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REVIEW

Renal Denervation With the Symplicity Spyral System: Current Evidence and Clinical Considerations for Uncontrolled Hypertension

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Keywords
Hypertension
Resistant Hypertension
Renal Denervation

September 2026
ISSN 2152-4343

Key Summary

- This narrative review assesses the Symplicity Spyral Renal Denervation (RDN) System (Medtronic) for adults with uncontrolled hypertension despite lifestyle measures and optimized medications, or with intolerance or adherence challenges.
- Three major RDN trials involving the Symplicity System are highlighted, where major adverse event rates were generally below 1%; the Global Symplicity Registry is also reviewed, which reported new renal artery stenosis rates of approximately 0.2% to 0.3% at 3 years without excess decline in estimated glomerular filtration rate.
- RDN with the Symplicity Spyral RDN System is a safe, durable adjunct that can provide clinically meaningful blood pressure reductions in appropriately selected patients with uncontrolled hypertension; further real-world and cost-effectiveness data are needed to refine its clinical role.

VASCULAR DISEASE MANAGEMENT. 2026;23(9):E140-E143

Abstract

Hypertension (HTN) is a major cardiovascular risk factor in the United States. Resistant HTN is blood pressure that remains above goal despite 3 maximally tolerated antihypertensive agents of different classes, including a diuretic. Poor control often stems from nonadherence, financial barriers, cultural biases, and psychological factors, underscoring the need for novel strategies. Renal denervation (RDN) offers a promising therapeutic alternative or adjunct. This manuscript reviews the clinical burden of HTN, the role of RDN (with emphasis on the Symplicity Spyral System [Medtronic], available devices, supporting clinical evidence, and its beneficial effects on patient outcomes.

Introduction

Hypertension (HTN) affects more than 1 billion adults worldwide and remains the leading modifiable risk factor for cardiovascular disease, stroke, and chronic kidney disease. A substantial proportion of patients fail to achieve guideline-recommended blood pressure (BP) targets despite optimized medical therapy because of true resistance, intolerance, or incomplete adherence.[1]

In recent years, high BP has been a primary contributing cause of hundreds of thousands of deaths annually in the United States.[2] Of 120 million adults in the United States with HTN, only about 23% have controlled BP readings under 130/80 mm Hg, and approximately 45% of those have uncontrolled BP readings of 140/90 mm Hg or higher.[3] Annual costs associated

with high BP were estimated at $219 billion in the United States, with medical costs for people with high BP substantially higher by $2759 than for those without.[4] These figures underscore the economic and personal burden carried by patients with HTN.

In hypertensive patients, the renin-angiotensin-aldosterone system contributes through multiple mechanisms. Angiotensin II increases sympathetic nervous system activity, resulting in increased tubular sodium and chloride reabsorption, potassium excretion, and water retention. It also promotes aldosterone secretion from the adrenal cortex (further enhancing water retention) and causes arteriolar vasoconstriction; the net effect elevates BP. Overactivity of the renal sympathetic nerves is a key driver of this pathophysiology, providing the rationale for catheter-based renal denervation (RDN), which interrupts afferent and efferent nerves in the periadventitial space of the renal arteries.

Three main RDN systems have been studied. The Symplicity Spyral RDN System (Medtronic) uses a catheter with 4 electrodes arranged in a spiral configuration to deliver radiofrequency energy that generates sufficient heat to ablate nerves in the renal artery periadventitial space while sparing the arterial wall. The Paradise Ultrasound RDN System (Recor Medical) delivers ultrasound energy via a catheter with an inflatable balloon that irrigates the vessel lumen with a cooling solution to protect the arterial wall. The Peregrine System Infusion Catheter (Ablative Solutions) delivers dehydrated alcohol through the renal artery into the perivascular space to treat the renal nerves. In November 2023, both the Symplicity Spyral and Paradise systems received US Food and Drug Administration approval as adjunctive treatments for patients with HTN in whom lifestyle modifications and antihypertensive medications do not adequately control BP.[5]

Symplicity Spyral Renal Denervation System

The Symplicity Spyral multi-electrode RDN catheter features a flexible, spiral-shaped, self-expanding nitinol element with 4 electrodes that can deliver simultaneous or selective radiofrequency energy. It is designed for vessels 3 to 8 mm in diameter and enables circumferential ablation covering 4 quadrants. The catheter is paired with a Symplicity G3 radiofrequency generator, which uses a real-time responsive algorithm that automatically adjusts power by monitoring temperature and impedance for safe energy distribution. The procedure is typically performed via femoral arterial access under fluoroscopic guidance, with sequential bilateral treatment of the main renal arteries and accessible branches.

Patient selection

Ideal candidates are adults with uncontrolled HTN (office and ambulatory confirmation) despite lifestyle measures and optimized pharmacotherapy, or those with medication intolerance or adherence challenges. Priority may be given to patients with higher cardiovascular risk (eg, coronary disease, diabetes, prior stroke/transient ischemic attack, or chronic kidney disease). Contraindications include renal artery diameter less than 3 mm or more than 8 mm, fibromuscular dysplasia, recent renal artery stenting (< 3 months), aneurysm, more than 50% stenosis, pregnancy, or abnormal kidney/adrenal tumors. Shared decision-making is essential, incorporating patient preferences regarding medications vs a one-time device-based procedure.[6]

Preprocedure imaging confirms suitable anatomy, and multidisciplinary input (HTN specialist and an interventionist) is recommended.

Clinical evidence and long-term outcomes

Early experience with first-generation devices included the SYMPLICITY HTN-3 trial of 535 patients with treatment-resistant HTN (systolic BP > 160 mm Hg despite ≥ 3 antihypertensive medications, including a diuretic). Although the primary endpoint was not met at 6 months, longer-term follow-up to 36 months showed sustained reductions favoring RDN: approximately –15.6 mm Hg change in 24-hour ambulatory systolic BP in the denervation group vs –0.3 mm Hg in the non-crossover sham group (adjusted treatment difference ~16.5 mm Hg).[7]

Subsequent second-generation trials with the Symplicity Spyral catheter provided more rigorous evidence. The SPYRAL HTN-OFF MED pilot and pivotal trials (patients with uncontrolled HTN not taking antihypertensive medications) demonstrated a reduction in 24-hour systolic BP of approximately 4 to 5 mm Hg greater than sham control.[5,8] In the pivotal trial, the treatment difference was –3.9 mm Hg for 24-hour ambulatory systolic BP and –6.5 mm Hg for office systolic BP at 3 months, with a high probability of superiority and an excellent safety profile.[8]

Longer-term data from the SPYRAL HTN-ON MED program (patients on background antihypertensive therapy) have shown durable benefits. At 24 months, RDN produced significantly greater ambulatory and office systolic BP reductions compared with sham, despite higher medication use in the control arm, with rare adverse events and no renal artery stenosis.[9] Real-world and registry data further support sustained reductions and increased time in the therapeutic BP range. A 10% increase in time in the therapeutic range after RDN through 6 months was associated with significant reductions in major adverse cardiovascular events, cardiovascular death, myocardial infarction, and stroke from 6 to 36 months.[10] Responders to RDN also demonstrate favorable long-term outcomes compared with nonresponders.[11]

Patient preference studies using discrete-choice methodology indicate that BP reduction is the dominant driver of treatment choice; many patients are willing to accept a minimally invasive procedure for meaningful ambulatory reductions of 5 to 10 mm Hg, particularly when facing additional medications or side effects.[6]

A 10 mm Hg reduction in systolic BP is associated with a 10% to 20% decline in cardiovascular morbidity and mortality.[12,13]

Guidelines and consensus documents have increasingly recognized RDN as a therapeutic option. The 2024 American Heart Association scientific statement concluded that RDN is an effective treatment for many patients with uncontrolled BP and has a favorable immediate safety profile.[1] In Europe, a 2023 clinical consensus statement from the European Society of Cardiology (ESC) Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions endorsed RDN for selected patients with resistant or uncontrolled HTN on the basis of sham-controlled trial evidence.[14] The 2023 European Society of Hypertension guidelines and the 2024 ESC HTN guidelines assigned RDN a Class IIb recommendation as an additional treatment option in appropriately selected patients (typically those with resistant HTN and estimated glomerular filtration rate [eGFR] > 40 mL/min/1.73 m²) after shared decision-making. Most recently, the 2025 American College of Cardiology/American Heart Association (AHA) high BP guideline similarly classified RDN as a Class IIb recommendation for adults with resistant or uncontrolled HTN in whom BP remains above goal despite lifestyle measures and antihypertensive medications, emphasizing multidisciplinary evaluation and its role as an adjunct rather than a replacement for pharmacotherapy.[15]

Contemporary RDN, particularly with the Symplicity Spyral RDN System, demonstrates a favorable safety profile across sham-controlled trials and real-world registries. Major adverse event rates in the SPYRAL HTN program were low (generally < 1% for the composite of mortality, end-stage renal disease, significant embolic events, renal artery perforation or dissection requiring intervention, major vascular complications, or new renal artery stenosis > 70%), with no instances of renal artery stenosis reported through 24 months in the ON MED cohort and stable kidney function.[6,13] Meta-analyses of radiofrequency RDN report an annual incidence of renal artery stenting of approximately 0.20%, comparable to background rates in untreated hypertensive patients, while the Global Symplicity Registry shows new stenosis rates of approximately 0.2% to 0.3% at 3 years with no excess decline in eGFR beyond expected age- and HTN-related changes.[5,11] The 2024 AHA scientific statement similarly concludes that RDN has a favorable immediate safety profile with very low major adverse events and no evidence of associated kidney dysfunction or progressive renal artery stenosis on medium- to longer-term follow-up.[1]

Conclusions

RDN with the Symplicity Spyral RDN System offers a safe, durable, adjunctive option that produces clinically meaningful BP reductions in appropriately selected patients with uncontrolled HTN. Shared decision-making should consider younger patients, men, those with higher baseline readings, greater medication burden, comorbidities, medication side effects, or adherence challenges. With proper patient selection, operator training, and multidisciplinary care, RDN can improve time in therapeutic range and potentially reduce cardiovascular events. Continued real-world data collection and attention to cost-effectiveness will further refine its role in clinical practice. ■

Affiliations and Disclosures

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The authors report no financial relationships or conflicts of interest regarding the content herein.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare-affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Manuscript accepted August 18, 2026.

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