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The influence of catheter-based renal sympathetic denervation on renal function and renal arteries

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ABSTRACT

Objective: Currently investigated non-pharmacological minimally invasive method for the treatment of resistant hypertension is percutaneous denervation of renal sympathetic nerve fibres by radiofrequency catheter-based ablation. We assessed its influence on renal function and renal arteries.

Methods: The first 38 patients treated with catheter-based renal denervation at our centre between September 2011 and December 2012 were included in the study. Changes in renal function and changes in renal artery morphology at 12 months after the procedure have been analyzed.

Results: Mean age was 57.6 ± 11 years, the majority (63.9%) were men. Average estimated glomerular filtration rates (eGF) were 1.25 ml/s/1,73 m^2 before denervation and 1.30 ml/s^{-1}/1.73 m^{-2} 12 months after intervention. Changes in eGF did not reach statistical significance. New haemodynamically non-significant renal artery stenosis (40%) has occurred in only one case after procedure.

Conclusion: In agreement with the results of several studies, our findings suggest that renal denervation (RDN) appears to be a safe therapeutic approach.

Introduction

Arterial hypertension is the most frequent cardiovascular disease [1]. Approximately 1 billion people worldwide suffer from hypertension, and it is projected that this number will increase to 1.5 billion by 2025 [2]. Its prevalence is expected to increase especially in developing countries [3]. Despite several available antihypertensive drugs and their unquestionable beneficial effects, hypertension control is still unsatisfactory [4,24]. This fact is attributed to a number of factors such as inappropriate blood pressure measurement, physician inertia, excessive salt intake or secondary causes of hypertension. Apart from the white coat syndrome, patient non-compliance to a pharmacological therapy is a very frequent phenomenon [5]. If these factors are excluded and uncontrolled hypertension persists despite the use of at least 3 antihypertensive drugs of different classes at maximally tolerated doses

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including a diuretic, we speak of resistant hypertension. The true prevalence of resistant hypertension remains unknown because of the absence of a specifically designed large prospective study with forced titration. Analyses of clinical trials suggest a prevalence to range from 10% to almost 30% of general hypertensive patients in different studies [6,7].

Accumulated evidence indicates that human sympathetic nervous system deregulation contributes to the development of arterial hypertension [8,9]. Sympathetic overactivity has been demonstrated in both essential and secondary forms of hypertension patients, such as obesity-related hypertension, end-stage renal disease hypertension and in obstructive sleep apnea [10].

Over the last few decades, growing knowledge about the role of the chronic sympathetic overactivity in hypertension pathophysiology has resulted in the development of an innovative non-pharmacological therapy that modulates sympathetic activation – percutaneous renal sympathetic denervation. It is an endovascular procedure that uses radiofrequency energy to destroy the perirenal sympathetic nerve fibres. RDN decreases both efferent and afferent renal sympathetic nerve activity. Anatomical regrowth of afferent renal nerves has not been shown and efferent renal nerves might be able to regrow to some extent [11]. Primary end point in the renal artery ablation sympathectomy is to reduce production of catecholamines, especially noradrenaline. The renin-angiotensin-aldosteron system is influenced simultaneously. After bilateral renal sympathectomy, the noradrenaline content in the kidney is reduced by 47% [12]. Renal perfusion is improved simultaneously [13]. Catheter-based sympathectomy does not affect negatively other organ systems and does not cause postural hypotension. It has a beneficial effect on myocardial remodelling and other vascular changes associated with severe hypertension and sympathetic overactivity [14].

Brandt and colleagues [15] demonstrated that RDN in resistant hypertension patients was associated with a regression of left ventricle hypertrophy and an improvement of the diastolic function at 6-months follow-up visit, compared with the control group. RDN may also influence other diseases associated with sympathetic hyperactivity like chronic heart failure, diabetes mellitus or sleep apnea syndrome [16].

Based on the available evidence from clinical studies, catheter-based renal denervation has a favourable short-term safety profile. During follow-up of patients from the multicenter, observational Symplicity HTN-1 trial [17] and from the randomized controlled Symplicity HTN-2 trial [18], no statistically significant changes in renal function and no vascular complications such as significant stenoses of treated renal arteries were seen.

The longest available follow-up was at 2 years in the Symplicity HTN-1 trial [19] with enlarged cohort of 153 patients at 19 centres in Australia, Europe and USA, in which renal function remained unchanged during the first year of follow-up. Estimated glomerular filtration rate data of 2 years after the intervention were only available for 10 patients, in which there was a mean reduction in eGF of 16 ml/min^{-1}/1.73 m^{-2}. Five of these 10 patients had spironolactone or other diuretic added to the antihypertensive treatment after the first year of follow-up. In the remaining patients without newly added spironolactone or other diuretic to the treatment, there was a reduction in estimated glomerular filtration rate (7.8 ml/min^{-1}/1.73 m^{-2}). No patient showed doubling of serum creatinine, development of chronic kidney disease stage IV or the requirement for dialysis.

Adverse effects of renal denervation on glomerular filtration rate or renal artery structure was not shown during 6 months of follow-up in the study of Mahfoud and colleagues [20].

Worthley and colleagues [2] studied the safety of renal artery denervation in 46 patients at 4 centres in Australia and Greece using the EnlighHTN catheter (multi-electrode system). The follow-up interval was 6 months. No acute or late serious vascular complications occurred and small, non-clinically relevant changes in average estimated glomerular filtration rate were reported (87 ± 19 ml/min^{-1}/1.73 m^{-2} before RDN compared with 82 ± 20 ml/min^{-1}/1.73 m^{-2} 6 months after RDN).

Gosain and colleagues [21] analyzed 19 studies investigating the effect of renal denervation on renal function and renal haemodynamics. They did not find a significant worsening of renal function, changes in renal artery anatomy or development of clinically significant stenosis.

The safety of renal sympathetic denervation has also been confirmed in a recently published multicentre, prospective, blinded, randomized and controlled Symplicity HTN-3 trial [22]. Only one new renal artery stenosis of more than 70% was verified at 6-month follow-up period.

Methods

Our aim was to analyze the safety of renal sympathetic denervation based on the changes in renal function and changes in renal artery morphology from baseline to 12 months.

A total of 39 patients underwent catheter-based renal denervation treatment at our centre from 1.9.2011 to 17.12.2012 with subsequent follow-up to 1 year. One patient was excluded from the study due to absence of 1-year follow-up visit. A total 38 patients were included in the analysis. All the patients were confirmed the diagnosis of resistant hypertension and met all indication criteria of renal denervation. Patients underwent procedure with the use of radiofrequency energy delivered by the Medtronic Ardian Symplicity^{TM} Renal Denervation System. The procedure was done in the catheterization laboratory in local anaesthesia by interventional cardiologist and arythmologist. Unfractionated heparin was administered with activated clotting time (ACT) monitoring. ECG and vital signs were monitored during the procedure. The intervention was performed via femoral access. A 6 French guiding catheter sheath was inserted to femoral artery, aortography with non-selective renal angiography using the pigtail catheter was performed subsequently. The lumen of the main renal artery was catheterized using RDND1 catheter (Medtronic, Denver, USA). After renal artery engagement and completion of a renal angiogram, the Symplicity ablation catheter was inserted to the renal artery minimally 5 mm from the main renal artery bifurcation and at the site where renal artery was minimally 4 mm in diameter.