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HEART RATE VARIABILITY OF CHILDREN WITH MITRAL VALVE PROLAPSE IN ORTHOSTATIC TEST

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The purpose of the research was to study the state of autonomic regulation in prepubertal children with mitral valve prolapse during an orthostatic test

Materials and methods. The study involved 2 groups: the main – 26 children aged 10-11 years with mitral valve prolapse, and a control group – 22 relatively healthy children. The adaptive mechanisms were monitored by analyzing heart rate variability. All children participated in a cardiorythmic examination at rest lying down and during an active orthostatic test.

Results and discussion. Among the indicators that had significant differences, the indicators of regulatory process adequacy index and mode amplitude should be noted. In the group of children with mitral valve prolapse, an increase of the regulatory process adequacy index indicated the predominance of the functioning of the sinus node over the activity of the sympathetic division of the autonomic nervous system. An increase in the adequacy index and mode amplitude indicates the connection of the central structures of rhythm control (subcortical rhythms) during a change in body position. Stress index also increased. This index of tension of regulatory systems shows the activity of the mechanisms of sympathetic regulation, the state of central regulation. Children in the control group had a well-coordinated response of the sympathetic nervous system to the orthostatic test: the low frequency spectrum and very low frequency indicators increased. While in main group, the value of low frequency spectrum (the work of the sinus node) increased, the value of very low frequency (the reaction of the central structures of the nervous system) decreased. This indicates dysfunction of the most important reactions, which also affects the daily activities of children, increases the risk of mitral valve prolapse complications.

Conclusion. In children with mitral valve prolapse, the absence of a pronounced typical reaction to an ortho test is a reflection of an adaptive-regulatory overstrain in conditions of morphological determina-

cy of connective tissue dysplasia, which are trying to ensure the adequacy of intracardiac hemodynamics. The data obtained will be useful for predicting the reaction of the body of children with mitral valve prolapse to physical activity of varying intensity.

Keywords: autonomic nervous system, heart rate variability, mitral valve prolapse, orthostatic test, pediatric patients.

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Introduction. Mitral valve prolapse (MVP) in children is an urgent problem of cardiology. This is due to its high prevalence among the children's population and the risk of complications that are life-threatening. According to domestic and foreign researchers, the prevalence of MVP ranges from 2.4-5 to 10-14% [1,2]. MVP is a syndrome that refers to the sagging / bending of the mitral valve cusps into the cavity of the left atrium during systole of the left ventricle. Clinical manifestations of MVP in children can be both minimal and significant. Complications such as bacterial endocarditis, stroke, and sudden death are rare, but can occur at a younger age [3].

30% of adolescents complain of chest pain. The etiology of this pain can be caused by such reasons:

- (1) excessive tension of the chords, which in turn leads to overstretching of the papillary muscles;
- (2) spasm of the coronary arteries;
- (3) disproportionate tachycardia during physical and / or emotional stress;
- (4) hyperadrenergic status, which increases myocardial oxygen demand, impaired regulation of

renin-aldosterone, abnormal secretion of atrial natriuretic factor [1,4,5];

- (5) microembolism of the coronary arteries due to increased aggregation of platelets and fibrinous deposits located in the corner between the left atrium and the posterior mitral valve.

At present, with echocardiography in children, three degrees of MVP are distinguished: for grade I, prolapse of the mitral valve cusps reaches 3-6 mm; with II degree – 6-9 mm; and at the III degree – more than 9 mm. It was found out that for children with MVP, pronounced disturbances in the vegetative balance in the body are characteristic. This is especially true of the sympathetic part of the autonomic nervous system (ANS), which dominates in such children amid weakening of the parasympathetic section of the autonomic nervous system. Some groups of children also showed an increase in the parasympathetic tone of the ANS [2,6].

Earlier studies (Lewis, Wooley, Kolibash & Boudoulas, 1987) noted that the exact association of anatomical mitral valve prolapse (flexible valve) with neuroendocrine disorder (MVP syndrome) remains unclear [3].

To control the tone of the autonomic nervous system in patients with MVP, they began to use the HRV analysis method developed by R. Baevskii (1965, 1971) [7,8]. In a study by Han, Ho, Yip & Chan (2000), it was observed that patients had a decrease in vagus nerve tone and a predominance of sympathetic tone compared with the control group [5].

However, in the studies of Belyakova (2011), Kushnir & Beyalkova (2012), the data of the cardio-intervalogram (CIG) allowed establishing not only the fact of autonomic imbalance in the autonomic contour of autonomic regulation in children with MVP, but also a significant difference in the main focus of the initial autonomic tone depending on the degree of prolapse. Therefore, when examining children with MVP 1 degree, there was a clear predominance of sympathetic tone, while in children with MVP 2 degree it turned out that more than half of them (59.5%) had a significant shift in the autonomic balance towards pronounced vagotonia, initiated by a decrease in compensatory sympathetic activity. It is believed that prolonged diastole in bradycardia, on the one hand, leads to an increase in the volume of the left ventricle, which somewhat eliminates the “redundancy” of dysplastically modified mitral valve cusps, and on the other hand, improves blood supply to the papillary muscles, which helps to increase their tone and better tension of the chords valve [9,10].

The purpose of the research was to study the state of autonomic regulation in prepubertal children with MVP during an orthostatic test.

Materials and methods. The study was carried out on the basis of the Mykolaiv general education

sanatorium boarding school No. 7. A total of 48 children aged 10-11 years were examined. The main group consisted of 26 children with MVP 1-2 degrees (10 girls, 16 boys). Since there were no significant differences between children with grade 1 and 2 prolapse in our study, we included them into one group. The electrocardiograms (ECG) of the patients did not reveal significant changes. Marfan syndrome, neuropathy, and atrial fibrillation were excluded. The control group consisted of 22 healthy children without MVP (14 girls, 8 boys). The children took no medicine.

All experiments were conducted in accordance with the Council of Europe Convention “On the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine Application of Biological and Medicine Achievements (ETS No. 164)” dated 04.04.1997, and the Helsinki Declaration of the World Medical Association (2008). Parents of each study children signed an informed consent to participate in the study and all measures to ensure anonymity of children were taken.

The work used data on heart rate variability (HRV). All children participated in a cardiorythmic examination at rest lying down and during an active orthostatic test (AOP).

Heart rate variability was studied using the multi-functional instrument “MPFI-rhythmograph 1” by “ASTER-AYTI” (Ukraine) and the EasyHRV v.2 program. The recording time in short sections was 5 minutes with monitoring 25 mm/s, 50 mm/mV. Extrasystoles were excluded from the analysis.

The statistical characteristics of the dynamic range of cardio intervals were calculated: the number of cardio intervals (RR); time series expectation (RRNN); root mean square of the successive differences (RMSSD); standard deviation of normal values of R-R intervals (SDNN); coefficient of variation (deltaX); fraction of consecutive R-R intervals, the difference between which exceeds 50 ms (pNN50,%). The numerical characteristics of the variational pulsogram are: “Mode” (Mo), “Mode amplitude” (AMo), “Stress-index” (SI), “Vegetative rhythm index” (VRI), “Regulatory process adequacy index” (RPAI).

Spectral analysis was performed using the fast Fourier transform method. All spectral maxima and spectrum powers in ms² were determined in the following ranges: super slow range (VLF – very low frequency) – from 0.003 Hz to 0.04 Hz; range of slow waves (LF – low frequency) – from 0.04 to 15 Hz; the range of high-frequency (respiratory) waves (HF) – from 0.15 to 0.40 Hz; total spectrum power (TP) in the range from 0.003 Hz to 0.40 Hz.

Checking the sample of heart rate variability data for normal distribution showed that the bulk of the indicators did not have a normal distribution. In this regard, nonparametric methods were used for statistical

studies – the Wilcoxon test (for comparing the differences within the same group), and the Mann-Whitney test (for comparing the differences between the main and control groups). Mathematical and statistical pro-

cessing of the observation data was carried out using the IBM SPSS Statistics 23.0 program.

Results and discussion. Table 1 presents the results of the frequency characteristics of HRV.

Table 1 – Descriptive statistics and geometric indicators for HRV results in children with MVP and healthy children in an orthostatic test

Indicators	Main group (n=26)		Control group (n=22)	
	Lying	Standing	Lying	Standing
Descriptive Statistics Indicators				
HR, beat/min	86.0650 (81.64; 90.44)	104.4000 (97.13; 113.67) Z=-4.457 p<0.001*	88.1800 (77.58; 96.06) Z=-0.538 p=0.591	97.8350 (87.67; 110.30) Z=-4.042 p<0.001* Z=-1.676 p=0.094
RRNN, ms	697.100 (663.57; 734.92)	574.500 (528.15; 617.77) Z=-4.457 p<0.001*	680.800 (624.60; 773.87) Z=-0.538 p=0.591	613.300 (544.05; 684.40) Z=-4.042 p<0.001* Z=-1.655 p=0.098
SDNN, ms	50.2050 (32.96; 60.64)	39.5950 (31.03; 51.93) Z=-2.045 p=0.041*	46.9300 (40.93; 62.74) Z=-0.248 p=0.804	55.7550 (38.16; 69.56) Z=-0.081 p=0.935 Z=-1.779 p=0.075
RMSSD, ms	43.5800 (26.79; 52.52)	23.0450 (16.22; 31.27) Z=-3.848 p<0.001*	40.1400 (26.43; 72.76) Z=-0.166 p=0.869	31.0100 (19.26; 41.79) Z=-3.263 p=0.001* Z=-1.304 p=0.192
pNN50, %	19.4900 (5.4; 29.37)	3.4650 (1.04; 8.41) Z=-3.949 p<0.001*	17.1000 (5.72; 43.13) Z=-0.145 p=0.885	8.1250 (1.94; 19.83) Z=-2.902 p=0.004* Z=-1.407 p=0.159
Mode, ms	675.00 (662.5; 725.0)	575.00 (525.0; 625.0) Z=-4.425 p<0.001*	650.00 (612.50; 787.50) Z=-0.757 p=0.449	625.00 (525.0; 675.0) Z=-3.503 p<0.001* Z=-1.615 p=0.106
AMo, %	38.3700 (33.91; 52.25)	44.9800 (36.38; 53.83) Z=-1.816 p=0.069	39.8000 (33.10; 49.00) Z=-0.168 p=0.867	36.2800 (28.37; 45.57) Z=-1.153 p=0.025* Z=-2.317 p=0.02**
deltaX, ms	300.00 (200.0; 300.0)	250.00 (200.0; 300.0) Z=-1.933 p=0.053	275.00 (200.0; 350.0) Z=-0.168 p=0.885	300.00 (200.0; 350.0) Z=-0.758 p=0.449 Z=-1.324 p=0.186
Geometric indicators (by R.M. Baevskii)				
VRI, 1/s ²	4.6000 (3.91; 8.0)	6.9600 (5.33; 10.53) Z=-3.175 p=0.001*	5.4250 (3.46; 8.0) Z=-0.104 p=0.917	5.8650 (4.57; 8.90) Z=-2.068 p=0.039* Z=-1.409 p=0.159
RPAI, %/s	53.600 (46.87; 78.57)	79.000 (58.20; 101.75) Z=-3.670 p<0.001*	58.200 (40.12; 78.40) Z=-0.083 p=0.934	58.900 (42.27; 84.72) Z=-1.218 p=0.223 Z=-2.214 p=0.027**
SI, %/s ²	88.200 (66.87; 200.47)	172.650 (95.07; 285.8) Z=-2.781 p=0.005*	108.800 (57.35; 171.62) Z=-0.145 p=0.885	106.750 (62.42; 197.80) Z=-1.282 p=0.200 Z=-1.904 p=0.057

Notes: * – p<0.01, differences in the values between the indicators in lying and standing position inside each group are reliable according to the Wilcoxon criterion; ** – p<0.01, differences in the values between the main and control group are reliable according to the Mann-Whitney criterion.

Resting state indices between the group of healthy children and the group with MVP did not have significant differences. However, if we compare the indicators in the state of orthostasis, the following reactions should be noted.

Heart rate indicators in children with MVP were slightly higher than in the control group. As a result of a change in position in children with MVP, SDNN decreased, indicating a decrease in total heart rate variability.

Indicators RRNN, RMSSD, pNN50 and Mode decreased in both of groups.

Opposite reactions between the main and control groups were noted in the indicator of the mode amplitude (AMo) – in 61.5% of children with MVP group this indicator increased, and in 54.5% of healthy children it decreased. An increase in this indicator means an increase in sympatho-adrenal activity during a change in body position [11].

Analyzing the group of geometric indicators (by R. M. Baevskii), in children with MVP, an increase of the RPAI was revealed. This indicates the predominance of the functioning of the sinus node by the activity of the sympathetic division of the autonomic nervous system. Stress index (SI) also increased. This index of tension of regulatory systems shows the activity of the mechanisms of sympathetic regulation, the state of central regulation. This indicator is calculated based on the analysis of the distribution graph of the cardiointervals-variational pulsogram. Activation of the central contour, strengthening of sympathetic

regulation during mental or physical exertion, stabilization, decrease in the spread of the duration of cardiointervals, the number of intervals of the same type (increase in AMo) [12].

Table 2 presents the results of the spectral characteristics of HRV. In healthy children in the position of orthostasis, among the frequency indicators, there was a significant increase in slow-wave (LF) intervals – a normal compensation reaction to a change in body position (reflects the response of the vasomotor center through the fibers of the sympathetic nerves). An increase in heart rate due to activation of the sympathoadrenal system and the release of catecholamines into the blood on the rhythmogram is reflected in an increase in low-frequency waves.

Changes in the spectral analysis of heart rate variability in healthy children and children with MVP are shown in **Figure 1**.

In 84.6% of children with MVP, there was a significant decrease in high-frequency (HF) intervals. This indicates inhibition of the parasympathetic link of regulation. The stimulating effects on the cardiovascular system increase, the number of high-frequency respiratory waves decreases. In 68.2% of healthy children, slight increases in this spectrum were noted.

Among the spectral indicators, opposite reactions between the groups were also noted, in terms of TP – in 53.8% of children of the MVP group this indicator decreased, and in 63.6% of healthy children it increased.

Table 2 – Indicators of the spectral analysis of HRV in children with MVP and healthy children in an orthostatic test.

Indicators	Main group (n=26)		Control group (n=22)	
	Lying	Standing	Lying	Standing
TP, ms ²	1468.50 (847.25; 2253.50)	1433.50 (829.25; 2055.0) Z=-0.775 p=0.439	1445.00 (1088.0; 2071.75) Z=-0.414 p=0.679	1903.500 (1196.50; 3484.75) Z=-1.477 p=0.140 Z=-1.531 p=0.126
VLF, ms ²	532.50 (227.25; 881.50)	467.00 (329.50; 796.25) Z=-0.610 p=0.542	541.00 (403.0; 978.50) Z=-1.066 p=0.287	807.00 (373.25; 1308.0) Z=-1.623 p=0.105 Z=-1.945 p=0.052
LF, ms ²	457.00 (265.25; 803.25)	577.00 (361.50; 901.0) Z=-1.130 p=0.258	398.50 (291.50; 671.25) Z=-0.310 p=0.756	622.00 (436.50; 1340.50) Z=-2.873 p=0.004* Z=-0.797 p=0.426
HF, ms ²	432.00 (271.75; 659.50)	232.00 (158.50; 363.75) Z=-3.518 p<0.001*	432.00 (159.0; 809.25) Z=-0.145 p=0.885	379.50 (183.75; 598.75) Z=-1.753 p=0.080 Z=-1.552 p=0.121
LF/HF	1.1600 (0.80; 2.19)	2.7350 (1.94; 3.43) Z=-3.480 p=0.001*	1.1150 (0.62; 1.98) Z=-0.238 p=0.812	2.0550 (1.66; 3.02) Z=-3.328 p=0.001* Z=-1.635 p=0.102

Notes: * – p<0.01, differences in the values between the indicators in lying and standing position inside each group are reliable according to the Wilcoxon criterion.

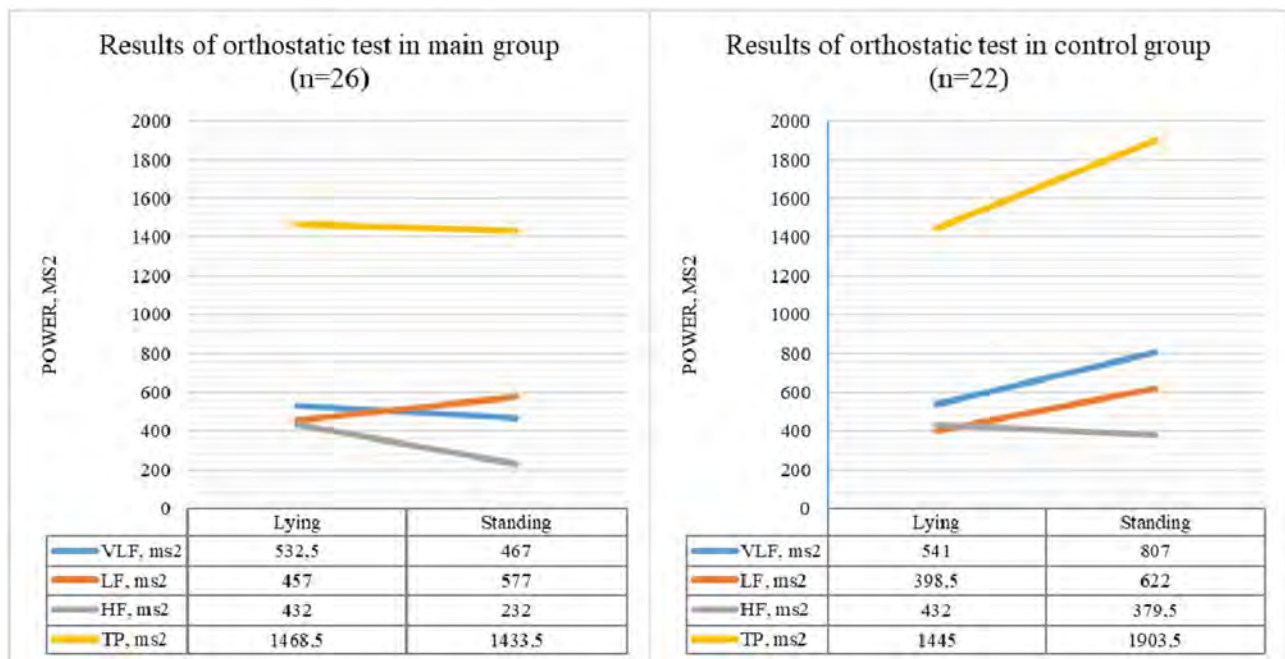


Fig. 1. Comparison of the results of an orthostatic test in main and control group

As shown in the figure, children in the control group have a well-coordinated response of the sympathetic nervous system to the orthostatic test: the LF and VLF indicators increase. While in main group, the value of LF (the work of the sinus node) increases, and the value of VLF (the reaction of the central structures of the nervous system) decreases. This indicates dysfunction of the most important reactions, which also affects the daily activities of children, increases the risk of MVP complications.

The study showed that the orthostatic load in children with MVP according to the indicator of the total spectrum power (TP, ms²) was accompanied by rather low values of changes in the wave characteristics of heart rate variability with a minimum frequency shift from the initial value. It is confirmed by the law of Weidler (1950) on the role of the initial values of the

function in the formation of the tension of the compensatory mechanisms in response to disturbing stimuli.

Conclusion. In children with MVP 1-2 degrees, the absence of a pronounced typical reaction to an orthotest is a reflection of adaptive-regulatory overstrain in conditions of morphological determinacy of connective tissue dysplasia, which are trying to ensure the adequacy of intracardiac hemodynamics.

The results of the study confirm the presence of a compensatory mechanism for regulating HRV in the form of a decrease in the work of the parasympathetic division of the ANS and the central contour of the nervous system during the orthostatic test.

Further research will focus on studying the control of the autonomic nervous system during exercise and developing criteria for a safe level of physical activity in children with MVP.

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ВАРІАБЕЛЬНІСТЬ СЕРЦЕВОГО РИТМУ У ДІТЕЙ З ПРОЛАПСОМ МІТРАЛЬНОГО КЛАПАНА В ОРТОСТАТИЧНІЙ ПРОБІ

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Резюме. Мета дослідження - вивчити стан вегетативної регуляції у дітей препубертатного віку з пролапсом мітрального клапана під час ортостатичної проби.

Об'єкт та методи. У дослідженні взяли участь 2 групи: основна - 26 дітей 10-11 років з пролапсом мітрального клапана та контрольна група - 22 здорових дитини. За адаптивними механізмами стежили за допомогою аналізу варіабельності серцевого ритму. Всі діти брали участь в кардіоритмічному обстеженні в спокої лежачи і під час активної ортостатичної проби.

Результати. Серед показників, що мали достовірні відмінності, слід відзначити показник адекватності процесів регуляції і амплітуду моди. У групі дітей з пролапсом мітрального клапана збільшення показника адекватності процесів регуляції свідчить про переважання функціонування синусового вузла. Підвищення амплітуди моди свідчить про підвищення симптоадреналової активності при зміні положення тіла. Індекс стресу також збільшився, що свідчить про активність механізмів симпатичної регуляції, переважання центральної регуляції. У дітей контрольної групи спостерігалася злагоджена реакція симпатичної нервової системи на ортостатичну пробу: збільшилися показники низькочастотного спектра (LF) і дуже низьких частот (VLF). У той час як в основній групі значення LF (робота синусового вузла) збільшується, а значення VLF (реакція центральних структур нервової системи) знижується. Це вказує на дисфункцію найбільш важливих реакцій, що також впливає на повсякденну діяльність дітей, збільшує ризик ускладнень пролапсу мітрального клапана.

Висновки. У дітей з пролапсом мітрального клапана відсутність вираженої типової реакції на ортотест є відображенням адаптивно-регуляторного перенапруги в умовах морфологічної детермінованості дисплазії сполучної тканини, які намагаються забезпечити адекватність внутрішньосерцевої гемодинаміки. Отримані дані будуть корисні для прогнозування реакції організму дітей з пролапсом мітрального клапана на фізичні навантаження різної інтенсивності.

Ключові слова: вегетативна нервова система, варіабельність серцевого ритму, пролапс мітрального клапана, ортостатична проба, діти.

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ВАРІАБЕЛЬНОСТЬ СЕРДЕЧНОГО РИТМА У ДЕТЕЙ С ПРОЛАПСОМ МИТРАЛЬНОГО КЛАПАНА В ОРТОСТАТИЧЕСКОЙ ПРОБЕ

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Довгань А. В., Куртасанов С. А., Ткаченко М. П.**

Резюме. Цель исследования - изучить состояние вегетативной регуляции у детей препубертатного возраста с пролапсом митрального клапана во время ортостатической пробы.

Объект и методы. В исследовании приняли участие 2 группы: основная – 26 детей 10-11 лет с пролапсом митрального клапана и контрольная группа – 22 здоровых ребенка. За адаптивными

механізмами следили при допомозі аналізу варіабельності серцевого ритма. Все діти брали участь у кардіоритмічному обстеженні в спокої лежачи і в час активної ортостатичної проби.

Результати. Серед показувачів, мавши достовірні відмінності, слід відзначити показувач адекватності процесів регуляції і амплітуду моди. В групі дітей з пролапсом мітрального клапана збільшення показувача адекватності процесів регуляції свідчить про перевагу функціонування синусового вузла. Підвищення амплітуди моди свідчить про зростання симпатико-адреналової активності при зміні положення тіла. Індекс стресу також збільшився, що вказує на активність механізмів симпатическої регуляції, перевагу центральної регуляції. У дітей контрольної групи спостерігалася спокійна реакція симпатическої нервової системи на ортостатичну пробу: збільшилися показувачі низькочастотного спектра (LF) і дуже низьких частот (VLF). В той час як в основній групі значення LF (робота синусового вузла) збільшується, а значення VLF (реакція центральних структур нервової системи) зменшується. Це вказує на дисфункцію найбільш важливих реакцій, що також впливає на повсякденну діяльність дітей, збільшує ризик ускладнень пролапсу мітрального клапана.

Висновки. У дітей з пролапсом мітрального клапана відсутність вираженої типової реакції на ортотест є відображенням адаптивно-регуляторного перенапруження в умовах морфологічної детермінованості дисплазії з'єднувальної тканини, які намагаються забезпечити адекватність внутрисерцевої гемодинаміки. Отримані дані будуть корисні для прогнозування реакції організму дітей з пролапсом мітрального клапана на фізичні навантаження різної інтенсивності.

Ключові слова: вегетативна нервова система, варіабельність серцевого ритма, пролапс мітрального клапана, ортостатична проба, діти.

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