American Journal of Medicine and Medical Sciences 2023, 13(10): 1469-1472
DOI: 10.5923/j.ajmms.20231310.23

Correlation Analysis in Assessing the Development of Pulmonary Hypertension in Children with Congenital Heart Defects

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Abstract Pediatric hypertensive vascular lung disease associated with congenital heart defects (CHD) is a condition in which the average pressure in the pulmonary artery (PA) at rest, determined by cardiac catheterization, is ≥2.0 mm Hg, and the general pulmonary resistance (OLS) is ≥ 3 U/ m2 for CHD with biventricular hemodynamics. [2,5].

Keywords Pulmonary hypertension, In children, Congenital heart defects, Endothelin-1, VEGF, NT-proBNP, Interleukin 1, Mean pulmonary artery pressure

1. Introduction

The development of hypertensive pulmonary vascular disease in CHD with abnormal intracardiac blood discharge depends on the anatomical variant, the size of the defect, and the volume of blood discharge through the defect. Children with не корригированнымиuncorrected common arterial trunk, transposition of great vessels with DMV, non -restrictive DMV and OAP are at risk for the earliest development of pulmonary vascular disease. The late-risk group consists of children with an atrial septal defect. The rate of development of pulmonary vascular disease also depends on the genetic predisposition. [8,9,10]

Numerous biomarkers have been shown to carry prognostic significance in PH and to correlate with other predictors of outcome. As CHD–PH differs significantly to other types of PH in terms of cardiac physiology and prognosis, it is indeed a worthwhile endeavor reviewing the evidence related to this expanding group of patients. In the present systematic review, we sought to evaluate the literature on the role of NT-proBNP, ED-1, and VEGF in the diagnosis, clinical management and prognosis of patients with CHD–PH. [6]

Objective: to analyze immunological and echocardiographic data using correlation.

2. Materials and Methods

For the period from 2019 to 2022, 139 children with congenital heart defects were examined and dynamically monitored (clinical base clinic TashPMI). Clinical symptoms of the disease, PH degree and functional class, hematological parameters, coagulogram, echocardiography, markers of endothelial dysfunction were analyzed at the beginning of the study - when the patient was admitted to the observation in the TashPMI clinic.

EchoCG diagnostics of heart damage was mainly performed at the TashPMI clinic, with color Doppler mapping performed on the Logic 400 device, according to an extended protocol, including assessment of the right heart using tissue pulse Dopplerography, standard approaches and positions were used, in accordance with ESC/ASE recommendations.

For the immunological study, blood was centrifuged at 3000 rpm. for 5 minutes to produce plasma, which was stored in a deep-freeze freezer (-80 gr. C) until the study is conducted: Todetect markers of endothelial dysfunction (ET-1, VEGF, IL - 1) and the concentration of the N-terminal fragment of the brain natriuretic peptide in the blood serum of patients by ELISA test systems, we used an automated HUMAREADER HS immunochemiluminescence analyzer (Biomedica, Germany).

Correlation analysis correlation dependence was performed to identify the statistical relationship of two or more random variables using the Pearson (r) method.

3. Research Results

The analysis of the parameters of the right heart was carried out using ultrasound assessment of the heart and large vessels, determining the severity of pulmonary

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Received: Aug. 7, 2023; Accepted: Sep. 16, 2023; Published: Oct. 10, 2023
Published online at http://journal.sapub.org/ajmms

vascular resistance. It was found that as the severity of arterial hypoxemia increases and the level of Npro-BNP increases, the stiffness of the vascular wall in the channel of the small circle increases and, accordingly, the increase in blood pressure in the pulmonary artery (Fig. 1).

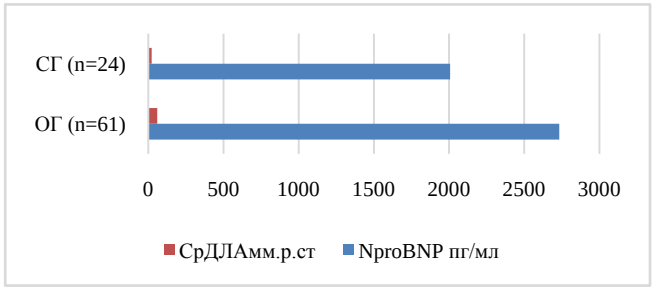

Figure 1. Indicators of pulmonary hypertension in children with congenital heart defects

So, in patients of the main group, the average value of systolic pressure in the pulmonary artery (SDLA) was 55 mm Hg, arterial hypoxemia was most pronounced: oxygen saturation at rest was 89.8%.

According to most researchers, in CHD with pulmonary hypertension, echocardiography can be used to assess the parameters of the right heart and determine early changes in the right heart to determine the possibility of surgical correction of the defect, and it is also possible to observe the rate of progression of right ventricular failure. [1,3,4].

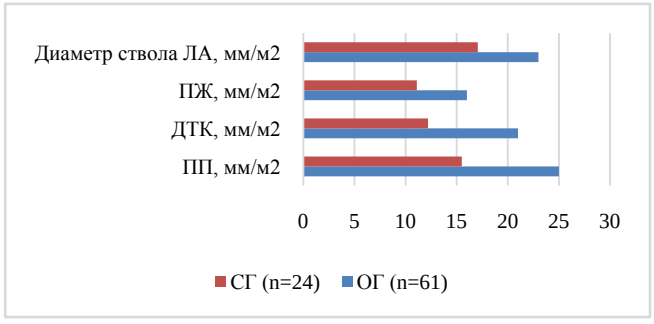

Figure 2. Morphological characteristics of the right heart in children with congenital heart defects

Our study shows that in the main group, when assessing the diameters of the right atrium, the size increased 2 times more from the comparison of the control group and 1.6 times more than the comparison group, and the diameter of the right ventricle, respectively, increased more than 2 times, due to the formation of myocardial hypertrophy. The increase in cavities contributed to the stretching of the atrioventricular ring of the tricuspid valve – its value was twice as high as the control level, and the expansion of the pulmonary artery trunk was also detected more than 2 times than the control group.

In all groups of observed patients, as well as in children of the control group, the functional state of the endothelium was studied by determining a number of functional characteristics of the endothelium: levels of endothelin 1, proinflammatory cytokine interleukin-1, as well as vascular endothelial growth factor in comparison with the severity of polycythemia, hypoxemia according to blood gas composition and blood coagulation system parameters.

We identified markers that cause the development of pulmonary hypertension due to the above mechanisms in our study patients. 3). The more the endothelium is affected, the more PH progresses and the level of ET-1 in plasma increases.

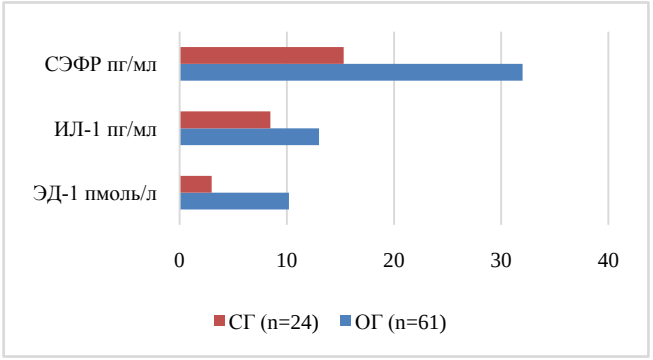

Figure 3. Markers of endothelial dysfunction in children with PH-CHD

It was found that damage to endothelial cells as the disease progresses is accompanied by an increase in the content of Endothelin 1. In the main group, the indicator was 27.8-28.6% higher than in the control group ($p < 0.01$), then in patients from the comparative group-by 167.2% more ($p < 0.05$). The concentration of the proinflammatory cytokine IL-1 significantly increased ($p < 0.001$) in the main group.

All subjects had a high level of EGFR: the main group showed a 2.3-fold increase from the level of the control group ($p<0.05$), and the comparative group showed a 1 – fold increase from the control group ($p<0.05$).

We also identified correlations between endothelial dysfunction and hemodynamic parameters, morphofunctional parameters of the right heart, and biochemical parameters of blood in order to apply these studies in the polyclinic unit (Table 1).

Table 1. Correlation analysis of morphofunctional parameters of the right ventricle and markers of endothelial dysfunction

	ED-1	IL-1	VEGF	MPAP, mmHg	RA	DSLA	RV	Npro-BNP
Npro-BNP	0,956	0,843	0,934	0,867	0,747	0,574	0,849	-
IL-1	0,781	-	0,783	0,744	0,663	0,402	0,729	0,843
ED-1	-0,781	0,781	0,823	0,758	0,669	0,572	0,801	0,956
VEGF	0, 823	0,783	-	0,919	0,784	0,546	0.838	0.934

Correlation analysis showed a strong positive relationship between markers of endothelial dysfunction: endothelin-1 and **Npro-BNP** (Fig. 4)

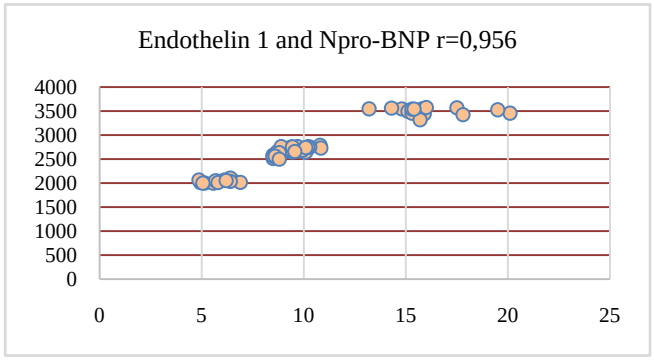

Figure 4

From the indicators that have a statically moderate dependence, i.e., an increase in the number of ET-1, manifested between the morphofunctional signs of the right heart, it follows that it has become evidence of pathogenetic mechanisms (Fig. 5).

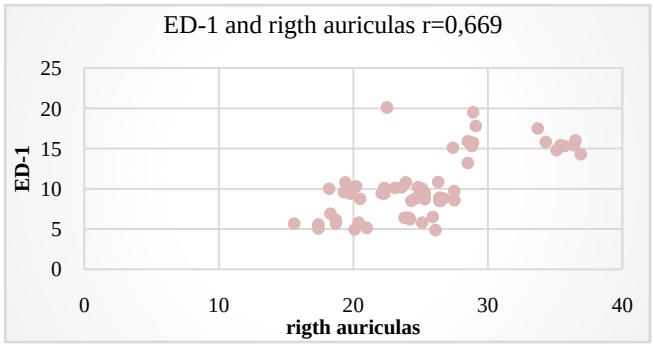

Figure 5

Another important marker is VEGF, which gave a strong positive correlation with IL-1 and D-demir, which indicates that the inflammatory process in the pulmonary arterioles increases and leads to intima proliferation, which leads to increased blood clotting and blood clot formation. (Figure 6).

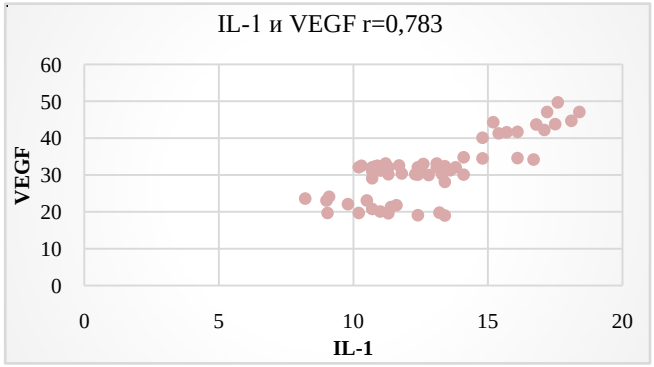

Figure 6

Also, the level of Npro-BNP increased significantly and correlated with the indicators of the right heart, especially with an increase in the size of the right ventricle (Figure 8). This makes it possible to determine the development of pulmonary hypertension and heart failure in the early forties. In addition, there were several statistically significant relationships presented in the table. And these connections serve as indicators that help in the early diagnosis of pulmonary hypertension in children with congenital heart disease and identify these processes in the polyclinic unit.

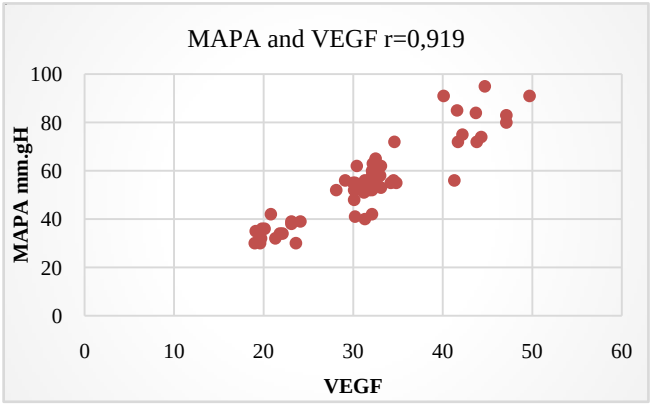

Figure 7

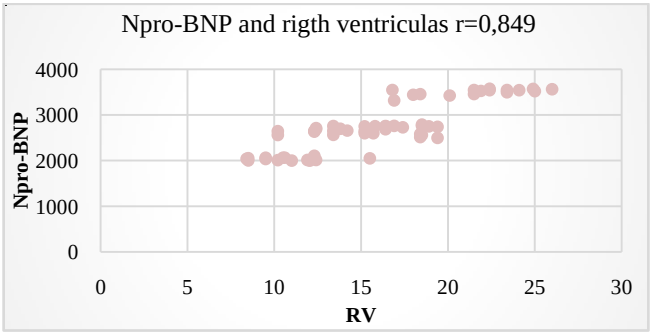

Figure 8

4. Conclusions

Our research has shown that immunological biomarkers and morphofunctional parameters of the right heart can be a prognostic indicator of the development of pulmonary hypertension in children with CHD.

Markers of endothelial dysfunction: ET-1, VEGF, IL-1, and NproBNP revealed strong positive and negative correlations between the morffunctional indicators of the right heart, which allows for early diagnosis of pulmonary hypertension in children with congenital heart disease and allows for early detection in polyclinic care.

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