

Early reduction of therapy-resistant hypertension in a patient after single-sided renal denervation approach

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Sirs,

Catheter-based renal denervation (RD) offers a relative new approach targeting the renal sympathetic nerves in order to decrease the blood pressure (BP) in patients with resistant hypertension associated with an increased risk of cardiovascular events. According to available evidence and expert suggestions, patients with treatment-resistant hypertension defined by office systolic BP ≥ 160 mmHg (≥ 150 mmHg in type 2 diabetes) despite treatment with at least three antihypertensive drugs (including one diuretic) are eligible for RD [1, 2]. Secondary hypertension, including renal artery stenosis $> 50\%$, must be ruled out and both-side denervation procedure is usually performed and some reports suggest higher responder rates in order to decrease the BP [3, 4].

Here, we report a RD procedure in a 47-year-old woman (BMI of 31.2 kg/m^2) with medically resistant hypertension on a treatment of seven antihypertensive drugs (β -blocker, angiotensin-II-blocker, calcium channel blocker, thiazide, α_2 -agonist, direct vasodilator, α -blocker). A secondary cause for the hypertension was excluded. No direct or indirect signs of hemodynamic relevant renal artery stenosis were seen in duplex sonography. End-organ damage was present with the detection of hypertensive cardiomyopathy, retinopathy and

nephropathy with micro-albuminuria. Automated blood pressure measurement over the daytime indicated baseline systolic/diastolic BP of $187 \pm 16 \text{ mmHg}/108 \pm 8 \text{ mmHg}$ ($n = 9$) before RD; the corresponding heart rate (HR) was $68 \pm 7 \text{ bpm}$. For performing RD, access via the right femoral artery with a 6F-sheath was used and fluoroscopic angiography indicated a normal configuration of the left renal artery (Fig. 1a), whereas the right renal artery with high-angle junction from abdominal aorta had a proximal stenosis of approximate 50% (Fig. 1b). Left artery denervation was performed with the application of five 8-W-radiofrequency ablation points using the standard solid-tip renal denervation catheter (Simplicity[®] catheter; Medtronic/Ardian Inc.). Mean temperature was $59.4 \pm 4.5 \text{ }^\circ\text{C}$ with a mean impedance drop of $19.6 \pm 1.7\%$ during the 120 s of ablation at each point. Remarkable intimal oedema and/or vasospasm without compromising the blood flow could be seen after the radiofrequency ablation procedure in the left renal artery (Fig. 1c). Due to right renal artery proximal stenosis, difficulty to advance the ablation catheter into the distal artery (using a 'RDC guiding catheter') and the patient's wish to not further elongate the procedure time, only a left-sided RD approach was chosen. Post-procedural performed controls revealed that the blood pressure could be significantly reduced 2 days after the RD procedure compared to the BP measured before the procedure in the same clinical environment ($141 \pm 12 \text{ mmHg}$ systolic and $85 \pm 8 \text{ mmHg}$ diastolic; $n = 7$; $P < 0.001$ vs. systolic and diastolic BP before RD); the HR was also reduced ($57 \pm 4 \text{ bpm}$; $n = 3$; $P = 0.048$ vs. HR before RD). Moreover, 1 month after the RD, ambulatory BP measurement revealed a mean systolic blood pressure of $122 \pm 17 \text{ mmHg}$ and diastolic of $77 \pm 20 \text{ mmHg}$ at daytime ($n = 45$; $P < 0.001$ vs. systolic and diastolic RR

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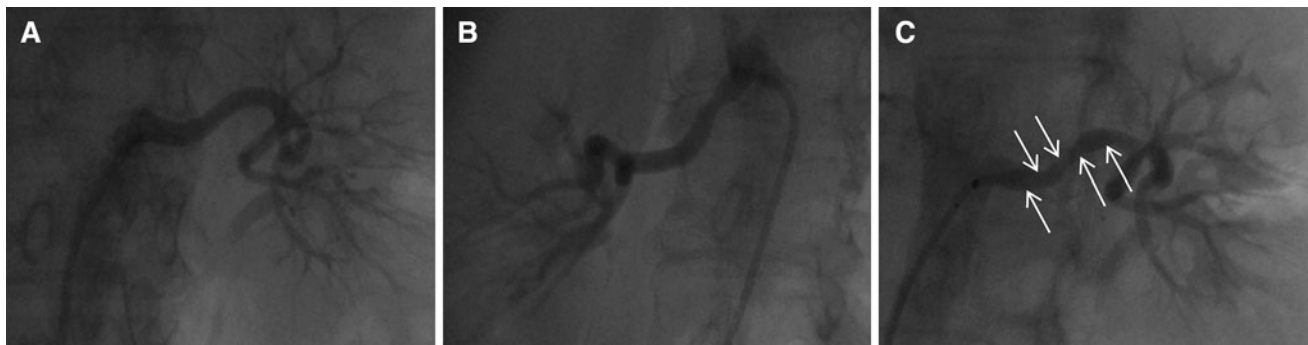


Fig. 1 Fluoroscopic angiography indicated a normal configuration of the left renal artery (a), whereas the right renal artery with high-angle junction from abdominal aorta had a proximal stenosis of approximate 50 % (b). Left renal artery denervation was performed with the

application of five 8-W-radiofrequency ablation points (arrows) and subsequent intimal oedema/vasospasm without compromising the blood flow was visible (c)

before RD) and measurement of the office blood pressure (125/75 mmHg) confirmed a normal BP level 3 months after RD, so that the dosage of four antihypertensive drugs could be reduced. The HR was still on a lower level compared to the HR before RD (59 ± 7 bpm; $n = 45$; $P = 0.002$). Renal function assessed by serum creatinine and urea nitrogen was unchanged (1 month, before RD, and 3 months after RD: 0.82, 0.72, 0.72 mg/dL and 16, 13, 13 mg/dL). The micro-albuminuria was reduced from 91 to 52 mg/g creatinine 3 months after RD. The duplex sonography indicated no renal artery abnormalities with a decrease of mean resistance index (RI) from 0.71 to 0.64 in the interlobar arteries of the right and 0.69 to 0.58 of the left kidney, respectively, comparing values prior to RD vs. 3 months after RD. The echocardiogram indicated a slightly reduced concentric left ventricular hypertrophy (end-diastolic posterior wall and interventricular septum thickness from 15 to 14 mm) and diastolic dysfunction (E/E' from 9.6 to 8.9) after RD.

In this single case we have seen a very early reduction in BP after the RD and in the following 3 months, although the denervation procedure was only performed single-sided. RI of interlobar arteries was decreased as described by other investigators [5]. Interestingly, the RI decrease was more pronounced on the interventional side. No adverse events were present and the mentioned laboratory and instrumental findings revealed an autonomic modulation (e.g. reduction of the heart rate) and a slight reduction of hypertension-related end-organ damage in this short follow-up period. These changes after single-sided RD (for summary see Table 1) exhibited a similar tendency compared to published studies examining the effect of standard both-sided RD on different organ systems; e.g. reduction of left ventricular heart hypertrophy and diastolic dysfunction [6, 7]. But these effects were less pronounced to some extent and it cannot exclude that they are related to the reduction of BP and only an indirect result of the single-

Table 1 A summary of relevant parameters and changes before and after the single-sided renal denervation (RD) is shown

	Before RD	Change after single RD
Blood pressure	Hypertensive (187/108 mmHg)	↓↓↓ Normotensive (125/75 mmHg)
Heart rate	Normal (68/bpm)	↓ Normal (59/bpm)
Serum creatinine	Normal range (0.82 mg/dL)	→ Normal range (0.72 mg/dL)
Urea nitrogen	Normal range (16 mg/dL)	→ Normal range (13 mg/dL)
Microalbuminuria	91 mg/g creatinine	↓ 52 mg/g creatinine
Renal resistance index (right/left)	0.71/0.69	↓ 0.64/0.58
Heart hypertrophy (IVSTd)	Moderate concentric (15 mm)	↓ Moderate concentric (14 mm)
Diastolic dysfunction (E/E')	9.6	↓ 8.9
Antihypertensive medication	7 drugs	↓ Dosage

For more details, please see the description in the text
IVSTd: end-diastolic interventricular septum thickness

sided RD. For speculating the underlying mechanism/reason for the early BP decrease, a high baseline sympathetic overactivity has to be taken into account [8–10]. However, the available evidence furthermore implicates an approach of both-side RD with its good vascular safety profile [1, 11]. But one has to consider that, if only single-sided RD is possible (e.g. unfavourable renal artery anatomy), this procedure might be successful in order to reduce BP and subsequently improve the hypertension-related end-organ damage.

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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