ORIGINAL ARTICLE

INSTRUMENTAL MARKERS OF THE RIGHT VENTRICLE FUNCTIONAL CONDITION WITH TISSUE DOPPLER IN CHILDREN WITH TETRALOGY OF FALLOT AFTER SURGICAL CORRECTION AND THEIR CONNECTION WITH VALVULAR FUNCTION OF PULMONARY ARTERY

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ABSTRACT

The aim: To improve efficacy of the right ventricle functional condition evaluation in children with tetralogy of Fallot after surgical correction by estimation of instrumental markers of myocardial dysfunction.

Materials and methods: We completely examined 35 children with tetralogy of Fallot after their surgical correction at the age of 3 – 17 years. For all the patients was presented tissue doppler. We evaluated peak myocardial velocities of right ventrical in different phases of the heart cycle (S, E`, A`), tricuspid annular plane systolic excursion (TAPSE), diastolic myocardial velocities ratio (E/E`), peak myocardial velocity during isovolumic contraction (IVV), isovolumic relaxation time (IVRT).

Results: All children of the study group had pulmonary insufficiency of different severity with main predominance of mild pulmonary regurgitation (20 patients, 57,14±8,36 %). Children with tetralogy of Fallot after surgical correction were admitted with: decreased TAPSE up to 1,39±0,28 cm, decreased S` up to 8,00±1,90 cm/s, and decreased IVV up to 5,69±0,95 cm/s that is significantly lower results of the healthy children. Severe pulmonary regurgitation usually followed by high chances of the right ventricle systolic dysfunction, exactly with: decresed TAPSE<1,5 cm (OR=0,500; 95% CI 0,323 – 0,775), S`<8,1 cm/s (OR=0,600; 95% CI 0,420 – 0,858) and IVV<5,9 cm/s (OR=0,250; 95% CI 0,117 – 0,534). As well we admitted significant decline of the velocities in earl and end diastole periods to compare with the results of the control group (E`= 12,11±1,22, A`= 4,56±0,92 cm/s (P=0,009 and P=0.0002)), boost of the E/E` ratio – 7,96±2,33 (P=0.01) and decline of the RV IVRT up to 43,49±6,04 ms (P=0.017).

Severe pulmonary regurgitation followed by high chances of the right ventricle systolic dysfunction development with TAPSE <1,5 cm (OR=0,500; 95% CI 0,323 – 0,775), S`<8,1 cm/s (OR=0,600; 95% CI 0,420 – 0,858) and IVV<5,9 cm/s (OR=0,250; 95% CI 0,117 – 0,534). As well we noticed high chances of the E/E`ratio > 6,0 in 1,5 times (95% CI 1,072 – 1,903) and decreased E` <12,2 cm/s (OR=0,200; 95% CI 0,083 – 0,481).

Conclusions: Apart of clinical symptoms of the heart failure in children with tetralogy of Fallot after surgical correction markers of the right ventricle myocardial dysfunction are presented by indices of myocardial velocities, received during tissue doppler in different phases of the heart cycle.

KEY WORDS: tetralogy of Fallot, children, right ventricle, myocardial dysfunction

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INTRODUCTION

Dominant position in a structure of congenital abnormalities is settled by congenital heart diseases that are more than 30-34 % among all the hereditary defects. According to 2016 analyze through European countries, as well North and South America, Asia, Russia and Ukraine – all of them occupy the same level around 8-10 children per 1000 newborns. In case of natural currency of the congenital heart disease (CHD) mortality rate can be above 40 %, though up to 70 % of children have no any chance to live up to the end of the first year of life [1,2,3].

One of the most common and complicated CHD is a tetralogy of Fallot (TF) – the most obvious "cyanotic" heart disease, that happens 1 in 3500 newborns, and the second for its frequency that has rate closely 7-10 % through all heart abnormalities [2]. Without surgical correction hemodynamic disorders and chronic hypoxemia lead to death in a short term in infant period and average duration of life of such patients doesn't exceed 12-15 years, the second decade of life will be just in 8 % of the patients [2]. Opposite all the above, majority of children that passed surgical correction of TF, for the long time don't have any clinical symptoms, as well as physical activity the same as in absolutely healthy kids [2]. At the same time residual pathology – as obstruction of the right ventricle outflow and chronic pulmonary regurgitation (PR) lead to progressive cardiomegaly, dilation and dysfunction of the right ventricle (RV). It is important to understand that diastolic dysfunction of the RV has asymptomatic course and in its majority manifests before systolic dysfunction,

Table I. Echocardiography indicators of the RV systolic function in children with TF and different stages of pulmonary regurgitation

RV systolic function indicators	Regurgitation severity			
	Mild n=20	Moderate n=10	Severe n=5	P value
TAPSE, (cm)	1,52±0,31	1,23±0,11	1,25±0,15	P=0.38
S`, (cm/s)	9,03±1,93	6,56±0,56	6,76±0,21	P=0.23
IVV , (cm/s)	6,28±0,54*	5,16±0,16**	4,40±0,29	P=0.005

* – the diffidence is significant between group of the mild and severe PR; ** – P=0.040 – the diffidence is significant between group of the mild and severe PR.

Table II. Echocardiography indicators of the RV diastolic function in children with TF and different stages of pulmonary regurgitation

RV diastolic function indicators	Regurgitation severity			
	Mild n=20	Moderate n=10	Severe n=5	P value
E`, (cm/s)	12,80±1,06	11,41±0,56	10,74±0,91	P=0.25
A`, (cm/s)	5,03±0,35*	3,84±1,31	4,10±0,19*	P=0.029
E/E`	6,52±1,29*	8,28±1,72	10,66±1,42*	P=0.042
IVRT, ms	43,85±5,56	40,60±3,89	47,80±9,14	P=0.48

* - the diffidence is significant between group of the mild and severe PR.

that is why clinical features by themselves cant be the only markers for heart failure (HF) estimation. That is why active search of the laboratory and instrumental markers that confirm development of myocardial dysfunction on preclinical stage is done.

THE AIM

The aims of this study were to improve efficacy of the RV functional condition diagnostic in children with TF after surgical correction by estimation of the noninvasive instrumental markers of the myocardial dysfunction.

MATERIALS AND METHODS

We had examined 35 children with TF after surgical correction at the age diapason between 3 – 17 years. Average age of the patients was 9,60±4,71 years. Al the children of the main group were divided according to the duration of the postoperative catamnesis on – up to 5 years and more than 5 years – 12 (34,28±8,02 %) andi 23 (65,71±8,03 %) children totally. For control group we examined 40 healthy children from 9 months up to 18 years (average age 9,44± 0,71 years).

Echocardiography (Echo-CG) was done for all the children with US-scanner «Phillips HDIIXE» by sensor from 3,5 to 7 MHz. The Echo-CG protocol was regulated according to Recommendations for Quantification Methods During the Performance of a Pediatric Echocardiogram: A Report From the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council 2010 with tissue doppler in impulse regime (TDI). With M-mode we checked tricuspid annular plane systolic excursion – TAPSE. TDI with myocardial velocity estimation was done on lateral part of the tricuspid fibrotic annular. As well we measured peak myocardial systolic velocities (S`), peak diastolic earl (E`) and late (A`) velocities, ratio E/E`, velocity during isovolumic contruction of the RV (IVV), isovolumic relaxation time of the RV (IVRT).

Results were statistically proceeded with computer programs IBMSPSS Statistics, version 12 (20). All data were expressed as mean ±SD. Estimation of differences between average meanings was done by coefficient «t» to Students method, percentage values were detected by Fishers method. Approvement of the differences was counted by standard possibility (p) – p<0,05. For difference between comparative values was evaluated ratio of risks. Assessment of the degree of influence of factor characteristics was evaluated by odds ratio for 95%.

RESULTS

All the children after surgical correction of TF had residual pathology: pulmonary insufficiency (mild – 57,14 %, moderate – 28,57 %, severe – 14,28 %) with constant PR of mild degree and residual pressure gradient on pulmonary artery was 10,83±4,45 mmHg. Children didn't have any complains during the examination period as well they were not detected with symptoms of HF during clinical examination.

Results of TDI in different phases of cardiac cycle and TAPSE in children with TF and group of control:

Results of TDI presented decreased meanings of velocity indices of RV myocardial contractions in children with TF after surgical correction to compare with a group of the healthy children, especially declined TAPSE to 1,39±0,28 cm (P=0,029), that on 35,05 % lower healthy children

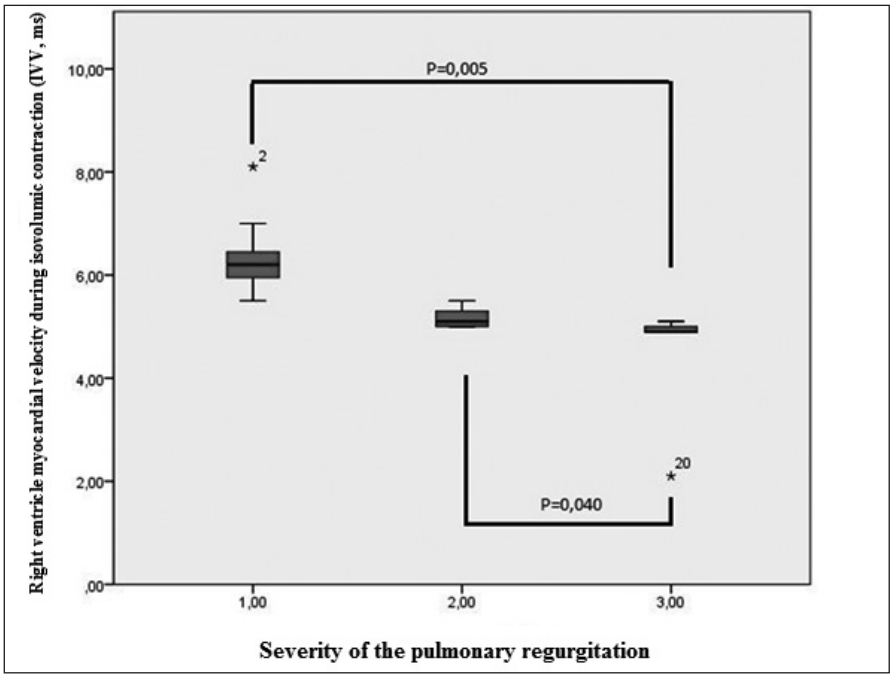

Fig. 1. Right ventricle myocardial velocity during isovolumic contraction (IVV) depending on severity of the pulmonary regurgitation.

result, declined S` to 8,00±1,90 cm/s (P=0,031), that lower results of the control group on 37,5 %, declined IVV to 5,69±0,95 cm/s (P=0.034), that on 33,91 % lower the estimated results of the healthy children.

As well we admit significant decline of the velocity indexes in earl and late diastole to compare with control group results (E`= 12,11±1,22, A`= 4,56±0,92 cm/s (P=0,009 and P=0.0002)), increasing ratio E/E` – 7,96±2,33 (P=0.01) and decreased IVRT RV to 43,49±6,04 ms (P=0.017), that indicated worsening of the RV relaxation in patients with TF after surgical correction to compare with healthy children.

TDI results in different phases of the heart cycle and TAPSE in children with TF according to stage of regurgitation on valve of pulmonary artery:

While studying correlation between stage of regurgitation on pulmonary artery valve and RV myocardial systolic function, we found out that TAPSE and peak myocardial systolic velocity S` didn't have any significant difference in varying degrees of PR (P=0,38 and P=0,23, accordingly) (tab.1).

At the same time IVV of the RV in case of severe PR was (4,40±0,29 cm/s) and was significantly lower than in case of mild (6,28±0,54 cm/s, P=0,005) and moderate (5,16±0,16 cm/s, P=0,040) (fig. 1).

As well we estimated that more intense PR usually followed by rising of the chance of systolic dysfunction of the RV with decreasing of TAPSE<1,5 cm (OR=0,500; 95% CI 0,323 – 0,775), S`<8,1 cm/s (OR=0,600; 95% CI 0,420 – 0,858) та IVV<5,9 cm/s (OR=0,250; 95% CI 0,117 – 0,534).

Investigation of the relaxation parameters of the RV according to the increase in degree of PR demonstrated that E` and IVRT RV didn't differ significant in three study groups. At the same time result of A` was significantly lower in case of severe PR (4,10±0,19 cm/s), than in variant of mild (5,03±0,35 cm/s, P=0,029) (Tab. 2).

Ratio of diastolic velocities on tricuspid valve demonstrated that progression of PR follows by significant elevation of E/E` ratio (P=0.042) and in severe case was 1,6 times higher than in mild variant (Fig. 2).

We estimated that chance to decrease results of the RV myocardial diastolic function correlates with the stage of PR , especially E` <12,2 cm/s (OR=0,200; 95% CI 0,083 – 0,481), that confirm rising of the unfavorable risk for RV diastolic function in severe variant of PR. As well we noticed increased chance of diastolic velocity ratio E/E` > 6,0 (OR=1,429; 95% CI 1,072 – 1,903), that indicates worsening of the relaxation characteristics of the RV in severe PR.

TDI results in different phases of the heart cycle and TAPSE in children with TF according to the duration of the postoperative follow-up:

Peculiarities of the RV myocardial function during systole in children with TF didn't differ in groups before 5 and after 5 years of the patients follow-up (Tab. 3).

Indices of the RV myocardial diastolic function as well were not different in children with period before 5 and after 5 years of the follow-up that indicates earl formation of the relaxation disorders and poor ability of the RV myocardium to compensate residual hemodynamic overloads after surgical correction of the TF (Tab. 4).

Evaluation of the recovery of RV myocardial functionality demonstrated that in postoperative catamnesis over 5 years chance to improve peak diastolic velocity of the tricuspid valve annular lateral part in earl diastole E` rises 2,78 times (OR = 2,783; 95% CI 1,007 – 7,690). Chance to improve other indices of the RV myocardial diastolic function wasn't significant (A` , (cm/s) (OR = 1,18; 95% CI 0,636 – 1,967); E/E` (OR = 1,357; 95% CI 0,635 – 2,899) IVRT, ms (OR = 1,148; 95% CI 0,519 – 2,539)).

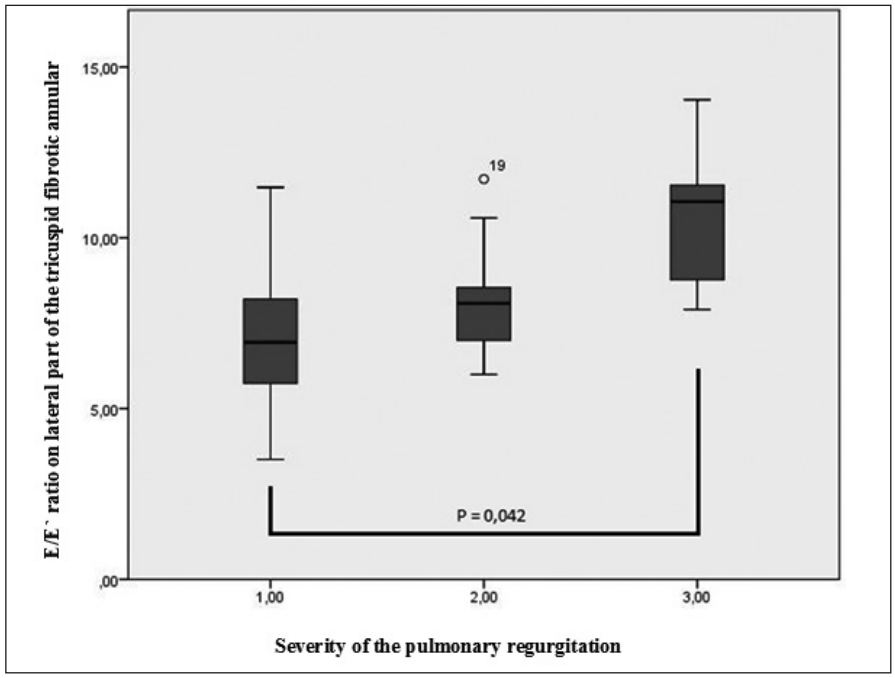

Fig. 2. E/E` ratio depending on severity of the pulmonary regurgitation

Table III. Echocardiography indicators of the RV systolic function in children with TF according to the duration of the postoperative period

Indicator	Children with TF, n=35		P value	Healthy children, n=40	P value
	Before 5 years, n=12	After 5 years, n=23			
TAPSE, (cm)	1.31±0.23*	1.44±0.29	P=0.72	2,14±0,19	P=0.0076
S`, (cm/s)	7.63±1.80*	8.19±1.96	P=0.83	12,80±1,09	P=0.017
IVV , (cm/s)	5.56±0.52*	5.76±1.11**	P=0.87	8,61±0,99	P=0.027

** P=0.12 – the diffidence is significant between results of the children with follow-up period over 5 years and healthy children.

Table IV. Echocardiography indicators of the RV diastolic function in children with TF according to the duration of the postoperative period

Indicator	Children with TF, n=35		P value	Healthy children, n=40	P value
	Before 5 years, n=12	After 5 years n=23			
E`, (cm/s)	11.38±1.02*	12.48±1.17	P=0.48	16,19±0,91	P=0.00094
A`, (cm/s)	4.63±0.53*	4.52±1.08	P=0.92	9,00±0,71	P=0.00001
E/E`	7.67±3.08	8.11±1.90*	P=0.90	1,81±0,17	P=0.0016
IVRT, ms	44.67±5.31*	42.87±6.40	P=0.83	60,68±3,61	P=0.016

* - the diffidence is significant between results of the children with different duration of the postoperative period.

DISCUSSION

Children after surgical correction of TF usually have residual pathology that influences on functional condition of RV, that possible may lead to development of myocardial dysfunction. Majority of them after the surgical correction for the long period of time stay assymptomatic that is why active search of the instrumental markers of the HF allows influence on their treatment in time.

Evaluation of the RV in children with TF while using standard echo methods causes several complications due to three anatomical parts places in three squares and can`t be visualized in two-dimensional Echo-CG [4,5]. RV has trabecular structure that complicates estimation of its borders. As well most of the muscle fibres of the RV have longitudinal position that is why determination of its contractility should be done at the same square [6].

TDI – is noninvasive methods that allows estimate longitudinal movement of the RV walls in different phases of the heart cycle and according to the results of myocardial velocities evaluate both systolic and diastolic function. Method is common and easy for calculation with normal reference values available for the pediatric population [7, 8, 9].

By Saxena N and others was estimated that S` of the RV at the level of the lateral part of the tricuspid valve > 10,5 cm/s associated with satisfactory RV function and normal pulmonary artery pressure. But in other studies was

demonstrated that TAPSE< 11.5 cm associated RV EF < 45 % with sensitivity 90 % and specify 85% [10].

In a study of 183 children with TF S`was compared to RV ejection fraction and RV end-diastolic index according to з magnetic resonance imaging (MRI). According to the results of the study S` correlated with RV ejection fraction (r = 0,66, P<0,001) and got negative correlation with S` and RV end diastolic volume index (r = -0,59, P<0,001), that allows to use TDI as alternative method instead of MRI for evaluation of the RV without additional radiation exposure [11]. In our study we checked for the correlation between echo signs of the RV systolic function (TAPSE, S`, IVV) and different stages of the PR. We estimated that TAPSE and S` doesn't have any significant difference in variety of pulmonary regurgitation stages but we found chances for the RV systolic dysfunction in case of more intense PR, lowering of the TAPSE<1,5 cm (OR=0,500; 95% CI 0,323 – 0,775), S`<8,1 cm/s (OR=0,600; 95% CI 0,420 – 0,858) and IVV<5,9 cm/s (OR=0,250; 95% CI 0,117 – 0,534).

E/E` ratio – is an integral sign with the meaning that positively correlates with the pressure of the ventricular filling. In NORRE Study, 2015 p. results of adult population presented for the RV and normal counted E/E` ratio <15 [12]. In our study we estimated correlation between E/E` ratio and stage of the PR. As well we found chance of the increase of E/E` ratio > 6.0 (OR=1,429; 95% CI 1,072 – 1,903), that indicates worsening of the relaxation characteristics of the RV in case of severe PR.

According to the type of the diastolic dysfunction E`, A`, and IVRT can be changed. With results of Radosław Pietrzak and Bożena Werner presented that velocity indices of E` and A`for RV in children with TF after surgical correction were 6,5±2,8 cm/s and 3,8±1,5 cm/s, and were lower than results of the control group (16,2±3,4 cm/s and 7,8±2,0 cm/s) [13]. In a study conducted by Savaş Demirpençe and others reflected similar results during the examination of the children with treated TF (E` – 0,11±0,03 m/s A` – 0,07±0,02 m/s), that is lower than results of the healthy children [14]. In our study we checked velocity indices that characterize relaxation ability of the RV and received similar results (E` – 12,11±1,22 cm/s A` – 4,56±0,92 cm/s), that was lower than results from the control group. Bülent Koca and others in their study compared results received during TDI and heart MRI. Their data shows that velocity indices get through out TDI can be used during follow-up in children with operated TF, but they didn't find any correlation between data received from the heart MRI [15].

Our study shows that some peculiarities of the RV myocardial contractility and relaxation doesn't differ in children before 5 and after 5 years of the follow up that confirm earl formation of the relaxation disorders and poor ability of the RV myocardium to compensate residual hemodynamic overloads after surgical correction of the TF.

CONCLUSIONS

In a practice of the family doctors, general practitioners, pediatricians , pediatric cardiologists should be counted influence of the residual pathology in case of TF after the surgical correction on functional condition of the RV. Except symptoms of the heart failure, earl indicators of the RV myocardial dysfunction are presented by myocardial velocities during TD in different phases of the heart cycle.

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Conflict of interest:
The Authors declare no conflict of interest.

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