

# Effects of Renal Sympathetic Denervation in Renal Artery Diameter Evaluated By Quantitative Angiography

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## ABSTRACT

**Background:** Percutaneous renal sympathetic denervation was developed as an adjunct method to treat clinical conditions associated to sympathetic hyperactivity. Percutaneous renal sympathetic denervation increases the renal blood flow and reduces vasoconstriction. The effects of percutaneous renal sympathetic denervation in renal artery diameter have not been reported. Our objective was to evaluate such effects by quantitative angiography. **Methods:** Prospective, observational, study including consecutive patients undergoing percutaneous renal sympathetic denervation. **Results:** Thirty-one patients were selected, 21 were submitted to percutaneous renal sympathetic denervation to control resistant arterial hypertension and 10 to control refractory ventricular arrhythmias. Seventeen patients did not perform renal arteriography in the follow-up due to clinical contraindications or because they did not complete the 6-month period established by the protocol. In addition, one patient performed a unilateral percutaneous renal sympathetic denervation and was also excluded from this analysis. Therefore, 52 renal angiographies (26 pairs) of 13 patients were analyzed. Mean maximal diameter of the right renal artery before the procedure was  $4.54 \pm 0.21$  mm and increased to  $5.2 \pm 0.44$  mm at 6 months ( $p = 0.01$ ). Likewise, there was a significant increase in the diameter of the left renal artery at 6 months of follow-up, increasing from  $4.37 \pm 0.42$  to  $5.23 \pm 0.77$  mm ( $p = 0.02$ ). **Conclusions:** The results of this analysis illustrate the significant increment in renal artery diameter after percutaneous renal sympathetic denervation. Randomized controlled clinical trials are required to consolidate our observations.

**DESCRIPTORS:** Hypertension. Drug resistance. Renal artery. Sympathectomy. Catheter ablation. Angiography.

## RESUMO

### Efeitos da Denervação Simpática Renal no Diâmetro da Artéria Renal Avaliados Pela Angiografia Quantitativa

**Introdução:** A denervação simpática renal percutânea surgiu como método adjunto no controle de condições clínicas associadas à hiperatividade simpática. Ela resulta em aumento do fluxo sanguíneo renal e em redução da vasoconstrição. Os efeitos da denervação simpática renal percutânea no diâmetro da artéria renal ainda não foram descritos. Nosso objetivo foi avaliar tais efeitos por meio da angiografia quantitativa. **Métodos:** Estudo prospectivo e observacional que incluiu pacientes consecutivos submetidos à denervação simpática renal percutânea. **Resultados:** Selecionamos 31 pacientes, sendo 21 submetidos à denervação simpática renal percutânea para controle da hipertensão arterial resistente e 10 para controle de arritmias ventriculares refratárias. Dezoito pacientes não realizaram arteriografia renal no seguimento por não completarem o período protocolar de 6 meses, ou por contraindicação clínica. Adicionalmente, uma paciente realizou denervação simpática renal percutânea unilateral, sendo também excluída desta análise. Assim, 52 angiografias renais (26 pares) de 13 pacientes foram analisadas. A média do diâmetro máximo da artéria renal direita, antes do procedimento, foi de  $4,54 \pm 0,21$  mm e aumentou para  $5,2 \pm 0,44$  mm aos 6 meses ( $p = 0,01$ ). Da mesma forma, observou-se aumento significativo do diâmetro da artéria renal esquerda aos 6 meses de seguimento, ampliando de  $4,37 \pm 0,42$  para  $5,23 \pm 0,77$  mm ( $p = 0,02$ ). **Conclusões:** Os resultados desta análise ilustram o incremento significativo dos diâmetros das artérias renais após denervação simpática renal percutânea. Ensaios clínicos randomizados e controlados são necessários para consolidar nossas observações.

**DESCRIPTORIOS:** Hipertensão. Resistência a medicamentos. Artéria renal. Simpatectomia. Ablação por cateter. Angiografia.

Approximately one billion people suffer from systemic arterial hypertension (SAH) worldwide.<sup>1</sup> It is well established that an increase in blood pressure is associated with an increased risk of cardiovascular disease. Conversely, small reductions in blood pressure (BP) substantially decrease the rates of stroke, coronary artery disease, and heart failure, also denoting a reduction in the number of hospitalizations, their related costs, and deaths, as well as an improvement in quality of life in patients with SAH.<sup>2,3</sup>

Based on the knowledge of the importance of hyperactivity of the sympathetic autonomic nervous system in the pathophysiology of SAH, percutaneous renal sympathetic denervation (RSD) has emerged as an adjunctive therapeutic strategy in selected groups of refractory hypertensive patients.<sup>4</sup> Benefits have also been observed with this method in other clinical contexts associated with chronic hyperactivity of the sympathetic nervous system (SNS), such as cardiac arrhythmias,<sup>5</sup> obstructive sleep apnea syndrome,<sup>6</sup> heart failure,<sup>7</sup> and metabolic syndrome.<sup>8</sup>

Despite the promising initial results of percutaneous RSD related to SAH, discrepancies have been observed among studies, in large part reflecting the variation in the technique used, the learning curve, the type of device used, and, especially, the different populations studied, with a wide variation of the importance of the sympathetic system in the genesis of SAH.

Sympathetic activity in the context of percutaneous RSD is measured by microneurography and by norepinephrine spillover.<sup>9</sup> However, although available, these procedures are not adopted routinely in clinical practice, due to limitations in their execution.

Chronic SNS stimulation progresses with an increase in plasma neurohormones, which in turn results in vascular (vasoconstriction, increased thickness, and reduced vascular compliance) and heart (development of myocardial hypertrophy, ischemia, arrhythmias, and heart failure) effects. In kidneys, an increased sympathetic activity leads to the activation of the renin-angiotensin-aldosterone system, increased reabsorption of sodium and water, reduction of renal blood flow and glomerular filtration rate, ischemia, and renal failure.<sup>10</sup>

Percutaneous RSD aims to reduce sympathetic activity. As a consequence, there is an increase in renal blood flow<sup>9</sup> and arterial vasodilation.<sup>10</sup> In this study; the aim was to evaluate the effects of percutaneous RSD on the diameter of the renal arteries, through the use of quantitative angiography.

## METHODS

### Selection of patients

Thirty-one consecutive patients undergoing percutaneous RSD at the Instituto Dante Pazzanese de

Cardiologia were selected. The indication for the procedure was for control of refractory hypertension in 21 of these patients and for control of refractory ventricular arrhythmias in the other ten.

### Procedure

In 26 patients, an open-irrigated tip catheter (ThermoCool® or Therapy Cool Path®) was used and, in five, the dedicated system EnligHTN® (St. Jude Medical Inc®, Westford, United States).

Four to six radiofrequency applications were performed in each renal artery with the irrigated catheter, starting at the most distal portion of the vessel, close to the bifurcation, toward the aorta, respecting the minimum distance of 5 mm between each application and the helical arrangement of them. The detailed technique for a percutaneous RSD with an irrigated catheter has been described previously elsewhere by our group.<sup>11</sup> Figure 1 shows a case in which six radiofrequency applications were conducted in the right renal artery.

EnligHTN® is a dedicated system for percutaneous RSD, designed with the aim of generating better-distributed renal artery lesions, and, therefore, four radiofrequency applications are performed with a minimal manipulation of the catheter. The device consists of a catheter with a basket at its distal end, which has four electrodes that sequentially emit the radiofrequency. Initially, the device was placed distally in the renal artery, wherein a first section of application was performed. After this step, the device was collapsed and retracted by about 1 cm, for a new application – a total of eight applications per treated renal artery were performed. The technique outlined for percutaneous RSD with the EnligHTN® dedicated system has been described previously elsewhere by the present group.<sup>12</sup>

### Quantitative angiography

Of those 31 patients selected, 17 did not undergo renal arteriography under the protocol during follow-up, or because they did not complete the six-month period, or due to clinical contraindication. Fourteen patients underwent angiography 6 months after percutaneous RSD, which allowed for the comparison of this examination versus the initial examination performed before the ablation. One case was excluded from this analysis, because the patient was submitted to ablation of only one renal artery. Thus, 52 renal arteriographies (26 pairs) from 13 patients were analyzed by quantitative angiography.

The quantitative renal angiography was interpreted with the help of QAngio XA software, version 7.3 (Medis Medical Imaging Systems BV, Leiden, The Netherlands). The maximum diameters of each renal artery were measured at three points: proximal, middle and distal thirds. The mean measure was calculated automatically by the program (Figure 2).

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