blood pressure (SBP) [Bhatt DL et al. *N Engl J Med* 2014]. This may in part explain the lack of efficacy for the primary endpoint of the trial. The purpose of this sub-analysis was to determine the significance of several potential confounders that may have driven the effect observed in the sham arm, including procedural changes, change in antihypertensive therapy, variability in adherence, and differences in patient populations according to different geographic regions.

In the prospective, sham-controlled, SYMPLICITY HTN-3 trial, 535 patients with severe resistant hypertension were randomly assigned in a 2:1 fashion to undergo renal denervation (RDN) or a sham procedure. Resistant hypertension was defined as patients who had been prescribed 3 or more antihypertensive medications at maximally tolerated doses. There was no significant difference in change in SBP between the 2 arms at 6 months, as the sham arm demonstrated a significant change in SBP from baseline ($p<0.001$).

In the sub-analysis, procedural variability was analyzed such that the mean number of ablations in patients who underwent RDN was matched 1:1 using propensity scores. Patients were categorized according to 4 quadrant ablations in both, one, or neither renal artery. As the number of ablations increased, there was a trend toward a progressive decrease in office SBP in the patients who underwent RDN. There was, however, a similar, trend in the patients who underwent the sham procedure, with BP decreasing with an increasing number of ablations.

Baseline predictors of BP improvement in patients in the sham arm included the use of alpha-blockers, higher baseline office BP readings, the use of aldosterone antagonists, and the total number of intervention attempts. However, vasodilator use was inversely associated with response in both the sham and RDN arms. A secondary analysis of potential racial differences demonstrated that black patients were less likely to improve in the sham arm compared with patients who were not black.

Geographic location also led to some notable differences. Patients who lived in the Northeastern United States (Boston-New York region) demonstrated a change in office BP, albeit to a lesser extent in ambulatory BP. However, the results for patients living in the Southwestern, Southern, or Western United States reflected that of the original trial. It is unclear as to why there was a difference based on geographic location.

Dr. Bakris concluded by stating that there were some limitations in the SYMPLICITY HTN-3 trial that may have led to the neutral results with RDN for the primary endpoint. He further suggested that the limitations discussed in his presentation were exploratory and were meant to be hypothesis-generating.

Renal Denervation Improves Systolic Ambulatory BP in Resistant Hypertension

Written by Emma Hitt Nichols, PhD

Systolic daytime ambulatory blood pressure (BP) was significantly decreased by renal denervation plus standardized medical treatment with the Symplicity catheter compared with standardized medical treatment alone in patients with confirmed resistant hypertension. Michel Azizi, MD, PhD, Hôpital Européen Georges Pompidou, Paris, France, presented 6-month data from the multicenter Renal Denervation in Hypertension study [DENER-HTN; NCT01570777]

The Symplicity catheter system delivers radiofrequency energy to target nerves through the renal artery wall to reduce sympathetic nervous system involvement in hypertension [Medtronic 2013]. The purpose of the open-label DENER-HTN trial was to evaluate the safety, efficacy, and cost-effectiveness of renal denervation with the single-electrode Symplicity catheter for patients with resistant hypertension.

In the parallel superiority DENER-HTN trial, 106 patients with resistant hypertension were randomly assigned to receive renal denervation or 4 weeks of standardized therapy alone, after 4 weeks of standardized therapy did not reduce BP to <135/85 mm Hg. Resistant hypertension was defined as office BP of 140/90 mm Hg despite stable antihypertensive therapy with ≥3 medications. All patients received new, standardized treatment for hypertension that included indapamide (1.5 mg), ramipril (10 mg, or irbesartan, if cough present), and amlodipine (10 mg) daily.

The primary endpoint of the trial was changes in daytime ambulatory systolic BP at 6 months. At baseline, the mean office BP was 163/95 mm Hg, and the daytime ambulatory BP was 153.9/93.0 mm Hg. The mean body mass index was 30.1 kg/m^2, and the mean glomerular filtration rate was 88.6 mL/minute. Patients were monitored with home BP; if the home BP was not <135/85 mm Hg at 2 months, then the patient received spironolactone (25 mg) daily. If BP was still not controlled by 3, 4, or 5 months, patients also received bisoprolol, prazosin, and rilmenidine, respectively.

Patients who underwent renal denervation experienced a significant decrease in systolic BP of 16 mm Hg and the treatment-only group experienced a decrease of 10 to 14 mm Hg, with a difference between the 2 arms of –5.9 mm Hg at 6 months (95% CI, –11 to –0.05; p=0.03). In addition, nighttime ambulatory BP decreased by 6 mm Hg. The proportion of patients who achieved

BP <135/85 mm Hg at 6 months was 42% in the renal denervation arm compared with 28% in the standardized treatment only arm; however, this was not significant. In both arms of the study at 6 months, >85% of patients required ≥4 antihypertensive agents, with about 30% requiring 7 antihypertensives.

Dr. Azizi concluded by stating that data from the DENER-HTN trial show that renal denervation with the Symplicity catheter results in a significant reduction in systolic daytime ambulatory BP in patients with resistant hypertension.

Perioperative Beta-Blockade Improves CEA Outcomes

Written by Emma Hitt Nichols, PhD

Perioperative beta-blockade for patients with coronary artery disease (CAD) who are undergoing carotid endarterectomy (CEA) appeared to prevent cardiac damage, resulting in a low mortality rate and no stroke events. George Galyfos, MD, Hippocration Hospital, Athens, Greece, presented data from a study evaluating the role of beta-blockage in asymptomatic cardiac damage in patients with CAD undergoing CEA.

The death rate after undergoing CEA is up to 50%, with most deaths occurring within the first 48 hours. Therefore, CEA is considered to be a procedure of intermediate cardiac risk according to guidelines of the American College of Cardiology and American Heart Association. In 2009, those guidelines and those of the European Society of Cardiology recommended preoperative beta-blockade with dose titration as Class IIa evidence [Bouri S et al. *Heart* 2013]. In addition, a review revealed that in most studies, beta-blockade in patients undergoing vascular surgery resulted in a decrease in cardiovascular events, mortality, heart rate, and blood pressure compared with control; however, there was also an increased risk of bradycardia and mortality [Brooke BS, *J Vasc Surg* 2010]. The purpose of this study was to further evaluate the effect of beta-blockade on the outcomes of patients undergoing CEA.

In the present study, 162 patients with CAD who were expected to undergo CEA were randomly assigned to receive a beta-blocker (n=70) or not (n=92). In addition, patients were categorized into 3 groups (low, medium, or high cardiac risk) according to their Vascular Study Group of New England Cardiac Risk Index score [Bertges et al. *J Vasc Surg* 2010]. On the basis of this index, most patients with low cardiac risk were asymptomatic (64%), whereas a majority of patients at high cardiac risk had a history of transient ischemic attack or amaurosis (83%).

Patients who received beta-blockade before CEA had less cardiac damage compared with patients who did not undergo beta-blockade (odds ratio, 0.25; 95% CI, 0.08 to 0.77; p=0.01). Following the CEA procedure, there were no strokes overall, and no events were observed in patients at high cardiac risk. In addition, 14% of patients experienced asymptomatic cardiac damage within the first 72 hours, but there were no cases of symptomatic cardiac damage. The mortality rate in the study was 0.6%.

Interestingly, troponin levels increased by the first day after CEA for patients at low and intermediate cardiac risk but not for patients at high cardiac risk (Table 1). At Days 3 and 7, the troponin levels decreased in patients at low and intermediate risk but remained the same for patients at high risk. This suggests that patients at high risk receive the greatest benefit from beta-blockade.

Table 1. Troponin Levels After Carotid Endarterectomya

	Cardiac Risk (n=162)		
	Low (n=70)	Intermediate (n=80)	High (n=12)
Preoperatively	0.007	0.008	0.004
Day 1	0.297 (0.018)	0.624 (0.015)	0.026
Day 3	0.102 (<0.05)	0.204 (0.028)	0.023
Day 7	0.016	0.025	0.003

According to Vascular Study Group of New England Cardiac Risk Index score. Parentheses indicate significant p values.

In conclusion, Dr. Galyfos stated that data from this study indicate that perioperative administration of beta-blockers appears to provide a protective effect from cardiac damage in patients with CAD who are undergoing CEA. In addition, he called for more trials with less bias to examine the benefit of beta-blockade in this population.

24-Hour ceABP Is a Better Measurement in Young Patients

Written by Emma Hitt Nichols, PhD

Twenty-four-hour central ambulatory blood pressure (ceABP) was shown to be significantly lower than peripheral ambulatory blood pressure (pABP) in adolescents and young adults. Higher blood pressure (BP) was found to be correlated with left ventricular mass index (LVMI) and common carotid intima-media thickness (cIMT). Angeliki Ntineri, MD, University of Athens, Athens, Greece, presented data from a study of 24-hour ceABP in adolescents and young adults.

pABP is known to be higher than ceABP in young patients (up to 30 mm Hg) because of amplification of the