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CORRESPONDENCE

Response to Wang *et al.*: mechanisms for catheter-based renal denervation to lower blood pressure: personal speculation

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INTRODUCTION

It is evident that catheter-based renal denervation (RDN) lowers blood pressure (BP), as has been confirmed by a recent crossover study;[1] however, the precise mechanisms regarding how RDN lowers BP remain un-established. I personally speculate the importance of volume-independent mechanisms to lower BP,[2] although intense discussions, such as by Wang *et al.*[3] are widely welcomed because the precise mechanisms are currently unknown.

There are three basic mechanisms for renal sympathetic activity to elevate BP:[4] (1) stimulation of renin secretion, (2) enhancement of tubular sodium reabsorption and (3) the increase in renal vascular resistance. All three of these mechanisms elevate BP, while the inhibition of these three mechanisms lowers BP. In fact, it has been shown that RDN reduces both renin secretion and renal vascular resistance,[5] while no evidence has supported these results due to enhanced natriuresis. In animal models, on the other hand, the pressure-natriuresis curve was shifted leftward without a change in the slope,[6] indicating that salt sensitivity was not altered with RDN. Because the slope of the pressure-natriuresis curve is determined by glomerulo-tubular balance of sodium,[7] the slope should be increased if natriuresis is enhanced. In fact, we have shown that diuretics, which enhance natriuresis, steepen the slope of the pressure-natriuresis curve and diminish the sodium sensitivity.[8,9] These findings may suggest that the enhanced natriuresis and the relief of salt and volume retention do not have important roles in lowering BP by RDN. Recently, three individual case reports[10–12] and a multi-center joint study[13] in hemodialysis patients were presented. All study participants, including some patients with no residual renal function who were therefore unable to excrete urine,[12] showed that BP could be successfully lowered without reducing either dry weight or body fluid volume. In addition, RDN does not cause BP-lowering effects in salt-sensitive models, such as in the DOCA-salt hypertension and the 1K–1C Goldblatt hypertensive models,[4] although RDN does lower BP in most models of hypertension.

These findings all strongly indicate that the control of salt and volume retention is not the key mechanism for lowering BP in RDN.

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1 Esler MD, Krum H, Schlaich M, Schmieder RE, Bohm M, Sobotka PA. Renal sympathetic denervation for treatment of drug-resistant hypertension: one-year results from the symplicity HTN-2 randomized, controlled trial. *Circulation* 2012; **126**: 2976–2982.
2 Kimura G. Future of catheter-based renal denervation: key issues to solve. *Hypertens Res* 2013; **36**: 492–493.
3 Wang Y, Denton KM, Golledge J. Control of salt and volume retention cannot be ruled out as a mechanism underlying the blood pressure-lowering effect of renal denervation. *Hypertens Res* 2013; **36**: 1006–1007.
4 DiBona GF, Esler M. Translational medicine: the antihypertensive effect of renal denervation. *Am J Physiol Regul Integr Comp Physiol* 2010; **298**: R245–R253.
5 Schlaich MP, Sobotka PA, Krum H, Lambert E, Esler MD. Renal sympathetic-nerve ablation for uncontrolled hypertension. *N Engl J Med* 2009; **361**: 932–934.
6 Roman RJ, Cowley AW Jr. Characterization of a new model for the study of pressure-natriuresis in the rat. *Am J Physiol* 1985; **248**: F190–F198.
7 Kimura G, Brenner BM. The renal basis for salt sensitivity in hypertension. *Hypertension: Pathophysiology, Diagnosis and Management* (edited by Laragh JH and Brenner BM) Raven Press, New York, 1995: 1569–1588.
8 Saito F, Kimura G. Antihypertensive mechanism of diuretics based on pressure-natriuresis relationship. *Hypertension* 1996; **27**: 914–918.
9 Akita S, Sacks FM, Svetkey LP, Conlin PR, Kimura G. Effects of the dietary approaches to stop hypertension (DASH) diet on the pressure-natriuresis relationship. *Hypertension* 2003; **42**: 8–13.
10 Prochnau D, Lauten A, Busch M, Kuehnert H, Figulla HR, Surber R. Catheter-based radiofrequency ablation therapy of the renal sympathetic-nerve system for drug resistant hypertension in a patient with end-stage renal disease. *Int J Cardiol* 2012; **154**: e29–e30.
11 Di Daniele N, De Francesco M, Violo L, Spinelli A, Simonetti G. Renal sympathetic nerve ablation for the treatment of difficult-to-control or refractory hypertension in a haemodialysis patient. *Nephrol Dialysis Transplant* 2012; **27**: 1689–1690.
12 Ott C, Schmid A, Ditting T, Sobotka PA, Veelken R, Uder M, Schmieder RE. Renal denervation in a hypertensive patient with end-stage renal disease and small arteries: a direction for future research. *J Clin Hypertens* 2012; **14**: 799–801.
13 Schlaich MP, Bart B, Hering D, Walton A, Marusic P, Mahfoud F, Bohm M, Lambert EA, Krum H, Sobotka PA, Schmieder RE, Ika-Sari C, Eikelis N, Straznicky N, Lambert GW, Esler MD. Feasibility of catheter-based renal nerve ablation and effects on sympathetic nerve activity and blood pressure in patients with end-stage renal disease. *Int J Cardiol* (e-pub ahead of print 4 March 2013; doi:10.1016/j.ijcard.2013.01.218).