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ORIGINAL ARTICLE

Angio-computed tomography reveals differences in the anatomy of renal arteries in resistant hypertension patients qualified for renal denervation versus pseudo-resistant hypertensive subjects

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Abstract

Background: *Renal denervation is a novel therapeutic option in resistant hypertension (RHT). The anatomy of renal arteries and the presence of additional renal arteries are important determinants of the effect of the procedure. The aim of this study was to assess the anatomy of renal arteries using angio-computed tomography in patients with RHT, who were qualified for renal denervation.*

Methods: *We analyzed angio-computed tomography scans of the renal arteries of 72 patients qualified for renal denervation. We divided the study population into two groups: a resistant hypertension group (RHT) and a pseudo-resistant hypertension group (NRHT). The biochemical and endocrine diagnostic procedures were performed to rule out secondary hypertension. We analyzed the morphology, the diameters, and the number of additional renal arteries.*

Results: *In both groups, we found additional renal arteries (ARN). ARN were more frequent in RHT than in patients with non-resistant hypertension (48.4% vs. 24.3%; $p < 0.05$). They were present more often on the left side (18 left side vs. 7 right side). The ARNs were longer than main renal artery — left side 41.7 ± 12.1 mm vs. 51.1 ± 11.8 mm, right side 49.2 ± 14.5 mm vs. 60 ± ± 8.6 mm, respectively ($p < 0.05$). The diameters of ARN were similar in both groups. In the group of patients with RHT the number of ARN was significantly higher ($p < 0.04$).*

Conclusions: *The ARNs occur more often in patients with RHT. It seems that there is no connection between the resistance of hypertension and the diameters of renal arteries.* (Cardiol J 2023; 30, 3: 379–384)

Key words: renal denervation, renal artery anatomy, resistant hypertension

Introduction

Resistant hypertension (RHT) is defined as an in-office blood pressure (BP) of at least 140 mmHg systolic (SBP) and/or 90 mmHg diastolic (DBP) in patients on maximal doses of three or more antihypertensive medications, including a diuretic [1]. Several studies estimate that RHT occurs in 10–15% of patients with hypertension [2–4]. The definition excludes secondary hypertension, white-coat hypertension, and other causes of uncontrolled BP, such as poor adherence or non-optimal medi-

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cation regimen and dosing. The latter situation is referred to as pseudo-resistant hypertension.

There are few data on the pathogenesis and causes of true-resistant hypertension. A possible explanation is that renal artery anatomy and/or function differ between patients with RHT and healthy individuals [5, 6]. One novel approach to the treatment of RHT is renal artery denervation (RDN). Although the safety of this technique has been demonstrated in several trials, its effectiveness is still being evaluated [7–10]. The anatomy of renal artery is crucial for the effect of the procedure.

Renal arteries arise from the abdominal aorta at the level of the L1/L2 vertebra. The right renal artery is usually longer than the left due to the position of the aorta, inferior vena cava, and right kidney. At the level of the renal hilum, renal arteries usually divide into five segmental arteries that supply independent renal segments. To qualify for RDN, patients must undergo an angiogram or angio-computed tomography (CT) of the renal arteries to assess their diameters and exclude abnormalities.

Studies suggest that several factors impact the efficacy of RDN [5, 6, 11]. After the unsatisfying results of the SYMPLICITY HTN-3 trial, even more effort was put into identifying the perfect candidates for RDN, who would gain the most from the procedure. The aim of this study was to assess renal artery anatomy using angio-CT in patients with RHT, who qualified for RDN.

Methods

This was a single-center study to assess the anatomy of renal arteries in patients initially diagnosed with RHT, who were referred for RDN. The group of 72 patients initially screened for eligibility for renal denervation, after exclusion of secondary hypertension and optimization of pharmacological treatment (including supervised drug administration), was dived into two groups:

- True-resistant hypertension group (RHT; n = 31) — resistant hypertension (defined as SBP > 140 mmHg and/or DBP > 90 mmHg despite three or more antihypertensive medications, including a diuretic, at a maximum tolerable dose);
- Non-resistant hypertension (pseudo-resistant hypertension; NRHT; n = 41) — patients in whom improving adherence or pharmacotherapy adjustment (dose increase and/or adding another antihypertensive agent) normalized the BP values.

Blood pressure measurements were obtained by taking the average of three office-based measurements and 24-hour ambulatory BP monitoring. Biochemical and endocrine diagnostic procedures were performed to rule out secondary hypertension. In all patients the following conditions were excluded: renal artery stenosis, Cushing disease, pheochromocytoma, primary hyperaldosteronism, hyperthyroidism, and coarctation of the aorta. Transthoracic echocardiography was performed using a Vivid E9 ultrasound system equipped with an M5S-D transducer (GE Healthcare).

Computed tomography scans were taken using a 64-row multi-slice CT scanner (Toshiba). CT data were analyzed on a Vitrea post-processing workstation (Vital Images) using two- and three--dimensional viewing modes and evaluated by two observers who reached a consensus.

The main renal artery was defined as the largest artery arising from the aorta to the kidney; other arteries were defined as additional renal arteries. We counted the number of additional renal arteries and measured the length, area of the ostium, diameter of the ostium (in anterior-posterior and superior-inferior axes), area of branching, and diameter of branching (in anterior-posterior axis and superior-inferior axis) of the main and additional renal arteries. Statistical analysis was performed using STATISTICA software. Values were expressed as mean (standard deviation) in the case of normal distribution or median (Q1;Q3) in the case of non-normal distribution. To compare quantitative variables the t-test (normal distribution) and U-Mann-Whitney test (non-normal distribution) were used.

Within the group with confirmed RHT, 15 patients who fulfilled the criteria and had no additional renal arteries underwent RDN using the Simplicity (Medtronic, USA) system. Clinical inclusion criteria for RND were as follows: age of 18+ years, uncontrollable treatment-resistant hypertension (defined as SBP > 160 mmHg despite three or more antihypertensive medications, including a diuretic, at a maximum tolerable dose, or ≥ 150 mmHg in patients with type 2 diabetes), main renal arteries with diameter > 4 mm, and trunk length of the main artery > 20 mm. The results of long-term follow-up were previously published [12].

The study was approved by the Ethics Committee and conformed to the Declaration of Helsinki. Informed written consent was obtained from all patients enrolled in the study.

Table 1. Baseline characteristics of the study groups.

Characteristics	Resistant hypertension (n = 31)	Non-resistant hypertension (n = 41)
Age (years ± SD)	66 ± 8.5	62 ± 12
Male	15 (48.3%)	21 (51.2%)
Body mass index [kg/m^2]	30.9 ± 4.1	29.8 ± 3.5
Medical history		
Type 2 diabetes	10 (32.3%)	14 (34.1%)
Left ventricular ejection fraction [%]	60.3 ± 5.5	60.7 ± 4.3
Family history of hypertension	22 (70.9%)	26 (63.4%)
No. of antihypertensive medication	5.03 ± 0.8	4.3 ± 0.6
Mean office systolic/diastolic BP [mmHg]	202 ± 31.5/107 ± 14.2	180.8 ± 19.9/104 ± 13.9
Mean 24 hours ambulatory systolic/diastolic BP [mmHg]	150.8 ± 12.9/87.2 ± 12.8	148.8 ± 10.7/85.8 ± 10.3

BP — blood pressure; SD — standard deviation

Results

Baseline characteristics of studied groups are presented in Table 1. Patients did not differ with regard to age, sex distribution, body mass index, and medical history of hypertension and diabetes. Mean office SBP values were non-significantly lower in the non-resistant group (202 ± 31.5 vs. 180.8 ± 19.9; p = NS); mean office DBP and ambulatory BP monitoring values were similar. The number of used antihypertensive drugs was higher in true RHT, but NRHT patients declared on average 4.3 medications.

The diameters of the main and additional renal arteries did not differ significantly between groups (Table 2). The right main renal artery was significantly longer than the left main renal artery in both groups (48.1 vs. 40.3 mm and 50.3 vs. 42.7 mm, respectively; $p < 0.05$).

Additional renal arteries (Figs. 1A–C) were observed more frequently in patients with RHT (15 patients, 48.4%) than in patients with NRHT (10 patients, 24.3%; $p < 0.05$). Moreover, patients with RHT had more additional renal arteries than patients with NRHT ($p < 0.04$). Additional renal arteries were present more often on the left side than on the right side (18 vs. 7 arteries, respectively; $p < 0.05$), were longer than main renal arteries (left side: 51.1 ± 11.8 vs. 41.7 ± 12.1 mm and right side: 59.9 ± 8.6 vs. 49.2 ± 14.5 mm, respectively; $p < 0.05$), and had smaller branching and ostium areas (Table 3).

We assessed the eligibility of all study patients for RDN using the SYMPLICITY and SPYRAL systems. The SYMPLICITY system requires that the main renal arteries be > 20 mm in length and > 4 mm in diameter; in our study, 52 (72%) patients had this anatomy. The SPYRAL system requires that the main renal arteries be > 20 mm in length and > 3 mm in diameter; in our study, 62 (86%) patients had this anatomy.

We also analyzed the relationship between the main renal artery anatomy and the outcome of RDN — data published previously [12]. We found no correlations between the anatomy or diameters of the main renal arteries and the efficacy of RDN at 24-month follow-up.

Discussion

Awareness of renal artery anatomy before RDN is crucial for the safety and success of the procedure. Von Achen et al. [13] reported that the anatomy of renal arteries impacts the outcomes of RDN. In the present study, the dimensions of the main renal arteries were similar between patients with and without resistant hypertension. However, additional renal arteries were longer and had smaller diameters than the main renal arteries, consistent with an earlier report [14].

In our population, we found that additional renal arteries were more common in patients with RHT than in patients with NRHT, which is similar to the result of a previous study [11]. Lauder et al. [14] showed that renal artery anatomy differs between hypertensive and normotensive subjects (accessory renal arteries in 22% vs. 9%, respectively) but does not differ between patients with poor and good BP control. Also, VonAchen et al. [13] reported that the presence of additional renal arter-

Table 2. The diameters of main and additional renal arteries in resistant and non-resistant hypertension subjects.

Characteristics	Resistant hypertension (n = 31)	Non-resistant hypertension (n = 41)	P
Right renal artery [mm]			
Length — mean (SD)	48.1 (15.2)	50.3 (14.1)	NS
Area of the ostium — median (Q1;Q3)	30.9 (22.6;42.3)	33.2 (28.3;39.8)	NS
AP ostium — median (Q1;Q3)	6.4 (5.2;7.9)	6.9 (5.7;7.8)	NS
SI ostium — median (Q1;Q3)	5.2 (4.6;7.0)	5.5 (4.6;6.9)	NS
Branching area — median (Q1;Q3)	22.7 (19.6;29.3)	26.2 (18.7;34.9)	NS
AP branching — mean (SD)	5.38 (1.46)	5.56 (1.53)	NS
SI branching — mean (SD)	4.85 (1.42)	5.07 (1.36)	NS
Left renal artery [mm]			
Length — mean (SD)	40.3 ± 10.7	42.7 ± 13.1	NS
Area of the ostium — median (Q1;Q3)	30.3 (24.7;47)	34.9 (27.8;48)	NS
AP ostium — mean (SD)	6.5 (1.8)	6.7 (2)	NS
SI ostium — mean (SD)	5.82 (2.1)	6.2 (1.9)	NS
Branching area — median (Q1;Q3)	22.4 (18.8;25.1)	24.1 (17.5;31.2)	NS
AP branching — mean (SD)	5.2 (1.1)	5.25 (1.4)	NS
SI branching –– median (Q1;Q3)	4.6 (4;5.4)	4.8 (4;6.3)	NS
Right additional renal arteries [mm] — mean (SD)	**N = 4**	**N = 3**	
Length	59.55 (10.6)	60.1 (9.1)	NS
Area of the ostium	11.8 (1.9)	13.2 (3.7)	NS
AP ostium	3.35 (1)	3.6 (1)	NS
SI ostium	2.85 (0.5)	3.3 (0.5)	NS
Branching area	9.9 (0.2)	11 (4.3)	NS
AP branching	3 (0.6)	2.9 (0.9)	NS
SI branching	2.6 (0.3)	3 (0.4)	NS
Left additional renal arteries [mm] — mean (SD)	**N = 11**	**N = 7**	
Length	52.9 (12.9)	49.9 (11.6)	NS
Area of the ostium	11.6 (3.2)	15.3 (6.03)	NS
AP ostium	4.1 (0.64)	4.4 (2.2)	NS
SI ostium	3 (0.58)	3.5 (1.7)	NS
Branching area	12.8 (4.3)	12.45 (2.5)	NS
AP branching	3.9 (0.8)	3.7 (0.9)	NS
SI branching	3.4 (1.1)	3 (0.78)	NS

AP — anterior posterior dimension; SI — superior inferior dimension; SD — standard deviation

ies is twice as common in patients with RHT than in healthy individuals. In our observation, additional renal arteries were more frequent in the RHT group than in patients with NRHT. Considering that the accessory renal arteries are a potential cause of renovascular hypertension [15], identifying them reveals a potential cause, while proper anatomy assessment makes it a therapeutic target at least in a fraction of patients with RHT.

These additional renal arteries had obviously different anatomy and diameters compared to those of main renal arteries, and not all additional renal arteries were eligible for RDN. Our findings also suggest that the SPYRAL system for RDN may be suitable for a larger number of patients due to the smaller dimensions of the catheter.

The ablation of additional renal arteries has been suggested to increase the efficacy of RDN [6].

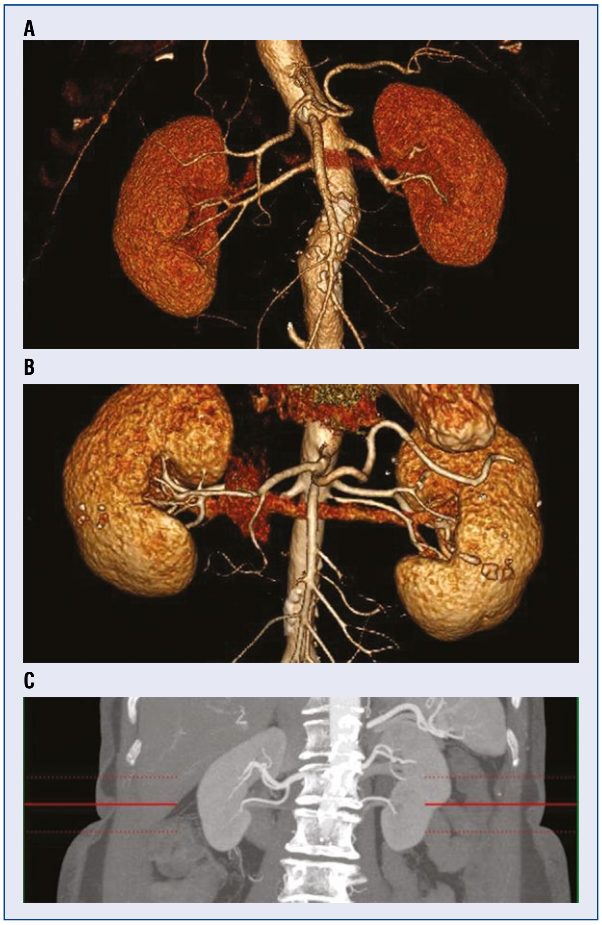

Figure 1. A–C. Additional renal arteries in patients from our study group.

However, denervation of additional renal arteries is not always possible due to their small diameter. Therefore, further development of catheters may enable the targeting of almost all accessory renal arteries in the future [16, 17].

In contrast to our study and the above-cited reports, Lauder et al. [14] do not report a significant difference between in the frequency and the number of additional renal arteries in RHT. This may be caused by several factors, one of which being the modality. Commonly used renal artery angiography is more likely to miss small additional renal arteries with non-typical ostium location than angio-CT. Our report is the first to present the use of angio-CT for renal artery assessment in a highly selective group of true-resistant vs. pseudo-resistant hypertension.

Our results suggest that the efficacy of RDN could be improved by treating patients with favorable renal artery anatomy, and attempting to denervate all renal arteries, including additional arteries.

Limitations of the study

The major limitation of the study is a low number of analyzed cases and a lack of healthy (non-hypertensive) control subjects for comparison of the results. However, the number of RHT (and pseudo-RHT) patients qualified for RDN and is low, even in high reference centers.

Table 3. Comparison of the diameters of main and additional renal arteries.

Characteristics	Main renal arteries	Additional renal arteries	P
Right side [mm] — mean (SD)			
Length	49.2 (14.5)	59.9 (8.64)	0.057
Area of the ostium	34.77 (12.82)	12.8 (3.23)	**< 0.001**
AP ostium	6.63 (1.77)	3.53 (0.95)	**< 0.001**
SI ostium	5.75 (1.86)	3.18 (0.53)	**< 0.001**
Branching area	25.9 (10.23)	10.7 (3.52)	**< 0.001**
AP branching	5.48 (1.49)	2.92 (0.83)	**< 0.001**
SI branching	4.98 (1.38)	2.89 (0.44)	**< 0.001**
Left side [mm] — mean (SD)			
Length	41.68 (12.1)	51.05 (11.8)	**0.004**
Area of the ostium	37.1 (14.59)	13.87 (5.34)	**< 0.001**
AP ostium	6.62 (1.92)	4.3 (1.76)	**< 0.001**
SI ostium	6.01 (2.03)	3.34 (1.39)	**< 0.001**
Branching area	24.88 (9.93)	12.59 (3.22)	**< 0.001**
AP branching	5.25 (1.3)	3.79 (0.89)	**< 0.001**
SI branching	4.93 (1.52)	3.19 (0.92)	**< 0.001**

AP — anterior posterior dimension; SI — superior inferior dimension; SD — standard deviation

Conclusions

Additional renal arteries occur more often in patients with resistant hypertension. The additional renal arteries have different anatomy and diameters in comparison to the main renal arteries.

Conflict of interest: None declared

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