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Pulse Wave Analysis in Children with Glomerulopathies

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Abstract

Sympathetic activation, hypertension, hyperlipidemia, and immunosuppressive treatment are risk factors for vascular damage in children with glomerulopathies.

Aim: To perform pulse wave analysis in children with glomerulopathies.

Material and Methods: We studied 33 children (22♂, 11♀) aged 13.3 ± 3.9 years with glomerulopathies: Henoch-Schonlein nephropathy 9 patients, IgA nephropathy 7 patients, membranoproliferative glomerulonephritis 4 patients, mesangioproliferative glomerulonephritis 3 patients, minimal change disease 3 patients, focal segmental glomerulosclerosis (FSGS) 3 patients, and other nephropathies 4 patients. We evaluated age at the disease onset, development of hypertension, body mass index (BMI) Z-score, selected biochemical variables, glomerular filtration rate (ac. to Schwartz formula), and pulse wave parameters determined using a SphygmoCor device (AtCor Medical, Australia): aortic systolic pressure (AoSP), diastolic pressure (AoDP) and pulse pressure (AoPP), augmentation pressure (AP), augmentation index (AIx), augmentation index corrected for heart rate of 75 beats per minute (AIx-75HR) [%], and an index of myocardial oxygen supply and demand, subendocardial viability ratio (SEVR) [%]. The control group included 20 healthy children matched for age and gender.

Results: Children with glomerulopathies showed trends for higher mean AP (P=0.08) and AIx (P=0.07), and a significantly higher mean AIx-75HR (P<0.05). Patients with hypertension (n=13) showed higher mean AoDP (P<0.05) and AIx-75HR (P<0.05) compared to normotensives (n=20). Six (18.2%) overhydrated patients had significantly (P<0.05) higher diastolic peripheral and aoritc diastolic blood pressure, as well as aortic systolic blood pressure than 27 (81.8%) normovolemic children. In 33 children, AoSP and AoDP correlated positively with proteinuria (r=0.44, P<0.05; and r=0.57, P<0.05, respectively); AoDP showed negative correlations with albumin (r=-0.42, P<0.05), total protein (r=-0.36, P<0.05), calcium level (r=-0.47, P<0.05). AoPP correlated positively with BMI Z-score (r=0.43, P<0.05), and SEVR negatively with total cholesterol level (r=-0.43, P<0.05).

Conclusions:

i. Patients with glomerulopathies show increased arterial stiffness compared to their healthy peers.

ii. In children with glomerulonephritis, hypertension is a risk factor for increased aortic stiffness, and hypercholesterolemia may be a risk factor for future myocardial ischemia.

iii. Overhydration in children with glomerulonephritis can increase peripheral and central blood pressure without influencing arterial stiffness.

Keywords: Children; Glomerulopathies; Pulse wave analysis

Introduction

Glomerulonephritis is an immune-mediated renal disease that presents with isolated asymptomatic proteinuria or erythrocyturia, overt hematuria, nephrotic syndrome, or nephritic syndrome. Among children, glomerulonephritis is the cause of end-stage renal failure in 14-29% of cases worldwide [1-3].

Adult patients with glomerulonephritis show an increased cardiovascular risk related to lipid abnormalities, coagulation abnormalities, increased sympathetic activity, and the treatment of the underlying disease [4,5]. New biochemical and imaging markers are needed to improve prediction and/or detection of cardiovascular system damage in patients at risk of atherosclerosis.

Applanation tonometry is a non-invasive method to evaluate the vascular system based on the analysis of pulse waveform in the radial artery. Pulse waveform is the sum of a wave generated by contraction of the left ventricle and propagating away from the heart within the arterial tree, and a reflected wave returning from the peripheral vessels [6]. With increased arterial stiffness, pulse wave velocity is large and the return of reflected wave coincides with the systolic phase of primary pulse wave, resulting in augmentation of late systolic aortic pressure [7]. In adult patients, the size of this augmentation of the central aortic pressure, expressed either as an absolute augmentation pressure (AP) or a relative augmentation index (AIx) was found to be an independent cardiovascular risk factor both in the general population [8-10] and in patients with renal failure [11,12].

Increased arterial stiffness evaluated by applanation tonometry was also reported in children with type 1 diabetes [13], hypercholesterolemia [14], low birth weight [15], end-stage renal failure treated with hemodialysis [16] and after kidney transplantation [17]. In addition, Yu et al. showed increased pulse wave velocity in patients with acute post-streptococcal glomerulonephritis [18]. However, there are no data in the literature regarding arterial stiffness in children with other glomerulopathies.

The aim of our study was to evaluate pulse waveform using applanation tonometry in children with glomerulonephritis.

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Material and Methods

We studied 33 children (22 boys and 11 girls) aged from 3.7 to 18.0 years (mean 13.3 ± 3.9 years) treated in the Department of Pediatric Nephrology due to glomerular disease.

In all children, arterial pulse waveform was evaluated using the Sphygmocor device (AtCor Medical, Australia). Before this evaluation, peripheral blood pressure [mm Hg] was measured oscillometrically in each patient on the right arm using the Welch Allyn ASM 300 Patient Monitor device.

Peripheral pressure waveforms were recorded from the radial artery at the right wrist, using applanation tonometry. After 20 sequential waveforms had been acquired, a validated generalized transfer function was used to generate the corresponding central aortic pressure waveform. We evaluated the following parameters: aortic systolic pressure (AoSP) [mmHg], aortic diastolic pressure (AoDP) [mmHg], aortic pulse pressure (AoPP) [mmHg], augmentation pressure (AP) [mmHg], augmentation index (AIx) [%], augmentation index corrected for heart rate of 75 beats per minute (AIx-75HR) [%], and an index of myocardial oxygen supply and demand, subendocardial viability ratio (SEVR) [%].

AP was calculated as the difference between the second (P2) and first (P1) systolic peak of the central pressure waveform. AIx was defined as the AP divided by pulse pressure and expressed as a percentage [19]. Because AIx is influenced by heart rate, an index normalized for heart rate of 75 bpm (AIx-75HR) was used [20]. SEVR was defined as the ratio of diastolic and systolic area under the curve [21].

Only high-quality recordings, defined as an in-device quality index >80%, were included in the analysis. All pulse wave analyses were performed in the sitting position in a quiet, temperature-controlled room (20 ± 5°C) after a period of rest (for at least 5 minutes).

In our clinical analysis, we also included data on the course of the underlying kidney disease including patient age at the disease onset [years], presence of hypertension and age at development of hypertension [years], and immunosuppressive and antihypertensive drugs used, body mass index (BMI) Z-score, and the following biochemical parameters: serum creatinine [mg/dL], urea [mg/dL], uric acid [mg/dL], total protein [g/dL], albumin [g/dL], calcium [mg/dL], total cholesterol [mg/dL], triglycerides [mg/dL], and daily proteinuria [mg/kg/24h]. Glomerular filtration rate was calculated using revised Schwartz formula [22]. Nephrotic-range proteinuria was defined as protein excretion >50 mg/kg/24h. The upper limit of normal cholesterol level was defined as 200 mg/dl, and the upper limit of normal triglyceride level was defined as 150 mg/dL as recommended by the American Heart Association and American Academy of Pediatrics [23].

Serum creatinine, urea, uric acid, total protein, albumin, calcium, total cholesterol, triglycerides were determined using dry chemistry (MicroSlide) and VITROS 5600 Integrated System (Ortho-Clinical Diagnostics Johnson & Johnson). Urine total protein concentration was determined using Exton's turbidimetric method.

The control group included 20 healthy children aged 8.1 to 18 years (mean 14.0 ± 3.0 years). The study and control groups did not differ significantly in regard to age and gender distribution.

Statistical analyses were performed using the Statistica 9.0 PL software (StatSoft, College Station, TX, USA). Normal variable distribution was tested using the Shapiro-Wilk test. Normally distributed variables are presented as mean values ± standard deviation, and non-normally distributed variables as medians and ranges. Differences in normally distributed variables were tested using the Student *t*-test, and differences in non-normally distributed variables were tested were tested using the Mann-Whitney U test. Differences in the frequency of analyzed variables between two groups were analyzed using the chi-square test or the Fisher exact test when appropriate. Pearson linear correlation coefficient was used to assess correlations between the variables. $P<0.05$ was considered statistically significant.

Results

Clinical characteristics of patients with glomerulopathies are shown in Table 1. Among 33 children with glomerulopathies, biopsy confirmed the diagnosis of glomerulonephritis in 30 patients. The most common diagnoses were Henoch-Schonlein nephropathy and IgA nephropathy. In three children, the clinical diagnosis of minimal change disease was made. Hypertension was diagnosed in 13 (39.4%) children aged 0.3 to 17.6 years (median 9.0 years), and duration of hypertension ranged from 1 to 144 months (median 19 months). Overweight was found in 7 (21.2%), and obesity in 6 (18.2%) children. Normal renal function was found in 22 (66.7%) children, chronic kidney disease (CKD) stage 2 in 6 (18.2%) children, CKD stage 3 in 2 (6.1%) children, and CKD stage 4 in 3 (9.0%) children. Lipid abnormalities were present in 19 (57.6%) children, including isolated hypercholesterolemia in 11 (33.3%), children, isolated hypertriglyceridemia in 3 (9.1%) children, and mixed

Age [years]	14.8 (3.7-18.0)
Boys/girls (n/n) (%/%)	22/11 (66.7% / 33.3%)
Renal disease (n) (%): **Henoch-Schonlein nephropathy** **IgA nephropathy** **Membranoproliferative glomerulonephritis** **Minimal change disease** **Focal segmental glomerulosclerosis** **Mesangioproliferative glomerulonephritis** **Other**	 9 (27.3%) 7 (21.2%) 4 (12.1%) 3 (9.1%) 3 (9.1%) 3 (9.1%) 4 (12.1%)
Presence of hypertension (n) (%)	13 (39.4%)
Age at the onset of renal disease [years]	7.9 (0.3-16.0)
Duration of renal disease [months]	31.0 (1.0-155.0)
Age at the onset of hypertension [years]	9.0 (0.3-17.5)
Duration of hypertension [months]	19.0 (1.0-144.0)
BMI Z- score	0.3 ± 1.3
Creatinine [mg/dL]	0.6 (0.3-10.1)
Urea [mg/dL]	25.0 (10.0-131.9)
Uric acid [mg/dL]	5.9 ± 2.0
GFR by Schwartz formula [mL/min/1.73m2]	110.3 (20.8-166.6)
Total protein [g/dL]	6.8 (3.4-8.1)
Albumin [g/dL]	3.8 (1.5 – 4.9)
Total cholesterol [mg/dL]	212.8 ± 60.3
Triglycerides [mg/dL]	139.6 ± 53.5
Calcium [mg/dL]	9.5 ± 0.6
Proteinuria [mg/kg/24h] n=15 (45.5%)	50.5 (4.5-322.1)
Immunosuppressive therapy	
Prednisone (n) (%) **Prednisone dose [mg/kg/24h]** **Cyclosporin A (n) (%)** **Azathioprine (n) (%)** **Mycophenolate mofetil (n) (%)**	23 (70.0%) 0.62 (0.03-1.43) 5 (15.1%) 3 (9.1%) 2 (6.0%)
Antihypertensive treatment	
Enalapril (n) (%) **Enalapril dose [mg/kg/24h]** **Losartan (n) (%)** **Amlodypine (n) (%)**	21 (66.7%) 0.11 (0.04-0.21) 5 (15.2%) 6 (18.2%)

BMI: Body Mass Index; GFR: Glomerular Filtration Rate.

Table 1: Clinical and biochemical characteristics of children with glomerulopathies.

hyperlipidemia in 5 (15.2%) children. At the time of pulse wave analysis, proteinuria was present in 15 (45.5%) children, including nephrotic-range proteinuria in 7 (21.2%) children. Immunosuppressive therapy was used in 23 (69.7%) children, including 15 (45.5%) treated with prednisone only, and 8 (24.2%) also receiving other immunosuppressive drugs. Of the latter, 3 (9.1%) received cyclosporin A, 3 (9.1%) received azathioprine, and 2 (6.0%) received cyclosporin A and mycophenolate mofetil. Among 13 (39.4%) children with hypertension, 5 (15.2%) were treated with enalapril, 5 (15.2%) with enalapril and amlodypine, 2 (6.0%) with losartan and amlodypine, and one patient (3.0%) was treated with enalapril and losartan. Nephroprotective therapy was also used in 12 of 20 (60.0%) normotensive patients, including 10 patients treated with enalapril, one patient treated with losartan, and one patient treated with enalapril and losartan.

Results of pulse wave analysis along with data on age and gender distribution in study and control groups are shown in Table 2. Compared to the control group, children with glomerulopathies were characterized by a trend for higher AP (P=0.08) and AIx (P=0.07), and significantly higher AIx-75HR (P<0.05).

Clinical and biochemical characteristics of 11 children with hypertension and 20 children without hypertension are shown in Table 3. Children with hypertension showed significantly lower total protein level (P<0.05), a trend for lower albumin (P=0.07) and calcium (p=0.07) levels, significantly lower total cholesterol level (P<0.05), and insignificantly higher proteinuria. Results of pulse wave analysis in patients with or without hypertension are shown in Table 4. Compared to normotensive children, patients with glomerulopathy and hypertension were characterized by higher mean peripheral and central diastolic pressure and higher AIx-75HR (P<0.05).

In the study group there were 15 (45%) children with proteinuria. Proteinuric patients had significantly lower concentration of total protein (6.5 (3.4-7.2) vs. 7.4 (4.7-8.1), P<0.05), albumin (3.6 (1.5-4.7) vs. 4.2 (2.0-4.9), P<0.01), and significantly higher concentration of cholesterol (250.5 ± 60.9 vs. 186.2 ± 44.7, P<0.005) and triglycerides (168.8 ± 51.8 vs. 120.7 ± 46.7, P<0.05) compared to non proteinuric patients. Results of pulse wave analysis in patients with or without proteinuria are shown in Table 5. Patients with proteinuria showed trend towards higher mean peripheral and central diastolic blood pressure (P=0,08 and P=0,07, respectively). Six among these 15 (40.0%) proteinuric patients had clinically evident overhydration with weight gain, peripheral edema, and effusions. Pulse wave parameters in this group of patients and 27 patients without overhydration were presented in Table 6. Overhydrated patients had significantly (P<0.05) higher diastolic peripheral and central diastolic blood pressure, as well as central systolic blood pressure.

Among 33 children in the study group, we found positive correlations of AoSP and AoDP with proteinuria (r=0.44, P<0.05, and r=0.57, P<0.005, respectively), and negative correlations of AoDP with albumin level (r=-0.42, P<0.05), total protein level (r=-0.36, P<0.05), and calcium level (r=-0.47, P<0.05). AoPP showed a positive correlation with BMI Z-score (r=0.43, P<0.05), and SEVR showed a negative correlation with total cholesterol level (r=-0.43, P<0.05) (Figure 1).

Parameter	Study group n=32	Control group n=20	P
Age [years]	14.8 (3.7-18.0)	14.7 (8.1-18.0)	NS
Gender (♂/♀) (n/n, %/%)	22/11 (66.7% / 33.3%)	15/5 (75.0% / 25.0%)	
SBP [mm Hg]	121.4 ± 10.9	122.4 ± 11.7	
DBP [mm Hg]	73.7 ± 10.7	70.8 ± 8.19	
PP [mm Hg]	47.7 ± 10.1	51.6 ± 9.1	
AoSBP [mm Hg]	102.8 ± 9.7	101.0 ± 9.7	
AoDBP [mm Hg]	75.7 ± 10.2	72.2 ± 8.4	
AoPP [mm Hg]	27.1 ± 5.3	31.5 ± 13.9	
AP [mm Hg]	- 0.4 ± 3.6	- 1.8 ± 2.1	P=0.08
AIx [%]	- 1.3 ± 13.3	- 6.6 ± 7.3	P=0.07
AIx- 75HR [%]	3.9 ± 15.2	- 4.2 ± 7.6	P<0.05
SEVR [%]	139.8 ± 37.6	154.0 ± 29.3	NS

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PP: Pulse Pressure; AoSBP: Aortic Systolic Blood Pressure; AoDBP: Aortic Diastolic Blood Pressure; AoPP: Aortic Pulse Pressure; AP: Augmentation Pressure; Aix: Augmentation Index; AIx- 75HR: Augmentation Index Corrected for Heart Rate of 75 Beats per Minute; SEVR: Subendocardial Viability Ratio.

Table 2: Pulse wave analysis in children with glomerulopathies and healthy controls.

Parameter	Patients with HTN n=13	Patients without HTN n=20	P
Age [years]	14.8 (6.4-17.8)	14.5 (3.7-18.0)	NS
Gender (♂/♀) (n/n, %/%)	7/6 (53.8% / 46.2%)	15/5 (75.0% / 25.0%)	
Renal disease (n) (%):			
Henoch- Schonlein nephropathy	1 (7.7%)	8 (40.0%)	
IgA nephropathy	3 (23.1%)	4 (20.0%)	
Membranoproliferative GN	3 (23.1%)	1 (5.0%)	
Mesangioproliferative GN	3 (23.1%)	0 (0.0%)	
Minimal change disease	0 (0.0%)	3 (15.0%)	
FSGS	2 (15.4%)	1 (5.0%)	
Other	1 (7.7%)	3 (15.0%)	
Age at the onset of renal disease [years]	7.9 (1.5-16.3)	9.6 (0.3-14.8)	
Duration of renal disease [months]	22.0 (2.0-144.0)	33.5 (1.0-155.0)	
BMI Z-score	0.2 ± 1.4	0.5 ± 1.2	
Creatinine [mg/dL]	0.6 (0.3-10.1)	0.6 (0.4-1.3)	
Urea [mg/dL]	31.0 (14.0-131.9)	24.0 (10.0-58.0)	
Uric acid [mg/dL]	6.5 ± 2.0	5.4 ± 2.0	
GFR by Schwartz formula [mL/min/1.73m2]	110.8 (20.8-166.6)	109.9 (50.4-137.3)	
Total protein [g/dL]	6.35 (3.8-7.8)	7.0 (3.4-8.1)	P<0.05
Albumin [g/dL]	3.6 (2.3-4.8)	4.1 (1.5-4.9)	P=0.07
Total cholesterol [mg/dL]	242.7 ± 71.5	191.7 ± 41.3	P<0.05
Triglycerides [mg/dL]	155.4 ± 60.4	129.4 ± 47.6	NS
Calcium [mg/dL]	9.32 ± 1.04	9.68 ± 1.24	P=0.07
Proteinuria n [%] [mg/kg/24h]	8 (54.5%) 80.4 (4.5-184.6)	7 (22.6%) 29.4 (6.7-322.1)	NS
Immunosuppressive therapy			
Prednisone (n) (%)	9 (69.2%)	14 (70.0%) 0.52	
Prednisone dose [mg/kg/24h]	0.96 (0.04-1.43)	(0.03-1.18)	
Cyclosporin A (n) (%)	3 (23.1%)	2 (10.0%)	
Azathioprine (n) (%)	2 (15.4%)	1 (5.0%)	
Mycophenolate mofetil (n) (%)	2 (15.4%)	0 (0.0%)	

BMI: Body Mass Index; FSGS: Focal Segmental Glomerulosclerosis; GFR: Glomerular Filtration Rate; GN: Glomerulonephritis.

Table 3: Clinical and biochemical characteristics of children with glomerulopathies with or without concomitant hypertension (HTN).

Discussion

Glomerulopathies are characterized by activation of the immune system leading to increased levels of proinflammatory cytokines,

Parameter	Patients with HTN n=11	Patients without HTN n=20	P
Age [years]	14.8 (6.4-17.8)	14.5 (3.7-18.0)	NS
Gender (♂/♀) (n/n, %/%)	7/6 (53.8% / 46.2%)	15/5 (75.0% / 25.0%)	
SBP [mm Hg]	123.4 ± 9.8	120.1 ± 11.7	
DBP [mm Hg]	78.9 ± 9.2	70.3 ± 10.4	P<0.05
PP [mm Hg]	44.5 ± 7.9	49.8 ±10.9	NS
AoSBP [mm Hg]	106.5 ±8.9	100.5 ± 9.7	P=0.08
AoDBP [mm Hg]	80.6 ± 8.4	72.6 ± 10.2	P<0.05
AoPP [mm Hg]	25.8 ± 4.5	27.9 ± 5.8	NS
AP [mm Hg]	0.8 ± 3.2	-1.2 ± 3.8	
AIx [%]	3.1 ± 11.9	-4.1±13.7	
AIx- 75HR [%]	11.3 ± 13.1	-2.5 ± 14.2	P<0.05
SEVR [%]	135.4 ± 23.3	142.7 ± 44.9	NS

SBP: Systolic Blood Pressure; DBP: diastolic blood pressure; PP: pulse pressure; AoSBP: Aortic Systolic Blood Pressure; AoDBP: Aortic Diastolic Blood Pressure; AoPP: Aortic Pulse Pressure; AP: Augmentation Pressure; Aix: Augmentation Index; AIx- 75HR: Augmentation Index Corrected For Heart Rate Of 75 Beats Per Minute; SEVR: Subendocardial Viability Ratio.

Table 4: Pulse wave analysis in children with glomerulopathies with or without concomitant hypertension (HTN).

Parameter	Patients with proteinuria n=15	Patients without proteinuria n=18	P
Age [years]	13.4 ± 3.5	13.1 ± 4.3	NS
Gender (♂/♀) (n/n, %/%)	11/4 (73.3% / 26.7%)	11 / 7 (61.1% / 38.9%)	
SBP [mm Hg]	124,1 ± 9,8	119,2 ± 11,6	
DBP [mm Hg]	77,2 ± 11,8	70,8 ± 8,9	P=0.08
PP [mm Hg]	46,9 ± 9,5	48,4 ± 10,8	NS
AoSBP [mm Hg]	105,7 ± 9,9	100,4 ± 9,1	
AoDBP [mm Hg]	79,2 ± 11,4	72,8 ± 8,3	P=0.07
AoPP [mm Hg]	26,5 ± 5,4	27,6 ± 5,4	NS
AP [mm Hg]	-0,7 ± 3,9	-0,1 ± 3,5	
AIx [%]	-3,3 ± 13,8	0,4 ± 13,1	
AIx- 75HR [%]	4,2 ± 13,4	3,6 ± 17,2	
SEVR [%]	131,8 ± 26,4	146,6 ± 44,5	

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PP: Pulse Pressure; AoSBP: Aortic Systolic Blood Pressure; AoDBP: Aortic Diastolic Blood Pressure; AoPP: Aortic Pulse Pressure; AP: Augmentation Pressure; Aix: Augmentation Index; AIx- 75HR: Augmentation Index Corrected For Heart Rate Of 75 Beats Per Minute; SEVR: Subendocardial Viability Ratio.

Table 5: Pulse wave analysis in children with glomerulopathies with or without proteinuria.

activation of the renin-angiotensin-aldosteron and sympathetic systems, frequent chronic hyperlipidemia, and the development of hypertension, with all these effects leading to vascular damage and atherogenesis [24]. In our group of children with glomerulopathies, we found higher AP (P=0.08) and AIx (P<0.05) than in the control group, indicating increased arterial stiffness compared to their healthy peers. As summarized by Schaefer, increased arterial stiffness in children with renal disease may be explained by increased sympathetic activity due to afferent renal nerve stimulation, and impaired catecholamine degradation by renalase [25-28]. Interleukin-6, a proinflammatory cytokine, may also have a role in the pathogenesis of increased arterial stiffness in glomerulopathies [29].

Our findings indicate that vascular changes develop already at an early stage of glomerulopathy, promoting increased arterial stiffness which might result in an increased risk of future cardiovascular events.

When we compared patients with or without hypertension among those with glomerulopathies, we found increased mean aortic diastolic blood pressure and increased AIx-75HR compared to normotensives. Higher augmentation index in this patient group suggests that elevated central aortic pressure is an additional cardiovascular risk factor in children with glomerulopathies. Of note, patients with hypertension were also characterized by more severe protein and lipid abnormalities which may also enhance the development of vascular changes.

Numerous studies in adult patients [9,29,30], including patients with end-stage renal failure [11] showed that elevated pulse wave analysis parameters (AIx, AIx-75HR, and AP) are risk factors for coronary artery disease. Among adult patients treated with hemodialysis, AIx-75HR was found to decrease following treatment [11], which was not confirmed in children [16]. Higher AIx was also associated with increased left ventricular mass in adults [9,31], and with smaller walking distance in patients with peripheral arterial disease [10].

Pulse wave analysis in the radial artery allows estimation of central aortic blood pressure and pulse pressure. In adults, central aortic pressure was found to be a better predictor of cardiovascular risk compared to peripheral arterial pressure [32,33]. Initial results of the Chronic Renal Insufficiency Cohort (CRIC) study in 2351 adult patients with CKD suggest that elevated central aortic pulse pressure is a risk factor for disease progression to end-stage renal failure [34].

In the studied children, we found a positive association between BMI and central aortic pulse pressure which suggests that obesity may be an additional cardiovascular risk factor in children with glomerulopathies. Unlike in adults [35], however, we did not confirm a correlation between BMI Z-score and AIx.

Our finding of a positive association between proteinuria and central aortic systolic and diastolic pressure indicates that hemodynamic changes develop in children with proteinuria. Increased sympathetic activity that might affect elevated central aortic pressure was found both in an experimental model [36] and in adult patients with nephrotic-range proteinuria [37,38]. Moreover, overhydrated proteinuric patients had significantly higher peripheral diastolic, as well as central systolic and diastolic blood pressure. Our results suggest

Parameter	Patients with overhydration n=6	Patients without overhydration n=27	P
Age [years]	14.8 (11.8-17.8)	14.8 (3.7-18.0)	NS
Gender (♂/♀) (n/n, %/%)	4/2 (67.7% /33.3%)	18 / 9 (67.7% / 33.3%)	
SBP [mm Hg]	128,7 ± 9,4	119,8 ± 10,8	
DBP [mm Hg]	83,5 ± 10,0	71,5 ± 9,7	P<0.05
PP [mm Hg]	45,2 ± 8,9	48,3±10,4	NS
AoSBP [mm Hg]	110,7 ± 8,6	101,1 ± 9,2	P<0.05
AoDBP [mm Hg]	85,2 ± 10,4	73,6 ± 9,1	P<0.05
AoPP [mm Hg]	25,5 ± 5,3	27,4 ± 5,4	NS
AP [mm Hg]	-1,8 ± 3,7	0,0 ± 3,6	
AIx [%]	-8,7 ± 16,0	0,4 ± 12,4	
AIx- 75HR [%]	0,2 ± 13,3	5,0 ± 15,7	
SEVR [%]	131,8 ± 14,4	141,6 ± 41,0	

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; PP: Pulse Pressure; AoSBP: Aortic Systolic Blood Pressure; AoDBP: Aortic Diastolic Blood Pressure; AoPP: Aortic Pulse Pressure; AP: Augmentation Pressure; Aix: Augmentation Index; AIx- 75HR: Augmentation Index Corrected For Heart Rate Of 75 Beats Per Minute; SEVR: Subendocardial Viability Ratio.

Table 6: Pulse wave analysis in children with glomerulopathies with or without overhydration.

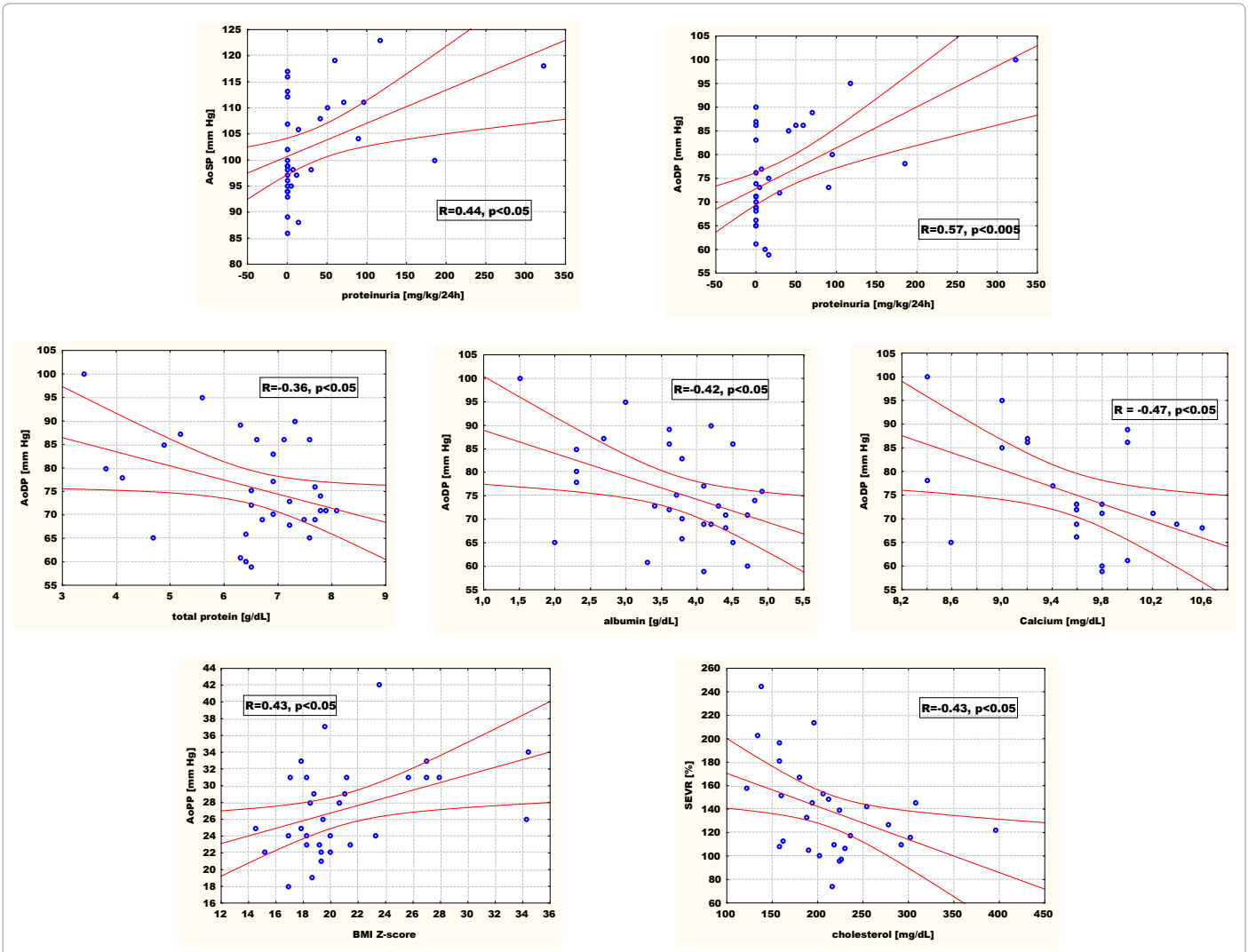

Figure 1: Correlations of AoSP and AoDP with proteinuria, of AoDP with albumin, total protein and calcium levels, of AoPP with Z-score, and of SEVR with cholesterol level.

that overhydration can increase peripheral and central blood pressure without influencing arterial stiffness.

In our study group, we noted a negative association between total cholesterol level and SEVR which suggests that in patients with hypercholesterolemia, coronary flow abnormalities lead to impaired myocardial perfusion. Abnormal pulse wave analysis parameters in children with glomerulopathy and concomitant lipid abnormalities that were found in our study suggest that this patient group may be at a higher risk of future myocardial infarction.

Further studies are necessary to evaluate arterial stiffness in children with glomerulopathies to identify predictors of cardiovascular risk in this population.

Conclusion

i. Patients with glomerulopathies show increased arterial stiffness compared to their healthy peers.

ii. In children with glomerulonephritis, hypertension is a risk factor for increased aortic stiffness, and hypercholesterolemia may be a risk factor for future myocardial ischemia.

iii. Overhydration in children with glomerulonephritis can increase peripheral and central blood pressure without influencing arterial stiffness.

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