Renal Denervation by Ablation with Innovative Technique in Resistant Hypertension

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Introduction

Hypertension is the cause of thousands of deaths annually[1], and half of the patients treated present controlled blood pressure (BP)[2]. Resistant hypertension (RH)is defined when the BP remains above the recommended targets with the use of three antihypertensive drugs with synergistic actions at maximum doses recommended and tolerated, preferably one being a diuretic, or when in use of four or more anti-hypertensive drugs, even with controlled BP[3]. It is estimated that 12%-15% of persons with hypertension are considered resistant, with high risk of cardiovascular morbidity and mortality[4].

The pathogenesis of hypertension is multifactorial, but the sympathetic activity plays an important role, especially in patients with resistant hypertension[2]. Efferent renal sympathetic activity stimulates renin release, increases sodium reabsorption and reduces renal blood flow and may be a mechanism for the development and maintenance of hypertension[2]. Genetic, behavioral and environmental factors influence increased sympathetic activity in persons with hypertension[5].

New therapies aiming to reduce sympathetic activity have been developed. Renal Sympathetic Denervation (RSD) by radiofrequency catheter ablation of renal arteries has been shown to control BP in resistant hypertension[6,7] and in associated clinical conditions such as sleep destructive apnea[8] and insulin resistance[9].

The main RSD clinical studies used a specific catheter not yet available in Brazil, but the radiofrequency ablation of arrhythmias is a procedure that has been performed by electrophysiologists through appropriate catheters for years in our country. Experimental studies of RSD with catheters used for ablation of arrhythmias indicated the possibility of using these to replace those used in international studies, considering the unavailability of those in our reality. Based on this, for the procedure to be reported, the model used for ablation in children (4 mm tip and 5F), which was proven to be more appropriate, was chosen. The objective of the report is to show the result of the first RSD in our community, with the aid of technology used in cardiac arrhythmias.

Keywords

Denervation; Hypertension; Catheter Ablation; Sympathetic Nervous System.

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Case report

39-year-old woman was admitted to our institution with a history of hypertension since age 17. At age 29, the patient began to experience episodes of hypertensive crisis associated with tachycardia, pallor, sweating and dry mouth, and pheochromocytoma was ruled out. After three years, the patient presented Cerebrovascular Accident (CVA) without neurological sequelae. Since then, it was harder to control hypertension and the patient has to use multiple antihypertensive drugs, while maintaining high levels of BP. In the last year, the patient was hospitalized due to hypertensive crises, reaching BP of 230/130 mmHg. On admission, she was using seven antihypertensive drugs at maximum dose (amlodipine, valsartan, furosemide, spironolactone, clonidine, hydralazine and atenolol). She denied the use of illegal drugs or other medications that would worsen hypertension. Her mother was hypertensive, died at age 40 from CVA, and two brothers were hypertensive.

Physical examination revealed BP 180/110 mmHg (lying position), 182/112 mmHg (standing position) and heart rate 120 bpm. Cardiovascular examination revealed no abnormalities and the remainder of the physical examination was normal. Investigation of secondary hypertension ruled out all probable causes. Doppler echocardiography showed no abnormalities and 24-hour Holter showed no arrhythmias.

As the patient presented hypertension resistant to several medications, the medical staff suggested RSD by ablation and the patient accepted after explanation of risks and benefits. The patient read and signed the Informed Consent Form, since it was the first procedure in Brazil.

The RSD procedure was conducted on August 25, 2011 by the Electrophysiology team. Access to the renal artery was through the femoral artery and anatomy eligible for the procedure was confirmed by angiography after selective catheterization. For renal ablation, a 5F catheter was used (Mariner Series AblationCatheters, Medtronics) and positioned in the aorta, retrograde in the renal artery, guided by radioscopy and connected to a radiofrequency (RF) generator. An electroanatomic map (EnSite System, StJude Medical) of the aorta and the renal arteries was constructed (Figure 1) and four RF applications in each renal artery were planned, distal to proximal, separated longitudinally and in rotation (helical), with markings on the map (white dots in Figure 1). After that, the catheter was introduced into each renal artery and four RF applications were made (8W, 60 °C, 120s) per artery in the regions previously marked (red dots in Figure 1). The patient was under general anesthesia, with BP monitored during the procedure, which occurred without complications. At the end, the patient was awakened from anesthesia reporting mild lower back discomfort that improved after administration of painkiller. A new selective angiography showed no abnormalities.

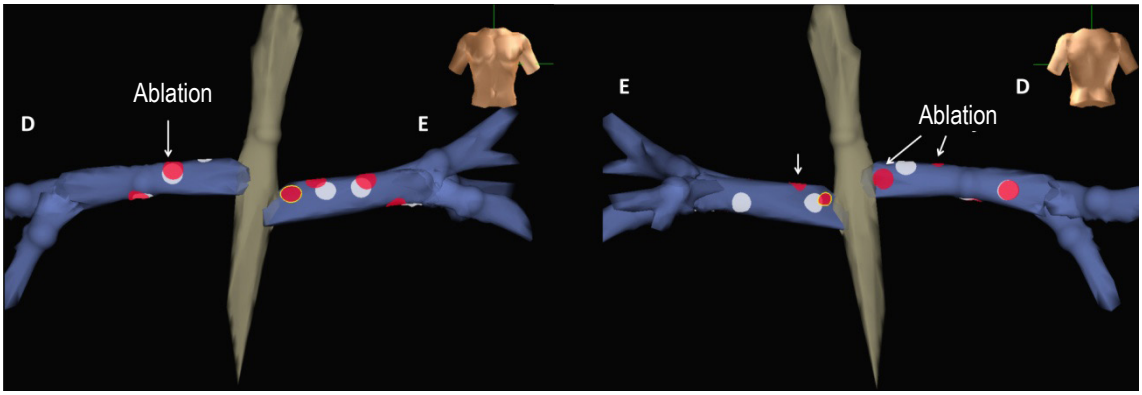

Figure 1 – *Electroanatomic map of the aorta and renal arteries with markings for ablation. The white dots show areas manually marked where application of RF was planned, and the red dots show the areas where RF application was done. On the left, anteroposterior view and on the right, posteroanterior view.*

Table 1 – Office and 24-h ABPM blood pressure, and arterial function parameters before and after renal denervation

Variables	Pre	6 months	1 year
Office BP (mmHg)	180/110	160/100	150/100
Daytime BP (mmHg)	190 / 121	162 / 107	146 / 100
Nighttime BP (mmHg)	170 / 117	120 / 77	111 / 75
Carotid distension (%)	4,65	6,95	-
APWV (m/s)	15,3	13,2	-

APWV: aortic pulse wave velocity; BP: blood pressure.

Six months after the procedure, the patient had lower office and ABPM BP, in use of four classes of antihypertensive drugs (Table 1). After one year, the patient remained little symptomatic, with improved quality of life, without any serious hypertensive crisis. Evolutionary office and ABPM BP data, as well as the arterial properties are shown in Table 1. After six months, angiography of renal arteries showed no stenosis.

Discussion

This is the first experience of RSD held in Brazil with catheter ablation used for arrhythmias in children. The results showed the safety of the procedure, and satisfactory BP control and quality of life results.

The first study using this technique demonstrated safety and significant BP reduction in 58 patients with resistant hypertension[10]. Average reduction in systolic and diastolic BP, respectively, was 22/11 mmHg in six months, and 27/17 mmHg in twelve months.

In 2010, an international multicenter trial studied 106 patients, 52 assigned to intervention and 54 assigned to clinical treatment. After six months, there was a decrease in office BP of 33/11 mmHg in those undergoing the procedure compared to the medical group. Among patients undergoing denervation, 20% reduced antihypertensive drugs and in 84% BP decreased 10 mmHg or more[2]. There were no serious complications related to the procedure.

All studies show high success rate after RSD in patients with resistant hypertension, with significant reduction in BP, decreased dose and/or number of drugs, without causing damage to the renal artery or impaired renal function[1,9,10].

Regarding the case reported, RSD using conventional electrophysiology catheter for ablation in children (5F) is safe and effective. Adding electroanatomic mapping, we can accurately assess renal artery sites where the applications were made, since the strategy used in the denervation procedures is based on the anatomy without immediate functional evaluations.

In the evolution, we observed improvement in 24-h, daytime and especially nighttime BP (Table 1). Increased sympathetic activity is one of the most important mechanisms of the absence of nocturnal blood pressure falls during sleep, which could explain the effect of a significant reduction in nocturnal BP in our patient.

We also assessed arterial properties through measurements of pulse wave velocity and carotid distension. These rates are markers of arterial function, whose changes may be involved in the mechanisms of difficulty in controlling BP. Increased sympathetic activity can increase arterial stiffness in patients with resistant hypertension and improvement of these parameters in the patient after denervation reinforces this interaction.

Ablation RSD is a safe and promising approach in reducing blood pressure, and improves quality of life in patients with resistant hypertension, even with catheters used in cardiac electrophysiology.

Author contributions

Conception and design of the research: Bortolotto LA, Midlej-Brito T, Scanavacca M; Acquisition of data and Analysis and interpretation of the data: Bortolotto LA, Midlej-Brito T, Pisani C, Costa-Hong V, Scanavacca M; Statistical analysis: Bortolotto LA, Midlej-Brito T; Writing of the manuscript and Critical revision of the manuscript for intellectual content: Bortolotto LA, Midlej-Brito T, Pisani C, Scanavacca M.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

References

1. Symplicity HTN-1 Investigators. Catheter-based renal sympathetic denervation for resistant hypertension: durability of blood pressure reduction out to 24 months. Hypertension. 2011;57(5):911-7.
2. Esler MD, Krum H, Sobotka PA, Schlaich MP, Schmieder RE, Böhm M; Symplicity HTN-2 Investigators Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. Lancet. 2010;376(9756):1903-9.
3. de Souza WS, Alessi A, Cordeiro A, da Rocha Nogueira A, Feitosa A, Amodeo C, et al. First Brazilian position on resistant hypertension. Arq Bras Cardiol. 2012;99(1):576-85.
4. Pimenta E, Calhoun DA. Resistant hypertension: incidence, prevalence, and prognosis. Circulation. 2012;125(13):1594-6.
5. Esler M. The sympathetic system and hypertension. Am J Hypertens. 2000;13(6 Pt 2):99S-105S.
6. DiBona GF. The sympathetic nervous system and hypertension: recent developments. Hypertension. 2004;43(2):147-50.
7. DiBona GF, Kopp UC. Neural control of renal function. Physiol Rev. 1997;77(1):75-197.
8. Baguet JP, Barone-Rochette G, Pépin JL. Hypertension and obstructive sleep apnoea syndrome: current perspectives. J Hum Hypertens. 2009;23(7):431-43.
9. Witkowski A, Prejbisz A, Florczak E, Kądziela J, Śliwiński P, Bieleń P, et al. Effects of renal sympathetic denervation on blood pressure, sleep apnea course, and glycemic control in patients with resistant hypertension and sleep apnea. Hypertension. 2011;58(4)559-65.
10. Krum H, Schlaich M, Whitbourn R, Sobotka PA, Sadowski J, Bartus K, et al. Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study. Lancet. 2009;373(9671):1275-81.