

## Renal Denervation to Treat Cardiac Fibrosis?

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**H**ypertension is extremely common across the world, and substantial resistance to pharmacological therapy occurs in a considerable subset, possibly >10% of afflicted patients.<sup>1</sup> The morbid consequences or comorbidities associated with hypertension are extensive and range from renal failure to myocardial infarction. For the most part, these comorbidities are more common with resistant hypertension.<sup>1</sup> Although we have seen gratifying decreases in the incidence and prevalence of many cardiovascular diseases in recent years, congestive heart failure, a well-known comorbidity of hypertension, is becoming a much greater problem.<sup>2</sup>

In this issue of the *Journal of the American Heart Association (JAHA)*, Doltra and colleagues report on the effects of renal denervation achieved through radiofrequency ablation on cardiac morphology assessed with magnetic resonance imaging. Specifically, these authors used the technique of observing delayed gadolinium enhancement to estimate how much cardiac fibrosis was present prior to and following renal denervation in 23 patients with resistant hypertension as well as 5 patients who had resistant hypertension and who did not undergo the renal denervation. Although the control group was admittedly small, significant decreases in blood pressure were observed with renal denervation that were not observed in the control hypertensive group. Of greater interest, the patients subjected to renal denervation showed decreases in left ventricular (LV) mass as well as the total extracellular volume, a parameter the authors contend represents the degree of fibrosis.<sup>3</sup> While decreases in LV mass have been reported with renal denervation in this category of patient (patients with resistant hypertension),<sup>4</sup>

this is the first report showing an ameliorative effect of renal denervation on a meaningful surrogate for cardiac fibrosis. When the authors looked at those patients who appeared to respond to the renal denervation with a 10 mm Hg drop in blood pressure compared with those who did not (responders versus nonresponders), they found that the changes in cardiac morphology were similar in the 2 subgroups.

Like most good articles, this study raises additional questions. The first question that will occur to any interested reader is whether the methodology used to assess LV morphology—in particular, LV fibrosis—is accurate. The literature is replete with articles speaking to the credibility of this approach.<sup>5–7</sup> That said, one would have hoped that other measurements of cardiac fibrosis (eg, urinary excretion of collagen breakdown products) or inflammation might have been measured, as other authors have proposed.<sup>8</sup> The next question would be how renal denervation achieves benefits, and whether these benefits are entirely linked to blood pressure reduction. It is very clear that there are a host of hormonal and cytokine alterations in response to renal denervation, and the importance of these factors in the pathogenesis of cardiac hypertrophy and fibrosis has only recently been appreciated.<sup>9–11</sup> Again, some measurement of candidate hormones and cytokines involved in cardiac remodeling (eg, concentrations of angiotensin II and aldosterone, sympathetic nervous system activity, concentrations of digitalislike substances<sup>12</sup>) would have been interesting, although performing such measurements (especially of the digitalislike substances) would have dramatically changed the scope of the article. Finally, one would wish to know if the advantageous effects of renal denervation on LV remodeling persist for long periods of time<sup>13</sup> and/or truly impact on clinical outcomes (eg, death, other comorbidities), but of course answering these studies would take additional resources, some of which are probably not available to the authors.

With the understanding that surrogate measurements may be misleading, the authors of this article may be on to something. Several large studies have shown that LV hypertrophy has substantial prognostic importance in hypertensive patients, regardless of whether hypertrophy is assessed by insensitive methods (eg, ECG) or overly sensitive methods (eg, echocardiography).<sup>14</sup> Magnetic reso-

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nance imaging measurements appear to provide more accurate measurements of LV mass than other modalities.<sup>15</sup> Regarding renal denervation, the jury is still out as to whether the benefits of this invasive and expensive modality are truly worth the costs, but additional data along the lines of this report would go a long way to answering this question.

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## Disclosures

None.

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**Key Words:** Editorials • fibrosis • high blood pressure • hypertension • hypertrophic cardiomyopathy • hypertrophy • magnetic resonance imaging