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## DETERMINING HEMODYNAMIC SIGNIFICANCE OF PATENT DUCTUS ARTERIOSUS USING ECHOCARDIOGRAPHIC DATA PROGNOSTIC TABLES

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**Key words:** patent ductus arteriosus (PDA), hemodynamic significance, transthoracic echocardiographic (TTE) examination

**Ключові слова:** відкрита артеріальна протока (ВАП), гемодинамічна значущість, трансторакальне ехокардіографічне дослідження (ТТЕ)

**Ключевые слова:** открытый артериальный проток (ОАП), гемодинамическая значимость, трансторакальное эхокардиографическое исследование (ТТЕ)

**Abstract. Determining hemodynamic significance of patent ductus arteriosus using echocardiographic data prognostic tables. Kulikova D.A., Safonova I.N., Chumak L.I., Poddubnaya I.N., Protsenko O.S., Dotsenko D.G.**

The paper presents an analysis of echocardiographic data of patients with PDA having different hemodynamic significance. Presently, the concept of “degree of hemodynamic significance” remains controversial. Criteria for determining the hemodynamic significance of PDA in term infants are not described. In our work, we used a classification of three degrees of hemodynamic significance: non-hemodynamically significant PDA – insignificant, moderately hemodynamically significant – moderately significant and large PDA – hemodynamically significant PDA. Aim – to work out an algorithm for determining the degree of PDA hemodynamic significance for prediction of its further development. The study involved children under 18 years old (80% of them – children under 3 years old) who were examined in the cardiac surgery department of the SI “IGUS n.a.V.T. Zaytsev NAMS of Ukraine” during 2013-2017 yy. Gestational age (from 37 weeks), the presence of left to right PDA shunt, absence of a ASD shunt and other congenital heart defects served as enrollment criteria for the trial. Two prognostic tables were formed with the main criteria for determining hemodynamic significance of PDA by the sum of the signs according to gradations (insignificant, moderately significant and hemodynamically significant) as an outcome of the trial. Based on the determination of the main and additional criteria of hemodynamic significance and the strength of their influence, a diagnostic algorithm is formed for a patient with PDA with the possibility of predicting a further clinical scenario. For determination of hemodynamic significance, an increase in pulmonary gradient with an information index of 1.135 and

*a prognostic factor of +5.90/-1.75 were dominant, while the left ventricular dilatation located from the A4C with an informational index of 1.020 and a prognostic coefficient of +3.69/-2.50 dominated in determining the degree of hemodynamic significance in the presence of secondary changes. The proposed mechanism for determining the level of hemodynamic significance of PDA for children with borderline changes will predict more precisely the development of the disease, determine the patient's observation tactics and regulate the decision-making process of surgical intervention.*

**Реферат.** **Визначення гемодинамічної значущості відкритої артеріальної протоки з використанням прогностичних таблиць за даними ехокардіографії.** Кулікова Д.О., Сафонова І.Н., Чумак Л.І., Піддубна І.Н., Проценко О.С., Доценко Д.Г. У статті представлений аналіз ехокардіографічних даних пацієнтів з відкритою артеріальною протокою (ВАП), що має різну гемодинамічну значущість. На цей час поняття "ступінь гемодинамічної значущості" залишається суперечливим. Критерії визначення гемодинамічної значущості ВАП у доношених дітей – не описані. У нашій роботі ми використовували класифікацію трьох ступенів гемодинамічної значущості: негемодинамічно значущий ВАП – незначний, помірно гемодинамічно значущий – помірно значущий та великий ВАП – гемодинамічно значущий ВАП. Мета – розробити алгоритм визначення ступеня гемодинамічної значущості ВАП для прогнозування його подальшого розвитку. У дослідженні брали участь діти до 18 років (80% з них – діти до 3 років), які пройшли обстеження в кардіохірургічному відділенні ДУ «ІЗНХ ім. В.Т. Зайцева НАМН України» протягом 2013-2017 рр. Гестаційний вік (від 37 тижнів), наявність шунта по ВАП зліва направо, відсутність шунта по ДМПП та інших вроджених вад серця служили критеріями включення до дослідження. Сформовано дві прогностичні таблиці з основними критеріями для визначення гемодинамічної значущості ВАП за сумою ознак за градаціями (незначущі, помірно значущі та гемодинамічно значущі) як результат дослідження. На основі визначення основних та додаткових критеріїв гемодинамічної значущості та сили їх впливу формується діагностичний алгоритм для пацієнта з ВАП з можливістю прогнозування подальшого клінічного сценарію. Для визначення гемодинамічної значущості визначальним було збільшення легеневого градієнта з інформаційним індексом 1,135 та прогностичним фактором +5,90/-1,75, тоді як дилатація лівого шлуночка в чотирьохкамерній позиції з інформаційним індексом 1,020 та +3,69/-2,50 домінувала при визначенні ступеня гемодинамічної значущості за наявності вторинних змін. Запропонований механізм визначення рівня гемодинамічної значущості ВАП для дітей із граничними змінами дозволить більш точно передбачити розвиток захворювання, визначити тактику спостереження за пацієнтом та регулювати процес прийняття рішень щодо хірургічного втручання.

Patent ductus arteriosus (PDA) is a congenital heart disease which occurs in absence of physiological closure of embryonal aorto-pulmonary communication after the birth. PDA frequency is 0.3%-0.8% in full-term newborns; twice as common in girls. Clinical manifestations of PDA depend not only upon its size, but also upon the ratio of systemic and pulmonary vascular resistance [1, 4, 11].

Characteristics of PDA significance can be represented by such concepts as "clinically obvious", "symptomatic" and "hemodynamically significant" (hs). The latter is understood as PDA with a shunt of significant volume on transthoracic echocardiographic (TTE) examination, which include direct and indirect signs. Hemodynamic significance can vary from minimal or absent, to one that leads to secondary changes not only in the heart itself, but also in the pulmonary system, and can lead to irreversible consequences [1, 8, 9, 12].

Presently, the concept of "degree of hemodynamic significance" remains controversial. Some authors offer classifications of significance in association with clinical manifestations. However, most of these studies are associated with deeply premature babies and, accordingly, with more pronounced clinical manifestations. Thus, Arlettaz R. in the study of PDA in premature newborns offers a classification of three degrees of hemodynamic

significance: hemodynamically insignificant PDA – insignificant, moderately hemodynamically significant moderately significant and large PDA hemodynamically significant PDA [3, 4, 5]. In our work we confined ourselves to the same classification. Patients with a diagnosis of "congenital heart disease: patent ductus arteriosus" do not always require urgent surgical intervention. Large, PDA that leads to secondary changes in the heart, pulmonary circulation hypervolemia with pronounced clinical manifestations requires consultation of a cardiac surgeon for determination of the duration and type of surgical treatment. Patients with small, moderately hs PDA, with minor secondary changes (for example, dilation of the left chambers to -1 by Z-score) require observation, and children of the first year of life have a chance of spontaneous closure of such a duct [6, 10, 11].

If there a shunt via PDA in the Color Flow Doppler (CFD), there are no signs of pulmonary overflow, no heart chambers dilation and clinical manifestations (including the presence of murmur during auscultation) respectively, as a rule, they do not require surgical treatment, but only need prevention from infectious endocarditis – as one of the rare complications [7]. For prediction of the disease development in such a patient, it is important to determine the degree of hs of the duct [13, 14].

Aim: to create a methodology for determining the degree of PDA hemodynamic significance in children who were born full-term.

#### MATERIALS AND METHODS OF RESEARCH

The study involved children under 18 years old (80% of them – children under 3 years old) who were examined in the cardiac surgery department of the SI “IGUS n.a.V.T. Zaytsev NAMS of Ukraine” during 2013-2017.

Gestational age (from 37 weeks), the presence of left to right PDA shunt, absence of a ASD shunt and other congenital heart defects served as enrollment criteria for the trial. We have analyzed all groups of signs of PDA hemodynamic significance, the main source of which were criteria of hs described in the literature [10, 13].

TTE examination was carried out according to the designed local protocol and was used for the study of additional specific parameters for PDA evaluating. Visualization of PDA shunt with CFD from the parasternal long-axis (PLAX) and short-axis (PSAX), ductal view position was the criterion for the diagnosis of PDA.

Retrospectively, according to the results of surgical treatment, all patients were divided into three groups according to the hemodynamic significance of PDA: group I – hemodynamically insignificant PDA (68 patients), group II – moderately hemodynamically significant (65 patients) and group III – hsPDA (66 patients). The hemodynamic significance of the duct was determined by intraoperative data.

For analysis, we selected 15 criteria of TTE, which demonstrated of statistically significant differences with values  $p < 0.05$  in the studied groups. Further, for these criteria, a sequential diagnostic procedure was carried out according to Wald, which is applicable for cases with any distribution of symptoms in groups. Relative values of the probability of the presence of each TTE criterion in the studied groups with their errors ( $P \pm m$ ), likelihood and prognostic coefficients, and an informativeness index were calculated. The criteria of TTE for different by hemodynamic significance groups of patients with PDA were ranked according to the index of informative value. To predict the degree of PDA hemodynamic significance, prognostic coefficients were calculated for each gradation of the criterion according to their significance.

The methodology was based on a consequential statistical procedure for pattern recognition by Gubler and the method of sequential analysis by A. Wald. The essence of the method is that there is a gradual accumulation of information until a certain

threshold value is reached, which depends on the chosen degree of probability. Using the table of threshold sums of diagnostic coefficients [2], the threshold value in our study was considered to be such a sum of diagnostic coefficients that was either (-13) or (+13), which corresponded to a 95% degree of probability.

If none of the thresholds sum can be reached, this means that there is lack of information for making a decision. The construction of prognostic tables means placing the criteria and their prognostic coefficients in a certain sequence in the order of decreasing informative value, which reduces the number of steps of the sequential A. Wald procedure, simplifying it.

Statistical processing of the study results was performed using the software product STATISTICA 6.1 (StatSoftInc., Serial № AGAR909E415822FA).

#### RESULTS AND DISCUSSION

Calculation of the degree of PDA hemodynamic significance involves taking into account a lot of parameters. While examining a patient with hemodynamically insignificant PDA, it is necessary to make a differential diagnosis with PDA of moderate hemodynamic significance, i.e. exclude all the most common secondary complications. Values of the criteria of TTE for hemodynamically insignificant and moderately significant PDA with their prognostic coefficients are presented in Table 1.

The set of criteria for TTE presented in the table is proposed as a base approach for the distribution of children in prognostic groups according to the hemodynamic significance of PDA. In a situation where the dilation of the left cardiac chambers according to TTE is insignificant or not clearly expressed, it is advisable to determine presence or absence of the criteria for echocardiographic diagnostics presented in Table 1 to define the hemodynamic significance.

If they are present, the prognostic coefficients corresponding to the “Yes” gradation are summarized, and if they are absent, the corresponding “No” gradations are summarized. If the sum of prognostic coefficients at a certain stage of the examination reaches a threshold (+13), this determines the PDA as moderately hemodynamically significant. Upon reaching the threshold (-13), PDA is considered hemodynamically insignificant. If the sum of prognostic coefficients for all the criteria of the Table 1 does not reach the thresholds (+13) or (-13), then the level of moderate hemodynamic significance can be considered conditional (Table 2).

Table 1

**Prognostic table for determining the absence of hemodynamic significance  
or the presence of insignificant hemodynamic significance of PDA in children**

Criterion of TTE	Its gradation	Informative index	Prognostic coefficients
Increase of gradient pressure on pulmonary artery	Yes	1.135	+5.90
	No		-1.75
Increase of gradient pressure on the left brunch of pulmonary artery	Yes	1.038	+5.13
	No		-1.83
Dilation of left ventricle (LV) in PLAX in M mode	Yes	0.459	+3.05
	No		-1.33
Increase of left atrium (LA) volume	Yes	0.416	+2.2
	No		-1.66
Dilation of LV in PLAX in B mode	Yes	0.389	+2.75
	No		-1.25
Increase of gradient pressure on aortic arch	Yes	0.352	+4.97
	No		-0.62
Dilation of LA in apical four-chambers view (A4C) in B mode	Yes	0.342	+2.71
	No		-1.11
Dilation of LV in A4C	Yes	0.325	+3.79
	No		-0.76
Dilation of LA in PLAX in B mode	Yes	0.322	+2.36
	No		-1.99
The presence of turbulent flow in the pulmonary artery	Yes	0.276	+2.98
	No		-0.81

The presence of hemodynamically insignificant PDA, confirmed by the sum of prognostic coefficients of TTE criteria (-13), determines very low probability of surgical treatment of malformation, and the tactics of conservative treatment of the child based on dynamic observation. The conditional

moderately hspDA, allocated with the sum of prognostic factors ranging from -12 to +12, shows that the child, at this stage of the examination, is in the favorable prognostic zone under observance of all rules of proper care, feeding and medical supervision.

Table 2

**Determining the degree of hemodynamic significance of PDA  
in children in the absence of dilation of the left heart chambers according to TTE**

Prognostic groups	Sum of the prognostic coefficients
Hemodynamically insignificant PDA	-13
Conditionally moderately hemodynamically significant PDA	from -12 up to +12
Moderately hemodynamically significant PDA	+13

Reaching the threshold of the sum of prognostic coefficients (+13), especially in the case of a step-by-step procedure according to A. Wald, taking into account the first 5-6 criteria of the table, should alert the cardiologist. In combination with a slight dilation of the left heart chambers, an increase of gradients on the pulmonary artery, descending aorta and others, the obtained coefficient is an evidence of the

hemodynamic borderline value of PDA in this child, which requires a more thorough examination using new modern TTE methods, as well as deep and frequent observation of the child in dynamics.

The decision on the tactics of management of a child is based on a complex of factors and on changes in his state in dynamics. If the course of the disease is unfavorable, there is a high probability of

the transition of hemodynamically insignificant PDA to hsPDA, which stipulates the necessity for surgical treatment of the patient.

In the presence of secondary changes in the heart, such as obvious signs of pulmonary overflow: dilation of the left heart chambers, an increase in the gradient on the right ventricular outflow tract, left branch of the pulmonary artery, the pressure gradient on the descending aorta and others, the hemodynamic significance should be differentiated between the II and III groups, namely between a moderate hemodynamically significant and hsPDA.

It is proposed to use prognostic table 3 for determination the degree of significance.

In the absence of pronounced secondary changes, a moderately hemodynamically significant PDA is confirmed by the sum of the prognostic coefficients of the ultrasound criteria (-13), and hemodynamically significant – by the sum (+13), respectively. The situation when the sum of the prognostic coefficients of the TTE criteria varies from -12 to +12, may be considered insufficient as for decision-making about the degree of hemodynamic significance of the PDA, this requires additional diagnostic methods (Table 4).

Table 3

**Prognostic table for determining the degree of hemodynamically significance PDA in children for moderately hemodynamically significant and hsPDA**

Criterion of TTE	Its gradations	Informative index	Prognostic coefficients
Dilation of LV in A4C	Yes	1.020	+3.69
	No		-2.50
Increase of LA volume	Yes	0.719	+1.74
	No		-3.70
Dilation of LA in PLAX in B mode	Yes	0.643	+2.09
	No		-2.74
Dilation of LA in A4C in B mode	Yes	0.635	+2.29
	No		-2.47
Increase of gradient pressure on pulmonary artery	Yes	0.563	+2.12
	No		-2.36
The presence of turbulent flow in the pulmonary artery	Yes	0.344	+2.20
	No		-1.38
Increase of gradient pressure on aortic arch	Yes	0.306	+2.76
	No		-0.97
Increase of gradient pressure on the left brunch of pulmonary artery	Yes	0.270	+1.48
	No		-1.60
Dilation of LV in PLAX in B mode	Yes	0.270	+1.53
	No		-1.55
Dilation of LV in PLAX in M mode	Yes	0.270	+1.53
	No		-1.55

There are two additional methods for determining the hemodynamic significance of PDA. The first method which we developed consists in calculating the ratio of the area of the PDA shunt volume to the area of the pulmonary artery (up to 20%, 20-40%, and more than 40%, respectively, in accordance to three groups of hemodynamic significance in ascending order). The second method consists in measuring the speed of PDA shunting during systole and diastole when measured by Continuous Wave Doppler. In the presence of a systolic-diastolic difference of more than 50%, the hemodynamic significance was regarded as insignificant, from 30-

50% – moderate, and if less than 30% – PDA was defined as hemodynamically significant [9].

Thus, offered by us mechanism for determining the level of hemodynamic significance of PDA for children with slight dilation of the left heart chambers allows to predict the process of the malformation development, determine the tactics of patient supervision and regulate the decision-making process as for surgical intervention if necessary. Using this technique makes it possible to implement an individual approach to each patient with PDA in practice.

Table 4

**Determining the degree of hemodynamic significance of PDA  
in children in the presence of secondary changes in the heart according to TTE**

Prognostic groups	Sum of the prognostic coefficients
Moderately hemodynamically significant PDA	-13
Conditionally hemodynamically significant PDA	from -12 up to +12
Hemodynamically significant PDA	+13

This technique allows using an individual approach to each patient with PDA. It should be noted that this technique should work in conjunction with other methods, take into account other important criteria, such as anamnestic, social and clinical ones. The application of the developed algorithm will significantly improve the diagnosing of the PDA significance with the help of TTE. In borderline cases using of additional methods developed by us will be necessary.

#### CONCLUSIONS

1. The determination of the hemodynamic significance of PDA in babies born full-term is a complex diagnostic problem, a key role in solving of which is to TTE.

2. Absence of essential clinical, instrumental and TTE criteria for diagnosing the significance of PDA forces developing diagnostic algorithms with a

statistical determination of the influence of each factor.

3. Based on the determination of the main and additional criteria of hemodynamic significance and the strength of their influence, a diagnostic algorithm is formed for a patient with PDA with the possibility of predicting a further clinical scenario.

4. For determination of hemodynamic significance, an increase in pulmonary gradient with an information index of 1.135 and a prognostic factor of +5.90/-1.75 were dominant, while the left ventricular dilatation in TTE in the A4C with an informational index of 1.020 and a prognostic coefficient of +3.69/-2.50 dominated in determining the degree of hemodynamic significance in the presence of secondary changes.

Conflict of interests. The authors declare no conflict of interest.

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