Introduction

Treating high blood pressure often involves making lifestyle changes and using medications. A newer technique that destroys parts of certain nerves has been proposed as a way to lower blood pressure when medication doesn’t work. For this procedure, a narrow tube (catheter) is inserted in an artery near the groin. The catheter is threaded up to the artery that supplies blood to the kidney and then maneuvered to the nerves in the wall of this kidney artery. A weak electrical current is released, and the heat kills parts of these nerves. It’s thought that because these nerves are damaged they will reduce the kidney’s production of specific hormones. The decreased amount of this hormone is thought to decrease blood pressure over time. Medical studies have conflicting results about whether this treatment works. This service is considered investigational (unproven).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
## Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiofrequency ablation of the renal sympathetic nerves</td>
<td>Radiofrequency ablation of the renal sympathetic nerves is considered investigational for the treatment of resistant hypertension.</td>
</tr>
</tbody>
</table>

## Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>0338T</td>
<td>Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery(ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; unilateral</td>
</tr>
<tr>
<td>0339T</td>
<td>Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery(ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; bilateral</td>
</tr>
</tbody>
</table>

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## Related Information

N/A

## Evidence Review
Description

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. RFA of the renal sympathetic nerves may act as a nonpharmacologic treatment for hypertension and has been proposed as a treatment option for patients with resistant hypertension.

Background

Resistant Hypertension

Hypertension is estimated to affect approximately 30% of the population in the United States.\(^1\) It accounts for a high burden of morbidity related to strokes, ischemic heart disease, kidney disease, and peripheral arterial disease. Resistant hypertension is defined as elevated blood pressure, despite treatment with at least three antihypertensive agents at optimal doses. Resistant hypertension is also a relatively common condition, given the large number of individuals with hypertension. In large clinical trials of hypertension treatment, 20% to 30% of participants meet the definition for resistant hypertension, and in tertiary care hypertension clinics, the prevalence is estimated at 11% to 18%.\(^1\) Resistant hypertension is associated with a higher risk for adverse outcomes such as stroke, myocardial infarction, heart failure, and kidney failure.

A number of factors may contribute to uncontrolled hypertension, and they should be considered and addressed in all patients with hypertension before labeling a patient resistant. They include nonadherence to medications, excessive salt intake, inadequate doses of medications, excess alcohol intake, volume overload, drug-induced hypertension, and other forms of secondary hypertension.\(^2\) Also, sometimes it is necessary to address comorbid conditions (ie, obstructive sleep apnea) to control blood pressure adequately.

Treatment

Treatment for resistant hypertension is mainly intensified drug therapy, sometimes with the use of nontraditional antihypertensive medications such as spironolactone and/or minoxidil. However, control of resistant hypertension with additional medications is often challenging and can lead to high costs and frequent adverse effects of treatment. As a result, there is a large
unmet need for additional treatments that can control resistant hypertension. Nonpharmacologic interventions for resistant hypertension include modulation of the baroreflex receptor and/or radiofrequency (RF) denervation of the renal nerves.

**RF Denervation of the Renal Sympathetic Nerves**

Increased sympathetic nervous system activity has been linked to essential hypertension. Surgical sympathectomy has been shown to be effective in reducing blood pressure but is limited by the adverse events of surgery and was largely abandoned after effective medications for hypertension became available. The renal sympathetic nerves arise from the thoracic nerve roots and innervate the renal artery, the renal pelvis, and the renal parenchyma. Radiofrequency ablation (RFA) 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.\(^3\)

The procedure is performed percutaneously with access at the femoral artery. A flexible catheter is threaded into the renal artery, and a controlled energy source, most commonly low-power RF energy, is delivered to the arterial walls where the renal sympathetic nerves are located. Once adequate RF energy has been delivered to ablate the sympathetic nerves, the catheter is removed.

**Summary of Evidence**

For individuals who have hypertension resistant to standard medical management who receive RFA of the renal sympathetic nerves, the evidence includes numerous randomized controlled trials (RCTs), numerous systematic reviews of the RCTs, as well as multiple nonrandomized comparative studies and case series. The relevant outcomes are symptoms, change in disease status, morbid events, medication use, and treatment-related morbidity. The largest trial, the Symplicity HTN-3 trial, used a sham-controlled design to reduce the likelihood of placebo effect and demonstrated no significant differences between renal denervation and sham-control patients in office-based or ambulatory blood pressure at six-month follow-up. The Symplicity HTN-3 results were in contrast to other studies not using a sham control design, including Symplicity HTN-2 and Renal Denervation for Hypertension (DENERHTN) trial, which reported efficacy in reducing blood pressure over a six-month time period compared with a control group. However, results from Symplicity HTN-3 have been supported by a number of subsequent smaller sham-controlled trials. Meta-analyses of the RCTs have also reported
inconsistent findings, with most analyses showing no significant benefit in blood pressure measurements following RFA. Single-arm studies with overlapping populations have reported improvements in blood pressure and related physiologic parameters, such as echocardiographic measures of left ventricular hypertrophy, that appear to be durable up to 24 months of follow-up. The strongest evidence comes from sham-controlled trials, the largest of which found no significant benefits with renal denervation. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

**Table 1: Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NCT02439775</td>
<td>Global Clinical Study of Renal Denervation With the Symplicity Spyral™ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension on Standard Medical Therapy (SPYRAL HTN-ON MED)</td>
<td>106</td>
<td>Feb 2024</td>
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<tr>
<td>NCT01673516</td>
<td>Effect of Renal Sympathetic Denervation on Resistant Hypertension and Cardiovascular Hemodynamic in Comparison to Intensive Medical Therapy Utilizing Impedance Cardiography</td>
<td>60</td>
<td>Aug 2022</td>
</tr>
<tr>
<td>NCT02439749</td>
<td>Global Clinical Study of Renal Denervation With the Symplicity Spyral™ Multi-electrode Renal Denervation System in Patients With Uncontrolled Hypertension in the Absence of Antihypertensive Medications (SPYRAL HTN-OFF MED)</td>
<td>433</td>
<td>Mar 2023</td>
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<tr>
<td>NCT02021019</td>
<td>Renal Denervation to Improve Outcomes in Patients With End-stage Renal</td>
<td>100</td>
<td>Dec 2022 (unknown)</td>
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<tr>
<td>NCT04307836</td>
<td>DENEX Renal Denervation in Patients With Hypertension on no or 1-3 Antihypertensive Medications (DENEX HTN-KORAS)</td>
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<td>Jan 2023</td>
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<tr>
<td>NCT No.</td>
<td>Trial Name</td>
<td>Planned Enrollment</td>
<td>Completion Date</td>
</tr>
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<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01911078</td>
<td>Renal Sympathetic Denervation in Metabolic Syndrome (Metabolic Syndrome Study)</td>
<td>20</td>
<td>Jun 2016 (completed)</td>
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<tr>
<td>NCT01901549</td>
<td>Renal Denervation in Patients After Acute Coronary Syndrome</td>
<td>80</td>
<td>Jun 2016 (unknown)</td>
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<tr>
<td>NCT02041130</td>
<td>Renal Sympathectomy in Heart Failure (the RESPECT-HF Study) - a Study of Renal Denervation for Heart Failure With Preserved Ejection Fraction</td>
<td>144</td>
<td>Dec 2016 (unknown)</td>
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<tr>
<td>NCT01522430</td>
<td>Denervation of Renal Sympathetic Activity and Hypertension Study</td>
<td>120</td>
<td>Dec 2016 (unknown)</td>
</tr>
<tr>
<td>NCT01932450</td>
<td>A Randomized, Open-label Study Investigating the Effect of Bilateral Renal Artery Sympathetic Denervation by Catheter-based Radiofrequency Ablation on Blood Pressure and Disease Progression in Autosomal Dominant Polycystic Kidney Disease</td>
<td>100</td>
<td>Jul 2015 (unknown)</td>
</tr>
<tr>
<td>NCT01628172a</td>
<td>Renal Sympathetic Denervation for the Management of Chronic Hypertension</td>
<td>96</td>
<td>Mar 2014 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial

*a Denotes industry-sponsored or cosponsored trial

**Practice Guidelines and Position Statements**

**American Heart Association et al**

The American Heart Association, American College of Cardiology, and American Society of Hypertension (2015) issued guidelines on the treatment of hypertension in patients with coronary artery disease.45 The guidelines noted that 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 American Heart Association, American College of Cardiology, and nine additional specialty societies (2018) published joint guidelines on the prevention, detection, evaluation, and management of high blood pressure in adults.46 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 American Heart Association (2018) published a Scientific Statement on the detection, evaluation, and management of resistant hypertension. The AHA Statement discussed the lack of benefit found in the Symplicity HTN-3 trial, as well as its methodological limitations. The AHA 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 AHA 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 for the management of hypertension in adults. These recommendations did not discuss the use of renal denervation.

**Medicare National Coverage**

There is no national coverage determination.

**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):

- Symplicity™ Renal Denervation System (Medtronic). In April 2018, the FDA approved an investigational device exemption pivotal trial, SPYRAL HTN. The trial will be randomized and sham-controlled and is designed to evaluate the RFA device as an alternative to exercise or lifestyle modification in patients with uncontrolled hypertension not treated with medication. Bohm et al (2020) has already published the 3-month results. The trial remains ongoing, however, with planned follow-up for 3 years for evaluation of long-term efficacy and safety. An additional randomized trial in patients with uncontrolled hypertension despite antihypertensive medication is ongoing (SPYRAL HTN-ON MED, NCT02439775).
• 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 OneShot™ Renal Denervation System (Covidien) is an irrigated RFA balloon catheter, consisting of a spiral-shaped electrode surrounding a balloon. (In 2014, Covidien abandoned development of its OneShot™ Renal Denervation program.)

• 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.

References


**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/15/12</td>
<td>New Policy. Radiofrequency ablation of the renal sympathetic nerves is considered investigational for the treatment of resistant hypertension.</td>
</tr>
<tr>
<td>12/04/13</td>
<td>Replace policy. Policy updated with literature review through July 31, 2013. References 5, 6, 17-21 added. No change in policy statement. Codes 0338T and 0339T added to policy; codes 36251-36254 removed from policy; they are no specific to the procedure.</td>
</tr>
<tr>
<td>11/20/14</td>
<td>Annual Review. Policy updated with literature review through July 31, 2014. References 4-5, 8-9, 11-12, 16, 19, 29-36, 38-43, and 45 added. No change to policy statement.</td>
</tr>
<tr>
<td>11/10/15</td>
<td>Annual Review. 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.</td>
</tr>
<tr>
<td>12/07/15</td>
<td>Update Related Policies. Removed 8.01.57 as it is archived.</td>
</tr>
<tr>
<td>12/01/19</td>
<td>Annual Review, approved November 6, 2019. Policy updated with literature review through July 2019; no references added. Policy statement unchanged.</td>
</tr>
</tbody>
</table>

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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