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Catheter-based renal denervation in Chinese patients with chronic kidney disease and uncontrolled hypertension

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Abstract

Sympathetic activation contributes to the progression of hypertension and chronic kidney disease (CKD). Ablation of renal sympathetic nerves lowers blood pressure (BP) and preserves renal function in patients with CKD and uncontrolled hypertension by reducing sympathetic nerve activity. But whether this approach is safe and effective in Chinese patients with CKD is unknown. We performed an observational study of eight patients with CKD stages from 1 to 5, office BP ≥150/90 mmHg, while on at least three antihypertensive drug classes including a diuretic, and diagnosis confirmed by 24 h ambulatory systolic BP measurement ≥135 mmHg. All patients underwent catheter-based renal denervation (RDN) using a newly designed RDN System (Golden Leaf Medtech, Shanghai, China). For up to 6 months after RDN, BP was monitored and renal function was assessed. Mean baseline office BP was 165.0 ± 13.9/97.8 ± 5.5 mmHg, despite treatment with three antihypertensive drugs. Six months after RDN, office BP was reduced by 22.1 ± 12.0 ($P = .002$)/11.0 ± 8.8 mmHg ($P = .012$) and average 24 h ambulatory BP by 18 ± 13.7 ($P = .01$)/9.3 ± 7.7 mmHg ($P = .016$). After RDN, heart rate and estimated glomerular filtration rate (GFR) had no significant change compared with before RDN. In Chinese patients with CKD, our observational pilot study found that treating hypertension with RDN lowers BP while not affecting renal function.

Brief Abstract: We performed RDN in eight Chinese patients with hypertension and CKD. The results showed that RDN lowered blood pressure of these patients significantly and eGFR was stable. No obvious adverse event was observed.

KEYWORDS
blood pressure, chronic kidney disease, hypertension, renal denervation

Senyan Liu, Rongrong Bian, Yixin Qian, and Huaqiang Liao contributed equally to this study.

1 | INTRODUCTION

Arterial hypertension is common in patients with chronic kidney disease (CKD), which has a bidirectional relationship with CKD and significant contributor to CKD progression.[1] Regardless of the cause of renal disease, increased systemic blood pressure (BP) in the setting of impaired autoregulation of glomerular pressure, leads to intraglomerular hypertension, glomerulosclerosis, and progressive decline of the glomerular filtration rate (GFR), perpetuating thus a vicious circle. Uncontrolled hypertension is also associated with an increased risk of major cardiovascular events. For most patients with CKD, the risk of death from cardiovascular disease outweighs the risk of progression to end-stage renal disease, and thus cardiovascular disease is responsible for much of the premature mortality in this patient group.[2] As a result, nephrologists caring for hypertensive patients with CKD must be well-versed in therapeutic options.

Plenty of experimental data have demonstrated the role of renal sympathetic overactivity in the pathogenesis of arterial hypertension and related disease states, including CKD.[3,4] Sympathetic renal denervation (RDN) is a minimally invasive, percutaneous procedure that involves the ablation of renal afferent and efferent nerves using a radiofrequency catheter. The thermal increase generated by the application of low-dose radiofrequency energy is effective in disrupting large portions of nervous fibers located within the adventitia of the renal artery. Recent sham-controlled, randomized studies have shown BP reduction in less severe hypertension similar to what one would expect with a single antihypertensive agent.[5–8]

In China, the number of patients with CKD has increased in the past few decades. A large proportion of hypertensive patients with CKD, despite conscientious clinical management, still fail to achieve their recommended BP treatment targets.[9] Whether RDN is safe and effective in Chinese patients with CKD is unknown. We, therefore, initiated this study to assess the short-term safety and efficacy of RDN in patients with uncontrolled hypertension and CKD.

2 | MATERIAL AND METHODS

2.1 | Trial design and patients

From May 2018 to December 2019, patients with CKD and uncontrolled hypertension were enrolled in this single-center pilot trial at our hospital. In brief, eligible patients (aged 18–65 years) had an office systolic BP of 150 mmHg or higher, an office diastolic BP of 90 mmHg or higher, and a mean 24 h ambulatory systolic BP of 135 mmHg or higher. Exclusion criteria of this study were pregnancy, vascular heart disease with significant hemodynamic consequences, stenotic vascular heart disease, in which a drop in BP could be dangerous, acute myocardial infarction, unstable angina, stroke, or transitory ischemic attack within the previous 6 months; renovascular anomalies (including renal artery stenosis, angioplasty with or without stenting, or double or multiple main arteries in the same kidney); Type 1 diabetes, or other secondary causes of hypertension (adrenal diseases, sleep apnea syndrome, severe obesity, high salt diet, and so on). This study was approved by the Ethic Committee of Changzheng Hospital (2017-02-01), and all patients gave written informed consent to participate in the study. The trial was designed in accordance with the Declaration of Helsinki.

2.2 | Screening

Following patient enrolment, an initial screening visit was done to verify initial eligibility criteria and to initiate medication washout. Patients were transferred to a treatment scheme of three standard antihypertensive drugs. Medications were required to be prescribed at 50% or more of the maximum manufacturer's recommended dosage of a thiazide-type diuretic, a dihydropyridine calcium channel blocker, or an angiotensin receptor blocker. After 4-week of standardized medication, the second screening visit confirmed the patient's BP. Patients underwent 24 h ambulatory BP monitoring (Mobil-O-Graph, IEM GmbH, Stolberg, Germany) if their office BP remained within the required range (systolic BP $\geq$150 mmHg and diastolic BP $\geq$90 mmHg), as measured by an automatic BP monitor (Omron, Shanghai, China). Every 30 min, ambulatory BP was measured. A minimum of 21 daytime (7:00 to 21:59) and 12 night-time (22:00 to 6:59) measurements were required for inclusion in the analysis. If the required number of readings were not obtained or if the average 24 h systolic BP was between 130 and 135 mmHg, the ambulatory BP monitoring could be repeated once. Patients who met all inclusion and exclusion criteria at the second screening visit were scheduled for a renal angiogram and then moved on to the next step if anatomical suitability was confirmed. Finally, eight patients with CKD stage 1–5 entered RDN procedure, none of them received dialysis.

2.3 | Procedures

In brief, a newly designed RDN catheter and radiofrequency generator (Golden Leaf Medtech, Shanghai, China) were used to perform circumferential radiofrequency ablation treatments in renal artery and branch vessels with diameters ranging from 4 to 8 mm. The treatment catheters were introduced into each renal artery via femoral access. We applied discrete radiofrequency ablations of 7 Watts or less lasting up to 2 min each. We performed 12 ablations separated both longitudinally and rotationally within each renal artery system. During ablation, the catheter system monitored tip temperature and impedance, altering radiofrequency energy delivery. All cases were performed by the same experienced proceduralist.

Patients returned for office follow-up visits at 1, 2, 3, and 6 months post-procedure. Unless the escape criteria were met, no antihypertensive drug changes were permitted for the next six months (office systolic BP $\geq$180 mmHg or <115 mmHg with symptoms of hypotension). Blood chemistries, including sodium, potassium, glucose, and serum creatinine, were obtained at each follow-up visit. The estimated GFR was calculated using the CKD-EPI formula. Renal artery

imaging using duplex ultrasound was performed during the 6-month office visit. If the duplex ultrasound was deemed non-diagnostic, a magnetic resonance angiography, computed tomography, or angiogram was recommended.

2.4 | Outcomes

The key efficacy endpoint was the BP change from baseline (measured at screening visit two) assessed at 6-month. This endpoint was based on the prespecified requirement for patients to be maintained on the same specified antihypertensive medication regimen through 6-month of follow-up. Between the two time points, the change in the office and 24 h BP measurements were compared. At 3- and 6-month, the office and 24 h heart rate change from baseline were assessed. Safety endpoints included all-cause mortality, end stage renal disease requiring dialysis, new renal artery stenosis larger than 70% (assessed at 6-month), any significant embolic event resulting in end-organ damage, admittance to hospital for hypertensive crises not related to medication nonadherence, new myocardial infarction, new stroke, renal artery re-intervention, major bleeding, major vascular complications, dissections, perforations, and increase in serum creatinine higher than 50% from screening assessment. End-stage renal disease was defined as two or more estimated GFR measurements lower than 15 ml/min/1.73 m^2 at least 21 days apart.

2.5 | Statistical methods

Continuous variables are presented as mean and standard deviation. Categorical data are reported as numbers and percentages. The paired sample *t*-test was used to make comparisons between continuous variables. A probability value of $P < .05$ was considered statistically significant. All statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, Illinois, USA).

3 | RESULTS

3.1 | Baseline characteristics of patients

Of the 26 initials patients, ten patients were excluded because of the small-sized renal artery (at least one renal artery diameter <4 mm) that contraindicated RDN, five patients retracted informed consent, and two patients were excluded because of hyperkalemia, one patient was excluded for low BP. Finally, eight patients finished RDN treatment and 6-month follow-up. Interestingly, there was a significant difference in eGFR between patients with or without renal artery stenosis (5.9 ± 3.3 vs. 46.5 ± 33.0, $P = .014$).

At baseline, average office systolic BP while seated was 165.0 ± 13.9 mmHg and diastolic BP was 97.8 ± 5.6 mmHg, with an office heart rate of 80 ± 5 beats/min. Baseline corresponding 24 h ambulatory BP monitoring showed an average systolic BP of 162.0 ± 21.4 mmHg and diastolic BP of 91.6 ± 9.3 mmHg. At baseline, the mean creatinine-based eGFR was 46.5 ± 33.0 ml/min/1.73 m2, and the mean plasma creatinine level was 298.8 ± 241.4 μmol/L.

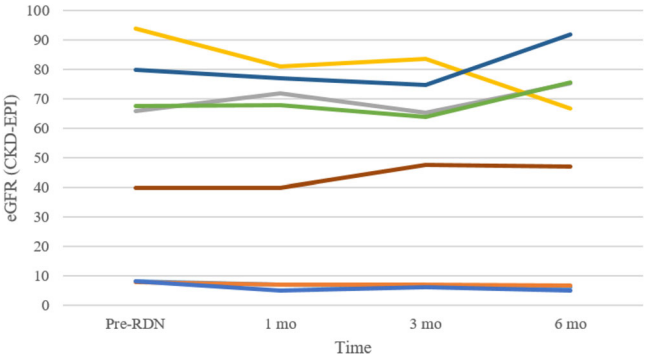

FIGURE 1 Individual changes in creatinine-based estimated GFR before RDN (pre-RDN); at 1-, 3-, and 6-month follow-up. GFR, glomerular filtration rate; RDN, renal denervation

3.2 | Effects of RDN on biochemical measures

No statistically significant differences in postprocedural serum biochemistry were observed ($P > .05$). There were no significant alterations in kidney function, as assessed by estimation of GFR according to serum creatinine levels. No disturbances in serum electrolytes were observed. Figure 1 depicts changes in creatinine-based eGFR in individual patients after the procedure at 1, 3, and 6-month.

3.3 | Effects of RDN on BP and heart rate

The mean decrease in seated office BP was 21.6/9.1, 21.8/12.5, and 22.1/11.0 mmHg for systolic BP and diastolic BP at 1, 3, and 6-month after the procedure, respectively. Mean 24 h ambulatory BP was significantly reduced at 3 and 6-month after RDN. Average 24 h BP had a decline of 14.1/7.1 mmHg at 3-month follow-up and 18.0/9.3 mmHg at 6-month follow-up (Figure 2). Similarly, both day-time and night-time BP were significantly lower at 3 and 6-month (Table 1). No marked post-procedure changes in night-to-day BP ratios were observed (Table 1). Compared with baseline, heart rate tended to be lower at 6-month after RDN (Table 1). But there was no significant difference.

3.4 | Safety

Of the eight patients who underwent RDN, no patient had bleeding at the puncture site of the femoral artery immediately after the procedure. Real-time renal artery imaging was used to assess internal structural changes caused by the procedure. There were no focal irregularities of the renal arteries observed postoperatively. At months 1

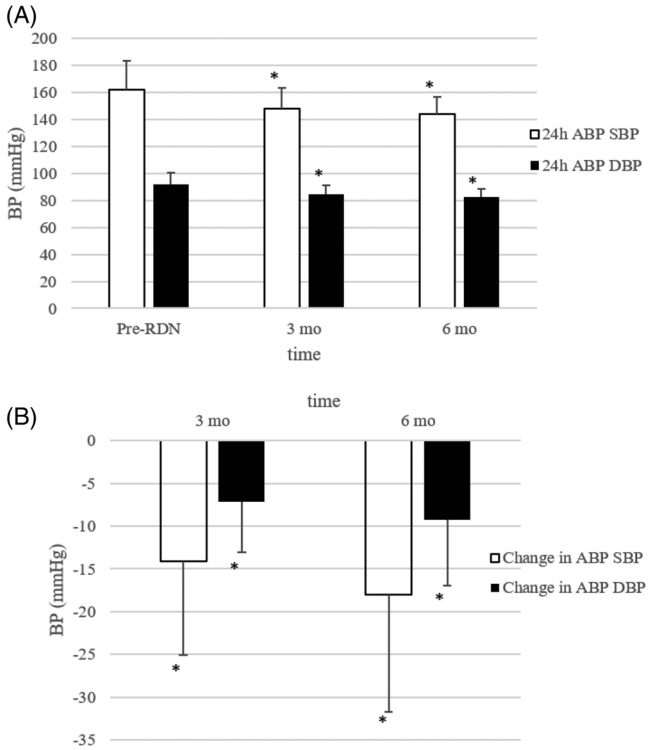

FIGURE 2 Mean 24 h ambulatory BP (ABP) values at follow-up. Changes in average ABP (A) and mean decrease in ABP (B) at follow-up. Error bars represent SDs. *$P < .05$ versus baseline (pre-RDN). ABP, ambulatory blood pressure; pre-RDN, pre-renal denervation; SD, standard deviation

and 6 after ablation, all patients underwent a Doppler scan of the renal arteries, which showed no evidence of stenosis or flow limitation.

4 | DISCUSSION

To our knowledge, our study is the first clinical experience with catheter-based renal nerve ablation in high-risk patients with CKD in China. Despite the relatively small number of patients ($n = 8$), We report on the safety and efficacy of radiofrequency-based RDN treatment applied in Chinese patients with CKD and uncontrolled hypertension. Bilateral RDN was associated with a significant and sustained decrease in BP measurements in our study, which was similar to other studies in hypertensive patients with normal or impaired renal function.[5–8,10,11] Our data confirmed and extended these findings by demonstrating significant BP reductions in a population with an eGFR below 45 ml/min/1.73 m2, which was previously excluded from some clinical trials.

Regardless of 24 h BP, nocturnal BP, and the night-to-day BP ratio have been found to predict all-cause mortality and cardiovascular events in hypertension.[12,13] High night-time and early morning BP levels have been associated with a higher risk of cardiovascular events. Wang et al. reported that nocturnal systolic hypertension was associated with higher risks for adverse outcomes in patients with CKD.[14] Several trials indicated that RDN treatment had a considerable effect on nocturnal and morning BP control.[15,16] Unfortunately, there was no significant change in the night-to-day BP ratio in our study. Future research should investigate the clinical significance of these findings.

TABLE 1 Office and ambulatory BP and heart rate before and after RDN

Measurement	Baseline ($n = 8$)	3-month ($n = 8$)	6-month ($n = 8$)	*P* values (baseline vs. 6-month)	*P* values (3- vs. 6-month)
SBP (mmHg)					
Office	165.0 ± 13.9	143.3 ± 17.2	142.9 ± 13.9	.002	.95
ABPM mean	162.0 ± 21.4	147.9 ± 15.6	144.0 ± 12.8	.01	.48
ABPM daytime	162.4 ± 20.4	148.4 ± 14.6	144.4 ± 12.9	.02	.51
ABPM night-time	159.1 ± 26.6	143.6 ± 22.3	143.1 ± 16.6	.02	.93
Night-to-day ratio	.98 ± .08	.96 ± .07	.99 ± .09	.50	.44
DBP (mmHg)					
Office	97.8 ± 5.5	85.3 ± 5.5	86.8 ± 8.6	.01	.71
ABPM mean	91.6 ± 9.3	84.5 ± 7.0	82.5 ± 6.3	.02	.53
ABPM daytime	92.1 ± 8.0	85.0 ± 7.2	83.0 ± 6.7	.03	.56
ABPM night-time	90.0 ± 15.4	80.0 ± 9.8	81.1 ± 8.7	.04	.75
Night-to-day ratio	.97 ± .09	.94 ± .07	.98 ± .10	.70	.34
Heart rate (beats/min)					
Office	80 ± 5	78 ± 10	76 ± 9	.09	.50
ABPM mean	80 ± 8	76 ± 7	75 ± 9	.07	.41

Values are expressed as mean ± SD. Data are shown as a one-way repeated-measures ANOVA between treatments. ABPM, ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; RDN, renal denervation; SBP, systolic blood pressure; SD, standard deviation.

Some studies indicated that bilateral sympathetic RDN decreased BP and slowed or even halted the decline of renal function.[10,17] Hering reported that RDN can slow further deterioration of renal function in CKD regardless of BP-lowering effects, which may be due to changes in intrarenal and glomerular hemodynamics caused by RDN's inhibition of sympathetic outflow.[10] In the SYMPLICITY Global Registry, 3 years after RDN, renal function declined by 7.1 ml/min/1.73 m2 in patients without CKD (eGFR ≥ 60 ml/min/1.73 m2) and by 3.7 ml/min/1.73 m2 in patients with CKD (eGFR < 60 ml/min/1.73 m2).[18] However, the observed eGFR decrease over 3 years was within the bounds of the expected decline in patients with severe hypertension. Additionally, one meta-analysis showed that renal function does not significantly change up to at least 9-month after RDN.[19] In our study, neither improvement nor further deterioration of renal function was observed, which was in line with most similar studies. It is worth noting that antihypertensive medication was not changed after RDN until after a 6-month follow-up. Therefore, our results further supported the hypothesis that RDN was safe and effective in high-risk patients with advanced CKD and persistent hypertension. Prospective trials in the population of patients with severe CKD and longer follow-up times are needed.

It was worthwhile to note the high prevalence of renal vascular abnormality in patients with advanced CKD. In our cohort, 77% of patients (10/13) with severe CKD (eGFR < 15 ml/min/1.73 m2) were excluded because of the thin renal artery. The difference in eGFR between patients with and without thin renal arteries was significant (5.9 ± 3.3 vs. 46.5 ± 33.0 ml/min/1.73 m2). In another study, end-stage renal disease patients with a mean diameter of the right renal artery were 3.7 mm (range 2.5–5.0 mm) and of the left renal artery was 3.6 mm (range 3.0–5.0 mm) received RDN successfully.[20] Two clinical studies confirmed that the BP-lowering efficacy of ablation was increased by ablation in the renal artery branches.[21,22] In this study, we established strict exclusive criteria for renal artery diameter while keeping safety in mind. In the future, we should explore smaller-sized arteries.

There were several different radiofrequency ablation systems. The first-generation radiofrequency ablation system (Symplicity Flex; Medtronic) utilizes a single unipolar electrode on a flexible (4F) catheter to perform RDN.[23] A newly developed second-generation radiofrequency ablation system (Symplicity Spyral, Medtronic) that uses a flexible 4-electrode array mounted on a 4F catheter to create four simultaneous lesions in a helical pattern was widely used.[24] In this study, we used a newly designed ablation system from a Chinese company, which had a unique expandable reticular electrode construction (Figure 3). This ablation system imitated a balloon, which could pass through small vessels in their original shape and fit vascular walls tightly after dilatation. RDN could be performed in six loci simultaneously using a system with six electrodes in different quadrants. Blood flow was not blocked all along, which took away heat generated by ablation. So, this system had some advantages compared with other systems.

We acknowledge several limitations of our study. This study was a single-center analysis, with a relatively small number of patients, and there was no control group. We have only a six-month follow-up.

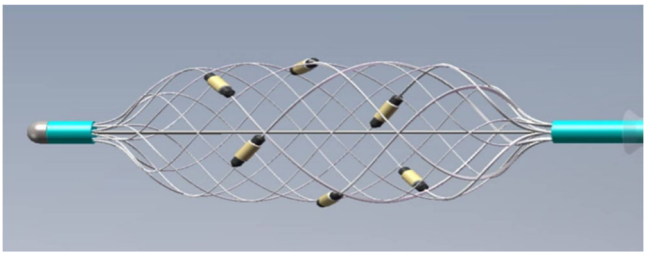

FIGURE 3 A new designed ablation system with unique expandable reticular electrode construction (Golden Leaf Medtech, Shanghai, China)

Renal nerve reinnervation, both functional and anatomical, has been observed in rats and sheep following RDN.[25,26] There is no evidence of similar reinnervation in patients who have undergone catheter-based RDN. However, in several clinical studies, the BP-lowering effect of RDN was sustained for up to 3 years.[18,27–29] Further studies are needed to resolve the issue of reinnervation in patients who received RDN. Furthermore, no simple physiological or biochemical markers can be used to determine the severity of RDN at the time of the procedure. As a result, we do not know if the procedure was successful in real-time. Furthermore, we lack an appropriate method for assessing RDN's effectiveness. Several immediate markers have been proposed, including renal blood flow parameters, blood levels of brain-derived neurotrophic factors, and the BP response to catheter-based renal nerve stimulation.[30–32] However, the sensibility and reliability of these markers need further study. It is of interest to note that the prospective, randomized, sham-controlled clinical trial examining the effect of RDN in CKD stage 3 (RDN-CKD study; NCT04264403) is currently ongoing. The Paradise Renal Denervation System will be used in this trial, which is a catheter-based device designed to use ultrasound energy to thermally ablate the nerves surrounding the renal artery. This randomized controlled trial will provide important information about the usefulness of RDN in CKD.

In conclusion, our observational pilot study in hypertensive patients with CKD in China found that RDN reduced office and 24 h ambulatory BP but had no effect on renal function. RDN is a safe and feasible strategy in advanced CKD patients with resistant hypertension. Further studies and clinical trials are needed to determine the long-term safety and efficacy of RDN in a larger CKD population.

AUTHOR CONTRIBUTIONS

Yuqiang Zhang and Senyan Liu carried out the studies, participated in collecting data and further analysis, and drafted the manuscript. Rongrong Bian and Yixin Qian participated in follow-up of patients, acquisition, and interpretation of data. Xiang Gao performed the statistical analysis. Huaqiang Liao and Weihua Dong participated in study design and performed RDN procedure. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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REFERENCES

1. Fay KS, Cohen DL. Resistant hypertension in people with CKD: a review. *Am J Kidney Dis*. 2021;77:110-121. https://doi.org/10.1053/j.ajkd.2020.04.017
2. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options. *Circulation*. 2021;143:1157-1172. https://doi.org/10.1161/circulationaha.120.050686
3. Grassi G, Bertoli S, Seravalle G. Sympathetic nervous system: role in hypertension and in chronic kidney disease. *Curr Opin Nephrol Hypertens*. 2012;21:46-51. https://doi.org/10.1097/MNH.0b013e32834db45d
4. Kaur J, Young BE, Fadel PJ. Sympathetic overactivity in chronic kidney disease: consequences and mechanisms. *Int J Mol Sci*. 2017;18:1682. https://doi.org/10.3390/ijms18081682
5. Townsend RR, Mahfoud F, Kandzari DE, et al. Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial. *Lancet*. 2017;390:2160-2170. https://doi.org/10.1016/s0140-6736(17)32281-x
6. Azizi M. Catheter-based renal denervation for treatment of hypertension. *Lancet*. 2017;390:2124-2126. https://doi.org/10.1016/s0140-6736(17)32293-6
7. Kandzari DE, Böhm M, Mahfoud F, et al. 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. *Lancet*. 2018;391:2346-2355. https://doi.org/10.1016/s0140-6736(18)30951-6
8. Böhm M, Kario K, Kandzari DE, et al. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED Pivotal): a multicentre, randomised, sham-controlled trial. *Lancet*. 2020;395:1444-1451. https://doi.org/10.1016/s0140-6736(20)30554-7
9. Yan Z, Wang Y, Li S, et al. Hypertension control in adults with CKD in China: baseline results from the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE). *Am J Hypertens*. 2018;31:486-494. https://doi.org/10.1093/ajh/hpx222
10. Hering D, Marusic P, Duval J, et al. Effect of renal denervation on kidney function in patients with chronic kidney disease. *Int J Cardiol*. 2017;232:93-97. https://doi.org/10.1016/j.ijcard.2017.01.047
11. Ott C, Mahfoud F, Mancia G, et al. Renal denervation in patients with versus without chronic kidney disease: results from the Global SYMPLICITY Registry with follow-up data of 3 years. *Nephrol Dial Transplant*. 2022;37:304-310. https://doi.org/10.1093/ndt/gfab154
12. Sega R, Facchetti R, Bombelli M, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation*. 2005;111:1777-1783. https://doi.org/10.1161/01.Cir.0000160923.04524.5b
13. Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA. Night-day blood pressure ratio and dipping pattern as predictors of death and cardiovascular events in hypertension. *J Hum Hypertens*. 2009;23:645-653. https://doi.org/10.1038/jhh.2009.9
14. Wang Q, Wang Y, Wang J, Zhang L, Zhao MH. Nocturnal systolic hypertension and adverse prognosis in patients with CKD. *Clin J Am Soc Nephrol*. 2021;16:356-364. https://doi.org/10.2215/cjn.14420920
15. Kario K, Bhatt DL, Brar S, Cohen SA, Fahy M, Bakris GL. Effect of catheter-based renal denervation on morning and nocturnal blood pressure: insights from SYMPLICITY HTN-3 and SYMPLICITY HTN-Japan. *Hypertension*. 2015;66:1130-1137. https://doi.org/10.1161/hypertensionaha.115.06260
16. Kario K, Weber MA, Böhm M, et al. Effect of renal denervation in attenuating the stress of morning surge in blood pressure: post-hoc analysis from the SPYRAL HTN-ON MED trial. *Clin Res Cardiol*. 2021;110:725-731. https://doi.org/10.1007/s00392-020-01718-6
17. Ott C, Mahfoud F, Schmid A, et al. Renal denervation preserves renal function in patients with chronic kidney disease and resistant hypertension. *J Hypertens*. 2015;33:1261-1266. https://doi.org/10.1097/hjh.0000000000000556
18. Mahfoud F, Böhm M, Schmieder R, et al. Effects of renal denervation on kidney function and long-term outcomes: 3-year follow-up from the Global SYMPLICITY Registry. *Eur Heart J*. 2019;40:3474-3482. https://doi.org/10.1093/eurheartj/ehz118
19. Sanders MF, Reitsma JB, Morpey M, et al. Renal safety of catheter-based renal denervation: systematic review and meta-analysis. *Nephrol Dial Transplant*. 2017;32:1440-1447. https://doi.org/10.1093/ndt/gfx088
20. Ott C, Schmid A, Ditting T, Veelken R, Uder M, Schmieder RE. Effects of renal denervation on blood pressure in hypertensive patients with end-stage renal disease: a single centre experience. *Clin Exp Nephrol*. 2019;23:749-755. https://doi.org/10.1007/s10157-019-01697-7
21. Fengler K, Ewen S, Höllriegel R, et al. Blood pressure response to main renal artery and combined main renal artery plus branch renal denervation in patients with resistant hypertension. *J Am Heart Assoc*. 2017;6:e006196. https://doi.org/10.1161/jaha.117.006196
22. Pekarskiy SE, Baev AE, Mordovin VF, et al. Denervation of the distal renal arterial branches vs. conventional main renal artery treatment: a randomized controlled trial for treatment of resistant hypertension. *J Hypertens*. 2017;35:369-375. https://doi.org/10.1097/hjh.0000000000001160
23. Krum H, Schlaich M, Whitbourn R, et al. Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study. *Lancet*. 2009;373:1275-1281. https://doi.org/10.1016/s0140-6736(09)60566-3
24. Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med*. 2014;370:1393-1401. https://doi.org/10.1056/NEJMoa1402670
25. Mulder J, Hökfelt T, Knuepfer MM, Kopp UC. Renal sensory and sympathetic nerves reinnervate the kidney in a similar time-dependent fashion after renal denervation in rats. *Am J Physiol Regul Integr Comp Physiol*. 2013;304:R675-R682. https://doi.org/10.1152/ajpregu.00599.2012
26. Booth LC, Nishi EE, Yao ST, et al. Reinnervation of renal afferent and efferent nerves at 5.5 and 11 months after catheter-based radiofrequency renal denervation in sheep. *Hypertension*. 2015;65:393-400. https://doi.org/10.1161/hypertensionaha.114.04176
27. Esler MD, Böhm M, Sievert H, et al. Catheter-based renal denervation for treatment of patients with treatment-resistant hypertension: 36 month results from the SYMPLICITY HTN-2 randomized clinical trial. *Eur Heart J*. 2014;35:1752-1759. https://doi.org/10.1093/eurheartj/ehu209
28. Kim BK, Kim HS, Park SJ, et al. Long-term outcomes after renal denervation in an Asian population: results from the Global SYMPLICITY Registry in South Korea (GSR Korea). *Hypertens Res*. 2021;44:1099-1104. https://doi.org/10.1038/s41440-021-00683-5
29. Mahfoud F, Kandzari DE, Kario K, et al. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): a randomised, sham-controlled

trial. *Lancet*. 2022;399:1401-1410. https://doi.org/10.1016/s0140-6736(22)00455-x. PMID:35390320
30. Dörr O, Liebetrau C, Möllmann H, et al. Brain-derived neurotrophic factor as a marker for immediate assessment of the success of renal sympathetic denervation. *J Am Coll Cardiol*. 2015;65:1151-1153. https://doi.org/10.1016/j.jacc.2014.11.071
31. de Jong MR, Adiyaman A, Gal P, et al. Renal nerve stimulation-induced blood pressure changes predict ambulatory blood pressure response after renal denervation. *Hypertension*. 2016;68:707-714. https://doi.org/10.1161/hypertensionaha.116.07492
32. de Jong MR, Hoogerwaard AF, Adiyaman A, et al. Renal nerve stimulation identifies aorticorenal innervation and prevents inadvertent ablation of vagal nerves during renal denervation. *Blood Press*. 2018;27:271-279. https://doi.org/10.1080/08037051.2018.1463817

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