denervation: 36-month results from SPYRAL HTN-ON MED trial. Hypertens Res 2023;46:280–288.
33. Mahfoud F, Kandzari DE, Kario K, et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): A randomised, sham-controlled trial. Lancet 2022;399:1401–1410.
34. Mahfoud F, Böhm M, Schmieder R, et al. Effects of renal denervation on kidney function and long-term outcomes: 3-year follow-up from the Global SYMPLICITY Registry. Eur Heart J 2019;40:3474–3482.
35. Al Ghorani H, Kulenthiran S, Recktenwald MJM, et al. 10-year outcomes of catheter-based renal denervation in patients with resistant hypertension. J Am Coll Cardiol 2023;81:517–519.
36. Mahfoud F, Mancia G, Schmieder RE, et al. Cardiovascular risk reduction after renal denervation according to time in therapeutic systolic blood pressure range. J Am Coll Cardiol 2022;80:1871–1880.
37. Kandzari DE, Townsend RR, Kario K, et al. Safety and efficacy of renal denervation in patients taking antihypertensive medications. J Am Coll Cardiol 2023;82:1809–1823.
38. Schmieder RE, Mahfoud F, Mancia G, et al. Clinical event reductions in high-risk patients after renal denervation projected from the global SYMPLICITY registry. Eur Heart J Qual Care Clin Outcomes 2023;9:575–582.
39. Rey-García J, Townsend RR. Renal denervation: a review. Am J Kidney Dis 2022;80:527–535.
40. Townsend RR, Walton A, Hettrick DA, et al. Review and meta-analysis of renal artery damage following percutaneous renal denervation with radiofrequency renal artery ablation. EuroIntervention 2020;16:89–96.
41. Panchavinnin P, Wanthong S, Roubsanthisuk W, et al. Long-term outcome of renal nerve denervation (RDN) for resistant hypertension. Hypertens Res 2022;45:962–966.
42. Vogt A, Dutzmann J, Nußbaum M, et al. Safety and efficacy of renal sympathetic denervation: A 9-year long-term follow-up of 24-hour ambulatory blood pressure measurements. Front Cardiovasc Med 2023;10:1210801.
43. Mahfoud F, Mancia G, Schmieder R, et al. Renal denervation in high-risk patients with hypertension. J Am Coll Cardiol 2020;75:2879–2888.
44. Balasubramanian P, Hall D, Subramanian M. Sympathetic nervous system as a target for aging and obesity-related cardiovascular diseases. GeroScience 2018;41:13–24.
45. Ewen S, Ukena C, Linz D, et al. Reduced effect of percutaneous renal denervation on blood pressure in patients with isolated systolic hypertension. Hypertension 2015;65:193–199.
46. Mahfoud F, Schmieder RE, Azizi M, et al. Proceedings from the 2nd European Clinical Consensus Conference for device-based therapies for hypertension: State of the art and considerations for the future. Eur Heart J 2017;38:3272–3281.
47. Fengler K, Ewen S, Höllriegel R, et al. Blood pressure response to main renal artery and combined main renal artery plus branch renal denervation in patients with resistant hypertension. JAHA 2017;6:e006196.
48. Xia M, Liu T, Chen D, et al. Efficacy and safety of renal denervation for hypertension in patients with chronic kidney disease: A meta-analysis. Int J Hypertens 2021;38:732–742.
49. Schmieder RE, Högerl K, Jung S, et al. Patient preference for therapies in hypertension: A cross-sectional survey of German patients. Clin Res Cardiol 2019;108:1331–1342.
50. Haribabu S, Sharif F, Zafar H. Recent trends in renal denervation devices for resistant hypertension treatment. Ir J Med Sci 2021;190:971–879.
51. Gulati R, Raphael CE, Negoita M, et al. The rise, fall, and possible resurrection of renal denervation. Nat Rev Cardiol 2016;13:238–244.
52. DeLalio LJ, Sved AF, Stocker SD. Sympathetic nervous system contributions to hypertension: Updates and therapeutic relevance. Can J Cardiol 2020;36:712–720.
53. Dorenkamp M, Bonaventura K, Leber AW, et al. Potential lifetime cost-effectiveness of catheter-based renal sympathetic denervation in patients with resistant hypertension. Eur Heart J 2013;34:451–461.