Renal Denervation Revisited: Promising Treatment for Resistant Hypertension?

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Renal sympathectomy has been in use since the 1930s to reduce blood pressure (BP) in patients with severe hypertension.[1] Radical surgical sympathectomy and therapeutic splanchnicectomy were used before the advent of modern pharmacologic treatments to treat severe hypertension[2,3] but these methods were largely abandoned with the availability of newer antihypertensive drugs that were both effective and had minimal side effects in the mid-late 1960s. Despite these newer efficacious drugs there remain patients with severe resistant hypertension.

Renal sympathetic nerves contribute to the development and perpetuation of hypertension, and sympathetic outflow to the kidneys is activated in patients with essential hypertension. Efferent sympathetic outflow stimulates renin release, increases tubular sodium reabsorption, and reduces renal blood flow. Afferent signals from the kidney modulate central sympathetic outflow and thereby directly contribute to neurogenic hypertension.[4,5] This was the basis for the use of nonselective surgical sympathectomy in the past. There has been a recent reemergence of interest in ablation of the renal sympathetic nerves using a catheter-based approach. A newly developed endovascular catheter technology enables selective denervation of the human kidney, with radiofrequency (RF) energy delivered in the renal artery lumen, accessing the renal nerves located in the adventitia of the renal arteries. This percutaneous, catheter-based approach is applied to selectively ablate the renal sympathetic nerves. In this approach, ablation is achieved percutaneously via the lumen of the main renal artery using a catheter connected to an RF generator. After gaining access via the femoral artery and confirmation of anatomic eligibility with renal angiography, the treatment catheter (Simplicity; Medtronic, Inc, Mountain View, CA) is introduced into each renal artery, and discrete RF ablations lasting ≤2 minutes each are applied to achieve ≤6 ablations separated both longitudinally and rotationally within each renal artery. Catheter tip temperature and impedance are constantly monitored during ablation, and RF energy delivery is regulated according to a predetermined algorithm.[6] The mean duration of the procedure is less than 40 minutes. Patients often report back pain during the procedure so conscious sedation and narcotics are generally used. Complications have been infrequent and fairly minor but do include pseudoaneurysms at the puncture site and rarely renal artery dissection, which has been managed by stenting.

An initial study of this approach showed successful renal denervation with both reductions of sympathetic activity and renin release in conjunction with reductions of central sympathetic outflow.[7] This study showed substantial reductions of BP without substantial procedure-related complications.

A larger study (Renal Denervation in Patients With Uncontrolled Hypertension [Symplicity 2]) was then performed using this RF catheter ablation procedure in a randomized trial of 106 patients with resistant hypertension despite treatment with an average of 5 antihypertensive medications including a diuretic.[8] The patients were evaluated at 6 months. RF ablation significantly decreased the office BP from 178/97 mm Hg to 143/85 mm Hg compared with no decrease in BP in patients who were maintained on baseline antihypertensive therapy. A systolic BP <140 mm Hg was attained significantly more often with RF ablation (19% vs 4%). There was no significant difference between the groups in kidney function. Complications related to RF ablation included one femoral artery pseudoaneurysm.

Long-term data regarding efficacy and safety of this procedure are limited. In a cohort study of 153 patients with resistant hypertension treated with catheter-based RF ablation, medical evaluation was performed in 64 patients at 12 months and 18 patients at 24 months.[9] Compared with baseline, BP was reduced by 23/11 mm Hg at 12 months and 32/14 mm Hg at 24 months. The average number of antihypertensive medications used was the same at last follow-up as it was at baseline. Renal artery stenosis was diagnosed and stented in 1 patient 6 months after RF ablation.

Another recent substudy assessed the effects of renal sympathetic denervation by RF ablation on BP reduction and sleep apnea severity in 10 patients with severe hypertension and sleep apnea. Antihypertensives were not changed during the study. Three and 6 months after renal denervation, in-office systolic BP and diastolic BP were decreased by 34/13 mm Hg. Significant decreases were also observed in plasma glucose concentration, glycated hemoglobin levels, and a decrease in apnea-hypopnea index at 6 months after renal denervation.[10]

This catheter-based approach to renal denervation presents a novel approach to severe resistant hypertension. Renal denervation has the potential to improve BP control most likely via interference with both

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efferent sympathetic and afferent sensory nerves and potentially through central sympathetic mechanisms. Data thus far show durable BP responses for at least 24 months. What is even more promising is the added potential for improved glucose control and reduction in sleep apnea. Use of this catheter is approved in Europe and a large phase 3 study is to be undertaken in the United States. Hurdles to overcome include assessment of responses with ambulatory BP monitoring, ensuring maximal drug treatment (for example, by ensuring mineralocorticoid antagonist failure) prior to denervation and demonstration of both short- and hopefully long-term beneficial cardiovascular effects.

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