SYMPLICITY HTN-3 Trial: No Blood Pressure Reduction in Patients With Resistant Hypertension Treated With Renal Denervation

Written by Muriel Cunningham

Previous research suggests that catheter-based renal artery denervation (RDN) reduces blood pressure (BP) in patients with resistant hypertension. Deepak L. Bhatt, MD, MPH, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented the results of the Renal Denervation in Patients With Uncontrolled Hypertension trial [SYMPLICITY HTN-3; Bhatt DL et al. *N Engl J Med* 2014]. This was a large, prospective, randomized, blinded sham-controlled study conducted to assess the safety and efficacy of percutaneous RDN in patients with resistant hypertension.

The study was conducted at 88 sites in the United States. Patients were eligible if they were aged 18 to 80 years at the time of randomization, were on a stable regimen of ≥3 antihypertensive medications of different classes (including a diuretic) with no changes in the previous 2 weeks and no expected changes in the next 6 months, and had a mean office systolic BP (SBP) ≥160 mm Hg. Patients with any of the following were excluded: an ambulatory BP monitor (ABPM) 24-hour average SBP <135 mm Hg, an estimated glomerular filtration rate of <45 mL/min/1.73 m^2, main renal arteries <4 mm diameter or <20 mm treatable length, multiple renal arteries, renal artery stenosis >50%, an aneurysm in either renal artery, or a history of prior renal artery intervention.

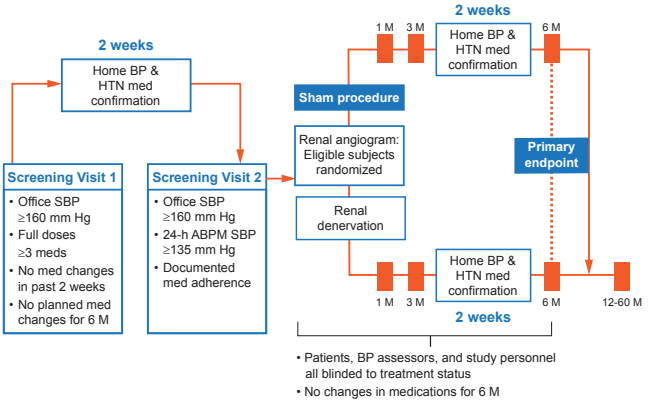
The study design is illustrated in Figure 1. Patients were randomized to either RDN or a sham procedure (renal angiogram). The primary endpoint was the change in SBP (office, superiority margin 5 mm Hg) at 6 months with the change in mean 24-hour ambulatory SBP as a secondary endpoint. The primary safety endpoint was a composite of death, end-stage renal disease, embolic events resulting in end-organ damage, renovascular complications, or hypertensive crisis at 1 month or new renal-artery stenosis at 6 months.

A total of 535 patients were randomized to RDN (n=364) and to the sham procedure (n=171). The mean age was 57 years, ~62% were male, ~70% were white, and patients were taking a mean of five antihypertensive agents. The mean baseline office SBP was 180 mm Hg, and the mean baseline ABPM was 160 mm Hg.

SBP in the two groups at 6 months was similar (difference of –2.39 mm Hg; 95% CI, –6.89 to 2.12; p=0.26) and SBP in both arms decreased from baseline to 6 months –14.1 mm Hg for the RDN group and –11.7 mm Hg for the sham group.

There was no difference in the major adverse event rate for RDN (1.4%) versus the sham arm (0.6%; p=0.67). The secondary efficacy analysis of the change in 24-hour mean systolic ABPM was also nonsignificant: –1.96 mm Hg (95% CI, –4.97 to 1.06).

Figure 1. Study Schematic



ABPM=ambulatory blood pressure monitor; BP=blood pressure; HTN=hypertension; M=months; SBP=systolic blood pressure.

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When presenting these results Dr. Bhatt concluded, "Further study in rigorously designed clinical trials will be necessary to confirm previously reported benefits of renal denervation in patients with resistant hypertension or to validate alternate methods of renal denervation."

Darapladib Without Significant CV Benefit in Stable Coronary Heart Disease (STABILITY)

Written by Wayne Kuznar

An investigational, selective, orally active inhibitor of lipoprotein-associated phospholipase A_2 (Lp-PLA_2) failed to significantly reduce the risk for cardiovascular (CV) death, myocardial infarction (MI), or stroke in stable coronary heart disease (CHD) patients on optimal medical therapy.

The design and results of the Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy trial [STABILITY; The STABILITY Investigators. *N Engl J Med* 2014] were presented by Harvey D. White, DSc, Auckland City Hospital, Auckland, New Zealand.

Elevated plasma levels of Lp-PLA_2 are associated with an increased risk of coronary events. The enzyme is secreted by T cells and macrophages and circulates largely bound to low-density lipoproteins [Zalewski A, Macphee C. *Arterioscler Thromb Vasc Biol* 2005]. Within atheromatous plaque, it hydrolyzes oxidatively modified polyunsaturated