腎除神経術は治療抵抗性高血圧に有益性をもたらさない

SYMPLICITY HTN-3：過去のトライアルにおいて認められた腎除神経術の強力な効果は新たな厳密なスタディにおいて消失した

SYMPLICITY HTN-3: Strong effects of renal denervation seen in earlier trials disappear with rigorous design of new study

重度の治療抵抗性高血圧患者において腎除神経術は一次および二次の有効性ゴールを満たさなかったが、一次安全性エンドポイントには合致したとの切実に待ち望まれていたSYMPLICITY HTN-3のデータが第63回American College of Cardiology学会で発表され、同時に*New England Journal of Medicine*オンライン版に掲載された。研究者らは、収縮期血圧160mmHg以上の治療抵抗性高血圧患者535人を腎除神経術群または血管造影のみの群にランダムに割り付けた。両群ともに3剤以上の降圧薬治療を継続された。両スタディ群とも6か月後にはベースラインと比較し統計学的に有意な血圧低下（腎除神経群 -14.1mmHgに対しシャム治療コントロール群-11.7mmHg）を示したが、2群間に認められた外来収縮期血圧の-2.29mmHgの差は有意ではなかった。24時間収縮期血圧の変化においても結果は同様で、2群間には有意でない-1.96mmHgの差が認められた。この極めて重要なトライアルは治療抵抗性高血圧治療として腎除神経術を行ったスタディの中で最大であり、盲検化およびコントロール群のシャム治療などは最も厳密にデザインされたものである。

Full Text

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 and simultaneously published online in the *New England Journal of Medicine*. 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 myocardial infarction and stroke for 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. Renal denervation is in clinical use for uncontrolled hypertension in more than 80 countries.

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 cardiologists, 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 hypertension, 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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