

Device Based Therapy for Treatment of Hypertension

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Systemic arterial hypertension is one of the leading cardiovascular diseases in the world and a major cardiovascular risk for coronary artery disease, cerebrovascular disease, and heart and renal failure. It is the leading attributable cause of mortality worldwide, causing 7.5 million deaths annually.^{1,2}

The treatment of hypertension is no longer limited to the drugs. For many patients, maximal medical therapy is insufficient to adequately treat hypertension. In addition, some patients may prefer to explore therapies that do not involve drugs as an initial step. Utilizing the knowledge of physiology of hypertension, new technology and interventions have been developed that allow for treatments that do not rely on medications. Number of devices have been developed to provide an alternative or supplemental approach to treating hypertension.

The Rheos device (CVRx Inc, Minneapolis, MN) is an implantable system that consists of leads implanted around the carotid sinus which connect to a generator. The Rheos system delivers electrical impulses to the carotid sinus baroreceptors, stimulating them and mimicking a high pressure/volume state. The physiologic result is a decrease in vascular tone, heart rate and cardiac contractility. There are also renal effects, with a resulting diuresis and decreased renin excretion.³ These effects lead to a fall in BP. The device is implanted under general anesthesia, with the leads tunneled subcutaneously into the space surrounding the carotid sinus. After implantation, the device-stimulation parameters can be adjusted.

Chronic baroreceptor stimulation causes sustained changes in heart rate variability and heart rate turbulence that are consistent with inhibition of

sympathetic activity and increase of parasympathetic activity in patients with drug-resistant systemic hypertension; these changes correlate with blood pressure reduction.⁴ The device has been evaluated in patients with resistant hypertension.

Rheos Pivotal Trial⁵ for chronic baroreceptor stimulation demonstrated that 54% of patients with the device had a >10-mm Hg reduction in SBP at 6 months and 88% had a sustained response at 12 months. In addition, there were significantly decreased short- and long-term adverse events in patients with the system. A total of 81% of patients were found to be “responders” to the Rheos system, with an average SBP decrease in these patients of 44 mm Hg at 12 months. Patients with the device also demonstrated a decline in left ventricular hypertrophy at 1 year. In addition, increases in arterial compliance, defined as stroke volume/pulse pressure, as well as reductions in left atrial dimension and mitral A wave velocity were noted, suggesting that this therapy might have clinical importance in patients with increased arterial stiffness and diastolic dysfunction.⁶

The concept of renal denervation as treatment for human hypertension is not new and even preceded the development of antihypertensive drugs. Non-selective surgical sympathectomy, which also denervates the kidney, was widely performed for the treatment of severe hypertension in the 1940s and 1950s.⁷⁻¹² However, the procedure was eventually abandoned because of post-procedural complications, e.g. anhidrosis, sexual and urinary dysfunction, orthostatic hypotension and tachycardia, prolonged postoperative recovery and the unpredictability of the results, as well as the development of safe and effective antihypertensive drugs.

The Symplicity catheter (Ardien, Inc, Mountain View, CA) system is designed to ablate these sympathetic renal pathways. It is inserted percutaneously through the femoral artery and into the renal arteries and radiofrequency pulses are delivered at several points throughout the renal arteries. The overactive sympathetic pathways are disrupted, resulting in a decrease in the inappropriately elevated sympathetic tone and a decrease in BP.

Initial trials have been favorable. In Simplicity HTN-1&2 study in patients with refractory hypertension, SBP was reduced by 14 mm Hg after 1 month and 27 mm Hg at 1 year.¹³ Further follow-up and pooled data demonstrated a 2-year SBP reduction of 32 mm Hg.¹⁴ This novel procedure may provide protection in patients with resistant hypertension and metabolic disorders at high cardiovascular risk.¹⁵

The RESPeRATE device (InterCure, Inc, New York, NY) uses biofeedback to progressively slow breathing. The system utilizes a controller unit, a respiration sensor, and headphones. Musical tones are played based on the patient's respirations, and the patient is instructed to follow the tones to adjust their breathing pattern. The device is used for 15 minutes daily. By progressively prolonging the expiratory phase, the patient's breathing cycle is slowed. A Slowed respiratory rates appear to have a beneficial effect on BP.¹⁶ As respiratory rates slow, lung inflation increases. This then increases activation of stretch receptors in the lungs, which feed back to the central nervous system, and leads to vasodilation.

The device decreased the SBP by 15 mm Hg at 2 months, compared with 11.3 in the placebo (music relaxation) group. Response appeared to persist beyond the period where the device was in use.^{17,18} Subsequent studies showed a more modest, but significant, 5-mm Hg decrease in SBP.¹⁹

Much of the evidence for these therapies comes from small studies with end points that typically include only BP. Clinical outcomes such as stroke or myocardial infarction have not been evaluated. These therapies are currently being evaluated for use in refractory hypertension. Should they prove

efficacious and safe their use as a first-line therapy may come into play. Longer-term clinical trials of the invasive therapies are ongoing and will further delineate their safety profiles. These therapies may be of particular use in patients who are reluctant to take medications or are in search of methods to reduce their BP further in combination with pharmacologic therapy.

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