Renal denervation

Clinical Policy ID: CCP.1283

Recent review date: 1/2021

Next review date: 5/2022

Policy contains: Renal sympathetic ablation; renal denervation; treatment-resistant hypertension.

AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas' clinical policies are not guarantees of payment.

Coverage policy

Renal denervation is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Antihypertensive medications.
- Diuretic therapy.

Background

The sympathetic nervous system is responsible for preparing the body for stressful or emergency situations, often referred to as the fight-or-flight response. Its effects target kidney function and systemic hemodynamics. Renal injury or hypoxia further enhances systemic and renal sympathetic activity. Sympathetic hyperactivity has been implicated in the initiation and progression of multiple conditions, including arterial hypertension, sleep apnea, metabolic syndrome, myocardial hypertrophy and heart failure, and cardiac arrhythmias (Bohm, 2014).

Renal denervation, also referred to as renal sympathetic ablation, is a minimally invasive percutaneous procedure that uses a radiofrequency catheter inserted through the femoral artery to selectively engage the sympathetic nerve fibers surrounding the renal artery. The desired result is to interrupt the influence of the

sympathetic reflexes on the kidney and systemic hemodynamics. The procedure usually takes from 45 to 60 minutes when a single catheter is used, or less time with a multi-electrode or balloon catheter. Analgesia and sedation are required (Böhm, 2014).

Renal denervation has been proposed as a non-pharmacologic treatment for treatment-resistant hypertension, which is common in patients with pre-existing comorbid atherothrombotic disease and obesity, and for other sympathetically driven conditions (Böhm, 2014). Renal denervation devices are available under investigational device exemption use only; none has received U.S. Food and Drug Administration (2020a, 2020b) approval for commercial use.

Findings

We included four systematic review/meta-analyses, three professional guidelines, and one cost-effectiveness analysis for this policy. Two systematic reviews/meta-analyses (Shafi, 2016; Fadl Elmula, 2015), the cost-effectiveness analysis (Geisler, 2012), and all three guidance documents (Lobo, 2015; Schlaich, 2013; National Institute for Health and Care Excellence, 2012) evaluated renal denervation for treatment-resistant hypertension. Two systematic reviews examined the role of renal denervation for treatment of Type 2 diabetes mellitus and obstructive sleep apnea (Pan, 2015; Shantha, 2015).

There is insufficient evidence to support the clinical use of catheter-based renal denervation for any indication. The evidence comprises observational data from multiple small case series and limited comparative clinical trials using the SYMPLICITY™ Renal Denervation System (Medtronic, Inc, Santa Rosa, California). The SYMPLICITY trials enrolled patients with severe treatment-resistant hypertension who were receiving a stable antihypertensive regimen of at least three drugs including a diuretic, and had adequate renal function:

- SYMPLICITY HTN-1 was the first in-human, proof-of-concept and safety study of 45 participants (Krum, 2014).
- SYMPLICITY HTN-2 was a multi-site, randomized controlled trial of 106 participants (Esler, 2014).
- SYMPLICITY HTN-3 was a multi-site, randomized controlled trial of 535 participants with sham controls (Bakris, 2014; Bhatt, 2014).

The evidence from these trials suggests that renal denervation in patients with treatment-resistant hypertension is safe, may be cost-effective, and lowers systolic blood pressure in the short term and medium term, but the results are highly variable. Long-term safety data beyond three years follow-up are lacking. Reduction in systolic blood pressure after renal denervation was greater in observational studies than randomized studies, and in studies that used office blood pressure measurement rather than ambulatory blood pressure measurement as an efficacy endpoint. Of note, while SYMPLICITY HTN-3, the most rigorously designed trial, met its primary safety endpoint with a major adverse event rate of only 1.4%, it failed to meet its primary and secondary efficacy endpoints; no statistically significant difference was shown in blood pressure measurement between the renal denervation treatment and sham control arms.

Results of the SYMPLICITY studies cannot be extrapolated to less severe or secondary forms of hypertension or to other catheter-based systems. Several factors may influence the findings, such as ethnicity, age, renal status, other comorbidities, and technical proficiency; efforts to address the design of future studies have been reported (Lobo, 2015; White, 2014). A growing body of evidence from non-randomized smaller studies suggests a potentially important role for renal denervation in the management of other disease states characterized by overactivation of sympathetic nerves. Further research using randomized, appropriately controlled, blinded designs, and large-scale registries is needed to identify optimal candidates for renal denervation, refine the technology, define procedural success and clinical efficacy of renal denervation in reducing blood pressure, and improve important clinical outcomes (e.g., risk of stroke, myocardial infarction, heart failure, and death).

In 2018, we added one new Cochrane review that found low- to moderate-quality evidence from randomized controlled trials did not support a clear benefit of renal denervation for treatment-resistant hypertension, and lacked long-term outcomes (Coppolino, 2017). The U.S. Food and Drug Administration has still not approved renal denervation for commercial use in the United States. No policy changes are warranted.

In 2019, we added one guideline from the American Heart Association (Carey, 2018). In the United States, renal denervation continues to be available under research protocols only. No policy changes are warranted. The policy ID was changed from CP# 09.03.04 to CCP.1283.

In 2020, we added four systematic reviews and meta-analyses confirming previous policy findings that renal denervation could safely reduce blood pressure compared with sham control, but incomplete medication adherence was common (Agasthi, 2019; Cheng, 2019; Liu, 2019; Lobo, 2019). Clinical studies to evaluate the safety and effectiveness of these devices are progressing (U.S. Food and Drug Administration, 2018). Such studies will employ randomization, sham controls, careful attention to medication adherence (on and off antihypertensive medications), careful ambulatory blood pressure measurement to evaluate efficacy, and careful attention to patient preferences to address the limitations that occurred in previous research. No policy changes are warranted.

In 2021, we added two registry studies (Lee, 2019; Rodriguez-Leor, 2020) and one longitudinal study (Naduvathumuriyil, 2020) that suggest renal denervation is safe and effective for patients with treatment-resistant hypertension with a clinically significant antihypertensive effect. In all instances, the authors called for randomized controlled trials to determine the specific context within which renal denervation should be considered a therapeutic option in antihypertensive care. To that end, Böhm (2020) published study design details of two ongoing randomized, sham-controlled clinical trials that enrolled subjects with uncontrolled hypertension in the absence (SPYRAL HTN-OFF MED Pivotal; clinicaltrials.gov identifier NCT02439749) or presence (SPYRAL HTN-ON MED Expansion; clinicaltrials.gov identifier NCT02439775) of antihypertensive medications. Both studies are sponsored by Medtronic, Inc. (Santa Rosa, California) with an estimated completion date of March 2023.

A new guideline by Hypertension Canada (Hiremath, 2020) does not recommend renal denervation for the routine treatment of hypertension, because the device has not been approved for use in Canada, but they recommend investigating the device in the context of controlled clinical studies. No policy changes are warranted.

References

On October 19, 2020, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “renal denervation,” “ablation,” “sympathectomy,” and “treatment resistant hypertension.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

11/2016: initial review date and clinical policy effective date: 2/2017

1/2018: Policy references updated.

1/2019: Policy references updated and policy ID changed.

1/2020: Policy references updated.

1/2021: Policy references updated.