

Renal denervation: back on track

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To the Editor:

Hypertension is a common cause as well as one of the main consequences of chronic kidney disease (CKD). In 2000, it was projected that more than 25% of the world's adult population had hypertension, two-thirds of them in developing countries. It is predicted that this amount will rise by ~60% to 1.56 billion in 2025 [1], becoming one of the most critical public health problems in the world. Hypertension control is poor in the presence of CKD, as show in the "Kidney Early Evaluation Program (KEEP)," in which only 13.2% of participants achieved good blood pressure control [2]. Such hypertensive subjects with CKD can benefit from catheter-based renal denervation.

However, the randomized, blinded, sham-controlled Symplicity HTN-3 trial [3] could not prove the superiority of renal denervation in reducing blood pressure compared with a sham group at 6 months post procedure. The unexpected and unresponsive results of the Symplicity HTN-3 trial have been extensively discussed and attributed to several possible confounding factors, including inadequate patient enrollment, unsatisfactory performance of the procedure, and lack of operator experience. Recently, the SPYRAL HTN-OFF MED study (Catheter-based renal denervation in uncontrolled hypertensive patients in the absence of antihypertensive treatment [SPYRAL

HTN-OFF MED]: a randomised, sham-controlled, proof-of-concept trial) [4], the SPYRAL HTN-ON MED (Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial) [5] and the RADIANCE-HTN SOLO (Endovascular ultrasound renal denervation to treat hypertension [RADIANCE-HTN SOLO]: a multicentre, international, single-blind, randomised, sham-controlled trial) [6] after a prolonged period of profuse controversy regarding the efficacy of renal denervation as an interventional tool to reduces blood pressure, have been demonstrating the role of renal denervation. Two studies, one performed with a multi-electrode radiofrequency ablation device in hypertensive subjects on concomitant medication usage (SPYRAL HTN-ON MED) and the other using a high-frequency ultrasound device in drug-naïve hypertensive patients (RADIANCE-HTN SOLO), show a substantial and clinically relevant reduction of ambulatory blood pressure in comparison to respective sham control groups. In concordance with the recently published SPYRAL HTN-OFF MED, meaningful evidence is now available from 3 consecutive and adequately designed randomized, sham-controlled trials, confirming the blood pressure depressing efficacy of catheter-based renal denervation approaches.

The SPYRAL HTN-OFF and ON MED studies showed that a massive sequence of radiofrequency ablated spots of renal nerves in the main renal artery and its branches lowers blood pressure, supporting its efficacy in a broad range of hypertensive individuals, including those who are drug-naïve or treated with antihypertensive medications. The RADIANCE-HTN SOLO study used an alternative approach based on endovascular ultrasound to successfully denervate the renal arteries, expanding the field further with the first sham-controlled evidence for

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safety and efficacy of this novel technique. The method consists of a circumferential energy delivery achieved by percutaneous placement of the endovascular catheter centered in the lumen of the main renal artery. According to these results undoubtedly, renal denervation lowers blood pressure in the absence and presence of concomitant antihypertensive medication, which is essential as a blood pressure reducing treatment for patients intolerant to antihypertensive medication, who do not adhere to the antihypertensive medication therapy, or have true drug-resistant hypertension. So far, blood pressure reduction is the unique palpable outcome variable producing the least organ damage, even though it has not proven by a prospective outcome trial. We expect that the 10 mmHg decrease in office blood pressure achieved in new renal denervation trials, if maintained long-term, would be associated with a reduction in cardiovascular events, especially heart failure and stroke, by ~25%. The resurrection of this powerful “new-old” tool to treat hypertension suggests that it will be possible, especially in hypertensive CKD patients, to control the progression of such diseases by interrupting the feedback loop, consequently reducing the associated mortality rate.

Conflicts of interest

The author has no conflicts of interest to declare.

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