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FEP Medical Policy Manual

FEP 7.01.136 Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension

Annual Effective Policy Date: January 1, 2024

Original Policy Date: March 2013

Related Policies:

8.01.57 - Baroreflex Stimulation Devices

Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension

Description

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Radiofrequency ablation (RFA) of the renal sympathetic nerves is thought to decrease both the afferent sympathetic signals from the kidney to the brain and the efferent signals from the brain to the kidney. This procedure decreases sympathetic activation, decreases vasoconstriction, and decreases activation of the renin-angiotensin system. Radiofrequency ablation of the renal sympathetic nerves may act as a nonpharmacologic treatment for hypertension and has been proposed as a treatment option for patients with uncontrolled hypertension despite the use of anti-hypertensive medications.

OBJECTIVE

The objective of this evidence review is to determine whether the use of radiofrequency ablation of the renal sympathetic nerves improves the net health outcome in individuals with uncontrolled hypertension.

POLICY STATEMENT

Radiofrequency ablation of the renal sympathetic nerves is considered **investigational** for the treatment of uncontrolled hypertension.

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

No RFA devices have been approved by the U.S. Food and Drug Administration (FDA) for ablation of the renal sympathetic nerves as a treatment for hypertension. Several devices have been developed for this purpose and are in various stages of application for FDA approval (FDA product code: DQY):

- The Symplicity Spyral™ Renal Denervation System (Medtronic) is a multielectrode RFA catheter system designed to deliver 4-quadrant ablations. On August 23, 2023 the FDA Advisory Committee for Circulatory System Devices voted that the Symplicity Spyral system met its safety endpoint as well as its efficacy endpoint, but after a tied vote in which the chairperson cast the final vote, the committee determined that the device did not achieve a positive balance of benefits and harms.
- The EnligHTN™ Multi-Electrode Renal Denervation System (St. Jude Medical) is an RFA catheter using a 4-point multiablation basket design. In January 2014, the EnligHTN™ Renal Guiding Catheter was cleared for marketing by the FDA through the 510(k) process, based on substantial equivalence to predicate devices for the following indication: percutaneous use through an introducer sheath to facilitate a pathway to introduce interventional and diagnostic devices into the renal arterial vasculature.
- The Vessix™ Renal Denervation System (Boston Scientific; formerly the V2 renal denervation system, Vessix Vascular) is a combination of an RF balloon catheter and bipolar RF generator technologies, intended to permit a lower voltage intervention.

Other RFA catheters (eg, Thermocouple Catheter™ [Biosense Webster]) used for other types of ablation procedures (eg, cardiac electrophysiology procedures) have been used off-label for RFA of the renal arteries.

In 2020, the FDA granted breakthrough therapy designation to 2 renal artery denervation systems - SoniVie"s Therapeutic Intra-Vascular Ultrasound (TIVUS) System and Recor's Paradise Renal Denervation System - for the treatment of patients with persistently elevated blood pressure. However, ultrasound-based renal denervation systems are outside of the scope of this evidence review.

RATIONALE

Summary of Evidence

For individuals who have uncontrolled hypertension, despite the use of anti-hypertensive medications, who receive radiofrequency ablation (RFA) of the renal sympathetic nerves, the evidence includes several randomized controlled trials (RCTs), numerous systematic reviews of the RCTs, and a multinational registry study. Relevant outcomes are symptoms, change in disease status, morbid events, medication use, and treatment-related morbidity. The proof of principle SPYRAL HTN-OFF MED study found that multielectrode renal denervation was superior to sham in the absence of background antihypertensive medication therapy, with between-group differences of -4.0 mmHg for 24-h systolic blood pressure (SBP) and -6.6 for office SBP at 3 months. The unpowered SPYRAL HTN-ON MED Pilot study also found significant between-group differences of -7.4 mmHg for 24-h SBP and -6.8 mmHg for office SBP at 6 months; however, results were only significant for the subgroup of patients non-adherent to medications. Long-term data from the SPYRAL HTN-ON MED study suggest that blood pressure reductions with multielectrode renal denervation are progressive and sustained over time. The SPYRAL HTN-ON MED Expansion study failed to meet its primary efficacy endpoint and found only 0.03 mmHg difference between renal denervation and sham control groups at 6 months follow-up. A significant reduction in office blood pressure was noted at 6 months (-4.1 mmHg). Confounding of these outcome estimates by unbalanced medication changes, missing 24-h SBP outcome data, and timing of antihypertensive medications related to 24-h SBP assessment may explain the discordant results between the pilot and expansion phases of this trial. Study interpretation is also complicated by short-term blinded follow-up and imputation of excluded crossover patient data. It is unclear which patients are most likely to derive benefit, and currently, there is no practical method to verify nerve destruction following ablation. Evidence from systematic reviews and meta-analyses are conflicting, but all available studies included evidence from both first and second-generation Symplicity catheters as well as multiple renal denervation methodologies such as ultrasound. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information" if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Heart Association et al

The American Heart Association (AHA), American College of Cardiology (AHA), and American Society of Hypertension (ASH; 2015) issued joint guidelines on the treatment of hypertension in patients with coronary artery disease.[21,] The guidelines noted the Symplicity HTN-3 trial did not find a significant benefit from renal denervation and stated that additional randomized controlled trials would be needed.

The AHA, ACC, and 9 additional specialty societies (2018) published joint guidelines on the prevention, detection, evaluation, and management of high blood pressure in adults.[22,] In discussing resistant hypertension, the guidelines indicated that studies using catheter ablation of renal sympathetic nerves "have not provided sufficient evidence to recommend the use of these devices."

The AHA (2018) published a Scientific Statement on the detection, evaluation, and management of resistant hypertension.[23,] The AHA Statement discussed the lack of benefit found in the Symplicity HTN-3 trial, as well as its methodological limitations. The statement also referred to the more recent positive data from the SPYRAL HTN-OFF MED trial, but noted that because the enrolled patients did not have resistant hypertension, "at best, this represents a proof-of-principle study demonstrating the role of the renal sympathetic nervous system in hypertension." The statement concluded that "the role of device-based sympatholytic treatments, as with renal denervation and baroreceptor stimulation, awaits clarification."

Eighth Joint National Committee

The Eighth Joint National Committee (2014), which was appointed to provide recommendations on hypertension treatment, published an evidence-based guideline on the management of hypertension in adults.[24,] These recommendations did not discuss the use of renal denervation.

European Society for Hypertension (ESH)

The ESH, with endorsement by the European Renal Association and the International Society of Hypertension, issued guidance on the management of arterial hypertension in 2023.[25,] The following recommendations were issued concerning renal denervation:

- Renal denervation can be considered as a treatment option in patients with an eGFR of > 40 ml/min/1.73m^2 who have uncontrolled blood pressure despite the use of anti-hypertensive drug combination therapy or if drug treatment elicits serious side effects. (Class of Recommendation: II, Level of Evidence: B)
- Renal denervation can be considered as an additional treatment option in patients with resistant hypertension if eGFR is > 40 ml/min/1.73m^2. (Class of Recommendation: II, Level of Evidence: B)
- Selection of patients to whom renal denervation is offered should be done in a shared decision-making process after objective and complete patient information is collected. (Class of Recommendation: I, Level of Evidence: C)
- Renal denervation should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure. (Class of Recommendation: I, Level of Evidence: C)

A class of recommendation I indicates a general consensus that the measure is useful, and a class II recommendation reflects that there is no general consensus and that only doubtful evidence exists. An 'A' level of evidence indicates that RCTs or meta-analyses with cardiovascular disease outcomes are available for this recommendation, a level 'B' suggests RCTs with surrogate measures, observational studies with cardiovascular disease outcomes or meta-analyses are available, and a C recommendation reflects either expert opinion or only observational or lower quality experimental evidence.

ESH recommendations did not discuss the specific use of radiofrequency renal denervation and included evidence from other modalities, such as ultrasound, in their evidence appraisal.

National Institute for Health and Care Excellence

In 2023, the National Institute for Health and Care Excellence (NICE) published an interventional procedures guidance on the use of percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension, recommending that the procedure should only be used with special arrangements for clinical governance, consent, and audit or research due to limited evidence.[26,]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
March 2013	New policy	Radiofrequency ablation of the renal sympathetic nerves is considered investigational for the treatment of resistant hypertension.
December 2013	Replace policy	Policy updated with literature review. References 5, 6, 17-20 added. No change in policy statement.
December 2014	Replace policy	Policy updated with literature review. References 4-5, 8-9, 11-12, 16, 19, 29-36, 38-43, and 46 added. No change to policy statement.
March 2016	Replace policy	Policy updated with literature review through August 3, 2015; references 4-5, 8, 12-13, 16-17, 51, 54-55, and 57-58 added. Policy statement unchanged.
December 2016	Replace policy	Policy updated with literature review. References 9-11, 15, 17, 21-22, 24-26, and 37 added. Policy statements unchanged.
December 2017	Replace policy	Policy updated with literature review through July 20, 2017; no references added. Policy statement unchanged.
December 2018	Replace policy	Policy updated with literature review through July 9, 2018; references 5-6, 11, 18-20, 28-29, 34-35, and 45 added. Policy statement unchanged.
December 2019	Replace policy	Policy updated with literature review through July 8, 2019; no references added. Policy statement unchanged.
December 2020	Replace policy	Policy updated with literature review through July 21, 2020; references added. Policy statement unchanged.
December 2021	Replace policy	Policy updated with literature review through July 23, 2021; no references added. Policy statement unchanged.
December 2022	Replace policy	Policy updated with literature review through September 29, 2022; references added. Minor editorial refinement to policy statement to include patients with uncontrolled hypertension; intent unchanged. Title updated to: "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Resistant or Uncontrolled Hypertension."
December 2023	Replace policy	Policy updated with literature review through August 25, 2023; references added. Editorial refinement to policy to include only evidence from the current generation Symplicity Spyral catheter and to omit earlier trials of the first generation device. Title updated to: "Radiofrequency Ablation of the Renal Sympathetic Nerves as a Treatment for Uncontrolled Hypertension." The indication for resistant hypertension was removed, and the indication for uncontrolled hypertension changed to: "Individuals with uncontrolled hypertension, despite the use of anti-hypertensive medications or who poorly tolerate blood pressure therapy, who receive radiofrequency ablation of the renal sympathetic nerves." Policy statement remains investigational.