Key Questions for Ongoing and Future Renal Denervation Trials

Dr. Ajay J. Kirtane discusses where renal denervation devices fit in the blood pressure control landscape, remaining questions to be addressed, ensuring patient access to this therapeutic option, and ideal goals for future trials.

Looking at the blood pressure control landscape in the United States, where do you think renal denervation (RDN) fits in? Its journey to FDA approval?

At least in the United States, we're thrilled to now have FDA approval of two devices for RDN: the Paradise ultrasound RDN system (Recor Medical) and the Symplicity Spyral RDN system (Medtronic). Despite widespread availability of medications and lifestyle modification, blood pressure control remains difficult for many patients. Although it's important to start with those two things for all patients, many patients still remain poorly controlled, and to have a device-based therapy that's in a sense independent of medication adherence is a welcome addition.

We're thrilled about the approvals because they reflect the remarkable perseverance it took to accomplish the clinical trials following a large negative clinical trial, SYMPLICITY HTN-3. There was a lot of resilience and collaboration between investigators around the world—as well as the FDA and industry colleagues—to perform rigorous science in the form of sham-controlled randomized trials, which allowed these devices to be approved.

What key questions remain to be addressed in ongoing/future RDN trials?

There are a number of things that remain to be studied and elucidated. First, can we predict some element of response or degree of response a patient is going to achieve? As a clinician, of course it's important to have randomized data showing the benefit of RDN, but we would like to be a little bit more precise in terms of estimating its effect. The procedure is irreversible, and we don't want to expose someone to a procedure that has limited efficacy for that patient.

A second issue relates to longer-term durability. In the past year, there have been a few publications looking at longer-term durability of the procedure, but some of these publications lack complete follow-up. We're going to be looking at not only the randomized trials that have been already conducted but also postmarket registries to assess questions of durability as a whole. As with any invasive procedure, although the safety data were reassuring within the randomized trials already conducted, we need larger patient numbers to continue to prove that. As a clinician, it's important to continue to be vigilant about safety and ensure these procedures are investigated in larger data sets.

Finally, the biggest question from a public health initiative is ensuring that patients have adequate education about and access to these types of technologies and procedures. That's especially important in an environment where reimbursement is a challenge right now. We want to ensure marginalized patients have access to this technology because we know that in many ways these patients have blood pressure that's the most poorly controlled and so could benefit from it. That's something that can be directly addressed by a study. In the postmarket studies, the FDA has been very cognizant of including specific patient groups to target for study who have been historically underrepresented in trials.

Is there an ideal study design that you would like to see for future trials evaluating RDN?

I've always also been a proponent of some sort of clinical outcome study with this technology, and I think the reason for that is severalfold. First, we are used to studies of clinical outcomes in cardiology. That's one of the reasons why I went into the field.

Second, there is always going to be some doubt as to whether lowering blood pressure with RDN might have the same effectiveness as was shown in trials like SPRINT of antihypertensive therapy. There are many people who feel it doesn't really matter how you reduce blood pressure—you're going to get clinical outcome benefits of blood pressure reduction regardless. That's not necessarily proven. So, an outcome study is probably warranted, but it doesn't have to be the size of the SPRINT study with those same endpoints. If we look at surrogate endpoints and combine them into a bigger picture, I think that those types of studies would potentially leverage benefits. If we could show those benefits, then in a sense we feel a lot more comfortable offering this therapy to a broader range of patients.

To summarize, I would say it's been a long-ish journey—one in which myself and many others have learned quite a bit, not just about technologies but about hypertension control, health care utilization, and health care delivery as a whole. And along with those lessons, it's nice to be here at this inflection point when it comes to treatments of hypertension. In many respects, it's been a privilege, and I'm excited for the future. ■

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