Renal resistive index in patients with true resistant hypertension: results from the RESIST-POL study

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A b s t r a c t

Background: Increased ultrasound Doppler renal resistive index (RRI) is a marker of atherosclerotic and hypertensive organ damage both at renal and systemic level.

Aim: To evaluate RRI in patients with true resistant hypertension (TRHT) in the RESIST-POL study.

Methods: From 204 patients diagnosed with TRHT in the RESIST-POL study, 151 patients (90 male, 61 female, mean age: 47.7 ± 10.4, range: 19–65 years) without secondary hypertension were included into the analysis. All patients were characterised by estimated glomerular filtration rate > 60 mL/min/1.73 m² and no history of diabetes prior to the study. As a control group we included 50 age- and gender-matched patients (35 male, 15 female, mean age: 46.8 ± 10.4, range: 19–65 years) with primary well-controlled hypertension. The groups also did not differ in respect to the number of years of known history of hypertension. The RRIs were evaluated on the basis of the Doppler ultrasound examination. Increased RRI was defined as ≥ 0.7.

Results: Both groups did not differ in terms of renal function. Patients with TRHT were characterised by higher RRI as compared with the group with well-controlled hypertension (0.62 ± 0.05 vs. 0.60 ± 0.05, p < 0.05). In the TRHT group RRI correlated significantly with age, clinic and ambulatory blood pressure measurement, diastolic blood pressure (DBP) levels, as well as with clinic pulse pressure (PP) (r = 0.297; p = 0.001), with daytime (r = 0.355; p < 0.001) and nighttime (r = 0.313; p < 0.001) PP, and with fasting glucose concentration (r = 0.215; p = 0.008) and E/E′ ratio (r = 0.289; p = 0.001) on echocardiography. RRI values were significantly higher in TRHT patients with newly diagnosed diabetes as compared with TRHT patients without diabetes (0.65 ± 0.05 vs. 0.62 ± 0.05, p = 0.022). Age, daytime DBP, daytime PP, and E/E′ ratio but not fasting glucose concentration correlated independently with RRI in the model. Among patients with TRHT, patients with increased RRI were characterised by older age (52.2 ± 4.9 vs. 47.3 ± 10.6 years, p = 0.012), higher body mass index (32.8 ± 6.0 vs. 29.7 ± 4.5 kg/m², p = 0.034), as well as lower daytime and nighttime DBP values and lower daytime and nighttime heart rate, as compared to patients with RRI < 0.7. The TRHT patients with increased RRI as compared to patients with RRI < 0.7 were characterised also by higher daytime and nighttime PP. Both groups did not differ in respect of renal function.

Conclusions: Our study showed that the patients with TRHT were characterised by significantly higher RRI values as compared to the subjects with well-controlled hypertension. It may also be suggested that in the subjects with TRHT renal vascular resistance is related to blood pressure values, selected echocardiographic abnormalities, and some surrogate markers for metabolic and cardiovascular events, including fasting glucose plasma concentration and PP, respectively.

Key words: resistant hypertension, resistive index, target organ damage, diabetes mellitus, pulse pressure

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INTRODUCTION

The Doppler-derived renal resistive index (RRI) has been used in a variety of clinical settings including the detection and management of renal artery stenosis or evaluation of progression risk in chronic kidney disease. More recently, evidence has been accumulated showing that an increased RRI not only reflects changes in intra-renal perfusion but also is related to systemic haemodynamics and the presence of subclinical atherosclerosis [1–4].

On the basis of these results, the evaluation of RRI has been proposed in the assessment and management of patients with primary hypertension (HT) to complement other signs of renal abnormalities. Increased RRI indicates the presence of hypertensive and atherosclerotic organ damage such as left ventricular hypertrophy (LVH) and carotid intima-media thickening and may therefore be taken as an indicator of increased cardiovascular risk profile [5–11].

Renal resistive index proved also to be an independent predictor of worse cardiovascular and renal outcomes, especially when combined with reduced estimated glomerular filtration rate (eGFR). Furthermore, an increased RRI has been demonstrated to predict the onset of diabetes mellitus in patients with primary HT [8, 10, 12, 13].

It should be noted that the indices of renal perfusion have not been extensively studied in patients with resistant hypertension (RHT). A recent study indicates that in patients with therapy-resistant hypertension RRI reflects functional and structural vascular parameters, and measurement of RRI in addition to low-grade albuminuria complements screening for target organ damage in RHT [10].

Therefore, the aim of our study was to evaluate RRI values in patients with true RHT in relation to ambulatory blood pressure measurement (ABPM) values, biochemical parameters, and echocardiographic parameters depicting early target organ damage. We also compared RRI values of patients with true RHT with age-matched patients with well-controlled HT.

METHODS
Study population

Evaluated patients were enrolled in the RESIST-POL study. The inclusion criteria were as follows: age 20–65 years, RHT confirmed on ABPM — mean daytime blood pressure (BP) > 135/85 mm Hg while on three antihypertensive drugs in optimal doses (including diuretic) — meeting the definition of true RHT. The exclusion criteria were: a history of other cardiovascular diseases (ischaemic heart disease, heart failure, transient ischaemic attacks, and previous stroke), decreased eGFR< 60 mL/min/1.73 m^2, neoplastic diseases, previous diagnosis of diabetes mellitus, alcohol or medicine addictions, advanced changes in the skeletal system, malignant HT, pregnancy, and lack of cooperation or agreement to participation in the study. The study protocol conforms to the ethical guide-

lines of the 1975 Declaration of Helsinki and was approved by the local Research Ethics Committee. Written informed consent was also obtained from each patient [14–18].

Since the principle goal of our present study was to evaluate the RRI in patients with RHT with regard to selected clinical parameters, we decided to exclude cases with secondary causes of HT characterised by other underlying mechanisms that could independently influence the RRI pattern. Therefore, from the original group of 204 patients with RHT we excluded 49 patients with secondary HT and five patients in whom renal arteries Doppler evaluation was not suitable for further analysis.

The full protocol and main results of the RESIST-POL study have already been published [16]. In brief, patients with true RHT were screened for coexisting conditions including metabolic abnormalities and obstructive sleep apnoea, secondary causes of HT, as well as being evaluated for target organ damage. As the methodology of the RESIST-POL study has been described extensively previously, we summarise below the definitions and methods used for the purpose of this analysis [16].

As a control group we included in our study 50 patients with well-controlled essential HT, being matched for age and gender. As criteria of BP control we assumed daytime ABPM levels below 135 mm Hg and 85 mm Hg for systolic and diastolic BP, respectively [19].

Office BP measurements

Blood pressure was measured by a trained nurse, with the patient in a sitting position after a 5-min rest, using an automated device (Omron 705IT, Omron Co., Kyoto, Japan). Based on the upper arm circumference an appropriately sized cuff was placed on the arm with the lower edge of the cuff 2 cm above the antecubital fossa. Three consecutive readings were performed. In cases where the difference between readings was higher than 10 mm Hg, further measurements were taken to obtain three consecutive consistent readings, the average of which was then recorded.

Ambulatory blood pressure monitoring

In all patients the ABPM was recorded using SpaceLabs 90207 or 90217 (Redmond, Washington, USA). Readings were obtained every 15 min during the day (06:00–22:00) and every 30 min during the night (22:00–06:00). Average 24-h daytime and nighttime systolic BP, 24-h daytime and nighttime diastolic BP, and average 24-h heart rate (HR) were analysed. Nocturnal decrease in BP was quantified as the relative decrease in nocturnal BP for both systolic and diastolic BP: [(daytime pressure – night-time pressure)/daytime pressure] × 100 and expressed as a percentage. Subjects were classified as dippers if the proportional decrease from waking to sleeping BP was ≥ 10%.

Laboratory methods

Biochemical evaluation of blood samples taken after overnight fasting were determined by routine methods, and included sodium and potassium, lipids, blood count, fasting plasma glucose (FPG), creatinine, and uric acid. eGFR was calculated using the Modification of Diet in Renal Disease formula [20]. Albuminuria was assessed using a 24-h urine collection. Microalbuminuria was defined as 24-h albumin excretion > 30 mg. Glucose and lipid metabolism abnormalities were diagnosed on the basis of the 2007 European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines [19]. For diagnosis of metabolic syndrome, three of five criteria had to be met: (1) BP ≥ 130 mm Hg/≥ 85 mm Hg — this criterion was met for all patients; (2) abdominal obesity — waist circumference, male > 102 cm, female > 88 cm; (3) high density lipoprotein cholesterol, male < 1.0 mmol/L, female < 1.2 mmol/L; (4) triglycerides > 1.7 mmol/L; and (5) FPG ≥ 5.6 mmol/L [19].

Renal ultrasound and Doppler studies

Ultrasonography examination and duplex Doppler imaging were performed with a Philips HD11 scanner with 2–4 MHz phased-array transducer. Patients were scanned in the supine position while in the fasting state. The intrarenal arteries were visualised in the colour duplex mode. Doppler ultrasonography spectral analysis included mean RRI and pulsatility index (PI). RRI was calculated as the difference between the peak systolic and end-diastolic blood velocities divided by the peak systolic velocity. PI was calculated as follows: peak systolic velocity – end diastolic velocity / mean velocity. RRI and PI were obtained from three Doppler curves at different sites of the each kidney. For calculations, the software of the duplex scanner was used. Measurements were made by two experienced investigators blinded to the clinical status of the patients. Interobserver and intraobserver coefficients of variance of RRI were 5.6% and 4.7%, respectively (n = 12) [21].

Echocardiography

All patients underwent a complete transthoracic echocardiographic study with a GE Medical System Vivid 7 (GE Healthcare) with a 2.5 MHz transducer. M-mode, two-dimensional, tissue Doppler echocardiography was used. The values of all echocardiographic parameters were obtained as the average of three consecutive cardiac cycles. The left ventricular (LV) mass (LVM) was calculated using the modified American Society of Echocardiography cube formula proposed by Devereux. Left ventricular mass index (LVMI) was obtained by normalising LVM to body surface area (BSA). LVH was defined as a LVMI ≥ 110 g/m^2 for women and ≥ 125 g/m^2 for men [19]. LV systolic function was evaluated by LV ejection fraction (LVEF) using biplane Simpson formula. LV diastolic function was evaluated by mitral inflow values and tissue Doppler imaging (TDI) velocities. Mitral inflow velocities were measured from the apical four-chamber view, with the sample volume placed at the mitral valve leaflet tips. The transmitral early diastolic (E-wave) and atrial (A-wave) velocities were measured and the E/A ratio was calculated. TDI examination was performed from the apical four-chamber view with the sample volume placed along the myocardial lateral wall 1 cm above the mitral annulus. Furthermore, the early diastolic velocity (E') was measured and the E/E' ratio was calculated [14, 15].

Statistical methods

Data analysis was carried out using statistical software PASW Statistics 18 (SPSS Inc., Chicago, IL, USA). The results are presented as mean ± one standard deviation, or median and interquartile range. The values of variables between groups were compared — continuous and discrete variables: Student's t test or Mann-Whitney test; categorical variables: χ^2 test or Fisher exact test. Parameters identified as statistically significant based on univariate analysis (p < 0.05) were included in the multivariate linear regression model in order to determine the combined effect of several variables on the renal resistive index. P < 0.05 was considered statistically significant.

RESULTS

The clinical characteristics of subjects with RHT and controlled HT are shown in Table 1. Patients with RHT, as compared with patients with controlled HT, were characterised by higher body mass index (BMI), higher frequency of abdominal obesity, higher BP levels in clinic measurements and ABPM, as well as higher FPG, low-density lipoprotein cholesterol levels, and number of antihypertensive drugs. There were no differences in age, gender distribution, known duration of HT, creatinine serum concentration, and eGFR between the groups (Table 1). In 16 (10.6%) patients with true RHT diabetes mellitus was diagnosed. Diabetes mellitus was not found in any of the patients with controlled HT. A comparison of echocardiographic parameters between RHT patients and the well-controlled group is shown in Table 2. Patients with RHT as compared with controls were characterised by significantly higher LVMI and E' velocity.

Renal resistive index values were significantly higher in RHT patients than in patients with controlled HT (0.62 ± 0.05 vs. 0.60 ± 0.05, p = 0.042) (Fig. 1). There was no difference in PI between the groups. When subjects were divided according to gender, men with true RHT were characterised by significantly higher RRI and PI as compared with men with controlled HT (0.62 ± 0.05 vs. 0.59 ± 0.03, p = 0.001 and 1.1 ± 0.2 vs. 1.0 ± 0.1, p = 0.001, respectively, for RRI and PI). No differences in RRI and PI values were found between women with true RHT and controlled HT.

In the RHT group RRI correlated significantly with age (r = 0.224, p = 0.006), clinic diastolic BP (r = –0.291, p = 0.001), daytime (r = –0.335, p < 0.001) and nighttime

Table 1. Clinical characteristics of patients with resistant hypertension (RHT) and control-group patients with well controlled hypertension (HT)

Characteristics	RHT	Controlled HT	P
N	151	50	
Males [%]	59.6	70.0	0.19
Age [years]	47.7 ± 10.4	46.8 ± 10.4	0.59
Clinic systolic BP [mm Hg]	159 ± 22	139 ± 22	< 0.001
Clinic diastolic BP [mm Hg]	96 ± 15	90 ± 14	0.051
Clinic PP [mm Hg]	63 ± 14	48 ± 15	< 0.001
Daytime systolic BP [mm Hg]	143 ± 18	130 ± 14	< 0.001
Daytime diastolic BP [mm Hg]	90 ± 13	82 ± 10	0.005
Daytime PP [mm Hg]	54 ± 11	48 ± 9	0.006
Daytime HR [bpm]	72 ± 11	70 ± 9	0.32
Nocturnal systolic BP [mm Hg]	129 ± 18	117 ± 13	< 0.001
Nocturnal diastolic BP [mm Hg]	78 ± 12	71 ± 8	< 0.001
Nocturnal PP [mmHg]	51 ± 11	47 ± 10	0.048
Nighttime HR [bpm]	66 ± 11	61 ± 7	0.020
Known history of hypertension [years]	10.7 ± 8.4	9.1 ± 6.7	0.26
Body mass index [kg/m^2]	29.9 ± 4.7	27.8 ± 3.2	0.001
Abdominal obesity	72.2%	29.6%	< 0.001
Metabolic syndrome	63.6%	34.8%	< 0.001
Smoking [%]	17.9	18	0.55
Sodium [mmol/L]	142 ± 3	140 ± 3	0.005
Potassium [mmol/L]	4.4 ± 0.4	4.3 ± 0.5	0.61
Fasting glucose [mmol/L]	5.8 ± 0.9	5.4 ± 1.0	0.042
Creatinine [μmol/L]	79 ± 18	81 ± 16	0.39
GFR [mL/min/1.73 m^2]	92.2 ± 16.1	93.9 ± 18.8	0.54
Uric acid [μmol/L]	354 ± 84	351 ± 80	0.84
Total cholesterol [mmol/L]	5.2 ± 1.1	5.1 ± 1.0	0.77
LDL-C [mmol/L]	3.3 ± 1.0	2.9 ± 1.1	0.019
HDL-C [mmol/L]	1.3 ± 0.4	1.8 ± 0.9	< 0.001
Triglycerides [mmol/L]	1.7 ± 1.1	1.5 ± 1.2	0.41
Number of antihypertensive medications	4 (3–5)	2 (1–3)	< 0.001

The results are presented as mean ± one standard deviation or median and interquartile range in the parentheses. Categorical variables are shown as frequencies; BP — blood pressure; GFR — glomerular filtration rate; HDL-C — high-density lipoprotein cholesterol; HR — heart rate; LDL-C — low-density lipoprotein cholesterol; PP — pulse pressure

(r = –0.305, p < 0.001) diastolic BP, clinic pulse pressure (PP) (r = 0.297, p = 0.001), daytime (r = 0.355, p < 0.001) and nighttime (r = 0.313, p < 0.001) PP, 24-h and daytime HR (r = –0.215, p = 013 and r = –0.182, p = 0.036, respectively) as well as with FPG (r = 0.215, p = 0.008) and E/E' ratio (r = 0.289, p = 0.001). Both RRI and PI values were significantly higher in RHT patients with newly diagnosed diabetes as compared with RHT patients without diabetes (0.65 ± 0.05 vs. 0.62 ± 0.05, p = 0.022 and 1.2 ± 0.2 vs. 1.1 ± 0.2, p = 0.025, respectively) (Fig. 2). There was no correlation between RRI values and BP nocturnal decline. No differences in RRI values were found between dippers and non-dippers.

A multivariate stepwise linear regression model that included variables correlated with RRI values at a significance of 0.05 or less was performed (Table 3). Age, daytime diastolic BP, and daytime PP and E/E' ratio correlated independently with RRI in the model that included: age, daytime diastolic BP, daytime HR, daytime PP, FPG levels, and E/E' ratio.

For the analyses of our study population we took an RRI of 0.7 as a threshold, which is in agreement with other studies performed in hypertensive patients without renal disease or renal allograft, in which a threshold of 0.7 was applied. Increased RRI was found in 11 (7.3%) patients with true RHT and in one patient with well-controlled HT.

Table 2. Echocardiographic parameters in patients with resistant hypertension (RHT) and control-group patients with well controlled hypertension (HT)

Characteristics	RHT	Controlled HT	P
N	151	50	
LVMI [g/m^2]	125 ± 28	105 ± 25	< 0.001
LVH	51.0%	28.6%	0.010
LVEF [%]	70 ± 5	70 ± 7	0.82
E-wave [cm/s]	0.73 ± 0.19	0.75 ± 0.15	0.55
A-wave [cm/s]	0.79 ± 0.17	0.78 ± 0.15	0.76
E/A	1.15 ± 0.42	1.06 ± 0.27	0.11
E' [cm/s]	10.4 ± 3.2	12.0 ± 3.8	0.020
E/E'	8.1 ± 2.7	7.1 ± 2.5	0.062

The results are presented as mean ± one standard deviation. Categorical variables are shown as frequencies; A-wave — late diastolic mitral flow velocity; E-wave — early diastolic mitral flow velocity; E'— early diastolic mitral annular velocity; LVH — left ventricular hypertrophy; LVEF — left ventricular ejection fraction; LVMI — left ventricular mass index

Table 3. Multivariate linear regression model (including age, daytime diastolic blood pressure, pulse pressure, daytime heart rate, daytime pulse pressure, fasting plasma glucose level, E/E' ratio) for variables associated with renal resistive index

Parameter	β standardised coefficient	P	VIF
Age	0.214	0.009	1.15
Daytime DBP	–0.394	< 0.001	1.35
Daytime PP	0.372	< 0.001	1.17
Daytime heart rate	–0.126	0.13	1.25
FPG level	0.019	0.81	1.18
E/E' ratio	0.169	0.034	1.35

DBP — diastolic blood pressure; FPG — fasting plasma glucose; PP — pulse pressure; VIF — variance inflation factors

Among patients with RHT, patients with increased RRI were characterised by older age, higher BMI, lower daytime and nighttime diastolic BP values, and lower daytime and nighttime HR as compared to patients with RRI < 0.7. The RHT patients with increased RRI as compared to patients with RRI < 0.7 were characterised also by higher daytime and nighttime PP. Both groups did not differ in respect of renal function (Table 4). There was a tendency towards higher E/E' index as well as lower E' velocity in patients with increased RRI (Table 5).

DISCUSSION

Our study showed that patients with true RHT were characterised by higher clinic and ambulatory BP values, BMI and FPG concentration, and higher incidence of abdominal obesity
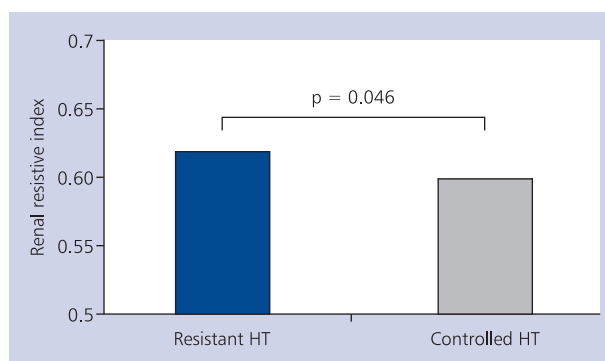

Figure 1. Renal resistive index values in patients with true resistant hypertension and in patients with well controlled essential hypertension; HT — hypertension
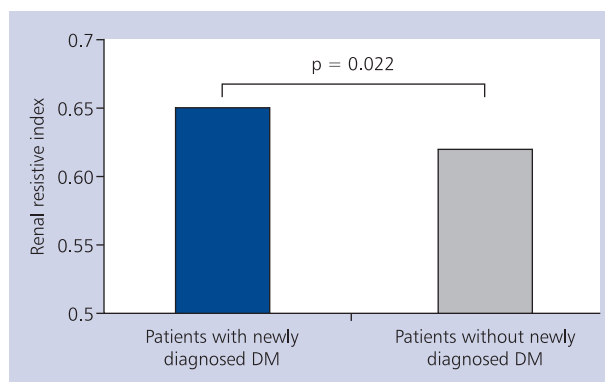

Figure 2. Renal resistive index values in patients with true resistant hypertension according to the presence of newly diagnosed diabetes mellitus; DM — diabetes mellitus

and metabolic syndrome as compared to the subjects with well-controlled hypertension, confirming previous reports [22–24].

The clinical relevance of renal Doppler indices has been discussed extensively. In the present study significant differences in RRI values were found between patients with RHT and an age-matched, well-controlled hypertensive group. Also among patients with RHT, patients with increased RRI > 0.7 were characterised by older age, higher BMI, and lower daytime and nighttime diastolic BP values as compared to patients with RRI < 0.7.

More recently it has been suggested that RRI values may be related to increased BP and duration of the disease, and early organ damage in patients with essential HT, including RHT [2, 10, 21, 22].

It should be noted that our study, representing a cohort being evaluated, differs in some ways from previous reports. We assessed a large group of patients with true RHT, characterised by moderately manifested target organ damage, with preserved renal function and without history of

Table 4. Clinical characteristics of patients with resistant hypertension with normal and increased resistive index (RI)

Characteristics	RI < 0.7	RI ≥ 0.7	P
N	140	11	
Males [%]	58.6	72.7	0.36
Age [years]	47.3 ± 10.6	52.2 ± 4.9	0.012
Clinic systolic BP [mm Hg]	159 ± 22	160 ± 25	0.88
Clinic diastolic BP [mm Hg]	96 ± 15	91 ± 13	0.31
Clinic PP [mm Hg]	62 ± 14	68 ± 2	0.20
Daytime systolic BP [mm Hg]	143 ± 19	141 ± 14	0.66
Daytime diastolic BP [mm Hg]	90 ± 13	81 ± 8	0.030
Daytime PP [mm Hg]	53 ± 11	60 ± 13	< 0.001
Daytime HR [bpm]	73 ± 10	60 ± 7	< 0.001
Nocturnal systolic BP [mm Hg]	129 ± 18	129 ± 11	0.98
Nocturnal diastolic BP [mm Hg]	78 ± 12	72 ± 5	0.004
Nocturnal PP [mm Hg]	51 ± 11	57 ± 11	0.073
Nighttime HR [bpm]	73 ± 10	60 ± 7	< 0.001
Known history of hypertension [years]	10.6 ± 8.5	11.7 ± 6.9	0.68
Body mass index [kg/m^2]	29.7 ± 4.5	32.8 ± 6.0	0.034
Abdominal obesity	71.4%	81.8%	0.46
Metabolic syndrome	62.9%	72.7%	0.51
Newly diagnosed diabetes	10%	18.2%	0.37
Smoking	17.2%	27.3%	0.40
Sodium [mmol/L]	142 ± 3	142 ± 1	0.86
Potassium [mmol/L]	4.4 ± 0.4	4.3 ± 0.3	0.58
Fasting glucose [mmol/L]	5.7 ± 0.9	6.1 ± 0.8	0.23
Creatinine [μmol/L]	78 ± 18	81 ± 13	0.59
GFR [mL/min/1.73 m^2]	92.4 ± 16.3	89.6 ± 13.9	0.58
Uric acid [μmol/L]	353 ± 85	364 ± 78	0.69
Total cholesterol [mmol/L]	5.2 ± 1.1	5.1 ± 1.1	0.84
LDL-C [mmol/L]	3.3 ± 1.0	3.5 ± 1.0	0.57
HDL-C [mmol/L]	1.3 ± 0.4	1.2 ± 0.3	0.28
Triglycerides [mmol/L]	1.7 ± 1.1	1.4 ± 0.8	0.48
Albuminuria [mg/24 h]	19.0 ± 18.9	21.2 ± 12.7	0.72
Number of antihypertensive medications	4 (3–5)	4 (3–5)	0.59

The results are presented as mean ± one standard deviation or median and interquartile range in the parentheses. Categorical variables are shown as frequencies; BP — blood pressure; GFR — glomerular filtration rate; HDL-C — high-density lipoprotein cholesterol; HR — heart rate; LDL-C — low-density lipoprotein cholesterol; PP — pulse pressure

other cardiovascular diseases, which was compared with the age-matched controls with well-controlled HT.

In other studies RRI was evaluated in patients with never treated or treated well-controlled essential HT, and in some of the studies they were older, had longer known duration of HT, and were characterised by higher prevalence of target organ damage. In a Veglio et al. [25] study including a relatively small group of 45 patients with essential HT it was shown that RRI was higher in subjects with a long-standing HT as compared to normotensive subjects and correlated with the severity and duration of the disease. The authors reported that baseline RRI was significantly higher in moderate and severe HT when compared to normal subjects and patients with mild HT [2, 10, 21, 25].

It should also be noted that some investigators evaluated RRI in patients with RHT but no comparison was performed with well-controlled subjects. The study of Raff et al. [10] showed that in patients with therapy-resistant hypertension RRI reflected functional and structural vascular parameters and measurement of RRI, in addition to other parameters, complements screening for target organ damage in RHT therapy. However, patients with RHT were not compared with those with controlled HT [10].

Table 5. Echocardiographic parameters of patients with resistant hypertension with normal and increased resistive index (RI).

Characteristics	RI < 0.7	RI ≥ 0.7	P
N	140	11	
LVMI [g/m²]	123.4 ± 27.1	138.9 ± 37.5	0.078
LVH [%]	50.7	54.5	0.81
LVEF [%]	70.8 ± 8.8	69.8 ± 6.5	0.75
E-wave [cm/s]	0.78 ± 0.17	0.84 ± 0.13	0.79
A-wave [cm/s]	0.73 ± 0.18	0.74 ± 0.23	0.34
E/A	1.1 ± 0.42	1.2 ± 0.45	0.57
E' [cm/s]	10.6 ± 3.2	8.8 ± 3.0	0.086
E/E'	7.9 ± 2.4	10.8 ± 4.6	0.072

The results are presented as mean ± one standard deviation. Categorical variables are shown as frequencies; A-wave — late diastolic mitral flow velocity; E-wave — early diastolic mitral flow velocity; E' — early diastolic mitral annular velocity; LVH — left ventricular hypertrophy; LVEF — left ventricular ejection fraction; LVMI — left ventricular mass index

Also in contrast to our results, in most studied groups preserved renal function and lack of cardiovascular disorders, as pre-specified criteria, were not employed. Derchi et al. [26] examined renal vascular resistance in 291 untreated patients with essential HT. However, the prevalence of mild renal dysfunction was 63%, and the investigated patients were older, had higher systolic BP and PP, and were characterised by higher RRI than those with normal renal function [26].

Our study showed that RRI values in true RHT were significantly higher in patients with newly diagnosed diabetes as compared to those without diabetes. Our observation is supported by other studies indicating that dynamic evaluation of RRI may be an early detector of renal vascular alterations in the presence of type 2 diabetes and HT, even before the onset of microalbuminuria. Also, another prospective study showed that subclinical functional and structural renal abnormalities are predictors of new onset diabetes in patients with essential HT. It is noteworthy that in a model including all the renal parameters, RRI was the only significant independent risk factor for the development of diabetes during the study period [5, 12].

In our group of RHT patients significant correlation was found between RRI and FPG concentration, but no relationship was found between RRI values and other features of metabolic syndrome, including abdominal obesity and dyslipidaemia.

It is noteworthy that in our group of RHT patients, significant correlation between RRI and ambulatory daytime and nighttime diastolic BP was found. Of note, Pontremoli et al. [9] and other authors showed a positive correlation not with diastolic but with systolic BP in different groups of hypertensive patients [9, 27]. However, it should be noted that in the current study BP measurements were documented by means of ambulatory BP. In a study by Raff et al. [10] including patients with therapy-RHT, systolic and diastolic BP as well as mean arterial pressure were not associated with RRI values.

In our study in patients with RHT significant correlation was found between RRI value and both clinic and ambulatory PP. Also other investigators reported a significant relationship between RRI value and PP, a factor known to be associated with vascular stiffness [2, 28–30]. However, in the study by Raff et al. [10] including patients with therapy-RHT PP was not associated with RRI values [2, 10].

The positive correlation between RRI and PP and the negative correlation between RRI and diastolic BP could have been expected, given the formula used to calculate RRI. PP is regarded as a principal determinant of RRI and is influenced by cardiac function systemic arterial compliance. It has also been postulated that renal diastolic flow correlates with femoral-to-aortic pressure gradient (i.e. PP amplification) and with aortic distensibility linking arterial stiffness and RRI [29].

The present study did not show a significant relationship between RRI values and LVH or LVMI. Also, Pontremoli et al. [9] and Okura et al. [31] did not find any association between RRI and LVMI and LVH. Okura et al. [31] concluded that this could suggest that the mechanism of hypertension-mediated progressive damage may differ between vessels and the myocardium. In a study by Tedesco et al. [32] a positive correlation was found between RRI values and LVMI. However, it should be noted that this group differs in some ways from patients included in our study and was distinguishing subjects with RRI < 0.7 from those with RRI > 0.7. The authors reported that hypertensive patients with RRI > 0.7 had increased LVMI with subclinical impairment of LV diastolic function [9, 31, 32].

In previous studies we found subclinical systolic and diastolic dysfunction in patients with RHT enrolled to the RESIST-POL Study. In the presented study RRI was significantly and independently correlated only with E/E' in RHT patients. In contrast Kuznetsowa et al. [30] demonstrated that RRI was significantly associated with LV systolic and diastolic Doppler parameters. This inconsistency in results may be secondary to differences in the groups of patients analysed in both of the studies [14, 15, 30].

It should be noted that our results are based on an observational study and that longitudinal, prospective studies are needed to evaluate the predictive role of RRI in RHT patients. It should also be kept in mind that the associations we observed between RRI and clinic and ambulatory BP values, biochemical parameters, and echocardiographic parameters reflect a selected hypertensive group without history of other cardiovascular diseases, without known diabetes, and with preserved renal function. Therefore, the results of this study cannot be extrapolated to the whole group of patients with RHT. Other limitations of the study may include also a relatively small group of patients with well-controlled HT.

CONCLUSIONS

In summary our study, evaluating cohort of patients with true RHT, indicates that patients with true RHT are characterised by significantly higher RRI values as compared with patients with well-controlled HT. It may also be suggested that in subjects with RHT renal vascular resistance is related to BP values, selected echocardiographic abnormalities, and some surrogate markers for metabolic and cardiovascular events, including FPG concentration and PP, respectively.

Conflict of interest: *none declared*

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Wskaźnik oporowości u chorych z prawdziwie opornym nadciśnieniem tętniczym: analiza wyników badania RESIST-POL

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Streszczenie

Wstęp: Postuluje się, że zwiększony ultrasonograficzny wskaźnik oporowości przepływu w tętnicach wewnątrznerkowych (RRI) może być wykładnikiem rozwoju miażdżycy i powikłań narządowych nadciśnienia tętniczego zarówno w obrębie nerek, jak i całego organizmu.

Cel: Celem pracy była ocena RRI i czynników związanych z jego wyższymi wartościami u chorych z prawdziwie opornym nadciśnieniem tętniczym (OPNT) włączonych do badania RESIST-POL.

Metody: Spośród 204 chorych z prawdziwie OPNT włączonych do badania RESIST-POL analizą objęto 151 osób (90 mężczyzn, 61 kobiet, średni wiek: 47,7 ± 10,4 roku, zakres: 19–65 lat), u których wykluczono wtórne postaci nadciśnienia tętniczego. Wszyscy chorzy charakteryzowali się zachowaną funkcją nerek (estymowany wskaźnik filtracji kłębuszkowej [eGFR] > 60 ml/min/1,73 m²) i brakiem wywiadu cukrzycy rozpoznanej przed włączeniem do badania. Grupę kontrolną stanowiło 50 dobranych pod względem wieku i płci pacjentów z dobrze kontrolowanym, pierwotnym nadciśnieniem tętniczym (35 mężczyzn, 15 kobiet, średni wiek: 46,8 ± 10,4 roku, zakres: 19–65 lat). Oceniane grupy nie różniły się także znanym czasem trwania nadciśnienia tętniczego. RRI oceniono w badaniu doplerowskim tętnic nerkowych. Za wartość podwyższoną uznano RRI ≥ 0,7.

Wyniki: Chorzy z prawdziwie OPNT charakteryzowali się wyższym RRI w porównaniu z pacjentami z dobrze kontrolowanym nadciśnieniem tętniczym pierwotnym (0,62 ± 0,05 vs. 0,60 ± 0,05; p < 0,05). Porównywane grupy nie różniły się pod względem parametrów funkcji nerek — stężenia kreatyniny w osoczu (78,6 ± 17,7 vs. 81,1 ± 16,1 μmol/l; p = 0,39) i eGFR (92,2 ± 16,1 vs. 93,9 ± 18,8 ml/min/1,73 m²; p = 0,54). W grupie chorych z prawdziwie OPNT wartości RRI korelowały istotnie z: wiekiem, wartościami rozkurczowego ciśnienia tętniczego (DBP) i ciśnienia tętna w pomiarach klinicznych oraz w całodobowej rejestracji ciśnienia tętniczego, jak również ze stężeniem glukozy na czczo (r = 0,215; p = 0,008) oraz ze wskaźnikiem E/E' (r = 0,289; p = 0,001) w badaniu echokardiograficznym. Wiek, wartości DBP oraz ciśnienia tętna z okresu dnia w całodobowej rejestracji oraz wskaźnik E/E', ale nie stężenie glukozy na czczo, korelowały niezależnie z RRI w analizie wieloczynnikowej w grupie chorych z prawdziwie OPNT. Podwyższony RRI stwierdzono u 11 chorych z prawdziwie OPNT (7,3%) i u 1 pacjenta z dobrze kontrolowanym nadciśnieniem tętniczym pierwotnym (2%). Chorzy z prawdziwie OPNT z podwyższonym RRI w porównaniu z pacjentami z prawdziwie OPNT i prawidłowym RRI charakteryzowali się starszym wiekiem (52,2 ± 4,9 vs. 47,3 ± 10,6 roku; p = 0,012), wyższym wskaźnikiem masy ciała (32,8 ± 6,0 vs. 29,7 ± 4,5 kg/m²; p = 0,034), a także niższymi wartościami DBP z okresu dnia i nocy oraz wyższym ciśnieniem tętna z okresu dnia i nocy w całodobowej rejestracji ciśnienia tętniczego. Chorzy z prawdziwie OPNT z podwyższonym i prawidłowym RRI nie różnili się pod względem stężenia kreatyniny oraz eGFR.

Wnioski: Wyniki wskazują, że chorzy z prawdziwie OPNT mogą się charakteryzować istotnie wyższymi wartościami RRI w porównaniu z pacjentami z dobrze kontrolowanym nadciśnieniem tętniczym pierwotnym, jak również że wartości RRI u chorych z prawdziwie OPNT mogą korelować z wartościami ciśnienia tętniczego i ciśnienia tętna oraz z wybranymi parametrami metabolicznymi i echokardiograficznymi.

Słowa kluczowe: nadciśnienie tętnicze oporne, wskaźnik oporowości, cukrzyca, powikłania narządowe, ciśnienie tętna

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