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Original Article

The Relationship Between the Renal Resistive Index and End Organ Damage Parameters in Hypertensive Pediatric Patients

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ABSTRACT

Background and Aim: This study aimed to investigate the strength of the relationship between renal resistive index with left ventricular mass index, microalbuminuria, and retinopathy to find a predictive value of the renal resistive index in early detection of end-organ damage.

Methods: Pediatric patients diagnosed with hypertension were included in this study between January 2020 and January 2022.

Results: A total of 41 consecutive patients who were never treated for essential hypertension were included in this study. Microalbuminuria was detected in 10 patients (24%). Retinopathy was detected in only 2 patients (4.9%). Echocardiographic data were available in 25 patients. The mean left ventricular mass index was 30±10 (17-53 g/m$^{2.7}$). Three male patients (12%) had left ventricular hypertrophy but none of the females had left ventricular hypertrophy. We categorized the patients into two groups according to the presence of microalbuminuria and compared the two groups. The value of the renal resistive index in the microalbuminuric group was significantly higher than in the nonalbuminuric group (0.8±0.2 vs. 0.6±0.2, P=0.047). We found a positive correlation between renal resistive index and urine microalbumin (r=0.636, P=0.014). In regression analysis, higher resistive index values were independently associated with microalbuminuria but not left ventricular hypertrophy. (OR=-0.633, 95% CI 24.4-187.2, P=0.015)

Conclusion: To our knowledge, this is the first study to analyze the correlation of RI with microalbuminuria in hypertensive children. We found a significantly higher resistive index in patients with microalbuminuria; we also found a correlation between these variables. This shows that this finding and an abnormal resistive index can be used as early signs of hypertension.

Keywords: Hypertension, Renal resistive index, albuminuria, Left ventricular hypertrophy, Retinopathy

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Introduction

Early diagnosis and appropriate treatment of hypertension (HT) at pediatric age are vital to prevent hypertensive end-organ damage, such as left ventricular hypertrophy (LVH), retinopathy, and microalbuminuria [1, 2]. Microalbuminuria reflects early kidney dysfunction [3]. Besides, LVH is a common complication of hypertension. Increased left ventricular mass index (LVMI) reflects LVH [4]. While the prevalence and incidence of retinopathy, namely various retinal microvascular lesions, are between 2% and 15% in the general population [5], previous studies have shown a higher prevalence (18%) of retinopathy in severe hypertension in the pediatric age group [6].

Renal resistive index (RRI) is a parameter to evaluate the renal vascular resistance [7] measured in renal Doppler ultrasonography. Blood pressure, glomerular filtration rate (GFR), and renal blood flow affect RRI [8-10]. This study was conducted to investigate the strength of the relationship between RRI with LVMI, microalbuminuria, and retinopathy to find a predictive value of RRI in the early detection of end-organ damage.

Materials and Methods

Pediatric patients diagnosed with hypertension were included in this study between January 2020 and January 2022. The patients underwent the following procedures, clinical and routine laboratory examinations, spot urine microalbuminuria/creatinine ratio measurement, echocardiography, Doppler ultrasonography, and ophthalmological examination. The exclusion criteria included having cardiac, and ophthalmologic disease, anatomical abnormalities of the urinary tract, or renal parenchymal disease. Pediatric hypertension was defined as having three numbers of systolic or diastolic blood pressure (BP) above the subject's normal blood pressure level determined by age, height, and sex and published in the hypertension guideline in 2017 [11]. Since BP measurements can vary between visits at different time points, we averaged the three measurements. At the time of data entry, demographic findings, data on the most recent anthropometric measurements, body mass index (BMI), office blood pressure measurements, and laboratory tests including routine biochemical parameters, complete blood count, spot urinary microalbumin creatinine ratio, lipid profile, and thyroid function tests were recorded. The findings of the ophthalmological examination were also recorded. The echocardiographic measurements were performed according to the guidelines issued by the American society of echocardiography [12]. Left ventricular mass was calculated according to the formula developed by Devereux [13, 14]. LVH was quantified and categorized by the Khoury LVMI percentile charts [15].

Doppler ultrasonographic examination was performed prospectively for both kidneys. The RRI was calculated according to the formula: ([peak systolic velocity–end-diastolic velocity]/peak-systolic velocity) [16, 17]. The measurements were performed twice by a well-trained ultrasonographer and the mean RRI of each kidney was calculated for all patients. Renal glomerular permeability was evaluated by urine microalbumin/creatinine (mg/mg) ratio [18]. Retinal changes were evaluated by two physicians according to the Keith, Wagener, and Barker classification.

Data analysis

Study data were analyzed by SPSS software v. 16.0. Results were shown as Mean±SD unless otherwise stated. Mann–Whitney U test and Chi-square test were used to assess the difference between the two groups. Pearson's correlation coefficient was used to examine the correlation between RRI values and LVMI, spot urine microalbumin/creatinine ratio, and other laboratory parameters, such as thyroid function tests and lipid profile. The level of significance was set at $P<0.05$.

Results

A total of 41 consecutive patients who were never treated with grade 1 or 2 essential hypertension (6 patients with grade 1 HT, 35 patients with grade 2 HT) were included in the study. The mean age of the patients was 176±31 months (72-204 months). The majority were men in the study population (78%). Microalbuminuria was detected in 10 patients (24%). Retinopathy was detected in only 2 patients (4.9%). Echocardiographic data were available in 25 patients; the mean LVMI was 30±10 (17-53 $g/m^{2.7}$). Three men (12%) had LVH but none of the women had LVH. Mean arterial systolic, diastolic pressure, and BMI were 147±15 mmHg, 92±10 mmHg, and 28±6 mmHg, respectively. We categorized the patients into two groups according to the presence of microalbuminuria and compared the two groups.

No significant difference was observed in gender distribution, age, BMI, LVMI, cholesterol, triglyceride, creatinine, thyroid stimulating hormone (TSH), and free thyroxine (T4) between the microalbuminuric (MA) and nonalbuminuric (NMA) groups. The RRI value was significantly higher in MA group than in the NMA group

(0.8±0.2 vs. 0.6±0.2, P=0.047). As expected, the mean urine microalbumin/creatinine ratio was significantly higher in the MA group than the NMA (60±22 vs. 8±6, P=0.039) (Table 1).

We found a positive correlation between RRI and urine microalbumin (r=0.636, P=0.014). On the other hand, no correlation was observed between urine microalbumin and systolic BP, BMI, LVMI, serum cholesterol, triglyceride, creatinine, TSH, and free T4 levels (Table 2).

In regression analysis, higher RRI values were independently associated with microalbuminuria but not left ventricular hypertrophy. (OR=-0.633, 95% CI 24.4-187.2, P=0.015)

Discussion

Target organ damage is a critical cause of morbidity in hypertensive patients. This study demonstrated that RRI has a predictive value in hypertensive nephropathy in pediatric patients. Previous studies have shown an inverse effect, that is, renal tissue compliance and vascular compliance have been reported to be the main factor affecting RRI [10]. Renin-angiotensin, kallikrein-kinin, and prostaglandin-thromboxane blunt vasodilatation and induce diffuse vasoconstriction so that the renal parenchyma exhibits increased RRI [19]. Our results have made us re-think the famous dilemma "which came first, the chicken or the egg?" for the case of the relationship between RRI and microalbuminuria.

Unlike previous studies, which proved that microalbuminuria levels were increased in patients with hypertension and correlated with LVH [20-22], we demonstrated no correlation between microalbuminuria and LVMI. Assadi et al. [23] suggested a positive correlation between HT grade and the level of MA and LVH, as evidenced by the observation that the higher the BP, the more the MA, and the worse LVH. However, our study included pediatric patients without chronic disease. The correlative studies mentioned above were on adults; the progression of LVMI takes a long time. We believe that age affected our correlation analysis. We hypothesized that microalbuminuria depends on the presence of renal vasculopathy. If hypertension does not affect the renal arteries, microalbuminuria is unlikely to be present.

We had 2 patients with grade 1 retinopathy. The proportion of patients with retinopathy is higher (42%) in adults and older patients [24]. Moreover, two of our patients had no microalbuminuria. Previous studies [25]

Table 1. Comparison of the demographic and laboratorial variables of patients with and without microalbuminuria

Variables	No.(%)/Mean±SD		P
	Microalbuminuria (n=10)	Non-Microalbuminuria (n=31)	
Gender Male	4(40)	27(87)	0.084
Age (months)	178±18	173±23	0.722
Systolic blood pressure (mmHg)	153±15	143±11	0.383
Body mass index (kg/m^2)	27±4	29±5	0.488
LVMI (g/m^2)	26±6	20±5	0.360
Retinopathy (n)	0	2	-
Urine microalbumin/creatine ratio	60±22	8±6	0.039
Cholesterol (mg/dL)	153±31	166±41	0.572
Triglyceride (mg/dL)	94±28	144±59	0.069
Creatinine (mg/dL)	0.6±0.1	0.7±0.1	0.568
TSH (mU/L)	2.2±0.9	1.9±0.8	0.611
Free T4 (ng/dl)	1.2±0.4	1.3±0.2	0.752
Renal resistive index	0.8±0.2	0.6±0.2	0.047

LVMI: left ventricular mass index; TSH: thyroid stimulating hormone.

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Table 2. Correlation coefficients between microalbumin/creatinine ratio and laboratory variables

Variables	Urine Microalbumin/Creatinine Ratio
Systolic blood pressure (mmHg)	r=0.068 P=0.685
Body mass index (kg/m²)	r=-0.048 P=0.859
LVMI (g/m²)	r=-0.226 P=0.529
Cholesterol (mg/dL)	r=-0.216 P=0.423
Triglyceride (mg/dL)	r=-0.254 P=0.343
Creatinine (mg/dL)	r=-0.390 P=0.168
TSH (mU/L)	r=0.237 P=0.436
Free T4 (ng/dL)	r=-0.252 P=0.429
Renal resistive index	r=0.636 P=0.014

LVMI: left ventricular mass index; TSH: thyroid stimulating hormone.

in adults have shown that the presence of retinopathy is not associated with more advanced end-organ damage. Moreover, the fundoscopic examination has a limited clinical value in the early phases of grade 1 and 2 hypertension. On the other hand, Dahlöf et al. found a positive correlation between retinal vascular involvement and left ventricular wall thickness on echocardiography in untreated hypertensive patients [26]. We did not find any studies analyzing the correlation between retinopathy and signs of end-organ damage in a pediatric age group. It would be prudent to conduct a similar study on pediatric patients.

Daniel et al. [27] reported that lean body mass and fat mass had a limited impact on LVM. Unlike their findings, we found no relationship between BMI and LVMI.

An interesting finding of our study was that the proportion of males and the triglyceride level were lower in the microalbuminuria group, although the difference was borderline statistically significant. A well-designed diagnostic accuracy study with a larger number of patients is needed to validate the findings of this study.

Our study has some limitations. First, relatively few study participants existed who underwent echocardiography, which may limit the generalizability of our findings. Second, in addition to grade 2 hypertensives, grade 1 hypertensive patients were observd which may affect our results regarding the correlation between MA and LVMI.

Conclusion

To our knowledge, this is the first study to analyze the correlation of RRI with microalbuminuria in hypertensive children. We found a significantly higher RRI in patients with microalbuminuria; we also found a correlation between these variables. In our patients, the prevalence of microalbuminuria was higher than the prevalence of the other signs of end-organ damage (i.e, retinopathy, LVH). Further studies are needed to test the association between microalbuminuria and LVH in pediatric patients with essential hypertension.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee of Kırıkkale University School of Medicine approved the study (date: 08.01.2020, No: 2020.01.07).

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Authors' contributions

Conceptualization, writing, original draft: Cihat Şanlı, Yaşar Kandur; Data curation, and writing, editing & review: Ayşegül Alpcan,Tevfik Oğurel, Salih Koç, Serkan Tursun, Fatma Hayvacı Canbeyli; Final approval: Yaşar Kandur.

All authors accept full responsibility for the work.

Conflict of interest

The authors declared no conflict of interest.

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