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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Myocardial dysfunction measured by tissue Doppler echocardiography in children with primary arterial hypertension

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Abstract

Background and aim: To evaluate myocardial function with the use of tissue Doppler echocardiography in children with primary hypertension.

Methods: A total of 64 subjects (34 with hypertension, 30 control) underwent echocardiographic evaluation of systolic and diastolic function with the use of standard and tissue Doppler echocardiography parameters.

Results: The left ventricular myocardial performance index was higher in children with hypertension (0.46 ± 0.08 vs. 0.35 ± 0.03; $p < 0.01$). The value of the A wave was higher in the hypertensive children group (0.59 ± 0.12 m/s vs. 0.49 ± 0.09 m/s; $p < 0.01$), while the E/A ratio was significantly lower in this group (1.58 ± 0.31 vs. 1.77 ± 0.28; $p < 0.01$). The values of isovolumetric relaxation time and deceleration time were significantly higher in patients with blood pressure elevation. The velocity of mitral flow propagation was lower (0.61 ± 0.08 m/s vs. 0.72 ± 0.10 m/s; $p < 0.01$) and E/Vp ratio was higher (1.50 ± 0.27 vs. 1.21 ± 0.23; $p < 0.01$) in hypertensive children. Evaluation of the left ventricle function with the use of tissue Doppler echocardiography showed significantly worse values of S′ and E′ septal, and S′ and E′ lateral in hypertensive children. The value of septal E′/A′ ratio was lower in children with hypertension (1.52 ± 0.24 vs. 1.69 ± 0.25; $p < 0.01$), while the value of this index for lateral wall was similar. The values of E/E′ septal and E/E′ lateral were higher in patients with hypertension.

Conclusions: In children with primary arterial hypertension, with the use of tissue Doppler echocardiography there are significantly lower values of diastolic and systolic parameters observed, which may be a sign of myocardial function deterioration.

Key words: diastolic dysfunction, Doppler tissue imaging, echocardiography, hypertension, systolic function

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INTRODUCTION

Arterial hypertension, next to obesity and overweight, has become a serious problem in the developmental-age population. It is estimated that arterial hypertension concerns 2–5% of children and even 10% of adolescents [1]. Primary arterial hypertension is diagnosed increasingly often and in younger and younger patients. In adolescents over 12 years of age it is one of the main forms of hypertension. Early diagnostics of organ complications due to hypertension enable prevention of morbidity and mortality caused by cardiovascular disorders in adulthood [1–3]. Echocardiographic examination is the main diagnostic tool enabling noninvasive evaluation of cardiac function. Tissue Doppler echocardiography has proven to be a feasible and useful method enabling estimation of many additional systolic and diastolic function parameters and allowing the detection of early myocardial dysfunction [4–7]. In the literature there are still few publications on the application of this method in the paediatric population [6, 8–12].

The aim of the study was to assess the myocardial function in children with primary arterial hypertension with the use of the tissue Doppler method.

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METHODS

Study patients

The case-control prospective study included 34 children (27 boys, 7 girls) aged 10–18 years with primary arterial hypertension, hospitalised in 2009–2013 in the Children's Cardiology and Rheumatology Department of the 2nd Chair of Paediatrics at the Medical University of Lodz, matched to a healthy volunteer group that included 30 children (23 boys, 7 girls) with normal arterial pressure similar for age. All examined children were normal weight and with no cardiac disease.

All studied patients underwent anthropometric assessment of nutritional status (height, weight, body mass index [BMI]), manual oscillometric measurements of arterial pressure with the use of proper cuff size, and ambulatory blood pressure monitoring (ABPM). The children were enrolled to the hypertensive group if mean values of blood pressure (BP) in manual measurements were over the 95th centile for gender and growth according to the Polish norms for schoolchildren and adolescents — OLAF project and ABPM measurement recordings were at least 25% of systolic BP and/or minimum 25% of diastolic BP above the 95th centile for gender and growth, and mean values of systolic BP over 24 h were equal or above the 95th centile [13, 14].

In order to evaluate only the effect of hypertension on myocardial function we excluded patients with arterial hypertension and associated overweight or obesity. We also excluded children treated with antihypertensive drugs.

Echocardiographic examination

Echocardiographic examination was performed using an Aloka Prosound α 10 device. Each patient underwent full transthoracic echocardiographic examination with cardiac anatomy and function evaluation after ABPM. Measurements of the right and left ventricular (LV) dimensions, interventricular septal thickness, posterior wall thickness, and LV mass were made by M-mode during diastole. The LV mass index (LVMI) was estimated by the de Simone formula as recommended in children, i.e. height in metres raised to the power of 2.7.

Assessment of systolic and diastolic function was made with the use of standard and tissue Doppler echocardiographic parameters.

The shortening fraction was estimated using M-mode in the parasternal long-axis view. The ejection fraction (EF) was obtained with the use of the biplane Simpson method. The mitral inflow velocities were measured from the apical four-chamber view. Measurements included the peak early mitral inflow velocity (E wave), the peak atrial mitral inflow velocity (A wave), the E/A ratio, and the deceleration time (DT; time interval of peak E-wave velocity to its extrapolation to the baseline). Next in the apical five-chamber view isovolumetric relaxation time (IVRT) and LV myocardial performance index (LVMPI) were calculated. This index is defined as the quotient of the sum of the isovolumetric contraction time and IVRT to LV ejection time [15]. The velocity of mitral flow propagation (Vp) was obtained by measuring the slope of the first aliasing velocity from the mitral tips to a position approximately 4 cm distally into the LV. E/Vp was calculated as the ratio of peak mitral E-wave velocity divided by Vp.

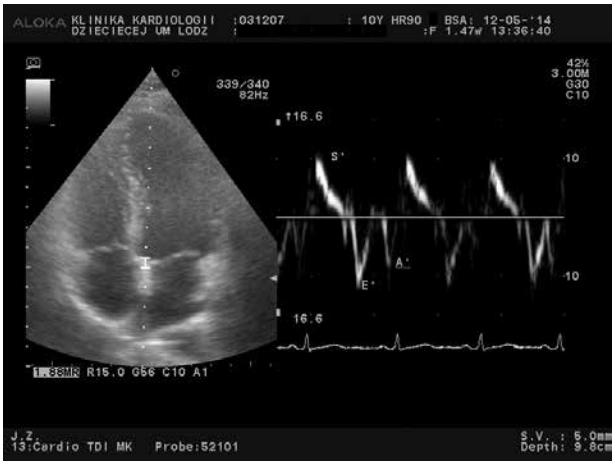

Figure 1. Tissue Doppler echocardiography velocity profile at septal mitral annulus

Colour and pulsed tissue Doppler imaging were performed in the apical four-chamber view. The filter setting was decreased to exclude high-frequency signals, and the gain minimised to allow for clear tissue signals with minimal background noise. The sample volume was positioned as parallel as possible with the lateral mitral annular motion.

The peak myocardial velocities at the interventricular septum (IVS) (septal) and lateral mitral annulus (lateral) during systole (S'), early (E'), and late (A') diastole were measured (Fig. 1). The ratio of the early to the late diastolic velocities was calculated for IVS (E'/A' septal) and for lateral wall (E'/A' lateral). The ratio of peak transmitral E velocity to early diastolic mitral annular velocity (E/E') was calculated for both IVS and lateral wall (respectively: E/E' septal; E/E' lateral). Each measurement was obtained for three cardiac cycles.

Statistical analysis

Distributions were checked for normality with the use of Kolgomorov-Smirnov test. In case of normal distribution the parameters were expressed as mean ± standard deviation. Parametric (Student's t-test) and nonparametric (Mann-Whitney) tests were performed to compare values between the examined groups. Statistical significance was defined as a p value < 0.05. The analysis of the dependence between the measured parameters was performed by calculating the Pearson correlation coefficient or Spearman's rank correlation coefficient. The statistical analysis was performed with the application of Microsoft SQL Server and PHP and Statistica version 10.

The study was approved by the Ethics Committee of the Medical University of Lodz.

Table 1. Patients' characteristics

	Study group (n = 34)	Control group (n = 30)	P
Age [years]	(10–18) 15.3 ± 2.1	(10–18) 15.4 ± 2.1	0.83
Body surface area [m^2]	1.71 ± 0.21	1.74 ± 0.25	0.60
Height [cm]	168.88 ± 11.79	172.50 ± 12.41	0.24
Weight [kg]	62.18 ± 10.95	64.20 ± 12.26	0.49
Body mass index [kg/m^2]	21.76 ± 2.05	21.33 ± 2.20	0.42
Heart rate [/min]	74.94 ± 10.90	70.60 ± 9.07	0.09

Table 2. Mean values of manual and ambulatory blood pressure (BP) measurements

	Study group (n = 34)	Control group (n = 30)	P
Systolic BP in manual measurements [mm Hg]	136.62 ± 6.01	120.37 ± 7.35	< 0.01
Diastolic BP in manual measurements [mm Hg]	78.38 ± 6.64	64.33 ± 4.30	< 0.01
Systolic BP load [%]	43.15 ± 17.05	4.70 ± 3.55	< 0.01
Diastolic BP load [%]	31.56 ± 20.16	2.03 ± 2.51	< 0.01
Systolic BP over 24 h [mmHg]	132.47 ± 5.53	118.87 ± 6.73	< 0.01

RESULTS

Physical examination did not reveal any statistically significant differences for height, weight, and BMI in the examined groups. No sex-based or racial/ethnic-based differences were present. The mean value of BMI was below the 90th centile in all patients.

Sex, age, and body surface area distribution were also comparable in both groups (Table 1).

In the hypertensive children group, both manual and ABPM measurements of arterial pressure showed statistically significant higher mean pressure values compared to the control group. All patients from the study group had the mean values of BP in manual measurements over the 95th centile for sex and height, which enabled identification of hypertension. In all those patients ABPM confirmed hypertension (Table 2).

Echocardiographic analysis

The echocardiographic LV diameters analysis did not reveal any significant difference in diastolic wall dimensions (IVS distolic dimension, LV posterior wall diameter) and the LV diameter referring to body surface area between the examined groups. In nine (26.5%) patients from the hypertensive children group there was increased IVS diastolic dimension, in four (11.8%) thickening of the LV posterior wall, and in three (8.8%) incorrect dimension of the LV lumen in diastole. In the control group all the above-mentioned parameters were within normal limits.

The LVMI according to the de Simone formula was significantly higher in children with arterial hypertension than in the control group and the LV hypertrophy, defined as LVMI over 95 centile for sex and age was observed in three (8.8%) patients only in the hypertensive children group.

The mean values of EF as well as shortening fraction (SF) did not differ significantly in the examined groups and were within normal limits. In the hypertensive group these values were respectively: EF 70.26 ± 4.99%, SF 40.41 ± 3.69%, and in the control group, respectively: EF 69.93 ± 5.64%, SF 38.70 ± 3.55%. The mean value of the LVMPI obtained in children with arterial hypertension was significantly higher than the mean value obtained in the control group (Table 3). In the study group as well as the control group there were no statistically significant correlations between myocardial performance index value and age (hypertensive group: r = 0.18, p = 0.31; control group: r = –0.15, p = 0.42), heart rate (hypertensive group: r = 0.05, p = 0.8; control group: r = –0.16, p = 0.4) or LVMI (hypertensive group: r = 0.2, p = 0.26; control group: r = 0.33, p = 0.08).

According to conventional diastolic function parameters, only the mean value of the E wave was similar between the two groups. The other diastolic function indices were significantly different. The mean value of the A wave was significantly higher in the hypertensive children group (0.59 ± 0.12 m/s vs. 0.49 ± 0.09 m/s; p < 0.01), while the mean value of E/A ratio in this group was significantly lower (1.58 ± 0.31 vs. 1.77 ± 0.28; p < 0.01). The mean values of IVRT and DT were significantly higher in patients with BP elevation (respectively: 95.32 ± 42.72 ms vs. 65.03 ± 15.41 ms; 136.32 ± 28.28 ms vs. 113.63 ± 22.18 ms). In the hypertensive children group there was positive correlation between the mean value of A wave and LVMI observed (r = 0.48; p = 0.005). On the other hand, the E/A ratio in this group of patients negatively correlated with the LVMI (r = –0.38; p = 0.03).

The mean values of velocity of mitral flow propagation and E/Vp ratio were also statistically different between the

Table 3. Echocardiographic parameters in examined groups

	Study group (n = 34)	Control group (n = 30)	P
LV dimensions			
Interventricular septum diameter [mm]	8.06 ± 1.81	7.37 ± 0.76	0.1
LV posterior wall diameter [mm]	8.12 ± 1.45	7.67 ± 0.63	0.06
LV end-diastolic diameter [mm]	45.76 ± 8.58	47.83 ± 5.08	0.25
LV mass index [g/m^2]	32.19 ± 7.33	28.05 ± 3.95	0.01
Systolic function			
Ejection fraction [%]	70.26 ± 4.99	69.93 ± 5.64	0.80
Shortening fraction [%]	40.41 ± 3.69	38.70 ± 3.55	0.06
LV myocardial performance index	0.46 ± 0.08	0.35 ± 0.03	< 0.01
Diastolic function			
E [m/s]	0.90 ± 0.10	0.85 ± 0.11	0.06
A [m/s]	0.59 ± 0.12	0.49 ± 0.09	< 0.01
E/A ratio	1.58 ± 0.31	1.77 ± 0.28	< 0.01
Deceleration time [ms]	136.32 ± 28.28	113.63 ± 22.18	< 0.01
Isovolumetric relaxation time [ms]	95.32 ± 42.72	65.03 ± 15.41	< 0.01
Vp [m/s]	0.61 ± 0.08	0.72 ± 0.10	< 0.01
E/Vp ratio	1.50 ± 0.27	1.21±0.23	< 0.01

LV — left ventricular

groups. The mean value of Vp was lower in the hypertensive children group (0.61 ± 0.08 m/s vs. 0.72 ± 0.10 m/s; $p < 0.01$), whereas the mean value of E/Vp ratio was significantly higher in those patients (1.50 ± 0.27 vs. 1.21 ± 0.23; $p < 0.01$). All these results are shown in Table 3.

Tissue Doppler echocardiography

Evaluation of the LV function with the use of tissue Doppler echocardiography showed significantly worse mean values of S' and E' septal, and S' and E' lateral in hypertensive children compared to the control group (Table 4). There was positive correlation between S' septal as well as S' lateral and age in the hypertensive group (respectively: $r = 0.39$, $p = 0.02$; $r = 0.42$, $p = 0.01$).

However, the mean values of A' septal and A' lateral did not significantly differ between the analysed groups. The mean value of the septal E'/A' ratio was significantly lower in the hypertensive children group (1.52 ± 0.24 vs. 1.69 ± 0.25; $p < 0.01$), while the mean values of this index for lateral wall were similar between the two groups. The obtained mean value of E/E' septal and E/E' lateral were significantly higher in patients with BP elevation (Table 4). There was statistically significant negative correlation between the mean value of A wave and E/E' septal ratio ($r = –0.34$; $p = 0.05$), while E/A positively correlated with this index ($r = 0.4$; $p = 0.02$).

Table 4. Tissue Doppler echocardiography parameters in examined groups

	Study group (n = 34)	Control group (n = 30)	P
Systolic function			
S' septal [m/s]	0.09 ± 0.13	0.11 ± 0.22	< 0.01
S' lateral [m/s]	0.11 ± 0.29	0.16 ± 0.33	< 0.01
Diastolic function			
E' septal [m/s]	0.14 ± 0.04	0.17 ± 0.03	< 0.01
A' septal [m/s]	0.10 ± 0.04	0.10 ± 0.03	1.00
E'/A' septal ratio	1.52 ± 0.24	1.69 ± 0.25	< 0.01
E' lateral [m/s]	0.18 ± 0.04	0.21 ± 0.03	< 0.01
A' lateral [m/s]	0.14 ± 0.18	0.13 ± 0.04	0.77
E'/A' lateral ratio	1.75 ± 0.56	1.73 ± 0.43	0.87
E/E' septal ratio	6.76 ± 1.94	5.14 ± 1.08	< 0.01
E/E' lateral ratio	5.20 ± 1.40	4.17 ± 0.62	< 0.01

DISCUSSION

To the best of our knowledge, this seems to be first study describing subclinical systolic dysfunction detected by tissue Doppler technique, despite preserved conventional systolic function parameters (EF, SF), in children with primary arterial hypertension. Our findings also confirm earlier reports on diastolic dysfunction in this group of patients [11, 16].

The increasing incidence of primary arterial hypertension in children and adolescents prompts the search for new diagnostic methods enabling early diagnosis of subclinical changes and proper treatment implementation in order prevent hypertensive heart disease in adult life.

The changes in the myocardial muscle take place in stages. Usually, prior to a systolic dysfunction, a diastolic dysfunction is observed. In arterial hypertension diagnostics, the evaluation of LV systolic and diastolic function is usually based on echocardiographic examination. The tissue Doppler echocardiography enables a precise quantitative evaluation of many additional parameters reflecting global as well as regional myocardial function [8–11, 17]. Another method of myocardial function evaluation is speckle-tracking echocardiography (STE). The advantage of this method is that it is independent from the angle of the ultrasonic beam. Hirth et al. [18] observed abnormal LV diastolic function using STE in children and adults after renal transplantation in childhood.

In our study, in line with Border et al. [11], LVMI according to the de Simone formula was significantly higher in hypertensive children compared to control group. The values of standard echocardiographic systolic parameters (EF, SF) were within normal limits and were similar in both groups of patients, which is consistent with the findings of other researchers [11, 19]. The index independent of parameters such as heart rate, respiratory movements, or chamber geometry is the LVMPI. It depends only on age. The LVMPI reaches a constant level over the third year of life when the cardiac muscle is functionally mature [20]. We confirmed this in our study. The youngest patient in our group was 10 years old; therefore, we could assume that LVMPI was fully independent. Elevation of this index indicates deterioration of LV function. The mean values of LVMPI obtained in children with arterial hypertension were significantly higher compared to the control group. Dhuper et al. [21] also found higher values of LVMPI in patients with arterial hypertension, but here hypertension was accompanied by obesity. Levent et al. [22] also showed significantly higher values of LVMPI in two groups of patients: obese children with normal BP (LVMPI 0.4 ± 0.1) and obese children with hypertension (LVMPI 0.5 ± 0.1). The evaluation of diastolic function with the use of standard echocardiographic indices revealed significantly higher values of the A wave and significantly lower values of the E/A ratio in hypertensive patients. Free inflow lower than active LV filling is associated with LV susceptibility abnormalities and is one of the symptoms of diastolic dysfunction. The mean values of early mitral inflow velocity (E wave) did not differ significantly in the examined groups. Similar findings in children with hypertension and obesity were observed by Persic et al. [23].

The significantly higher values of IVRT and DT obtained in children with hypertension also determine LV diastolic dysfunction. The IVRT itself depends on LV filling abnormalities and is the parameter that changes early. However, due to the large variability and dependence on the heart rate, it has low specificity. Therefore, an incorrect value of IVRT does not have to indicate pathology but still is a helpful indicator valued by researchers. Similar to our observations, Border et al. [11] revealed prolongation of IVRT in hypertensive children.

The mean values of velocity of mitral flow propagation were significantly lower in children with hypertension. The reduction of free inflow velocity is direct evidence of diastolic dysfunction; therefore, this parameter enables initial assessment of relaxation abnormalities and differentiation of normal and pseudo-normal mitral inflow profile.

In line with other findings, the E/Vp ratio in hypertensive children was significantly higher [11, 12]. This index is precisely connected with elevated LV end-diastolic pressure and has big prognostic value. Larrazet et al. [24] showed the advantage of this index over the E/E' ratio in the assessment of left atrial pressure in children after cardiosurgical operation.

Estimation of diastolic mitral annulus velocity profiles with the use of tissue Doppler echocardiography is a supplementing method. Border et al. [11] described diastolic function abnormalities in 1/3 of studied patients with hypertension. In children between 10 and 13 years of age early diastolic mitral annular profile (E' wave) and E/E' were abnormal in 38% of patients, whereas in children between 14 and 18 years of age the value of E' wave and E/E' ratio were abnormal, respectively, in 56% and 50% of patients. Similar to our findings, Urbina et al. [25] observed significantly higher values of the E/E' ratio for IVS as well as lateral wall in children with hypertension. Agu et al. [26] also observed higher values of the lateral wall E/E' ratio in hypertensive patients group. These researchers also found significantly lower values of the E'/A' ratio in hypertensive patients for both IVS and lateral wall. Our analysis revealed lower values of the E'/A' ratio for IVS and lateral wall in children with hypertension but statistically significant was only the septal E'/A' index [25].

The analysis of systolic mitral annular velocity profile for IVS and lateral wall showed significantly lower values in children with hypertension compared to the control group. There is no data in the literature on values of these parameters in children with primary arterial hypertension. However, in available reports on hypertension in adults, authors also observed significantly lower values of systolic mitral annular velocities, despite preserved LV systolic function using conventional parameters (EF, SF) [7, 27]. In our study we found positive correlation between systolic values of mitral annular velocity at the IVS as well as the lateral level and age in hypertensive patients, which is similar to other authors [6, 8–10].

CONCLUSIONS

Summing up, it should be noted that in children with primary arterial hypertension there are significantly worse values of diastolic and systolic parameters observed with the use of tissue Doppler echocardiography method. This finding can indicate deterioration of myocardial function. Tissue Doppler echocardiography is a useful tool in the evaluation of subclinical LV systolic dysfunction, while conventional echocardiographic parameters are still within normal limits. The wider application of tissue Doppler echocardiography may be

helpful in planning treatment of hypertension in young people as well as in monitoring the progression of organ damage, especially LV function.

Conflict of interest: *none declared*

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Zaburzenia funkcji mięśnia sercowego u dzieci z nadciśnieniem tętniczym pierwotnym: ocena z wykorzystaniem tkankowej echokardiografii doplerowskiej

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Streszczenie

Wstęp i cel: Celem pracy była ocena funkcji mięśnia sercowego z wykorzystaniem tkankowej echokardiografii doplerowskiej u dzieci z nadciśnieniem tętniczym pierwotnym.

Metody: Analizie poddano łącznie 64 dzieci (34 z nadciśnieniem tętniczym, 30 — grupa kontrolna), u których przeprowadzono echokardiograficzną ocenę funkcji skurczowej i rozkurczowej z użyciem standardowych parametrów echokardiograficznych oraz wskaźników z wykorzystaniem tkankowej echokardiografii doplerowskiej.

Wyniki: Wskaźnik globalnej wydolności mięśnia sercowego był wyższy u dzieci z nadciśnieniem tętniczym (0,5 ± 0,1 *vs*. 0,4 ± 0,03). Wartość fali A była istotnie wyższa w grupie dzieci z nadciśnieniem tętniczym (0,6 ± 0,1 m/s *vs*. 0,5 ± 0,1 m/s), podczas gdy wartość wskaźnika E/A była w tej grupie pacjentów istotnie niższa (1,6 ± 0,3 *vs*. 1,8 ± 0,3). Wartości czasu rozkurczu izowolumetrycznego i czasu deceleracji były znamiennie wyższe u pacjentów z podwyższonymi wartościami ciśnienia tętniczego. Prędkość propagacji wczesnej fali napływu mitralnego (Vp) była istotnie niższa (0,6 ± 0,1 m/s *vs*. 0,7 ± 0,1 m/s), a stosunek E/Vp był istotnie wyższy (1,5 ± 0,3 *vs*. 1,2 ± 0,2) w grupie dzieci z nadciśnieniem tętniczym. Ocena funkcji lewej komory przy użyciu tkankowej echokardiografii doplerowskiej wykazała istotnie niższe wartości profilu prędkości skurczowej (S') i prędkości wczesnoroskurczowej (E') na poziomie przegrody międzykomorowej i ściany bocznej lewej komory w grupie dzieci z nadciśnieniem tętniczym. Wartość wskaźnika E'/A' mierzonego na poziomie przegrody międzykomorowej była niższa u dzieci z nadciśnieniem tętniczym (1,5 ± 0,2 *vs*. 1.7 ± 0.3), podczas gdy wartość tego wskaźnika mierzona na poziomie ściany bocznej nie różniła się między grupami. Wartości wskaźników E/E' zarówno na poziomie przegrody międzykomorowej, jak i ściany bocznej lewej komory były wyższe u pacjentów z nadciśnieniem tętniczym.

Wnioski: U dzieci z nadciśnieniem tętniczym pierwotnym, na podstawie oceny parametrów uzyskanych z wykorzystaniem metody doplera tkankowego, obserwuje się zaburzenia funkcji rozkurczowej i skurczowej lewej komory.

Słowa kluczowe: dysfunkcja rozkurczowa, tkankowa echokardiografia doplerowska, echokardiografia, nadciśnienie, funkcja skurczowa

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