Cautious Enthusiasm for Renal Denervation

Krishna J. Rocha-Singh, MD, FACC, FAHA, FSCAI, FSVM, shares his thoughts on the potential for this procedure and the methodical path required to get there.

In what ways have your impressions about the potential benefits of renal denervation (RDN) in treating resistant hypertension changed over the past several years?

My impressions regarding the potential benefits of RDN have evolved since the time we treated our first patient in 2009. Over the past 4 years, I have come to understand that it is essential that the correct patient with severe treatment-resistant hypertension be selected through a meticulous, clinically rigorous evaluation process. This has, of course, resulted in a significant screen failure rate—a rate that potentially increases given the patient's renal anatomy.

Additionally, as data from Symplicity HTN-1 and -2 3-year follow-up have recently been reported, the results underscore my impression that appropriate patient selection is essential and that inappropriate selection will reflect negatively on the perceived utility of the devices and procedures. Furthermore, the issue of severe treatment-resistant hypertensive patients who are post-RDN "responders" or "nonresponders"—arbitrary binary definitions that have been used to infer treatment success in this patient cohort—I believe may ultimately prove an impediment to advancing the science regarding appropriate patient selection. Medtronic is yet to reveal the exact systolic blood pressure values of these "nonresponders," other than to state that these patients have a blood pressure response < 10 mm Hg. Of course, there may be multiple reasons why this occurs, which will be discussed at length at upcoming conferences. Although my enthusiasm remains high, it has been tempered by my appreciation that the current applicability of this therapy is germane to a relatively small and highly select group of patients with severe treatment-resistant hypertension.

Which other studies, results, or developments in particular have shaped your opinions?

Clearly, the small, single-center reports demonstrating the "collateral benefits" of sympathetic system modulation via RDN have been of interest. However, although these observations are encouraging, it is important to note that they are preliminary and must be corroborated in larger, better-defined, prospective, multicenter, adjudicated evaluations. It also increasingly appears that in addition to potentially having a benefit in patients who have treatment-resistant hypertension associated with obstructive sleep apnea or type 2 diabetes, there may be a role in the treatment of patients with advanced chronic kidney disease and end-stage renal disease. Additionally, there have been encouraging case reports regarding its potential role in maintaining normal sinus rhythm after atrial fibrillation ablation and incessant ventricular dysrhythmias. Of course, we all look to emerging signals from Germany and the United Kingdom regarding its use in patients with heart failure, both systolic and diastolic.

Which other developments have given you new optimism?

With publications of Symplicity HTN-1 and -2 and the recent European Society of Cardiology 3-year follow-up in 88 patients, there appears to be an emerging consistent signal of the benefit associated with selecting the correct patient, as well as the safety and durability of the treatment effect. This would suggest that the possibility of regrowth of renal nerves is unlikely and that continued benefit, potentially through vascular remodeling in this cohort of patients, does occur. Additionally, there appears to be no clinically relevant decline in renal function in this cohort of patients, which was a positive sign.

What is the most critical challenge concerning RDN?

I believe it is important that we dissociate the emerging very positive clinical science from the interests of the multiple stakeholders involved in this therapy. One of my biggest concerns is the depth and breadth of clinical evidence that will be required by the Centers for Medicare & Medicaid Services (CMS) in order to reimburse this procedure in the United States. Clearly, as we all understand, the potential indications for this procedure will extend far beyond the treatment of severe treatment-resistant hypertension to potentially include patients with moderate treatment-resistant hypertension (systolic blood pressure of 140–160 mm Hg on three antihypertensive medications), possibly atrial fibrillation, and forms of heart failure. This could indeed be a "budget buster" for CMS. I understand that CMS cannot, by statutory law, consider the cost of any intervention; however, they can "prioritize" reimbursement. I do believe that Medtronic, Inc. (Minneapolis, MN) has been extremely proactive in engaging CMS in a parallel pathway for reimbursement and regulatory approval. Their forward thinking in this regard should be congratulated.

What other factors are critical to the progress of this therapy?

Any device or therapy has a cycle. This is characterized by initial enthusiasm that subsequently evolves into tempered introspection with regard to appropriate patient selection and the associated costs and complications; more clinical data become available, and, finally, there is the understanding that this is just the first therapy for RDN, and more effective iterations are needed. I believe that understanding more about appropriate patient selection and preprocedure markers or demographics that predict a poor response or no response are essential. Additionally, providing the interventionist with an intraprocedural feedback assessment that will better assess "anatomic" denervation will allow us to understand more about the resulting "clinical" denervation; if a patient has no clinical response to a successful anatomic denervation, we can then state that these patients have severe hypertension for other reasons. These are but two essential shortcomings that require further elucidation by physicians and industry.

Is it too early to ask what the next breakthrough in resistant hypertension therapy will be beyond RDN?

I think it is essential that we understand that RDN represents a first-generation, new-era technology to successfully percutaneously address modulation of the sympathetic nervous system. Other technologies will evolve that will either be competitive or complementary in modulating the sympathetic system. Specifically, those companies that target ablation of chemoreceptors or the stimulation of mechanoreceptors to influence these sympathetic pathways will be closely watched. Understand that a patient with severe treatment-resistant hypertension of 180 mm Hg may have a significant 20-mm Hg drop in blood pressure; however, he or she is still left with significant cardiovascular risk, facing lifelong antihypertensive therapy. I can imagine the day when this type of patient also undergoes a complementary therapy, whether carotid body ablation or mechanoreceptor stimulation, in order to further reduce this individual's cardiovascular risk by further lowering blood pressure.

How can various specialties work together in order to avoid turf wars that might slow or stagnate the progress of this and other hypertensive innovations?

It is essential that the various specialties within the medical, surgical, radiology, cardiology, and interventional cardiology fields work together very early on to promote the clinical science in the treatment of these patients. It is important to understand that the interventionist may not be the true "customer" for the medical device company; as such, these device companies must reach out with new educational programs targeting the general internists, family practitioners, and nephrologists and educate as to the importance of this therapy. Frankly, once the referral is made, it is less important which competent proceduralist performs the denervation, whether it is an interventional cardiologist, radiologist, vascular surgeon, or even a cardiac electrophysiologist. It is essential that whoever performs the actual procedure be well accomplished and competent in performing renal artery interventions and know the potential associated complications. However, as we all understand, there are no curative properties associated with this intervention, and as such, continued communication with and long-term follow-up by the patient's primary caregiver is essential. ■

Krishna J. Rocha-Singh, MD, FACC, FAHA, FSCAI, FSVM, is Medical Director, Prairie Research and Education Cooperative, St. John's Hospital in Springfield, Illinois. He has disclosed that he is a consultant to Medtronic, Inc., Vessix Vascular, Inc. (now Boston Scientific Corporation), ev3 Inc. (now Covidien), CardioSonic Ltd., and Cibiem. Dr. Rocha-Singh may be reached at ksingh@prairieheart.com.