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12-Month Blood Pressure Results of Catheter-Based Renal Artery Denervation for Resistant Hypertension

The SYMPLICITY HTN-3 Trial

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ABSTRACT

BACKGROUND Results of the SYMPLICITY HTN-3 (Renal Denervation in Patients With Uncontrolled Hypertension) trial confirmed the safety but not the efficacy of renal denervation for treatment-resistant hypertension at 6 months post procedure.

OBJECTIVES This study sought to analyze the 12-month SYMPLICITY HTN-3 results for the original denervation group, the sham subjects who underwent denervation after the 6-month endpoint (crossover group), and the sham subjects who did not undergo denervation after 6 months (non-crossover group).

METHODS Eligible subjects were randomized 2:1 to denervation or sham procedure. Subjects were unblinded to their treatment group after the 6-month primary endpoint was ascertained; subjects in the sham group meeting eligibility requirements could undergo denervation. Change in blood pressure (BP) at 12 months post randomization (6 months for crossover subjects) was analyzed.

RESULTS The 12-month follow-up was available for 319 of 361 denervation subjects and 48 of 101 non-crossover subjects; 6-month denervation follow-up was available for 93 of 101 crossover subjects. In denervation subjects, the 12-month office systolic BP (SBP) change was greater than that observed at 6 months (-15.5 ± 24.1 mm Hg vs. -18.9 ± 25.4 mm Hg, respectively; $p = 0.025$), but the 24-h SBP change was not significantly different at 12 months ($p = 0.229$). The non-crossover group office SBP decreased by -32.9 ± 28.1 mm Hg at 6 months, but this response regressed to -21.4 ± 19.9 mm Hg ($p = 0.01$) at 12 months, increasing to 11.5 ± 29.8 mm Hg.

CONCLUSIONS These data support no further reduction in office or ambulatory BP after 1-year follow-up. Loss of BP reduction in the non-crossover group may reflect decreased medication adherence or other related factors. (Renal Denervation in Patients With Uncontrolled Hypertension [SYMPLICITY HTN-3]; NCT01418261) (J Am Coll Cardiol 2015;65:1314–21) © 2015 by the American College of Cardiology Foundation.

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The SYMPLICITY HTN-3 (Renal Denervation in Patients With Uncontrolled Hypertension) study was a prospective, blinded, randomized, sham-controlled trial that used ambulatory blood pressure measurement (ABPM) as part of the inclusion criteria as well as a pre-specified secondary endpoint. All participants were evaluated at baseline and 6 months for changes in ambulatory, home, and office blood pressure (BP). Primary results of the trial

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demonstrated safety of the renal denervation procedure but failed to show a greater reduction in office or ambulatory systolic BP (SBP) than that with the sham procedure at 6 months (1). This paper presents the detailed office and 24-h ABPM results of SYMPLICITY HTN-3 after 1 year of follow-up in the original cohort randomized to the procedure as well as in those who were either not eligible to be crossed over and those who were crossed over and who underwent renal denervation at 6 months.

METHODS

STUDY POPULATION. SYMPLICITY HTN-3 was a prospective, randomized, sham-controlled, multicenter clinical trial. Primary results and detailed methods were published previously (1). Adult subjects with uncontrolled hypertension receiving a stable antihypertensive medication regimen that included maximally tolerated doses of ≥3 medications of complementary classes, including a diuretic agent, were randomized 2:1 to undergo renal denervation or sham procedure. Subjects were required to have a seated office SBP of ≥160 mm Hg at their first screening visit with the pressure confirmed before randomization at the second screening visit. The protocol provided escape criteria to allow changes in antihypertensive medication during the 2-week period between screening visits. Subjects were also required to have a 24-h ambulatory SBP of ≥135 mm Hg before to randomization. Details of the ABPM procedures were reported previously (2).

Additional clinical exclusion criteria included known secondary causes of hypertension or more than 1 hospitalization for hypertensive emergency in the previous year. Anatomic exclusion criteria included >50% renal artery stenosis, renal artery aneurysm, prior renal artery intervention, multiple renal arteries, renal artery diameter of <4 mm, or treatable segment of <20 mm in length.

The Symplicity renal denervation system (Medtronic, Santa Rosa, California) was used to deliver radiofrequency energy within the main renal arteries to ablate surrounding efferent and afferent nerves. Subjects randomized to the sham control group received a renal angiogram and were blinded by the use of conscious sedation, blindfolding, music (to cover procedural sounds), and lack of experience regarding the procedure.

After 6-month primary safety and efficacy endpoints were ascertained, subjects were unblinded to their treatment, and those in the sham control group who still met eligibility requirements were allowed to crossover to receive the denervation procedure (crossover group). Subjects with a BP lower than required or who otherwise did not choose to undergo renal denervation were followed as the non-crossover group.

ABBREVIATIONS AND ACRONYMS

ABPM = ambulatory blood pressure monitoring

DBP = diastolic blood pressure

SBP = systolic blood pressure

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