

## Bibliography

This bibliography includes articles that support the approved U.S. FDA indication for use for the Symplcity Spyrals™ renal denervation (RDN) system for uncontrolled hypertension and therefore deemed to be relevant to aid in the payer decision-making process. This includes randomized controlled trials, real-world evidence, clinical practice guidelines, society recommendations, and systematic reviews. This list is current as of August 14, 2025 and is not exhaustive of all articles on the Symplcity RDN system.

### Randomized Controlled Trials (RCTs)

#### Study: SPYRAL HTN-ON MED

Kandzari DE, Mahfoud F, Townsend RR, et al. Long-Term Safety and Efficacy of Renal Denervation: 24-Month Results From the SPYRAL HTN-ON MED Trial. *Circ Cardiovasc Interv.* Published online May 20, 2025. doi: 10.1161/circinterventions.125.015194

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Kandzari DE, Cao, KC, Ryschon AM, Sharp ASP, Pietzsch JB. Catheter-Based Radiofrequency Renal Denervation in the United States: A Cost-Effectiveness Analysis Based on Contemporary Evidence. *J Soc Cardiovasc Angiogr Interv.* 2024;3(10):102234. Doi:10.1016/j.jscv.2024.102234

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Townsend RR, Ferdinand KC, Kandzari DE, et al. Impact of Antihypertensive Medication Changes After Renal Denervation Among Different Patient Groups: SPYRAL HTN-ON MED. *Hypertension.* 2024;81(5):1095-1105. doi: 10.1161/HYPERTENSIONAHA.123.22251

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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(19):1809-1823. doi: 10.1016/j.jacc.2023.08.045

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PubMed Abstract: <https://pubmed.ncbi.nlm.nih.gov/35390320/>

Kandzari DE, Hickey GL, Pocock SJ, et al. Prioritised endpoints for device-based hypertension trials: the win ratio methodology. *EuroIntervention.* 2021;16(18):e1496-e1502. Published 2021 Apr 2. doi: 10.4244/EIJ-D-20-01090

PubMed Abstract: <https://pubmed.ncbi.nlm.nih.gov/33226002/>

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. *The Lancet*. 2018;391(10137):2346-2355. doi: 10.1016/S0140-6736(18)30951-6

PubMed Abstract: <https://pubmed.ncbi.nlm.nih.gov/29803589/>

### **Study: SPYRAL HTN-OFF MED**

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. *The Lancet*. 2020;395(10234):1444-1451. doi: 10.1016/S0140-6736(20)30554-7

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## Non-Randomized Studies

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Kindermann I, Wedegärtner SM, Mahfoud F, et al. Improvement in health-related quality of life after renal sympathetic denervation in real-world hypertensive patients: 12-month outcomes in the Global SYMPPLICITY Registry. *J Clin Hypertens (Greenwich)*. 2017;19(9):833-839. doi: 10.1111/jch.13007

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### **INDEPENDENT STUDIES DEMONSTRATING LONG-TERM EFFECTS**

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## **STUDY DEMONSTRATING PATIENT PREFERENCE**

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## **Clinical Practice Guidelines & Society Recommendations**

Jones DW, Ferdinand KC, Taler SJ, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Hypertension.* Published online August 14, 2025. doi:10.1161/HYP.0000000000000249  
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## **CONSENSUS STATEMENTS & POSITION PAPERS**

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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(15):1313-1330. doi: 10.1093/eurheartj/ehad054. Erratum in: *Eur Heart J.* 2023 Jul 14;44(27):2439.

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Kandzari DE, Townsend RR, Bakris G, et al. Renal denervation in hypertension patients: Proceedings from an expert consensus roundtable cosponsored by SCAI and NKF. *Catheter Cardiovasc Interv.* 2021;98(3):416-426. doi:10.1002/ccd.29884

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MCG Care Guidelines: A-1034 Renal Sympathetic Nerve Ablation. 2025. Accessed via Blue Cross Blue Shield of Tennessee website on August 1, 2025 via <https://provider.bcbst.com/tools-resources/manuals-policies-guidelines/>.

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## Symplivity Spyral™ renal denervation system

### BRIEF STATEMENT

#### Indications

The Symplivity Spyral™ renal denervation system is indicated to reduce blood pressure as an adjunctive treatment in patients with hypertension in whom lifestyle modifications and antihypertensive medications do not adequately control blood pressure.

#### Contraindications

The Symplivity Spyral system is contraindicated in patients with any of the following conditions: • Renal artery diameter < 3mm or > 8mm • Renal artery fibromuscular dysplasia (FMD) • Stented renal artery (<3 months prior to RDN procedure) • Renal artery aneurysm • Renal artery diameter stenosis >50% • Pregnancy • Presence of abnormal kidney (or secreting adrenal) tumor • Iliac/femoral artery stenosis precluding insertion of the catheter.

#### Warnings and Precautions

A thorough understanding of the technical principles, clinical applications, and risks associated with vascular access techniques and percutaneous transluminal catheterization in renal arteries is necessary before using this device.

The safety and efficacy of the Symplivity Spyral system has not been established in patients with isolated systolic hypertension or in patients with prior renal artery interventions including renal stents, renal angioplasty, or prior renal denervation. The Symplivity Spyral system has not yet been studied in patients who are breastfeeding, under the age of 18, or with secondary hypertension • Avoid treatment with the Symplivity Spyral™ catheter within 5 mm of any diseased area or stent. • Implantable pacemakers (IPGs) and implantable cardioverter defibrillators (ICDs) or other active implants may be adversely affected by RF ablation. Refer to the implantable device's Instructions for Use. • The patient's heart rate may drop during the ablation procedure. • Proper pain medication should be administered at least 10 min before ablating renal nerves.

#### Potential Adverse Events

Potential adverse events associated with use of the renal denervation device or the interventional procedures include, but are not limited to, the following conditions: • Allergic reaction to contrast • Arterial damage, including injury from energy application, dissection, or perforation, • Arterial spasm, or stenosis • Arterio-enteric fistula • AV fistula • Bleeding • Blood clots or embolism • Bruising • Cardiopulmonary arrest • Complications associated with medications commonly utilized during the procedure, such as narcotics, anxiolytics, or other pain or anti-vasospasm medications • Death • Deep vein thrombosis • Edema Electrolyte imbalance • Heart rhythm disturbances, including bradycardia • Hematoma • Hematoma - retroperitoneal • Hematuria • Hypertension • Hypotension (may cause end organ hypoperfusion) • Infection • Kidney damage including renal failure or perforation • Myocardial infarction • Nausea or vomiting • Pain or discomfort • Peripheral ischemia • Pulmonary embolism • Proteinuria • Pseudoaneurysm • Radiocontrast nephropathy • Renal artery aneurysm • Skin burns from failure of the dispersive electrode pad • Stroke • Other potential adverse events that are unforeseen at this time.

Please reference appropriate product *Instructions for Use* and *User Manual* for more information regarding indications, contraindications, warnings, precautions, and potential adverse events.

**CAUTION:** Federal (USA) law restricts this device to sale by or on the order of a physician.

For further information, please call and/or consult Medtronic at 800-633-8766 or the Medtronic website at [medtronic.com](http://medtronic.com)

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