Lessons Learned in Trial Design and Patient Selection

With many questions yet to be answered in the clinical study of renal denervation, Martin W. Bergmann, MD, PhD, FESC, discusses how previous results have shaped his practice.

What are some of the most important lessons that have been learned about how to best define endpoints in renal denervation trials?

So far, office-based systolic blood pressure was the best-defined endpoint. Twenty-four-hour ambulatory blood pressure is also significantly altered. However, this parameter is less sensitive; the study population sizes needed to demonstrate a significant change are higher. In the future, end-organ damage such as heart failure with preserved ejection fraction and/or biomarkers may become more important.

What do we know now that we did not when the initial trials began? What is an example of an endpoint that was previously seen as important but is now regarded as less so, if at all?

Indeed, the 24-hour ambulatory blood pressure has been replaced by office-based systolic blood pressure as a more sensitive and meaningful parameter. The procedure was shown to have a significant effect in approximately 70% to 80% of patients treated. Higher baseline blood pressure was the best predictor for response.

What is one important lesson you have learned about patient selection since you began your work as a trialist in this field?

High blood pressure plus beginning end-organ damage (heart failure with preserved ejection fraction, systolic heart failure, renal failure) is best treated with this approach.

What are you currently using as your criteria for patient selection in your practice?

Invasive and/or office-based systolic blood pressure are the best criteria. The available studies included patients with office-based systolic blood pressure > 160 mm Hg on three or more antihypertensive drugs; if diabetes was present, the threshold was 150 mm Hg. With the new European Society of Cardiology guidelines on diagnosis and treatment of hypertension published a few weeks ago, the threshold of "uncontrolled" blood pressure was lowered to 140 mm Hg since several studies found progressive end-organ damage if blood pressure was above this threshold. New studies on renal denervation will therefore take this threshold; given the perfect safety profile of the procedure and the devastating consequences of uncontrolled hypertension (stroke, renal failure, heart failure), we already offer the procedure to all patients with systolic blood pressure > 140 mm Hg and beginning end-organ damage or diabetes.

How do you believe the field should weigh current lessons learned about the nonresponder population versus the evolution of technique and technology and future ability to treat a larger population?

We found a second renal denervation procedure employing the Symplicity system (Medtronic, Inc., Minneapolis, MN) to be effective in a number of nonresponders; this would argue in favor of more effective ablation to have additional effects. We offered this approach to all patients who had persisting symptoms and/or progressive end-organ damage 6 to 9 months after the first procedure with a systolic blood pressure reduction of < 10 mm Hg. Small renal arteries with a diameter < 4 mm appear to be at risk of renal artery stenosis (one patient in our cohort) and should therefore be treated with a different approach such as irrigated low-level radiofrequency energy renal denervation, bipolar, or ultrasound ablation. ■

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