Renal denervation shows no benefit in resistant hypertension

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Renal denervation fell short of primary and secondary efficacy goals in patients with severe resistant hypertension but did meet the primary safety endpoints, according to keenly awaited data from SYMPLICITY HTN-3 presented at the American College of Cardiology's 63rd Annual Scientific Session. This pivotal trial is the largest study conducted of renal artery denervation as a treatment for resistant hypertension and the most rigorously designed, including blinding and a sham treatment in the control arm.

Hypertension increases risks for heart attack and stroke for more than 77 million Americans and up to one billion adults worldwide. People with severe resistant hypertension – high blood pressure not controlled with three classes of medications – are a very challenging subset of patients. During the renal denervation procedure with the Symplicity device used in this trial, a catheter is threaded through arteries to deliver radiofrequency energy that inactivates kidney nerves, interrupting electrical signals to and from the kidney, an organ that performs a major role in regulating blood pressure. Although renal denervation is in clinical use for uncontrolled hypertension in more than 80 countries, it is still considered an experimental approach in the United States.

This study randomly assigned 535 patients with resistant hypertension and systolic blood pressure of 160 mmHg or higher to renal denervation or angiography alone. Both groups remained on treatment regimens of three or more antihypertensive drugs, including a diuretic, at the highest tolerated doses. Renal denervation failed to achieve the primary efficacy

endpoint of a decrease in systolic blood pressure measured in the doctor's office from baseline to six months or the powered secondary efficacy endpoint of decrease in average 24-hour levels by ambulatory blood pressure monitoring, which provides more reliable readings. Although both study groups showed a statistically significant decrease at six months compared with baseline (-14.1 mmHg for renal denervation compared to -11.7 mmHg for the sham treatment control), the difference of -2.29 mmHg in office systolic blood pressure between the two arms was not significant. Results were similar for change in 24-hour systolic blood pressure, with a non-significant difference between the two arms of -1.96 mmHg.

"That is a fascinating result because it highlights the importance of a properly done, rigorous randomized trial that is both blinded and sham controlled," said Deepak L. Bhatt, M.D., M.P.H., executive director of interventional cardiovascular programs, Brigham and Women's Hospital Heart and Vascular Center, professor of medicine at Harvard Medical School, and co-principal investigator. "This is the first blinded trial or sham controlled trial in the field of renal denervation. It seems that these factors really mattered. We saw no added treatment benefit of renal denervation for patients with severe resistant hypertension who were closely monitored and optimally treated with medications."

Bhatt commented on the value of the study's cooperation between interventional and non-interventional blood pressure doctors, which demonstrated that a "good proportion" of patients with resistant hypertension in this study responded to expert medical therapy. However, new treatment options are still needed for patients with uncontrolled high blood pressure, he said.

The major adverse event rate of 1.4 percent for renal denervation comfortably met the safety goal of 9.8 percent, compared with 0.3 percent in the sham treatment arm. Although a particular area of concern

was potential renal stenosis, there was only one case in the renal denervation group and none in the sham group.

"The field has really exploded with several devices in clinical practice despite lack of compelling data to support their use. Now we have some definitive data with one device," Bhatt said. "However, we do think research in the field should continue, especially to see if renal denervation is useful in other areas, such as heart failure or with alternative approaches. We've shown renal artery denervation is very safe."

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