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1 message

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Dr. dr Hasyim Kasim:

We kindly inform that we have reached a decision regarding your submission to Arterial Hypertension, entitled "Renal Resistive Index in Hypertensive Patients: One Centre Study".

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Case report

Renal Resistive Index in Hypertensive Patients: One Centre Study

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Abstract

Introduction: Hypertension is a leading cause of kidney dysfunction. Renal resistive index (RRI) was an index to evaluate arterial compliance and/or resistance, reflecting the reduction of kidney function and microalbuminuria. We investigated the relationship of RRI in hypertensive patients to detect kidney dysfunction early detection.

Methods: This was a cross-sectional study at Wahidin Sudirohusodo hospital in June-November 2022. All hypertensive patient was evaluated for RRI. RRI was examined with intrarenal doppler ultrasound, and a cut-off ≥0.70 were used.

Results: This study included 61 subjects. Thirty-five subjects were female, and 26 subjects were male 90.2% of subjects were below 60 years. Estimated glomerular filtration rate (eGFR) level was 90.29±25.19 in RRI <0.7 and 64.91±31.79 in RRI ≥0.7. Our study found there was a significant difference between anti-hypertensive treatment and eGFR level with the RRI group (*p*-value <0.05). There was no significant difference in sex, age, proteinuria, and hypertension control status in both RRI groups.

Conclusion: The renal resistive index is a useful marker for early renal dysfunction in hypertensive patients despite normal eGFR.

Keywords: hypertension, renal resistive index (RRI), eGFR level, proteinuria

Introduction

Renal resistive index (RRI) is an ultrasonographic Doppler measurement of flow velocities in intraparenchymal renal arteries [1]. It is a non-invasive and repeatable method for assessing arterial compliance and/or resistance. RRI appears to have a significant role in assessing various secondary hypertension patients. RRI is related to subclinical indicators of target organ damage and represents renal disease progression beyond albuminuria and creatinine clearance. Also, the RRI can evaluate cardiovascular and renal risk [2]. Several studies indicate that this index reflects systemic hemodynamic and depends on the aortic pulse pressure, which is affected by parameters like age, presence of hypertension (HTN), or diabetes. In patients with widespread atherosclerosis or reduced vascular compliance, RRI may be increased even with normal kidney function [2]. An elevated RRI (≥0.70) is usually associated with impaired renal function, increased proteinuria, and poor prognosis [3]. Evaluation of RRI may also contribute to therapeutic decision-making. Given its straightforward assessment, RRI appears as a simple approach and "multifunctional" instrument that might aid in evaluating renal disease progression. The purpose of this review was to evaluate RRI in hypertensive patients.

Material and Method

Subjects

Sixty-one patients with hypertension at Wahidin Sudirohusodo Hospital were chosen as a subject. All patients had signed a consent form and confirmed their voluntary participation in this research study. They were given an explanation regarding the purpose, benefits, and what was done in this study and agreed to participate in this research voluntarily. During the study, they had been given the right to ask questions or ask for clarification from researchers if there were still things that were not clear.

All essential hypertension patients were evaluated for renal RI at the initial visit. Hypertension was defined as systolic blood pressure of 140 mm Hg and/or diastolic blood pressure of 90 mm Hg, measured three times in the sitting position using a brachial sphygmomanometer or therapy with antihypertensive medication. The exclusion criteria were chronic kidney disease with dialysis. The ethics committee of the Faculty of Medicine, Hasanuddin University, authorized the study with ethical number UH22090548. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices.

Blood and urine collection

Using an automated analyser, haemoglobin, creatinine, sodium, potassium, and chloride were determined. The estimated glomerular filtration rate was computed utilizing the equation of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).

Duplex doppler ultrasonography

Doppler ultrasonography was used to investigate renal hemodynamics utilizing an HI VISION Avius (Hitachi Aloka Medical, Tokyo, Japan.) and a 3.5-MHz convex probe fitted with a Doppler system. Doppler flow was measured in the interlobar arteries of both kidneys at three distinct places (superior, middle, and inferior) using colour flow mapping as a reference. Then, peak systolic velocity (PSV) and end-diastolic velocity (EDV) were calculated. The average resistive index (RI) was computed using the following formula: RI = (PSV – EDV)/PSV[4].

Statistical analysis

Statistical analysis was implemented using the statistical package for social sciences (SPSS) software, version 25.0 for Windows. Data are expressed as mean +/- SD or median (interquartile range). Both data and normality were analysed using the Kolmogorov-Smirnov test. The chi-square test was used to evaluate significant differences between variable with normal data distribution. Statistical significance was defined as *p*-value < 0.05.

Results

This study included 61 patients (Tables 1 and 2). Thirty-five subjects were female, and 26 subjects were male. 90.2% of subjects were below 60 years. Antihypertensive treatment usage was calcium channel blocker (50.8%), angiotensin receptor blocker (9.8%), angiotensin converting enzyme inhibitor (ACEi) (6.6%), a combination of calcium channel blocker (CCB) and angiotensin receptor blocker (ARB) (27.9%), a combination of CCB and ACEi (3.3%), and three combination drugs (1.6%). Based on the RRI group, 88.5% had the RRI value of <0.7, and 11.5% had an RRI value of ≥0.7. Based on proteinuria, 42.6% had proteinuria and 57.4% had no proteinuria. Based on hypertensive control, accounted 31.1% of subjects had controlled hypertension, and 68.9% of subjects were uncontrolled. In Table 3, the average eGFR RRI <0.7 is 90.29 ± 25.19 and the average RRI ≥ 0.7 is 64.91± 31.79. With a *p*-value of 0.030, there was a significant difference between eGFR and RRI. Age, systolic, diastolic, pulse rate, haemoglobin, creatinine, and potassium were not significantly different on the RRI (P value > 0.05). In the RRI 0.7 group, there were 27 CCB subjects, 6 ARB subjects, 4 ACEi subjects, 14 CCB+ARB subjects, 2 CCB+ACEi subjects, and 1 person receiving a combination of all three medicines. In the RRI >0.7 group, 4 participants had CCB, 0 had ARB, 0 had ACEi, 3 had CCB+ARB, 0 had CCB+ACEi, and 0 had a combination of all 3 medications. There was a correlation between antihypertensive therapy and RRI (*p*= 0.04) (Table 4).

Discussion

This study showed a significant relationship between RRI values and eGFR even though the average eGFR value was more than 60 ml/min/1.73 m^2. Renal vasodilating capacity was reduced before the onset of established renal damage and in normal RRI values, meaning that functional rather than structural alterations might already be present, indicating a subclinical stage of renal damage. In predicting Chronic Kidney Disease (CKD)

progression and poor outcomes in cases with mild to moderate renal impairment, RRI was superior to renal function assessment alone [5]. Four RRI has been linked to a quicker loss in renal function in individuals with proteinuria CKD or diabetics with microalbuminuria, even when GFR levels are normal [6]. In table 3, there was a significant relationship between RRI and eGFR in 61 hypertensive patients (Table 3). It seems that lower eGFR values were associated with higher RRI values. A similar relationship was reported by Gaurav et al. who reported that there was a significant negative correlation between RRI and eGFR[7].

This study did not show a significant association with proteinuria. It could be due to the fact that this study did not assess microalbuminuria or proteinuria in 24 hours. Hashimoto et al. studied 133 hypertension individuals and found that each 0.1 increase in RRI was related to a 5.4-fold increase in the incidence of albuminuria [8]. In a investigation involving 66 patients with critical hypertension (HTN), a strong correlation was seen between high RRI and future increases in urine albumin excretion [9].

The only variable that substantially predicted an >50% rise in the urine albumin to creatinine ratio over two years was RRI. The ideal RRI cut-off value that predicted this increase was 0.71 (sensitivity 52.4% and specificity 84.0%). This cut-off value was consistent with other studies indicating that RRI values >0.7 are more prevalent in patients with left ventricular hypertrophy or advanced carotid atherosclerosis and are associated with higher mortality in hypertensive patients with CKD and no clinically significant renal artery stenosis [10,11].

The assessment of RRI may have therapeutic consequences as well. Our study found there was a significant difference ($p<0.05$) between RRI and antihypertensive treatment. During chronic antihypertensive medication, there was evidence that changes in RRI parallel changes in urine albumin excretion[11]. In addition, an increase in RRI indicated intrarenal stiffness and urges care in titrating renin-angiotensin system inhibitors to prevent renal function decline, particularly in CKD patients, diabetics, and the elderly. In particular, Renin angiotensin system inhibitors (RASi) such as valsartan and lisinopril can improve renal function in individuals with essential HTN, particularly those with microalbuminuria, by decreasing renal vascular resistance and so avoiding eventual renal failure [12,13].

Details on the effect of treatment and RRI are given in Table 5. Overall, the majority of patients have RRI of less than 0.7. RRI values were affected by the type of therapy received by either the controlled or uncontrolled hypertension. While monotherapy therapy is effective for controlled and uncontrolled hypertension, combined therapy is less effective for uncontrolled therapy. Despite the treatment, none showed statistically significant ($p< 0.05$).

Conclusion

RRI is a useful marker for renal dysfunction in hypertensive patients.

Authorship

Hasyim Kasim*: Conceptualization, data collection, writing, funding acquisition. Khadijah Khairunnisa Hasyim: data collection, methodology. Andi Makbul Aman: methodology, writing. Dimas Bayu: Data modelling. Nur Fitriani: writing - review & editing.

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Conflict of interest

The authors declare no conflict of interest.

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Table 1. Data descriptive

	Minimum	Maximum	Average	Std. Deviation
Age (years)	32.0	63.0	50.7	8.6
Systolic (mmHg)	110.0	214.0	155.4	21.9
Diastolic (mmHg)	63.0	127.0	89.6	12.2
Heart rate (beat/min)	62.0	121.0	88.1	11.2
Haemoglobin (g/dL)	7.4	16.9	12.8	2.3
Creatinine (mg/dL)	0.4	3.4	0.9	0.5
GFR (mL/min/ 1.73 m^2)	14.8	138.0	87.4	26.9
RRI	0.5	0.8	0.6	0.1
Natrium (mEg/L)	127.0	150.0	139.3	4.2
Potassium (mEg/L)	2.8	5.3	3.9	0.6
Chloride (mEg/L)	96.0	113.0	104.8	4.0

Table 2. Data descriptive

Variable	**n**	**%**
Sex		
Female	35	57.4

Male	26	42.6
Age		
<60 Years	55	90.2
>=60 Years	6	9.8
Antihypertensive treatment		
CCB	31	50.8
ARB	6	9.8
ACEi	4	6.6
CCB+ARB	17	27.9
CCB+ACEi	2	3.3
3 Combination	1	1.6
RRI		
<0,7	54	88.5
>=0,7	7	11.5
Proteinuria		
normal	35	57.4
Proteinuria	26	42.6
Hypertensive control		
Controlled	19	31.1
Uncontrolled	42	68.9

Note: Our study found there was a significant difference between antihypertensive treatment and eGFR level with the RRI group (*p*-value <0.05)

Table 3. RRI Profile in hypertensive patient

Variable	<0,7 (n= 54)	≥0,7 (n=7)	*p*-value*
Age	50.0 ± 8.8	55.5 ± 4.1	0.10
Systolic	156.1±21.3	150.1± 27.2	0.50
Diastolic	90.5±12.3	83.1±9.9	0.14
Heart rate	88.8±11.3	83.1±9.5	0.21
Haemoglobin	12.7±2.2	13.3± 3.1	0.51
Creatinine	0.9±0.3	1.4 ±0.9	0.10**
eGFR	90.3±25.2	64.9±31.8	0.03**
Potassium	3.9±0.5	4.2±0.5	0.19

Note: *t-test at $p<0.05$

** Mann Whitney test, the value was significant at $p<0.05$

Table 4. Relationship of RRI and Independent Variable

Variable	RRI (n,%)		*p*-value*
	<0,7 (n=54)	≥0,7 (n=7)	
Sex			
Female	32 (91.4)	3 (8.6)	0.41
Male	22(84.0)	4(15.4)	
Age			
<60 Years	49(89.1)	6(10.9)	0.67
>=60 Years	5(83.3)	1(16.7)	
Anti-hypertensive treatment			
CCB	27(87.1)	4(12.9)	
ARB	6(100.0)	0(0)	0.04
ACEi	4 (100.0)	0(0)	
CCB+ARB	14(82.4)	3(17.6)	
CCB+ACEi	2(100.0)	0(0)	
3 Combination	1(100.0)	0(0)	
Proteinuria			
normal	29(82.9)	6(17.1)	0.10

Proteinuria	25(96.2)	1(3.8)	
Hypertensive control			
Controlled	16(84.2)	3(15.8)	0.47
Uncontrolled	38(90.5)	4(9.5)	
Value (Average±SD)			
Creatinine	0.88±0.32	1.37 ±0.93	0.10**
GFR	90.29±25.19	64.91±31.79	0.03**

Note: *t-test at $p<0.05$

** Mann Whitney test, the value was significant at $p<0.05$

Table 5. RRI values for controlled and uncontrolled hypertension patients

Note: the value was significant at $p<0.05$

Hypertension			RRI <0,7	RRI ≥0,7	Total	*p*-value
Controlled	monotherapy	N	12	3	15	0.52
hypertension		%	80.0%	20.0%	100.0%	
	combination	N	7	0	7	
	therapy	%	100.0%	0%	100.0%	
	Total	N	19	3	22	
		%	86.4%	13.6%	100.0%	
Uncontrolled	monotherapy	N	26	1	27	0.08
hypertension		%	96.3%	3.7%	100.0%	
	combination	N	9	3	12	
	therapy	%	75.0%	25.0%	100.0%	
	Total	N	35	4	39	
		%	89.7%	10.3%	100.0%	