

# The Effects of Percutaneous Renal Sympathetic Denervation on Cardiac Function and Exercise Tolerance

## Abstract

About 100 million people worldwide suffer from chronic heart failure (CHF), which has a 50% five-year survival rate despite the fact that pharmacological therapy can relieve symptoms. Sympathetic hyperactivity, a significant contributor to the onset and progression of heart failure (HF), is associated with both the severity and prognosis of HF.

## Introduction

Recent studies have shown that ablating the renal afferent and efferent nerves using an unique catheter-based renal sympathetic denervation (RDN) approach can reduce excessive sympathetic nerve activation and may have a potential therapeutic benefit in disorders linked to sympathetic activation. RDN has been shown to lower blood pressure (BP) in patients with resistant hypertension in several investigations on the condition, with a mean reduction of 33/12 mmHg [1]. A prior study supported the 6-min walk distance of patients with HF can be increased with RDN utilising a 3.5F Symplicity ablation catheter, but echocardiography measurements of ejection fraction (EF) and left ventricular capacity are not improved. In preliminary animal studies, our research team has shown that employing a 5F ablation catheter from Medtronic Inc, Dublin, Ireland, percutaneous RDN can enhance cardiac function and decrease left ventricular volume in pigs with rapid pacing-induced HF. A 5F ablation catheter was employed in the current investigation to treat RDN in patients with CHF, and safety parameters including cardiac function, exercise tolerance, blood pressure, and creatinine (Cr) were measured [2].

CHF diagnosis, EF 45% on echocardiography, >2 HF episodes in the previous 6 months, medication with HF medications such as beta-blockers, ACEIs or ARBs, and spironolactone, and no acute HF decompensation in at least 1 month of medication therapy were inclusion criteria. A history of renal artery stenosis (RAS) or imaging evidence of RAS, glomerular filtration rate 30 ml/min/1.73 m<sup>2</sup>, type 1 diabetes, pregnancy or intending to become pregnant during the study period, acute phase of myocardial infarction (MI) or cerebrovascular accident, and systolic blood pressure 100 mmHg were the exclusion criteria. In the trial, 14 patients were enrolled, including four with hypertensive HF, two with dilated cardiomyopathy, and eight with coronary artery disease. The average blood pressure at rest was 138.622.1/81.111.3 mmHg. ALL informed consent forms for receiving percutaneous procedures were signed by all patients [3].

RDN the Putuo Hospital Ethics Committee of Shanghai University of Traditional Chinese Medicine in China gave its approval to the study. This trial had only one arm and was prospective, open, and without a control or dummy group [4]. All of the patients who were included received biliary percutaneous RDN. evaluation of pre-renal denervation The New York Heart Association functional class, echocardiographic parameters, 6-min walk distance, and standard blood biochemistry markers were all evaluated in all included patients. Prior to percutaneous RDN, bilateral renal artery ultrasonography or computed tomography angiography was carried out to rule out RAS [5]. Before the intervention, the RDN group received 300 mg of chewable enteric-coated aspirin or 300 mg of clopidogrel, as well as 6000–8000 U of intravenous unfractionated heparin. After cleaning the skin and disinfecting the right inguinal area, RDN. The Putuo Hospital Ethics Committee of Shanghai University of Traditional Chinese Medicine in China gave its approval to the study. For bilateral renal angiography, the right femoral artery

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was perforated, a 7F catheter sheath was placed, and then a JR catheter. Then, using a 39D72X Stockert EP Shuttle RF Generator (Johnson & Johnson Medical) with temperature control (8-10 W, 50°C), a 5F radiofrequency catheter was implanted for rotational ablation. There were 4-6 ablation spots applied to each renal artery, with a 0.5 cm gap between adjacent points, and the effective ablation time per point was 60-90 s (impedance reduction >10%). An angiography of the kidney was done following the percutaneous intervention [6,7].

After the procedure, all patients stayed in the hospital for seven days to be observed. On the seventh day, BP and a 6-minute walk distance were recorded. Six months after being discharged, echocardiography, a 6-minute walk test, routine blood work, and monthly blood pressure and 6-minute walk tests were conducted. All patients were given HF medicines, such as beta-blockers, ACEIs, ARBs, and spironolactone, at the highest tolerable dose. According to the patients' blood pressure, heart rate, and other factors during the follow-up period, the medicine dosage was modified [8,9].

Six months after RDN, compared to before RDN, certain modifications in HF medicines were seen. Due to the removal of peripheral edoema and the lack of HF symptoms including chest discomfort and shortness of breath, six patients lowered or stopped using loop diuretics. No patient used loop diuretics more frequently. ARB dose was decreased in six patients and raised in one, while the dosage of beta-blockers was decreased in six patients and increased in one [10]. A number of trials conducted in 2009 and 2010 showed that RDN is probably an efficient therapeutic approach for treating resistant hypertension. 4,5 But regrettably, the more recent HTN-3 trial<sup>8</sup> revealed that RDN had a similar BP-lowering impact to that in the sham group, sparking significant doubt regarding RDN's efficacy. Studies on RDN, particularly those focusing on its effects in HF, have not yet come to an end as a result of this. RDN is viewed as a potential strategy for the treatment of HF because it has the ability to block renal sympathetic nerves, which prevents the activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS) [11].

## Discussion

All fourteen patients in our study had elevated

EF on echocardiography during the follow-up period. Findings from the 6-minute walk test showed significant increases in heart health and endurance following RDN. Due to better control of HF symptoms and symptoms-related indicators, the dosage of loop diuretics was also decreased. According to the study's findings, these HF patients who had bilateral RDN experienced no problems such renal artery dissection or RAS. There were no hypotensive events noted during the six-month follow-up period, and renal function did not alter appreciably. Another investigation into the effects of percutaneous RDN involved the Renal Artery Denervation in Chronic Heart Failure (REACH-Pilot) experiment, which had seven HF patients. According to the trial's findings, RDN increased exercise tolerance and 6-min walk distance, which is in line with the findings of the current investigation. In contrast to the REACH-Pilot study, the current study likewise showed considerable improvements in EF and left ventricular volume on echocardiography. This variance is probably due to different methods and the ablation catheter that was used. In this investigation, a 5F ablation catheter was employed. A 5F catheter makes more contact with blood vessels than a 3.5F Simplicity catheter (Medtronic Inc.), which allows radiofrequency energy to more easily penetrate the artery wall and ablate nerve plexuses [12,13].

Additionally, when a 5F ablation catheter is utilised as opposed to lesser diameters, thermal energy is more likely to build up and result in vascular stenosis. This study includes HF from both hypertension and no hypertensive etiologies. The findings showed that RDN is more effective in improving cardiac function (particularly EF) in individuals with hypertension HF, likely as a result of RDN's ability to lower blood pressure. This suggests that RDN may be most beneficial for HF patients who also have hypertensive heart disease. Numerous research have looked into how RDN and HF are related. Published a study showing that RDN applied prior to MI dramatically lowered ventricular filling pressure and enhanced cardiac function in rats. More recently, verified the dependency of angiotensin receptor expression in a rabbit HF model generated by rapid pacing, on the sympathetic nervous system. They also noticed that renal denervation decreased the expression of the angiotensin II type 1 receptor in renal cortical vessels and the expression of the angiotensin II type 2 receptor in HF rabbits. Similar to this,

found that unilateral RDN in a rabbit model of rapid pacing-induced HF inhibited sympathetic nerve activity, which was advantageous for cardiac sympathovagal balance in HF rabbits. All of these findings are consistent with the notion that RDN might reduce sympathetic and RAAS activation to enhance cardiac function [14].

## Conclusion

It was made plain at the 2016 European Society of Cardiology Congress that despite the HTN-3 study's underwhelming findings, RDN research will continue. Several ongoing investigations confirm the clinical efficacy of RDN in the treatment of heart failure. The current study's findings suggest that RDN utilising a 5F ablation catheter can boost exercise tolerance in HF patients, improve heart function, and lessen HF symptoms and indicators. But in order to verify the findings, a sizable, protracted, randomised controlled trial is required, as the current investigation was merely a clinical observation with a small sample and a brief follow-up time.

## Acknowledgement

None

## Conflict of Interest

None

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