

## Case report

# Treatment of Resistant Hypertension with Renal Denervation in a Diabetic Patient

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## Abstract

**Introduction.** High risk patients, such as diabetic patients, with treatment-resistant hypertension benefit greatly from the procedure of renal denervation by lowering blood pressure and preserving renal function.

**Case report.** A 62-year-old female came to our clinic for uncontrolled hypertension. She was obese (BMI 32) diabetic patient with neuropathy and retinopathy and renal insufficiency stage II (MDRD/CKD-EPI formula for eGFR: 66/72ml/min/1,73m<sup>2</sup>), but without diabetic nephropathy. All of the antihypertensive drugs were given at best tolerated dosage. Despite the therapy with 6 antihypertensive drugs (aldosterone was added to the treatment) the patient was not able to control her blood pressure and ambulatory blood pressure monitoring showed a resistant hypertension (RH): non-dipper pattern, with day average systole/diastole: 149/78mmHg, maximum values of 208/130 mmHg, pulse pressure 68mmHg and frequency 80 per minute. The patient was admitted to the hospital for testing the compliance, and the result was excellent. Thus, a device related therapeutic procedure remained as a treatment alternative, and renal artery denervation is the only possible option in Croatia.

**Results.** Renal sympathetic denervation was done at seven sites on both arteries without any procedure-related complications. After the procedure, the patient was stable, without worsening of the renal function and good control of blood pressure. BP measurements at 1 and 3 months follow-up visits were compared to baseline values.

**Conclusions.** Renal denervation is a safe and effective procedure to cure RH in patients with diabetes.

**Key words:** resistant hypertension, renal denervation, cost-benefit analysis

## Introduction

Resistant hypertension is defined as high blood pressure that remains uncontrolled despite treatment with at least three antihypertensive agents (one of which is a diuretic) at best tolerated doses [1]. Before a resistant hypertension

diagnosis can be made, obvious causes of elevated blood pressure should be sought (non-compliance, under-dosing, white-coat hypertension etc.) as well as secondary arterial hypertension. Prevalence of resistant hypertension in Croatia is not known, but in USA and in Western Europe it ranges from 9 to 13% [2,3].

Despite guideline treatment strategies, many patients with hypertension fail to achieve blood pressure control and remain at risk for cardiovascular disease [1]. Sympathetic nervous system activation has been implicated in the development and progression of hypertension, as well as associated metabolic, cardiovascular and renal disease states. Renal denervation is a successful device-based therapeutic therapy for resistant hypertension [4] and some subsequent studies reported beneficial effect on glucose tolerance, sleep apnoea, left ventricular hypertrophy, and cardiac function [5,6]. The cost of this procedure is around 65,000 HRK (8500 EUR) and it is not paid by the Croatian Institute for Health Insurance. It is considered a high cost procedure and it is not included in Diagnosis-related groups. In patients with coronary artery disease, carotid arteries disease, chronic kidney disease (CKD) uncontrolled hypertension undeniably leads to possible stroke, myocardial infarction and end-stage renal disease with a need of haemodialysis. Prices of treatment for one stroke granted by the Croatian Institute for Health Insurance are 24508,89 HRK; treatment of one myocardial infarction 24635,23 HRK and one haemodialysis treatment is around 900 HRK; all prices are given as Diagnosis-related groups. Patients with resistant hypertension are also at higher risk for poor cardiovascular outcomes, including death, MI, heart failure, stroke, or chronic kidney disease, meaning that "recognizing these patients and identifying means of minimizing their risk will be important to improve their overall prognosis, and there is a strong evidence for the use of spironolactone as a highly effective antihypertensive agent [7,8].

Patients with multiple comorbidities are usually refused for renal denervation, but we present a case of patient who gained benefit from this procedure with evidence of preserved renal function, improved diabetes control and lower pharmacological therapy.

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## Case report

A 62-year-old female came to our clinic for resistant hypertension (RH). She was obese (body mass index 32), diabetic patient (since 1976) with complications including polyneuropathy and retinopathy, history of hypertension (since 1972) and chronic kidney disease stage II (MDRD/CKD-EPI formula for eGFR: 66/72ml/min/1,73m<sup>2</sup>). Blood-pressure (BP) control was defined as <140/<90 mm Hg. So, the patient has controlled BP to <140/<90 mm Hg being on four or more blood-pressure medications and was classified as having controlled apparent treatment-resistant hypertension. Optimal therapy for this patient with uncontrolled apparent treatment-resistant hypertension was prescribing a diuretic and two or more other blood-pressure medications, with each medication at  $\geq 50\%$  of the maximum recommended or approved dose for hypertension. She was given losartan 200 mg/hydrochlorothiazide 25 mg, amlodipine 10 mg, nebivolole 5 mg, moxonidine 0,6 mg, spironolactone (Aldactone)100 mg, indapamide 1,5 mg, statins, aspirin and insulin therapy; all of antihypertensive drugs at best tolerated dosage. Despite the therapy ambulatory blood pressure monitoring showed a non-dipper pattern, with day average systole/diastole: 149/78 mmHg, maximum values of 208/130 mmHg, pulse pressure 68 mmHg and frequency 80 per minute. Serum creatinine was 77  $\mu\text{mol/L}$ , potassium 4,3 mmol/L, glucose 7,5-10.0 mmol/L, without albuminuria. The patient was admitted to the hospital for testing the compliance, and the result was excellent. Aldosterone antagonist was not given because of high levels of serum potassium. Thus, a device related therapeutic procedure remained as a treatment alternative, and renal artery denervation (RDN) was done at seven/sites on both arteries without any procedure-related complications. After the procedure, the patient was stable, without worsening of the renal function. Laboratory values after the procedure showed stable serum creatinine 71  $\mu\text{mol/L}$  with albumin/creatinine ratio 0,5 mg/mmol. HbA1c value before RDN was 7,6% and after 3 months (with the same therapy) 7,2%. One month after RDN the ambulatory blood pressure monitoring (ABPM) showed non-dipper pattern, with day average systole/diastole: 131/68 mmHg, maximum values of 179/123 mmHg, pulse pressure 62 mmHg and frequency of 73 per minute. Three months after RDN the ABPM showed non-dipper pattern, with day average systole/diastole: 127/62 mmHg, maximum values of 148/84 mmHg, pulse pressure 64 mmHg and frequency of 65 per minute. One and 3 months after RDN, office systolic blood pressure values were significantly lower ( $P < 0.001$ ). Nevertheless, after RDN the number of antihypertensive drug classes required was 5 which was not statistically different from the baseline.

## Discussion

Optimal therapy for patients with controlled apparent treatment-resistant hypertension was defined as prescription of a diuretic and three or more other blood-pressure

medications, with each medication at  $\geq 50\%$  of the maximum recommended or approved dose for hypertension [1]. To improve treatment of uncontrolled hypertension, physicians should search for secondary causes of hypertension, rule out white-coat hypertension, expend energy to improve patient compliance, and prescribe an optimal drug regimen and adequate dosage [9]. Approximately 1 in 7 of all uncontrolled hypertensives and 1 in 2 with uncontrolled RH are prescribed  $\geq 3$  BP medications as optimal regimens. We need to answer some basic questions when treating a patient with treatment-resistant hypertension: is the patient's pressure elevated outside the office? Is the prescribed treatment adequate, and is the patient taking the medications that have been prescribed [10]. When pharmacological therapy has failed, there are new options for treating patients with resistant hypertension (RH). Renal Sympathetic Denervation (RDN), an endovascular catheter-based intervention, has been applied as a novel concomitant treatment of drug-resistant hypertension (rHT). This was the case with our patient.

## Conclusions

Renal sympathetic denervation is safe and effective procedure that lowers blood pressure in patients with resistant hypertension. The most beneficial effect of the procedure has been shown in patients with multiple comorbidities such as diabetic patients, coronary arteries disease, carotid arteries disease and chronic kidney disease. These patients should not be excluded from the procedure since they will benefit greatly from it by prolonging dialysis-free time, preventing stroke and myocardial infarction and improving quality of life. For better understanding of the efficacy and safety of RDN we need clinical trials in patients with rHT and various co-morbidities.

*Conflict of interest statement.* None declared.

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