Catheter-based Radiofrequency Renal Sympathetic Denervation for Resistant Hypertension

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ABSTRACT

Purpose: To evaluate the feasibility, efficacy, and safety of catheter-based radiofrequency renal sympathetic denervation for treatment of resistant hypertension.

Materials and Methods: Twenty-four patients with essential hypertension unresponsive to at least three antihypertensive agents underwent renal denervation (RDN). Three patients had variant renal anatomy. Comorbidities included diabetes ($n = 11$), renal failure ($n = 4$), and obstructive sleep apnea ($n = 2$). The effect on 24-hour ambulatory blood pressure (BP) was assessed at 6 months. Patients with a decrease in systolic BP of at least 10 mm Hg were considered responders.

Results: RDN was bilateral in 19 patients and single-sided in five. The 19 patients with bilateral RDN showed mean reductions in 24-hour ambulatory BP of 20.7/8.7 mm Hg ± 18.1/9.9 (systolic/diastolic; $P = .0001/P = .0012$). Sixteen bilaterally treated patients (84.2%) showed a systolic BP reduction of at least 10 mm Hg and were considered responders, whereas only one of the five patients with single-sided RDN showed a response. Two responders with sleep apnea showed improvement in polysomnography indices, and one with left concentric ventricular hypertrophy showed complete cardiac remodeling 11 months after the RDN procedure. Renal function remained unchanged in all patients, including those with renal failure. Optical coherence tomography of the renal arteries in one patient showed sporadic endothelial scarring. Renal angiograms at 9 months (one patient) and 12 months (two patients) had normal findings.

Conclusions: Catheter-based RDN was carried out safely, even in patients with comorbidities, abnormal renal arteries, or anatomic variants. The response rate for bilateral RDN (84.2%) was comparable to previous reports.

ABBREVIATIONS

ACT = activated clotting time, BP = blood pressure, CPAP = continuous positive airway pressure, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, RDN = renal denervation, RF = radiofrequency, SBP = systolic blood pressure

Hypertension is the most common risk factor for cardiovascular disease, affecting approximately 40% of the adult population and accounting for an estimated 5% of mortality worldwide (1,2). The hypertensive state is also frequently associated with other cardiovascular risk factors, such as type 2 diabetes and metabolic syndrome (3). Hypertension is traditionally classified as essential (90% of cases) or secondary, with essential hypertension generally requiring lifelong pharmacologic therapy. Historically, surgical sympathicectomy was used between 1930 and 1960 for treatment of malignant hypertension, but the advent of antihypertensive drugs has led to its demise (4,5). However, this procedure highlighted the role of hyperactivity of the sympathetic nervous system in hypertension. In addition, the centrality of the kidney in regulating arterial blood pressure (BP), even in pathologic conditions, has also been demonstrated (6,7). Despite the numerous drugs available, some hypertension cases prove resistant to pharmacologic treatment. Whether this is true drug resistance or apparent resistance caused by

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intolerance or noncompliance, the end result is the same (8). Additionally, hypertensive patients are susceptible to organ damage, which can affect the heart, kidneys, central nervous system, or retina.

A novel method, endovascular renal denervation (RDN) by application of radiofrequency (RF) energy, has been investigated for the treatment of hypertension (9–11). This revisiting of sympathetic denervation with the use of a minimally invasive procedure has led to a renewed interest in nonpharmacologic control of hypertension. This technique has demonstrated a high success rate, durability of BP decrease, and relative safety (12). In addition, RDN has been shown to improve glucose metabolism in patients with insulin-resistant diabetes (13). Currently, RDN has been evaluated for conditions including refractory heart failure (14), polycystic ovary syndrome (15), obstructive sleep apnea (16), and chronic renal failure (17). The aim of the present study was to evaluate the safety and effectiveness of catheter-based RDN in an interventional radiology setting while extending the inclusion criteria to candidates previously considered unsuitable for the procedure, such as those with variant renal artery anatomy or conditions requiring single-sided denervation.

MATERIALS AND METHODS

Patients

This prospective study was approved by the ethics committees of the two institutions involved. All enrolled patients gave written informed consent for each procedure, including imaging methods and follow-up. From November 2010 to March 2012, 24 consecutive patients (19 men, five women) with a mean age of 65.9 years ± 11.8 underwent RDN. In the event of stenosis of the contralateral artery, denervation was single-sided. Inclusion criteria were age 18–85 years, office-based BP measurement of greater than 160 mm Hg (> 150 mm Hg in patients with type 2 diabetes mellitus), and 24-hour ambulatory BP greater than 140/90 mm Hg (> 130/80 mm Hg for patients with type 2 diabetes) despite previous pharmacologic treatment. Exclusion criteria, modified from previous studies (9,11), were renal artery diameter less than 4 mm or length shorter than 20 mm, non–catheter-accessible renal arteries, aortic valve stenosis, untreatable carotid artery stenosis, myocardial infarction or cerebrovascular incident in the previous 6 months, unstable angina pectoris, and pregnancy. Baseline population characteristics are shown in **Table 1**.

Preprocedural Assessment

All patients were assessed before RDN via office-based and 24-hour ambulatory measurements of systolic BP (SBP) and diastolic BP (DBP). In addition, routine blood chemistry analysis was performed, including fasting glucose measurement, renal function tests including estimated glomerular filtration rate (eGFR) calculated per Modification of Diet in Renal Disease equation (18), plasma renin and aldosterone measurements, and urinary catecholamine levels. All patients also underwent electrocardiography, echocardiography, color Doppler analysis of

Table 1. Demographics and Baseline Parameters (N = 24)

Variable	Value
Age (y)	65.9 ± 11.8
Sex	
Male	19
Female	5
Office-based SBP (mm Hg)	184.6 ± 13.0
Office-based DBP (mm Hg)	104.7 ± 22.8
24-h ambulatory SBP (mm Hg)	161.5 ± 14.6
24-h ambulatory DBP (mm Hg)	90.7 ± 8.0
Serum creatinine (mg/dL)	
Mean	1
Median	1.2
eGFR (mL/min/1.73 m^2)	69.8 ± 21.4
Mean body mass index	27.6
Antihypertensive medications (%)	
ACE inhibitors	33
ARBs	67
Direct renin inhibitors	29
β-blockers	79
Calcium-channel blockers	83
Diuretics	71
Aldosterone antagonists	33
Vasodilators	4
α-1 blockers	37
No. of antihypertensive medications per patient	4.4 ± 1.0
Comorbidities	
Heart failure	1 (4)
Renal failure	
Stage 3	2 (8)
Stage 4	2 (8)
Coronary artery disease	3 (12)
Vertebral aneurysm	1 (4)
Abdominal aorta aneurysm	1 (4)
Renal artery aneurysm	1 (4)
ICA stenosis, previously stented	1 (4)
TIA/stroke	2 (8)
Obstructive sleep apnea	2 (8)
Type 2 diabetes mellitus	11 (46)
Obesity	11 (46)
Patients with variant renal artery anatomy	
Two left renal arteries	1 (4)
Three right renal arteries	1 (4)
Three right and two left renal arteries	1 (4)
Patients with renal artery pathology	
Right renal artery stenosis	3 (12)
Left renal artery stenosis	2 (8)

Values presented as mean ± standard deviation where appropriate. Values in parentheses are percentages.
ARB = angiotensin receptor blocker, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, ICA = internal carotid artery, SBP = systolic blood pressure, TIA = transient ischemic attack.