BP Reduction by Renal Denervation Maintained Over 24 Months in the EnligHTN I Trial

Written by Emma Hitt Nichols, PhD

The EnligHTN renal denervation system reduced office blood pressure (BP) with no serious periprocedural adverse events over 24 months of follow-up. Costas Tsioufis, MD, PhD, University of Athens, Athens, Greece, presented long-term data from *the* first-in-human *Safety and Efficacy Study of Renal Artery Ablation in Resistant Hypertension Patients trial* [EnligHTN I; NCT01438229].

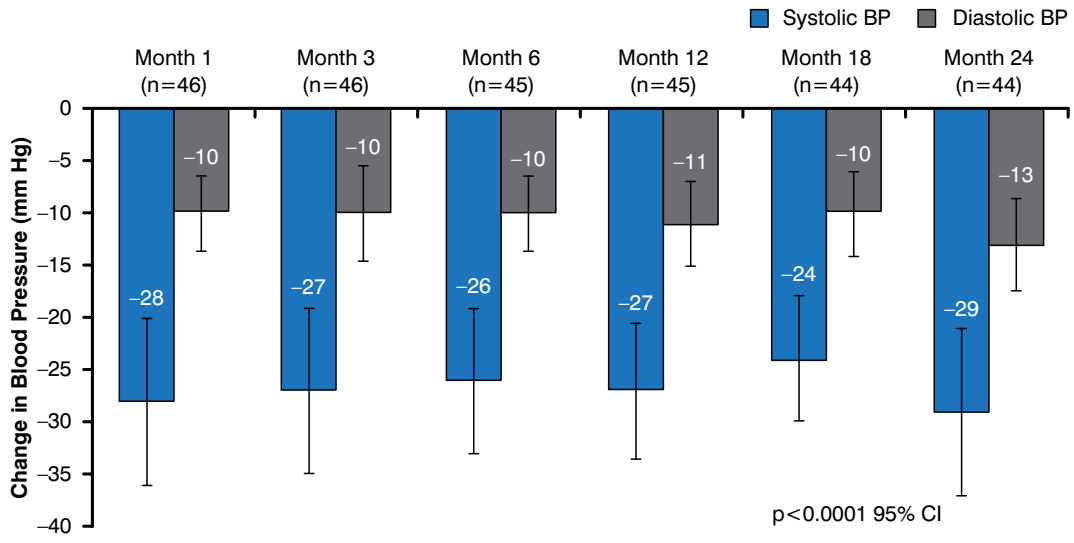
The EnligHTN renal denervation system uses a multielectrode device to produce acute lesions with a predictable pattern. During the procedure, after being positioned proximal to the bifurcation of the renal artery, the basket is expanded, and a diagnostic check is performed to ensure electrode contact. Ablation is performed for 90 seconds per electrode. The basket is collapsed, pulled back 1 cm, then rotated and expanded, wherein the diagnostic check is performed, followed by ablation. The purpose of this study was to determine the long-term safety and efficacy of renal denervation with the EnligHTN renal denervation system.

In the open-label interventional EnligHTN I trial, 46 patients with resistant hypertension received renal denervation and were followed for 24 months. No control group was enrolled. Resistant hypertension was defined as office systolic BP of ≥160 mm Hg that did not respond to ≥3 concurrent antihypertensive medications at maximally tolerated doses for a minimum of 14 days before enrollment. Patients aged 18 to 80 years were excluded if they had a history of renal artery intervention, renal artery stenosis >30%, multiple main renal arteries, main renal arteries <4 mm in diameter or <20 mm in length, a glomerular filtration rate of <45 mL/minute/1.73m^2, type 1 diabetes, identified cause of secondary hypertension, or significant valvular heart disease.

The primary objective was to evaluate all adverse events and office BP. At baseline, mean systolic and diastolic BP (SBP and DBP) were 176 and 96 mm Hg, respectively, with a mean number of antihypertensives of 4.7. In addition, 33% of patients had diabetes; 30% had sleep apnea; 59% had hyperlipidemia; 20% had coronary artery disease; and the mean body mass index was 32 kg/m^2. The mean number of left and right renal artery ablations performed were 7.4 and 7.7, respectively, with a mean of 15 total ablations performed per patient. The mean procedure time was 34 minutes.

In the EnligHTN I trial, renal denervation resulted in a significant decrease in office SBP and DBP at 1 month that was maintained to 24 months (p<0.0001; Figure 1). Similarly, ambulatory BP was significantly decreased from baseline following renal artery denervation (p<0.0001). At 24 months, 77% of patients were considered to have responded to renal denervation, with a reduction of office SBP by >10 mm Hg from baseline.

Figure 1. Office Blood Pressure Following Renal Denervation by the EnligHTN Renal Denervation System



BP=blood pressure.

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In addition, at 24 months, 39% of patients experienced an office SBP of <140 mm Hg.

Through 24 months of follow-up, there were no serious periprocedural events in the EnligHTN I trial. Serious device- or procedure-related events included 1 case of worsening preexisting proteinuria, 1 case of symptomatic hypotension, and 2 events in 1 patient of worsening of preexisting renal artery stenosis with a new stenotic lesion.

Prof. Tsioufis concluded that data from the EnligHTN I trial indicate that renal denervation with the EnligHTN system is effective in lowering office BP with an acceptable safety profile.

Metabolic Syndrome Elevates Risk of Microalbuminuria Despite BP Control

Written by Emma Hitt Nichols, PhD

Fimasartan reduced blood pressure (BP) and albumin-creatinine ratio (ACR) in patients with or without metabolic syndrome; however, patients with metabolic syndrome at baseline and 3 months were at a greater risk of elevated ACR at 1 year. Jeong Bae Park, MD, Cheil General Hospital, Kwandong, Korea, presented 3-month and 1-year data from a 3-year multicenter study designed to evaluate the effect of early correction of metabolic syndrome on organ damage for patients with hypertension [K-METS]. The design of this study has been published [Kim C et al. *Pulse* 2013].

The antihypertensive agent fimasartan is derived from losartan and is expected to have greater efficacy and potency [Kim TW et al. *Bioorg Med Chem Lett* 2012]. In clinical trials of fimasartan, risk of cardiovascular disease was reduced with the correction of metabolic risk factors in addition to BP control. The purpose of the observational K-METS study was to determine the effect of the early correction of metabolic syndrome on organ damage, as well as the future development of diabetes and cardiovascular disease, for patients with hypertension.

In the prospective single-arm K-METS study, 5481 patients with hypertension received open-label fimasartan and are being followed for 3 years. At baseline, 17% of patients had diabetes, mean weight was 67.3 kg, mean body mass index was 25.3 kg/m^2, and the mean number of years taking an antihypertensive agent was 3.58. Baseline systolic and diastolic BPs (SBP and DBP, respectively) were 144 and 88 mm Hg, respectively. Metabolic syndrome was present in 57% of the study population.

The primary end point of the K-METS study is cardiovascular mortality, stroke, myocardial infarction, hospitalization for heart failure, and the development of diabetes at 3 years. At 3 months, patients with hypertension or metabolic syndrome received therapy for correction. At 1 year, BP, insulin resistance, diabetes, and cardiovascular events were assessed. At 3 years, incidence of diabetes and cardiovascular disease will be evaluated. Patients were categorized into 4 groups according to the presence of metabolic syndrome:

1. *Group 1:* metabolic syndrome at baseline and 3 months
2. *Group 2:* metabolic syndrome at baseline but not at 3 months
3. *Group 3:* no metabolic syndrome at baseline but metabolic syndrome developed by 3 months
4. *Group 4:* no metabolic syndrome at baseline or 3 months

At 1 year, SBP and DBP significantly decreased to 127 and 79 mm Hg, respectively ($p<0.0001$), as well as ACR from 41.2 to 26.6 mg/g ($p<0.0001$). The proportion of patients with metabolic syndrome also decreased to 44% ($p<0.0001$). Although all groups experienced a decrease in ACR, patients in Group 1 or 2 experienced the greatest decrease in ACR. Patients in Group 1 had the highest ACR rates compared with Groups 2, 3, and 4. In addition, patients in Group 1 were at a greater risk of ACR ≥30 mg/g compared with Groups 2, 3, and 4 (odds ratio, 1.62; 95% CI, 1.33 to 1.97).

Dr. Park stated that data from the K-METS trial suggest that fimasartan treatment results in a substantial decrease in BP and ACR at 3 months and 1 year.

Multiple Factors Examined for Contributing to SYMPLICITY HTN-3 Failure

Written by Emma Hitt Nichols, PhD

Multiple factors associated with the Renal Denervation in Patients With Uncontrolled Hypertension trial [SYMPLICITY HTN-3; NCT01418261] may have contributed to its failure to meet the primary endpoint of change in office blood pressure at Month 6, according to George L. Bakris, MD, University of Chicago Medicine, Chicago, Illinois, USA, who presented data from a subanalysis of this trial.

The sham arm of the SYMPLICITY HTN-3 trial demonstrated a greater than expected reduction in systolic