Myocardial hypertrophy and intracardial hemodynamics in children with bicuspid aortic valve

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Bicuspid aortic valve is one of the most common congenital heart diseases with low manifestation in childhood and severe consequences in adults that determines the importance in early diagnostics of myocardial changes in this anomaly. According to the literature the polymorphisms in the genes of *NFATC* family could result both in impaired embriogenetic valves formation and development of postnatal myocardial hypertrophy.

The aim of the study was to detect the early changes of intracardial hemodynamics at aortic valve in children with bicuspid aortic valve (BAV) and establish their interrelations to the signs of myocardial hypertrophy in these children.

Materials and methods: Dopplerograhphic study of basic intracardiac hemodynamics parameters in 38 children with BAV and in 28 children of control group was conducted. The results were processed statistically by Student's t-test, correlation analysis and multiple regression.

Results: In the result of study the moderate concentric left ventricle myocardial hypertrophy development was detected in 62 % of children with BAV which is accompanying to significant increasing of blood flow velocity and pressure gradient at aortic valve. There were not established significant correlations between the parameters of hemodynamics at valve and left ventricle's posterior wall depth and septum depth whereas the highest inputs of these values were obtained in the left ventricle systolic dimension and volume and less in the hypertrophic signs.

Conclusions: In children with BAV the moderate concentric myocardial hypertrophy with significant changes of intracardial hemodynamics at aortic valve takes place with the highest inputs in left ventricle volumetric values The obtained data serves as a substantiation for the treatment and prevention of it further development.

Гіпертрофія міокарда та внутрішньосерцева гемодинаміка в дітей із двостулковим аортальним клапаном серця

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Двостулковий аортальний клапан є однією з найпоширеніших вроджених вад серця, котра має малосимптомний перебіг у дитинстві та важкі прояви в дорослому віці, що визначає важливість ранньої діагностики змін у міокарді при цій аномалії. Згідно з науковими літературними даними, поліморфізми генів сімейства *NFATC* можуть впливати як на ембріогенетичний формування клапанів серця, так і на розвиток постнатальної гіпертрофії міокарда.

Мета роботи – визначення ранніх змін внутрішньосерцевої гемодинаміки на аортальному клапані в дітей із двостулковим клапаном серця (ДАК) і встановлення взаємозв'язків цих параметрів із показниками гіпертрофії міокарда.

Матеріали та методи. У 38 хворих із ДАК та у 28 умовно здорових дітей контрольної групи здійснили доплерографічне дослідження параметрів внутрішньосерцевої гемодинаміки зі статистичним опрацюванням даних за критерієм Стьюдента, методами кореляційного аналізу та множинної регресії.

Результати. У результаті дослідження в 62 % хворих із ДАК встановлена наявність помірної концентричної гіпертрофії міокарда, що поєднувалася зі значним підвищенням градієнта тиску та швидкості кровотоку на аортальному клапані. Водночас не встановили значущих кореляцій між параметрами гемодинаміки на клапані та товщиною задньої стінки лівого шлуночка й міжшлуночкової перетинки з наявністю найбільших внесків даних, що отримали, в систолічний об'єм і розмір лівого шлуночка та менших – у показники, що відбивають міокардіальну гіпертрофію.

Висновки. У дітей із ДАК наявна помірна концентрична гіпертрофія міокарда лівого шлуночка, що супроводжується суттєвими змінами гемодинаміки аортального клапана з найбільшим впливом цих змін на волюметричні показники лівого шлуночка.

Гипертофия миокарда и внутрисердечная гемодинамика у детей с двустворчатым аортальным клапаном сердца

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Двустворчатый аортальный клапан является одним из наиболее распространённых врождённых пороков сердца, имеет малосимптомное течение в детском возрасте и тяжёлые осложнения у взрослых, что определяет важность ранней диагностики изменений в миокарде при этой патологии. Согласно научным литературным данным, полиморфизмы генов семейства NFATC могут влиять как на эмбриогенетическое формирование клапанов сердца, так и на развитие постнатальной гипертрофии миокарда.

Цель работы – определение ранних изменений внутрисердечной гемодинамики на аортальном клапане у детей с двустворчатым клапаном сердца (ДАК) и выявление взаимосвязей этих параметров с показателями гипертрофии миокарда.

Материалы и методы. У 38 больных с ДАК и у 28 условно здоровых детей контрольной группы было проведено допплерографическое исследование параметров внутрисердечной гемодинамики с последующей статистической обработкой полученных данных при помощи критерия Стьюдента, методами корреляционного анализа и множественной регрессии.

Результаты. В результате исследования у 62 % больных с ДАК установлено наличие умеренной концентрической гипертрофии миокарда, которая сочеталась с повышением градиента давления и скорости кровотока на аортальном клапане. В то же время не выявлено значимых корреляций между параметрами гемодинамики на клапане и толщиной задней стенки левого желудочка и межжелудочковой перегородки при наличии наибольших вкладов полученных параметров в систолический объём и размер левого желудочка и, соответственно, меньших – в показатели, отражающие гипертрофию у этих больных.

Выводы. У детей с ДАК имеет место умеренная концентрическая гипертрофия миокарда левого желудочка, которая сопровождается существенными изменениями гемодинамики аортального клапана с наибольшим влиянием этих изменений на волюметрические показатели левого желудочка.

Introduction

Congenital heart defects (CHD) in children has recently attracted the attention of the medical community. The permanent increasing in CHD incidence could be attributed to environmental influence producing genotoxic effects as well as infections during pregnancy affecting the genome at formation the heart structure. At the same time, in the general structure of CHD there is also a growing number of cardiac defects involving valve abnormalities, and, as we know, the consequences of these defects in the form of acute cardiovascular events occur mainly in adulthood. Nevertheless, until recently the most widespread CHD like bicuspid aortic valve (BAV) with the populational prevalence is from 10 to 20 cases per 1000 was considered as the small anomaly of the heart. That's why the problem of children management with BAV currently remains quite actual [1,2]. First of all, because oBAV is the most widespread congenital heart disease which is mainly revealed occasionally by heart ultrasound and has low manifestation during childhood. In adults the defect is complicated with aortal dissection, aortal valve failure and aortal stenosis [3]. At the same time, this anomaly is often accompanied by other aortal defects and genetic syndromes [4,5]. It is also must be emphasized that one of the BAV manifestations is the myocardial hypertrophy with slow progression caused either by morphologic and functional features of this CHD or by independent co-morbid condition related to polymorphisms of NFATC genes that, by turn, leads to formation of valve anomalies within the embryogenesis and postnatal stress-induced myocardial hypertrophy. These genes are represented by 5 modifications with an expression in different tissues and also participate in hypertrophic response of bones and heart muscles. From the other hand, in some studies the role of NFATC proteins in development of cardiac dysfunction and myocardial hypertrophy was proven [6,7].

The aim of the study was to detect the early changes of intracardial hemodynamics at aortic valve in children with BAV and established their interrelations to the signs of myocardial hypertrophy in this cohort of patients.

Materials and methods

There was conducted a study of basic dopplerographic parameters in 38 children with BAV. In the control group 28 healthy children without differences in their age, sex and body weight compared to BAV patients were included (10.2 y. o. ± 0.7 y. o. and 10.9 y. o. ± 0.8 y. o. respectively;

p > 0.05, BMI 17.08 kg/m² ± 0.70 kg/m² and 18.9 kg/m² ± 0.84 kg/m² respectively; p > 0.05). Most of patients in both comparable groups were the boys (28 (75 %) and 17 (62 %) respectively; p > 0.05). All the children were free of signs of heart failure. Dopplerographic study was conducted with "Medison – 8000" scaner and 2.5 MHz transducer with detection of dopplerographic data and calculation of left ventricle myocardial mass by Devereux R. B. – 1.04 [(LVold + VSd + LVPWd)³ – LVold³] -13,6) [8] and index of left ventricle myocardial mass – by P. Gosse – M/H²·⁷ [9], where the LVold is left ventricle diastolic volume in ml, VSd is diastolic ventricular septum depth in mm, LVPWd is left ventricle posterior wall depth in mm, M is left ventricle mass and H is height were done to all children. The relative left ventricle posterior wall depth (rLVPWd) was calculated by Ganau (2*LVPWd/LVDd) [10], where LVPWd is the left ventricle posterior wall depth and LVDd is the left ventricle diastolic dimension. The left ventricle geometry type was established by P. Verdecchia [11] in dependence of left ventricle myocardium mass index and relative left ventricle posterior wall depth values. The data were processed consequently with Statistica 6.0 program by using Student t-test, Spearman correlations and multiple regressions by counting the beta regression coefficients. The study was approved by the Ethics Committee of the Hospital and Medical University. The informed consent from the parents was taken.

Results and discussion

At the first stage of the study the comparative analysis of basic anatomical data and heart hemodynamics in two above mentioned groups of patients was conducted. This data is represented in the *Table 1*.

As it is shown in *Table 1* there are basic signs of disorders in heart hemodynamics concerned to bloodstream at aortal valve with an essential increasing of peak flow velocity (6.90 m/s ± 3.67 m/s against 0.97 m/s ± 0.05 m/s respectively; p < 0.05) and peak pressure gradient (17.56 mm Hg ± 3.89 mm Hg and 3.38 mm Hg ± 0.33 mm Hg respectively; p < 0.05) that was in correspondence to this anomaly. There was also the established increasing of left ventricle mass (146.51 g ± 30.4 g against 80.13 g ± 12.01 g in control group; p < 0.05) and index of left ventricle mass (61.37 g/m²·⁷ ±17.51 g/m²·⁷ and 27.97 g/m²·⁷ ± 4.46 g/m²·⁷ respectively; p < 0.05). In 24 from 38 patients with BAV the left ventricle posterior wall depth (LVPWd) and ventricular septum depth was more than 8 mm and their rLVPWd was 0.49 mm ± 0.04 mm compared to those with LVPWd

Table 1. Morphologic and functional echodopplerographic signs in children with bicuspid aortic valve and in the control group

Parameters of heart hemodymamics	M ± m	
	Children with BAV, (n = 38)	Control, (n = 28)
PA (diameter of pulmonary artery), mm	19.35 ± 0.49	19.25 ± 0.42
Ao (diameter of aorta), mm	19.36 ± 3.06	19.25 ± 0.46
Left atrium longitudinal dimension, mm	25.82 ± 1.11	22.91 ± 0.94
Left atrium transversal dimension, mm	24.72 ± 0.74	22.94 ± 0.83
Right atrium longitudinal dimension, mm	25.89 ± 1.11	23.68 ± 1.03
Right atrium transversal dimension, mm	25.00 ± 0.78	23.18 ± 0.85
Right ventricle longitudinal dimension, mm	44.7 ± 1.31	43.24 ± 1.46
Right ventricle transversal dimension, mm	22.43 ± 0.54	21.94 ± 0.57
LVDd (left ventricle diastolic dimension), mm	41.42 ± 1.37	40.61 ± 1.11
LVDs (left ventricle systolic dimension), mm	25.39 ± 1.06	26.25 ± 0.93
LVold (left ventricle diastolic volume), ml	81.9 ± 6.64	75.57 ± 5.43
LVols (left ventricle systolic volume), ml	26.06 ± 2.86	26.33 ± 2.35
S Vol (systolic volume), ml	56.41 ± 4.32	50.78 ± 3.19
Ejec F (ejection fraction), %	69.57 ± 1.26	66.71 ± 1.05
VSd (ventricular septum depth), mm	8.35 ± 0.40	7.24 ± 0.28
LVPWd (left ventricle posterior wall depth), mm	8.37 ± 0.41	7.21 ± 0.26
MVV (mitral valve peak bloodstream velocity), m/s	0.91 ± 0.04	0.89 ± 0.05
MVPG (mitral valve peak pressure gradient), mm Hg	7.87 ± 3.86	5.39 ± 3.55
AVV (aortal valve peak bloodstream velocity), m/s	6.90 ± 3.67*	0.97 ± 0.05
AVPG (aortal valve peak pressure gradient), mm Hg	17.56 ± 3.89*	3.38 ± 0.33
TVV (tricuspid valve peak bloodstream velocity), m/s	2.15 ± 1.51	7.99 ± 4.99
TVPG (tricuspid valve peak pressure gradient), mm Hg	4.49 ± 2.81	4.75 ± 3.57
PAV (pulmonary artery peak bloodstream velocity), m/s	6.24 ± 3.69	4.52 ± 3.57
PAVPG (pulmonary artery valve peak pressure gradient), mm Hg	8.82 ± 3.60	10.77 ± 4.85
LVMM (left ventricle myocardial mass), g	146.51 ± 30.4*	80.13 ± 12.01
ILVMM (index of left ventricle myocardial mass), g/m$^{2.7}$	61.37 ± 17.51*	27.97 ± 4.46
rLVPWd (relative left ventricle posterior wall depth), mm	0.41 ± 0.02*	0.35 ± 0.01

*: $p < 0.05$.

less than 8mm where this value was 0.34 mm ± 0.01 mm ($p < 0.05$). In the same time, indexes of left ventricular myocardial mass were 104.25 g/m$^{2.7}$ ± 33.10 g/m$^{2.7}$ and 42.66 ± 17.13 g/m$^{2.7}$ respectively ($p < 0.05$). Thus, in 63.2 % of these patients with increasing both relative LVPWd and index of left ventricle mass the concentric hypertrophy of left ventricle took place, whereas in other 14 patients (36.8 %) there was normal left ventricle geometry. In addition, there was not any significant difference revealed with the parameters of heart hemodynamics at aortal valve and dimensions of heart chambers in children with BAV and control group. This has led to the systematic study of the correlation relationship between the LVPWd, VSd and aortal valve's hemodynamics in patients with BAV. The obtained data is represented in *Table 2*. As it is shown in *Table 2*, both in children with BAV and control group the most significant correlations between the left ventricle posterior wall depth and ventricular septum depth to the diameters of aorta and pulmonary artery, transversal dimension of left atrium, longitudinal and transverse dimension of right ventricle, left ventricle diastolic dimension and the diastolic volume were obtained. Comparatively to the control group in children with BAV there were not significant correlations between left atrium longitudinal dimension and LVPWd (R = -0.04), VSd (R = 0.1), LVDs and LVPWd (R = 0.11) to VSd (R = 0.16), LVol s or LVPWd and VSd (R = 0.25 and 0.58 respectively; $p < 0.05$), PAV or LVPWd (R = -0.11) and VSd (R = -0.09).

At the same time, in BAV patients the significant correlations between right atrium transverse dimension or LVPWd and VSd were found (R = 0.37; $p < 0.05$ and R = 0.45; respectively, $p < 0.05$), that distinguishes this group of patients from the in control. It should be also emphasized that comparatively to control in children with BAV the opposite direction of LVPWd or VSd and Ejec F correlations with low values of coefficients were found (R = 0.32 and R = -0.34 respectively; $p < 0.05$).

The other feature of conducted correlation analysis in children with BAV was an absence of significant inter-relations between the blood flow velocity at aortal valve and LVPWd or VSd. In both above mentioned groups the obtained correlation coefficients to the aortal valve pressure gradient were non significant.

Thus, despite the stated increase of bloodstream velocity and pressure gradient at aortic valve in BAV children, these parameters of intracardiac hemodynamics were not influenced significantly on the myocardial hypertrophy whereas in control group the medium and high level of interrelations were established (*Table 2*). Based on obtained data the individual comparative inputs of peak AVPG and peak AVV in the LVPWd and VSd were estimated by multiple regression method in children with BAV and in control group.

These data is shown in the *Table 3*. As it is seen from the *Table 3*, the mentioned parameters of hemodynamics at aortal valve had small inputs on LVPWd and VSd either in BAV children or in control. It also should be noted, that highest significant inputs in heart chambers dimensions in the control group were the peak pressure gradient into the left atrium longitudinal dimension (beta = 1.57) and peak bloodstream velocity with negative input value into the atrium's transversal dimension (beta = -0.81).

Taking into account the opposite direction of these inputs it could be assumed an adaptation influence of pressure gradient increasing at aortal valve into left atrium lengthening as well as flow velocity into decreasing of their transversal dimension respectively, that is, the general elongation of left atrium in the control group in response to increasing of blood flow and pressure gradient at aortal valve was marked. On the other hand, these tendencies were not seen in children with BAV in whom the increased LVPWd took place.

Based on these results the inputs of blood flow parameters at aortic valve into left ventricle hemodynamics in both groups of patients were established. The data are represented in the *Table 4*.

In *Table 4* it is shown that in children with BAV in comparison to the control the highest inputs had the valve's pressure gradient into LVDs (-2.43 against 0.71 respectively; $p < 0.05$), gradient pressure and blood flow velocity into LVold (1.50 against -1.33 respectively; $p < 0.05$ and 1.50 against -1.08 respectively; $p < 0.05$) and the blood flow velocity into S Vol. However, the inputs of mentioned blood flow parameters at the aortal valve into the LVPWd and VSd were insignificant both as in control as in children with BAV.

Thus, the marked signs of left ventricular hypertrophy in children with BAV did not have direct interrelations with the parameters of hemodynamics at aortal valve. It should be also emphasized that in BAV children the total

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number of obtained significant correlations compared to the control group were less both to LVPWd (3 against 9, respectively) and to VSd (11 against 13 respectively). The results of multiple regression analysis in children with BAV showed an absence of important inputs of aortal valve's hemodynamics into left atrium dimensions compared to the control, which has become the another confirmation of early myocardial desadaptive changes in this cohort of patients.

At the same moment, in children with BAV the significant influences of the aortal valve bloodstream velocity on the left ventricle diastolic parameters and on the sys-

Table 2. Correlation coefficients (R) between left ventricle posterior wall (LVPWd) and ventricular septum (VSd) depths and the parameters of heart hemodynamics in children with bicuspid aortic valve and in the control group

Parameters of hemodynamics	R (p)			
	LVPWd		Vsd	
	BAV	control	BAV	control
PA (diameter of pulmonary artery), mm	0.37 (0.02)	0.62 (<0.01)	0.34 (0.03)	0.66 (<0.01)
Ao (diameter of aorta), mm	0.41 (<0.01)	0.64 (<0.01)	0.36 (0.02)	0.67 (<0.01)
Left atrium longitudinal dimension, mm	-0.04 (0.8)	0.34* (0.05)	0.1* (0.54)	0.38 (0.03)
Left atrium transversal dimension, mm	0.35 (0.03)	0.39 (0.02)	0.50 (<0.01)	0.44 (<0.01)
Right atrium longitudinal dimension, mm	0.25 (0.12)	0.26 (0.14)	0.37 (0.02)	0.30 (0.08)
Right atrium transversal dimension, mm	0.37 (0.02)	0.24 (0.17)	0.45 (<0.01)	0.28 (0.1)
Right ventricle longitudinal dimension, mm	0.61 (<0.01)	0.55 (<0.01)	0.61 (<0.01	0.60 (<0.01)
Right ventricle transversal dimension, mm	0.51 (<0.01)	0.47 (<0.01)	0.48 (<0.01)	0.49 (<0.01)
LVDd (left ventricle diastolic dimension), mm	0.45 (0.04)	0.65 (<0.01)	0.47 (<0.01)	0.69 (<0.01)
LVDs (left ventricle systolic dimension), mm	0.11 (0.51)	0.67* (<0.01)	0.16 (0.31)	0.70* (<0.01)
LVold (left ventricle diastolic volume), ml	0.40 (0.01)	0.62 (<0.01)	0.43 (<0.01)	0.64 (<0.01)
LVols (left ventricle systolic volume), ml	0.26 (0.1)	0.55 (<0.01)	0.25 (0.12)	0.58 (<0.01)
S Vol (systolic volume), ml	0.49 (0.01)	0.60 (<0.01)	0.50 (<0.01)	0.63 (<0.01)
Ejec F (ejection fraction), %	0.32 (0.04)	-0.34* (0.03)	0.29 (0.07)	-0.38* (0.01)
MVV (mitral valve peak bloodstream velocity), m/s	-0.12 (0.47)	0.05 (0.81)	0.009 (0.95)	0.10 (0.59)
MVPG (mitral valve peak pressure gradient), mm Hg	-0.04 (0.83)	0.19 (0.32)	0.06 (0.74)	0.15 (0.45)
AVV (aortal valve peak bloodstream velocity), m/s	0.23 (0.17)	-0.33* (0.08)	0.19 (0.24)	-0.33* (0.09)
AVPG (aortal valve peak pressure gradient), mm Hg	0.18 (0.26)	-0.03 (0.85)	0.20 (0.22)	-0.04 (0.86)
TVV (tricuspid valve peak bloodstream velocity), m/s	-0.01 (0.95)	-0.26 (0.18)	0.13 (0.45)	-0.33 (0.09)
TVPG (tricuspid valve peak pressure gradient), mm Hg	0.04 (0.83)	-0.18 (0.36)	0.12 (0.49)	-0.25 (0.21)
PAV (pulmonary artery peak bloodstream velocity), m/s	-0.11 (0.50)	-0.53* (<0.01)	-0.09 (0.58)	-0.58* (<0.01)

*: statistic significance between correlation coefficients.

Table 3. The inputs of peak pressure gradient and peak bloodstream velocity at aortic valve into heart chamber dimensions in children with bicuspid aortic valve by the data of obtained regression quotients (beta) compared to control group

Parameters of hemodynamics	peak bloodstream velocity		peak pressure gradient	
	BAV	control	BAV	control
Left atrium longitudinal dimension, mm	-0.65	1.08	-0.45	1.57*
Left atrium transversal dimension, mm	-0.14	-0.81*	-0.30	-0.71
Right atrium longitudinal dimension, mm	0.62	-0.70	0.88	-0.81
Right atrium transversal dimension, mm	-0.07	0.97	-0.31	0.19
Right ventricle longitudinal dimension, mm	-0.09	-0.03	-0.08	-0.21
Right ventricle transversal dimension, mm	-0.21	-0.32	-0.34	0.05
VSd, mm	0.23	0.16	-0.11	0.31
LVPWd, mm	-0.16	-0.45	0.51	-0.38

*: p < 0.05.

Table 4. The inputs of peak bloodstream velocity and peak gradient pressure at aortic valve into the left ventricle hemodynamics, left ventricle posterior wall depth and ventricular septum depth by the data of obtained regression coefficients (beta) in children with bicuspid aortic valve compared to control group

Parameters of hemodynamics	AVV		AVPG	
	BAV	control	BAV	control
LVDd (left ventricle diastolic dimension), mm	-2.96*	1.42*	-2.43*	0.71
LVDs (left ventricle systolic dimension), mm	-0.03	-0.18	-0.16	-0.15
LVold (left ventricle diastolic volume), ml	1.50*	-1.08	1.51*	-1.33
S Vol (systolic volume), ml	1.40*	0.31	0.80	1.05
Ejec F (ejection fraction), %	-0.25	-0.18	0.0001	-0.64
VSd, mm	-0.13	-0.56	0.1	-0.32
LVPWd, mm	0.19	0.16	0.13	0.11

*: p < 0.05; **AVV**: arterial valve bloodstream velocity; **AVPG**: arterial valve pressure gradient.

tolic volume were obtained, that were correspondent to decreasing of left ventricle diastolic dimension and to compensatory increasing of the ejection fraction in LVPWd and VSd thickening.

Conclusions

1. In children with BAV the parameters of hemodynamics at aortal valve have the highest inputs into the left ventricle diastolic dimension, systolic dimension and volume.

2. In children with BAV in absence of the heart failure and clinical manifestations the moderate concentric hypertrophy of left ventricle takes place which is combined to significant disorders of intracardial hemodynamics at aortic valve.

3. The detected features of myocardial hypertrophy in its early manifestation in children with BAV create a theoretical substantiation for the prevention, diagnostics and therapy of this anomaly.

References

[1] Hales, A. R., & Mahle, W. T. (2014) Echocardiography screening of siblings of children with bicuspid aortic valve. *Pediatrics*, 133, e1212. doi: 10.1542/peds.2013-3051.

[2] Petit, C. J., Gao, K., Goldstein, B. H., Lang, S. M., Gillespie, S. E., Kim, S. I., & Sachdeva, R. (2016) Relation of Aortic Valve Morphologic Characteristics to Aortic Valve Insufficiency and Residual Stenosis in Children With Congenital Aortic Stenosis Undergoing Balloon Valvuloplasty. *Am J Cardiol.,* 117(6), 972. doi: 10.1016/j.amjcard.2015.12.034.

[3] Siu, S. C., & Candice, K. (2010) Bicuspid aortic valve disease. *Journal of the American College of Cardiology*, 55(25), 2789–2800. doi: 10.1016/j.jacc.2009.12.068.

[4] Hanedan Onan, S., Baykan, A., Sezer, S., Narin, F., Mavili, E., Baykan, Z., et al. (2016) Evaluation of cardiovascular changes in children with BAVS. *Pediatr Cardiol.*, 37(3), 472–481. doi: 10.1007/s00246-015-1302-6.

[5] Calloway, T. J., Martin, L. J., Zhang, X., Tandon, A., Benson, D. W., & Hinton, R. B. (2011) Risk factors for aortic valve disease in bicuspid aortic valve: A family-based study. *American journal of medical genetics,* 155(5), 1015–1020. doi: 10.1002/ajmg.a.33974.

[6] Lunde, I. G. (2011) Molecular mechanisms of heart failure; Nuclear Factor of Activated T-cell (NFAT) signaling in myocardial hypertrophy and dysfunction. Dissertation for the degree of Philosophiae Doctor (PhD). Oslo, Norway. Series of dissertations submitted to the Faculty of Medicine, University of Oslo, №1307.

[7] Wu, B., Baldwin, H. S., & Zhou, B. (2013) Nfatc1 directs the endocardial progenitor cells to make heart valve primordium. *Trends in Cardiovascular Medicine,* 23(8), 294–300. doi: 10.1016/j.tcm.2013.04.003.

[8] Devereux, R. B., Alonso, D. R., Lutas, E. M., Gottlieb, G. J., Campo, E., Sachs, I., & Reichek, N. (1986) Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am. J. Cardiol.*, 57(6), 450–458. https://doi.org/10.1016/0002-9149(86)90771-X.

[9] Gosse, P., Jullien, V., Jarnier, P., Lemetayer, P., & Clementy, J. (1999) Echocardiographic definition of left ventricular hypertrophy in the hypertensive: which method of indexation of left ventricular mass? *J. Hum. Hypertens.*, 13(8), 505–9.

[10] Ganau, A., Devereux, R. B., Roman, M. J., de Simone, G., Pickering, T. G., Saba, P. S., et al. (1992) Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J. Am. Coll. Cardiol.*, 19(7), 1550–1558. doi: 10.1016/0735-1097(92)90617-V.·

[11] Verdecchia, P., Porcellati, C., Zampi, I., Schillaci, G., Gatteschi, C., Battistelli, M., et al. (1994) Asymmetric left ventricular remodeling due to isolated septal thickening in patients with systemic hypertension and normal left ventricular masses. *Am. J. Cardiol*, 73(4), 247–52. doi: https://doi.org/10.1016/0002-9149(94)90228-3.

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