Tackling Resistant Hypertension – Is There a Role for Renal Denervation Therapy?

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THE STUDY: Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med* 2014; 370(15):1393-401

BACKGROUND

Resistant hypertension is defined as a blood pressure of 140/90 mm Hg or higher, despite using 3 maximally tolerated antihypertensive medications, including a diuretic at an appropriate dose [1]. It is associated with increased cardiovascular morbidity and mortality. A novel treatment option explored in the past is catheter based radio frequency renal artery denervation. This procedure basically decreases the sympathetic tone of the renal arteries by disrupting renal nerves traveling in the adventitia of the renal arteries.

Numerous studies have demonstrated significant reductions in blood pressures in resistant hypertension and the procedure is being used routinely in many centers across the world. The Symplicity HTN-1 and 2 trials, demonstrated a significant reduction in blood pressures of patients with resistant hypertension who received renal denervation therapy [2, 3]. Although the later study was randomized, it was not blinded. Similar weakness existed amongst other studies, which is why a well designed study addressing these aspects was needed.

WHY WAS THE STUDY CONDUCTED?

Earlier studies and trials had some shortcomings as stated above. Thus, the authors designed a prospective, randomized control trial that was single blinded.

THE STUDY

It was a prospective, randomized, sham controlled and single blind trial done in the USA from October 2011 to May 2013. Five hundred and thirty five patients with resistant hypertension, defined as a blood pressure of 160 mm Hg or higher while on at least three anti-hyp-ertensive medications that were maximally tolerated including a diuretic at an appropriate dose were randomly assigned in a 2:1 ratio into treatment and control groups. Patients in the treatment group underwent renal artery denervation with delivery of radiofrequency energy by a renal denervation catheter designed by Medtronic. The control group only underwent angiography. Neither group knew which procedure they underwent or what treatment they received.

Three endpoints were defined:

- A primary efficacy endpoint was defined as a mean change in the office blood pressure from baseline at 6 months (with a superiority margin of 5 mm Hg).
- A secondary efficacy end point was defined as a mean change in 24 hour ambulatory systolic blood pressure at 6 months (with a superiority margin of 2.5 mm Hg).
- The primary safety end point was a composite of major adverse effects including death, end stage renal disease, embolic events resulting in end organ damage, renal artery or other vascular complications or hypertensive crisis within 30 days. The criterion for this safety point was a rate of major adverse events of 9.8% derived from historical data.

WHAT DID THE STUDY FIND?

The mean change in office blood pressures at 6 months in the treatment group was -14.12±23.93 mm Hg and -11.74±25.94 mm Hg in the sham procedure group, for a difference of -2.39 mm Hg (95% confidence interval, P=0.26 with a superiority margin of 5 mm Hg). The change in ambulatory blood pressures at 6 months was -6.75 ± 15.11 mm Hg in the treatment group and -4.79±17.25 mm Hg in the sham procedure group (95% confidence interval, for a difference of -1.96 mm Hg , P=0.98 with a superiority margin of 2 mm Hg). There were few adverse effects; five in the treatment group (1.4%) and 1 in the control group (0.8%).

WHAT ARE THE STRENGTHS AND LIMITATIONS OF THE STUDY?

The Symplicity HTN-3 trial described no statistically significant reduction in office or ambulatory blood pressure after renal denervation compared to a sham control 6 months after the procedure. Its results contradict findings of the previous Symplicity trials. The strengths of this study relative to previous trials included double blinded, sham-control design which helped in making findings more authentic and dependable.

There were a few clear limitations. Firstly, since the catheter worked by delivering a specific amount of energy, there was no definitive marker to assess the right amount of energy delivered and to estimate a successful denervation. This may have contributed to a lack of efficacy and thus the negative results in the denervation group.

Secondly, medication adherence could also not be confirmed, although stringent measures were taken to ensure as much adherence as possible.

Thirdly, the results of the trial are specific to the catheter used in this study which was the simplicity renal denervation catheter designed by Medtronic; they cannot be generalized to other denervation systems, since a wide variety of such systems are in use, with different documented efficacies.

Weighing these pros and cons, this trial does provide us with valuable information about renal denervation therapy as a novel modality for resistant hypertension. Further trials will help to calrify the findings of the simplicity HTN-3 trial.

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