News and Views From the Literature

Hypertension

Left Ventricular Hypertrophy and Cardiac Function in Patients With Resistant Hypertension

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Renal Sympathetic Denervation Reduces Left Ventricular Hypertrophy and Improves Cardiac Function in Patients With Resistant Hypertension

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Resistant hypertension is a common clinical problem faced by both primary care clinicians and hypertension specialists, including cardiologists, nephrologists, and endocrinologists. Although the exact prevalence of resistant hypertension is unknown, small studies demonstrate a prevalence of resistant hypertension that ranges from 5% in general medical practice to > 50% in nephrology clinics.[1] The exact prognosis of resistant hypertension is unknown as it has not been well studied, but cardiovascular risk is increased in these patients because they often have comorbidities, including obesity, sleep apnea, diabetes, and chronic kidney disease (which themselves can contribute to the evolution of controlled hypertension to resistant hypertension). The diagnosis of resistant hypertension requires the use of good blood pressure technique to confirm persistently elevated blood pressure levels. Pseudoresistance, including lack of blood pressure control secondary to poor medication and dietary sodium restriction adherence; use of anti-inflammatory agents, decongestants, and vasoactive herbal agents; and white coat hypertension must be excluded before a diagnosis of resistant hypertension is entertained. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure defines resistant hypertension as failure to achieve goal blood pressure (< 140/90 mm Hg for the overall population and < 130/80 mm Hg for those with type 2 diabetes mellitus [DM] or chronic kidney disease) when a patient adheres to maximum tolerated doses of three antihypertensive drugs, including a diuretic.[2]

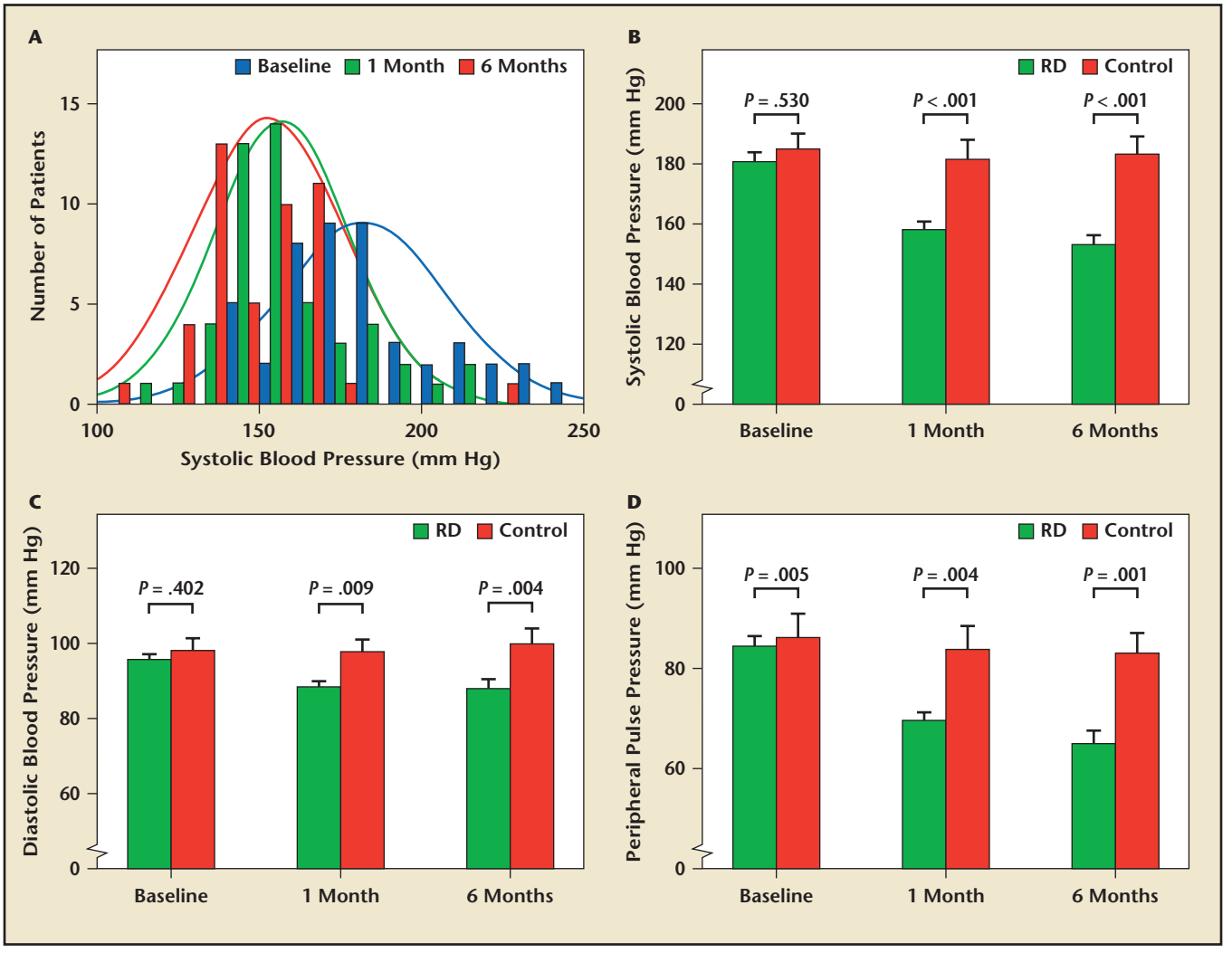
The renal nerves play an essential role in the long-term regulation of blood pressure through reduction of renal blood flow, excess renin production (efferent nerves), and outbound renal sympathetic signaling (afferent nerves), causing an upregulation of systemic sympathetic outflow. Catheter-based renal denervation (RD) is a percutaneous procedure that leads to a significant reduction of blood pressure in resistant populations.

The percutaneous application of discrete low-dose radiofrequency energy to the renal artery endothelial surface results in the effective blocking of nerve conduction through sympathetic nerve fibers, reducing β- and α-receptor–mediated sympathetic hyperactivity, thus leading to an effective reduction of blood pressure.

The investigators studied 74 patients who had an office systolic blood pressure ≥ 160 mm Hg (≥ 150 mm Hg for patients with DM) despite treatment with at least three antihypertensive drugs, including a diuretic. Patients with secondary causes of hypertension were excluded and 24-hour blood pressure recordings were performed to exclude white coat hypertension; 46 patients underwent bilateral RD and 18 patients served as control subjects. Transthoracic echocardiography was performed at baseline, 1 month, and 6 months of treatment. In patients treated with RD, systolic and diastolic blood pressure (−22.5/−7.2 mm Hg at 1 month and −27.8/−8.8 mm Hg at 6 months; $P < .001$ at each time point) where blood pressure remained unchanged in the control group (Figure 1). In the control group, the number and dosage of antihypertensive drugs remained constant during follow-up. After RD, the number of antihypertensive drugs could be reduced in seven patients (15%), resulting in an average of 4.5 antihypertensive drugs at 6 months versus 4.7 at baseline ($P = .402$).

The left ventricular (LV) mass index decreased continuously in the RD group, from 53.9 g/m$^{2.7}$ at baseline to 47.0 g/m$^{2.7}$ at 1 month ($P < .001/.01$) and 44.7 g/m$^{2.7}$ at 6 months ($P < .001/.001$) versus baseline, whereas LV mass slightly increased in the control group, from 55.7 g/m$^{2.7}$ at baseline to 58.6 g/m$^{2.7}$ at 6 months ($P = .007/.009$ vs RD) (Figure 2). In the RD group, 63% and 33% had LV hypertrophy (indexed to height$^{2.7}$) at baseline and after 6 months, respectively. After RD, but not in control patients, there was a significant reduction of the

Figure 1. Effect of RD on BP and pulse pressure in patients with resistant hypertension. **(A)** Distribution of SBP in the RD group at baseline (*blue*), and after 1 month (*green*) and 6 months (*red*). **(B)** SBP, **(C)** DBP, and **(D)** pulse pressure in patients who underwent RD (*green*) and in control patients (*red*) at baseline, 1 month, and 6 months. *P* values RD vs control are indicated above the columns. In the treatment group, *P* for statistical trend was $P < .001$ for SBP **(B)**, $P < .001$ for DBP **(C)**, and $P < .001$ for pulse pressure **(D)**. Values are presented as mean ± standard error. BP, blood pressure; DBP, diastolic blood pressure; RD, renal sympathetic denervation; SBP, systolic blood pressure. Reprinted with permission from Cardiosource.



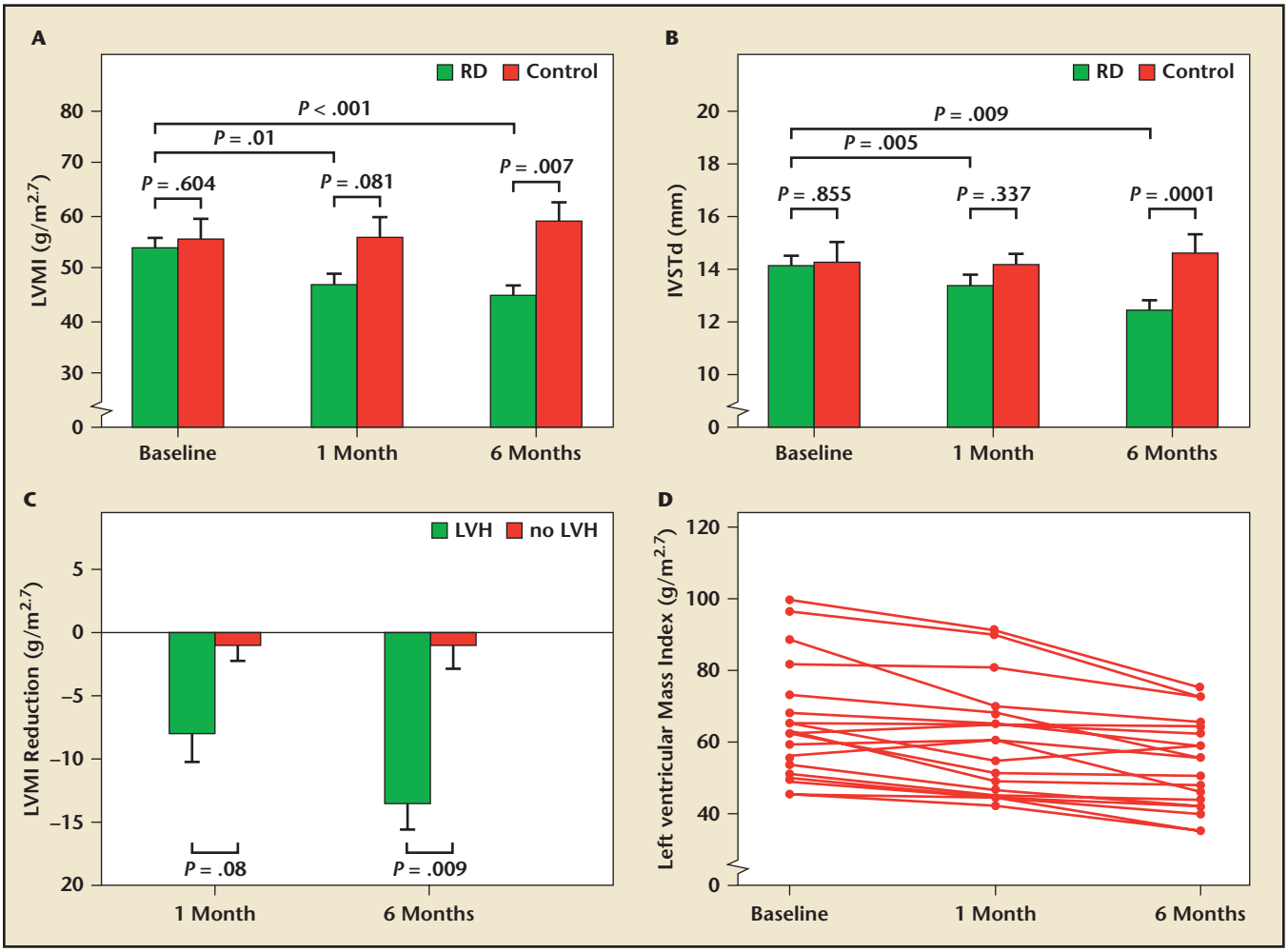


Figure 2. Impact of RD on LV mass. **(A)** LV mass/height$^{2.7}$ and **(B)** IVSTd measured in RD and control patients at baseline, 1 month, and 6 months. Although there was a steady decrease in the average LV mass and IVSTd after RD, these parameters slightly increased in control patients. In the treatment group, *P* for statistical trend was $P = .004$ for LV mass/height$^{2.7}$ **(A)**. $P = 0.007$ for IVSTd **(B)**. **(C)** Differential effect of RD on LV mass regression depends on the degree of LVH at baseline. LV mass/height$^{2.7}$ regression by RD was significantly greater in those patients with LVH at baseline. Values are presented as mean ± standard error. **(D)** Regression of LV mass after RD in individual patients with an LVH at baseline (n = 29). IVSTd, interventricular septum thickness; LV, left ventricular; LVH, left ventricular hypertrophy; LVMI, left ventricular mass index; RD, renal sympathetic denervation. Reprinted with permission from Cardiosource.

interventricular septum thickness from a mean of 14.1 mm at baseline versus 13.4 mm at 1 month ($P = .005$), to further reduction at 6 months to 12.5 mm ($P = .009$). The LV end-systolic volume was significantly reduced by RD with a significant increase of the LV ejection fraction.

RD was also accompanied by an improvement of diastolic functional parameters, such as shortening of mitral E-wave deceleration time, isovolumic relaxation time, and a decrease in the ratio of mitral inflow velocity to annular relaxation velocity (lateral E/E), whereas in control patients, a trend toward progression of diastolic dysfunction was observed. Left atrial size also decreased after RD, whereas in the control group the size had actually increased.

It appears, therefore, that the reduction of blood pressure seen in this resistant hypertensive population is associated with reductions in cardiac mass and improvements in both systolic and diastolic function. Remarkably, this improvement was observed as early as 1 month following the procedure. Not all therapies that reduce blood pressure are associated with equivalent decreases in cardiovascular event rates or positive cardiac remodeling. Atenolol is the perfect case in point, as it does reduce peripheral blood pressure (not central blood pressure) without a significant effect on event rates or cardiac remodeling. The association of RD with both blood pressure reduction and cardiac enhancements makes us optimistic that it will be associated with reductions in cardiovascular event rates. ■

References

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2. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206-1252.