

Predictors of myocarditis in children with acute respiratory infections across different age groups

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Abstract. Introduction. Acute viral respiratory infections continue to lead in frequency among infectious diseases in adults and children in the modern world. Severity and speed of the development of clinical symptoms of these pathologies, as well as the frequency of complications, directly depend on the pathogenicity of the pathogen and the state of the body's innate immune response. **Aim.** To improve early diagnosis and risk stratification of myocarditis in children with acute viral respiratory infections (AVRI) based on a comprehensive assessment of clinical, anamnestic, laboratory, and instrumental predictors across different age groups. **Materials and Methods.** Between 2023 and 2025, 195 patients aged 1-14 years with acute viral respiratory infections were studied. Of 195 patients, 112 children (57.44%) were diagnosed with laboratory- and instrumentally confirmed myocarditis and constituted the study group, while the comparator group consisted of 83 patients aged 1-14 years. Anamnestic, clinical, laboratory, and instrumental research methods were used. The findings were statistically processed using parametric and nonparametric criteria by methods of variational statistics. **Results and Discussion.** Echocardiography has the greatest diagnostic significance, recording a decrease in ejection fraction, chamber dilation, and regional contractility disorders, all being the markers of inflammation severity. ECG changes, such as repolarization disorders and tachycardia, were early functional indicators of myocardial damage. Elevated levels of troponin T and I demonstrated maximum sensitivity and specificity for inflammatory myocardial damage, while CK-MB and LDH complemented the picture of cytolysis and metabolic imbalance, and CRP enhanced the prognostic significance of other systemic inflammation biomarkers. The prognostic model has a high risk-stratification accuracy (AUC = 0.981) in early diagnosis and determination of the strategies for the management of such patients. **Conclusions.** The leading predictors of myocarditis in children are TnT > 34 pg/ml, CRP > 20 mg/l, decreased left ventricular ejection fraction, a combination of sinus tachycardia and ST-T changes, and a history of frequent acute viral respiratory infections.

Keywords: acute viral respiratory infections, children, myocarditis, early diagnosis.

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Предикторы миокардита у детей с острыми респираторными инфекциями в разных возрастных группах

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Реферат. Введение. Острые респираторные вирусные инфекции в современном мире продолжают лидировать по частоте в структуре инфекционных заболеваний у взрослых и детей. Тяжесть и скорость развития клинической симптоматики этих патологий, как и частота осложнений, напрямую зависят от патогенности возбудителя и состояния врожденного иммунного ответа организма. **Цель.** Совершенствование ранней диагностики и стратификации риска миокардита у детей с острыми респираторными вирусными инфекциями на основе комплексной оценки клинических, анамнестических, лабораторных и инструментальных предикторов в различных возрастных группах. **Материал и методы.** В период 2023-2025 гг. изучены 195 больных с острыми респираторными вирусными инфекциями в возрасте 1-14 лет. Из 195 пациентов лабораторно и инструментально подтвержденный диагноз миокардит констатировали у 112 (57,44%) детей, которые составили основную группу, группу сравнения составили 83 пациента 1-14 лет. Применены анамнестические, клинические, лабораторные и инструментальные методы исследования. Статистическую обработку проводили с использованием параметрических и непараметрических критериев методами вариационной статистики. **Результаты и их обсуждение.** Эхокардиография обладает наибольшей диагностической значимостью, фиксируя снижение фракции выброса, дилатацию камер и региональные нарушения сократимости – маркеры тяжести воспаления. Изменения на электрокардиограмме – нарушение реполяризации и тахикардия, выступили ранними функциональными индикаторами миокардиального повреждения. Повышение тропонинов Т и I продемонстрировало максимальную чувствительность и специфичность в отношении воспалительного поражения миокарда, в то время как креатинфосфокиназа-МВ и лактатдегидрогеназа дополнили картину выраженности цитолиза и метаболического дисбаланса, С-реактивный белок усиливал прогностическую значимость других биомаркеров системного воспаления. Прогностическая модель имеет высокую точность стратификации риска (AUC = 0,981) при ранней диагностике и определении тактики ведения таких пациентов. **Вывод.** Ведущими предикторами миокардита у детей являются: TnT > 34 пг/мл, С-реактивный белок > 20 мг/л, снижение фракции выброса левого желудочка, сочетание синусовой тахикардии и изменений ST-T, а также частые острые респираторные вирусные инфекции в анамнезе.

Ключевые слова: острые респираторные вирусные инфекции, дети, миокардит, ранняя диагностика.

Introduction. Acute viral respiratory infections (AVRI) continue to lead in terms of frequency in the structure of infectious diseases in adults and children in the modern world. In the Russian Federation, 70–80 thousand cases of AVRI per 100 thousand children are registered each year, with no downward trend, while in the adult population this figure is 3.3 times lower [1]. According to the World Health Organization, the seasonal complex of AVRI pathogens in the autumn/winter period includes dozens of simultaneously circulating viruses (> 200 genetic groups from 6 families and 10 genera), which practically do not differ in their clinical picture [2].

In cases of acute viral respiratory infections, multi-viral etiology is confirmed in 4–33% of children, which increases the risk of adverse clinical outcomes [3]. Every year, up to 80% of the world's population suffers from respiratory infections: children under the age of 5 experience an average of 6–8 episodes of AVRI per year [4]. In preschool institutions, the incidence of AVRI is particularly high in the first and second years of attendance: 10–15% higher than in children who do not attend preschool. However, schoolchildren get sick more often, with the incidence of AVRI being the highest between September and April, with the peak incidence occurring in February/March and a decline in incidence consistently recorded in the summer months, when it decreases by 3–5 times [5].

Globally, AVRI is one of the leading causes of morbidity and mortality, with nearly 2 million children under 5 years dying from this disease each year [6]. Every year, 290,000–650,000 people worldwide die from the influenza virus [7]. Over 80% of home visits are made to AVRI patients, and the economic damage from these diseases reaches 86% of all infectious diseases [8].

Studies have proven the effect of AVRI on the cardiovascular system: All heart membranes may be involved, but infectious myocarditis is more common, occurring

in 2% of patients with AVRI and 8% of hospitalized patients with this pathology [9]. Enteroviruses cause the maximum number of cardiovascular complications in 5–15% of cases, and influenza viruses in 5% [10].

It is still difficult to early diagnose myocarditis. It has been proven that all patients with cardialgia against the background of acute viral respiratory infection, ECG changes, and the onset and worsening of heart failure should have their serum creatine phosphokinase and troponin levels determined [11]. However, the concentrations of these markers increase in only 35% of patients with suspected myocarditis and demonstrate a sensitivity of 53% [12].

These data dictate the need for further studies of early and reliable markers of myocarditis, especially in children, and for the development of an algorithm to ensure the early comprehensive diagnosis of myocarditis in children with AVRI, which is the subject of this study.

Aim. To improve early diagnosis and risk stratification of myocarditis in children with acute viral respiratory infections based on a comprehensive assessment of clinical, anamnestic, laboratory, and instrumental predictors across different age groups.

Materials and methods.

The study was conducted using a cluster sampling method at a children's clinical hospital between 2023 and 2025. It included 195 patients aged 1–14 years with confirmed cases of influenza or other acute viral respiratory infections. Respondents for the study were selected by random sampling with subsequent prospective observation. Of the 195 patients, 112 children (57.44%) were diagnosed with laboratory- and instrumentally confirmed myocarditis, forming the study group (SG). The comparator group (CG) consisted of 83 patients aged 1-14 years, comparable in gender to SG. The control group (ConG) included 20 healthy children of comparable age, i.e., 1-14 years (Fig. 1).

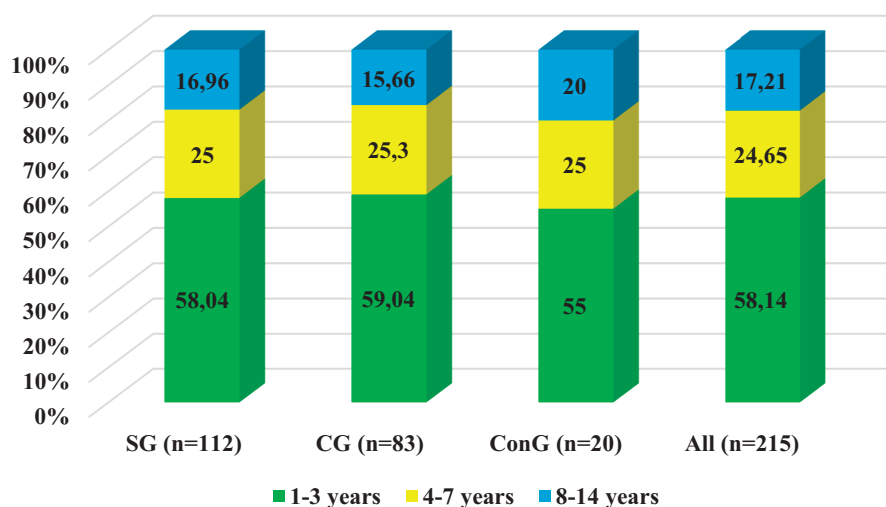


Figure 1. Distribution of age groups among the patients examined
Рисунок 1. Распределение возрастных групп исследуемых пациентов

Boys predominated in this study (68 (60.71%) in SG, 49 (59.04%) in CG, and 12 (60.0%) in ConG) at a ratio of 3 : 2 in all groups ($\chi^2 = 0.84$; $p = 0.66$). Thus, children aged 1-3 years predominated in this study, accounting for 58.14%, children aged 4-7 years accounted for 24.65%, and children aged 8-14 years accounted for 17.21%, which emphasizes the great medical and social significance of this work. Intergroup statistical comparative analysis found no statistically significant differences in age and gender ($\chi^2 = 0.42$; $p = 0.81$).

Criteria for inclusion of patients in the study: Patients of both sexes and aged 1–14 years; presence of laboratory- and instrumentally confirmed myocarditis; no congenital cardiovascular or other anomalies; no history of cardiovascular disease; no oncological, hematological, psychiatric, or other systemic diseases; voluntary informed consent of the child's parents to participate in this study according to the design; and willingness of parents to ensure the child's presence at the necessary time for dynamic observation studies.

Criteria for exclusion of patients from the study: Age under 1 year and over 14 years; refusal of the patient's parents to undergo the planned examination according to the patient examination design or the proposed treatment; any organic pathology of organs or systems prior to hospitalization; history of specific inflammatory processes (tuberculosis) or other pathology of the cardiorespiratory system; presence of any oncological, hematological, mental, or other systemic diseases; and inability to follow up the patient within the established time frame for any reason.

Ethical considerations. The study was conducted in accordance with the principles of the Declaration of Helsinki. The parents or legal guardians of all subjects signed informed consent forms. The study protocol was approved by the local ethics committee.

Our study used anamnestic, clinical, laboratory, and instrumental research methods. The anamnestic method of examination involved actively collecting the patient's medical history and the history of the diagnosed pathology for which the patient was hospitalized in this study. During the clinical examination, the general condition of the patients was assessed, with a focus on syndromes and symptoms characteristic of AVRI and acute respiratory pathologies, myocarditis, and other cardiovascular pathologies, as well as the condition of the skin, visible mucous membranes, internal organs, and systems. All patients were examined by a cardiologist.

Chest X-rays were performed in the frontal (anterior or posterior) and lateral projections with the child in an upright position (if possible) during inspiration; in younger children, they were performed with the child lying down and immobilized.

Electrocardiography (ECG) was performed on all subjects in 12 standard leads (I, II, III, aVR, aVL, aVF, V1-V6) using pediatric electrodes and a recording speed of 25 or 50 mm/s.

Echocardiography (ECHO) was performed transthoracically in B-mode, Doppler (CW, PW, and color) and spectral imaging using sector or linear probes (2–8 MHz) in standard projections (parasternal, apical, subcostal, and supraclavicular), tissue Doppler imaging and global

longitudinal strain imaging were evaluated for early detection of subclinical changes, with sedation or restraint used in younger children to minimize motion artifacts.

All subjects underwent routine laboratory diagnostics: complete blood count and urinalysis, coagulogram, biochemical analysis of peripheral venous blood with determination of standard indicators (followed by calculation of the de Ritis ratio, i. e., AST/ALT) and levels of C-reactive protein (CRP), troponins (Tn I and TnT), creatine phosphokinase (CPK and CPK-MB), and lactate dehydrogenase (LDH 1 and 2).

The research results were statistically processed using variational statistics methods with the help of IBM SPSS Statistics v.27.0.1.0 and Microsoft Office Excel 2019 software programs, calculating the arithmetic mean of the studied indicator (M), standard deviation (SD), standard error of the mean (m), and relative values (frequency, %). In case of deviation from the normal distribution of values, we calculated the medians with interquartile range (Me [Q1; Q3]) %. The normality of the distribution was checked using the Shapiro-Wilk criterion. The correlation of nonparametric data was determined by Spearman's coefficient (r), and parametric data by Pearson's criterion. For intergroup comparisons, we used the χ^2 test, Mann-Whitney U test for quantitative data, and Fisher's exact test for categorical variables [13]. We determined the degree of influence of factors and differences from the control group using Cohen's d. The statistical significance of the comparison of mean values was determined using Student's t-test and Welch's t-test with the determination of df (degrees of freedom) and the calculation of the probability of error (p) when testing the normality of the distribution. We calculated the relative risk (RR), attributable risk (AR), attributable fraction (EF), and odds ratio (OR). The statistical significance of the results had the following levels: "high $p < 0.001$, medium $p < 0.01$, low (marginal) $p < 0.05$, and insignificant (unreliable) $p > 0.05$." [13]

Results and discussion.

In this study, we determined the frequency of each variant of the clinical course of AVRI in the study groups. The data are presented in *Table 1*.

In both study groups, the distribution of clinical variants of AVRI showed a pronounced age-dependent patterns with a similar overall structure. At an early age (1–3 years), respiratory and abdominal variants dominated: in SG, they were recorded in 35.38% and 32.31% of children, respectively, and in CG, in 36.73% and 30.61%, respectively. Kawasaki-like syndrome in this age group was found in approximately one in four children (23.08% in SG and 24.49% in CG), which emphasizes the significance of the hyperinflammatory phenotype in young children. At the same time, cardiac and hypoperfusion variants in 1–3 years were quite rare (in SG 6.15% and 3.08%; in CG 6.12% and 2.04%, respectively).

At the age of 4–7 years, the general trend remained: respiratory and abdominal variants remained the most common (32.14% and 28.57% in SG, 33.33% and 28.57% in CG, respectively), with a moderate proportion of Kawasaki-like syndrome: 21.43% in SG and 19.05% in CG. Cardiac and hypoperfusion variants were more

Table 1

Frequency of clinical course of acute viral respiratory infections in the patients examined

Таблица 1

Частота встречаемости клинического течения острой респираторной вирусной инфекции у исследуемых пациентов

Clinical variant of AVRI	SG (n = 112)						CG (n = 83)					
	1 -3 years (n = 65)		4 -7 years (n = 28)		8 -14 years (n = 19)		1 -3 years (n = 49)		4 -7 years (n = 21)		8 -14 years (n = 13)	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Respiratory	23	35,38	9	32,14	3	15,79	18	36,73	7	33,33	2	15,38
Abdominal	21	32,31	8	28,57	3	15,79	15	30,61	6	28,57	2	15,38
Kawasaki -like	15	23,08	6	21,43	1	5,26	12	24,49	4	19,05	1	7,69
Cardiac	4	6,15	3	10,71	7	36,84	3	6,12	2	9,52	5	38,46
Hypoxic	2	3,08	2	7,14	5	26,32	1	2,04	2	9,52	3	23,08

common in this group than in younger children but remained secondary: 10.71% and 7.14%, respectively, in SG and 9.52% each in CG.

The most pronounced shift in structure was observed in children aged 8 - 14 years - the proportion of the cardiac variant increased sharply: By 36.84% in SG and by 38.46% in CG; as did the hypoperfusion variant: 26.32% in SG and 23.08% in CG, while the respiratory and abdominal variants decreased to 15–16%. The Kawasaki-like variant was rare in the group of older patients: 5.26% in SG and 7.69% in CG.

Overall, intergroup differences were minimal, and the leading factor in variability was age, reflecting a shift in dominant clinical phenotypes from predominantly catarrhal and gastrointestinal to cardio and hemodynamic.

As can be seen from the data presented, young children (aged 1–3 years) prevailed in our study: 58.04% in SG and 59.04% in CG. The odds ratio (OR) of developing myocarditis in age group I was 0.96 (95% CI 0.56 - 1.65; $p = 0.89$) compared to older children, indicating no significant age predisposition in this sample.

For age group II (4–7 years), the OR was 1.04 (95% CI 0.56 - 1.96; $p = 1.00$), which indicates no statistically significant association with an increased risk of myocarditis compared to children in subgroups I (1–3 years) and III (8–14 years), emphasizing the uniform distribution of pathology in this cohort.

For age group III (8–14 years), OR = 0.96 (95% CI 0.47–1.96; $p = 1.00$), which indicates a minimal deviation from neutral risk and the absence of age dependence in older children.

Gender also did not affect the risk: For boys OR was 1.07 (95% CI 0.78–1.47; $p = 0.67$), while for girls it was 0.93 (95% CI 0.68–1.28; $p = 0.68$). Perinatal risk factors were also significant, with low birth weight (< 2500 g) found in 28 children (25.0%) in SG group versus 12 (14.46%) in the GS group (OR = 1.96; 95% CI 1.12–3.47; $p = 0.048$). A history of perinatal hypoxia was noted in 34 patients (30.36%) in SG and 16 patients (19.28%) in CG (OR = 1.83; 95% CI 1.15–3.19; $p = 0.047$). Premature birth (before 37 weeks of gestation) occurred in 22 children (19.64%) in SG versus 9 (10.84%) patients in CG (OR = 2.01; 95% CI 1.13–3.62; $p = 0.044$).

One year prior to the index episode, 76 (67.86%) children in SG had experienced AVRI ≥ 3 times, compared to 38 (45.78%) children in the CG (OR = 2.51; 95% CI 1.62–3.89; $p < 0.001$). Severe previous AVRI was observed in 41 children (36.61%) in SG, compared with 17 children (20.48%) in CG (OR = 2.24 (95% CI 1.35–3.71; $p = 0.002$). Frequent AVRI and episodes of severe disease in medical history showed a significant association with an increased risk of myocarditis. In the SG children, the frequency of recurrent infections and previous hospitalizations was significantly higher, as confirmed by OR > 2.

No influenza vaccination was registered in 89 children (79.46%) in SG and in 52 patients (62.65%) in CG (OR = 2.28; 95% CI 1.39–3.74; $p = 0.001$), and lack of pneumococcal vaccination was observed in 72 patients (64.29%) in SG versus 41 children (49.40%) in CG (OR = 1.85; 95% CI 1.18–2.90; $p = 0.007$).

The main ECG signs of myocarditis in SG were as follows:

Sinus tachycardia (HR > 140 bpm at rest), observed in 89 children (79.5%), with maximum severity in the first age group (1–3 years), in 84.6% of patients, where the average HR reached 152 ± 18 beats/min ($p < 0.001$ compared to CG);

Conduction disturbances: first - degree AV block was observed in 24 patients (21.4%), second -degree AV block in 8 children (7.1%), with a predominance in the second age group (4–7 years) (OR = 2.3; 95% CI 1.03–5.12; $p = 0.042$);

ST-T segment changes in the form of ST depression greater than 0.1 mV were observed in 62 children (55.4%), T wave inversion in 47 (41.9%), with a frequency of 68.2% in group III (8–14 years), where a strong direct correlation was observed with QTc duration > 440 ms ($r = 0.62$; $p < 0.001$).

The most typical findings in this study were ST segment depression, T wave inversion, and nonspecific ventricular repolarization abnormalities. In terms of ECG changes, 71.4% of patients in SG showed regression by day 7, with complete normalization by month 3 in 94.6%. In CG, nonspecific tachycardia occurred in 38.6% of cases, but without signs of ischemia ($p < 0.001$). No abnormalities were recorded in the ConG.

Thus, the combination of sinus tachycardia and ST-T changes is an early marker of myocarditis with a sensitivity of 82% and specificity of 76% (AUC = 0.81), especially in younger age groups, where metabolic stress exacerbates electrophysiological shifts. The overall sensitivity of ECG to myocarditis was 78.6%, with non-specific changes prevailing in 92.9% of cases.

In SG, the most common findings on echocardiography were as follows:

A reduction in LVEF below 55% was initially observed in 76 children (67.9%) (mean $48.2 \pm 8.4\%$) and was statistically significant compared to the control group ($p < 0.001$), where LVEF was reduced by only 6.3% in group I ($p = 0.018$);

LV GLS $> -15\%$ was recorded in 54 patients (48.2%), with the highest prevalence in group III (OR = 1.9; $p = 0.031$) against the background of a strong inverse correlation with troponins ($r = -0.71$; $p < 0.001$);

Heart chamber dilatation greater than + 2 SD was diagnosed in 42 patients (37.5%).

Pericardial effusion greater than 5 mm was observed in 31 patients (27.7%), with a frequency of 42.1% in group II.

The dynamics showed recovery of EF $> 55\%$ by the 7th day in 83.3% of SG patients, with LVEDD becoming less than -18%. In CG, LVEF was $62.4 \pm 5.2\%$ ($p < 0.001$), without deformation. In the ConG, LV GPD was $-20.1 \pm 1.8\%$.

Echocardiographic markers (LVEF + GLS) demonstrate an AUC = 0.92 for early diagnosis, with age specificity: In children aged 1–3 years, effusion more often mimics tamponade, requiring differentiation from pericarditis.

The sensitivity of the method reached 91.1% (95% CI 85.3 - 95.2%), while its specificity was 98.2% (95% CI 95.3 - 99.9%) with high reproducibility in dynamics (intraclass correlation coefficient ICC = 0.92). The echocardiographic picture in children with myocarditis is characterized by high heterogeneity, reflecting a spectrum of pathophysiological processes ranging from mild transient dysfunction to severe inflammatory myocardial damage.

In SG, the key radiological findings were as follows:

Cardiomegaly (cardiothoracic index (CTI) greater than 0.55) was observed in 67 children (59.8%), with an average CTI of 0.58 ± 0.07 ; the difference with the GS was statistically significant ($p < 0.001$); the most pronounced cardiomegaly was found in group I (64.6%; $p = 0.022$);

Interstitial changes (increased pulmonary pattern, Curley lines) were diagnosed in 54 children (48.2%), with a moderate direct correlation with venous stasis ($r = 0.58$; $p < 0.001$).

Pleural effusion was recorded in 29 children (25.9%), predominantly left - sided, more often in group II (OR = 1.8; $p = 0.045$).

Dynamic monitoring allowed us to establish regression of cardiomegaly by the 7th day in 72.4% of patients, and normalization of the pulmonary pattern in 85.7% by the time of discharge. In CG, cardiomegaly was initially found in 18.1% of patients, and interstitial changes were found in 24.1% of patients, which was statistically significantly less than in SG ($p < 0.001$). In the control group, the mean CTI was 0.48 ± 0.04 . The sensitivity of chest X - ray for myocarditis was 69.6% (95% CI 63.1 - 79.6%), and the specificity was 75.9% (95% CI 66.5 - 85.3%) with a predominance of combined findings (cardiomegaly + interstitial syndrome) in 76.8% of cases.

A comparative analysis of instrumental methods revealed their complementarity: ECHO is superior in sensitivity (91.1%), while ECG in accessibility (78.6%), and radiography in terms of complications (69.6%). The overall AUC for the combined panel is 0.94 (95%CI 0.91–0.97), with age specificity; in group I, the AUC of EchoCG reaches 0.93, and in group III only 0.89 (Fig. 2). The dashboard allows for early diagnosis in 95.5% of cases, with the greatest effectiveness in children aged 1–7 years, where initial myocarditis is more likely to occur subclinically.

An increase in troponins was recorded in 104 children (92.86%) of SG, which significantly exceeds the indicators of CG (11 children (13.25%)) and in CG (none) and has statistical significance ($p < 0.001$). The average TnT level at admission to the exhaust gas was 128.4 ± 96.7 pg/mL (Me = 98.2 pg/mL), TnI reached

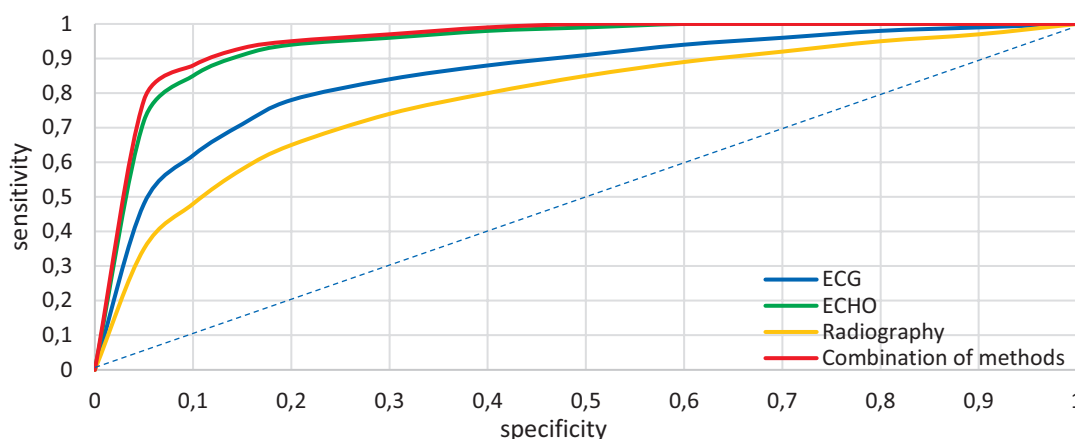


Figure 2. ROC curves for instrumental methods of diagnosing myocarditis in children
Рисунок 2. ROC-кривые инструментальных методов диагностики миокардита у детей

Table 2

Independent predictors of myocarditis

Таблица 2

Независимые предикторы миокардита

Predictors	β	SE	Wald	OR (95% CI)	p
TnT > 34 pg/mL	3,21	0,68	22,31	24,8 (6,5 -94,6)	<0,001
CRP > 20 mg/L	2,18	0,61	12,76	8,8 (2,7 -29,1)	<0,001
LVEF < 55%	1,94	0,59	10,82	7,0 (2,2 -22,3)	0,001
Sinus tachycardia + ST-T	1,67	0,57	8,59	5,3 (1,7 -16,4)	0,004
≥ 3 AVRI in the previous year	1,12	0,47	5,68	3,1 (1,2 -7,8)	0,017
Constant	-6,84	1,42	23,21	-	<0,001

142.6 $\pm$ 118.3 pg/ml (Me = 112.5 pg/ml). The maximum TnT values were observed in age group I (1–3 years) and amounted to 156.8 $\pm$ 104.2 pg/ml, which is statistically significantly higher than in group III (8–14 years): 89.3 $\pm$ 62.4 pg/ml ($p = 0.002$). ROC analysis confirmed the high diagnostic value: TnT – AUC = 0.96 (95%CI 0.94–0.98), threshold 34 pg/ml, the analysis had the sensitivity of 93.8% with the specificity of 95.2%; Tnl: AUC = 0.97 (95%CI 0.95–0.99), threshold 42 pg/mL, characterized by the sensitivity of 94.6%, and the specificity of 96.4%. Combination of TnT + Tnl yielded AUC = 0.98 (95%CI 0.97–0.99).

CK-MB concentration in serum was increased at baseline in 86 children (76.79%) of SG and had a mean value of 42.6 $\pm$ 28.4 U/L at a rate of up to 24 U/L, while the relative proportion of CK-MB exceeded 6% of the total CK in 68 patients (60.71%). The level of CK-MB normalized on the 7th day in 89.3% of patients.

The LDH flip-flop phenomenon (LDG-1 > LDG-2) was detected in 79 children (70.54%) of SG, the average ratio of LDH-1/LDH-2 = 1.18 $\pm$ 0.36 versus 0.82 $\pm$ 0.14 in CG, the difference is statistically significant ($p < 0.001$).

The de Ritis ratio (AST / ALT) > 2.0 was recorded in 64 patients (57.14%) of SG with the mean group value of 2.46 $\pm$ 0.78 versus 1.12 $\pm$ 0.31 in CG, the difference being statistically significant ($p < 0.001$).

CRP at admission was increased in 108 children (96.43%) of SG with the average value of 48.6 $\pm$ 32.4 mg/l (maximum 178 mg/l), and in CG, an increase was noted in 62 patients (74.70%) with an average level of 18.4 $\pm$ 12.6 mg/l, the difference being statistically significant ($p < 0.001$). Normalization on the 7th day was noted in 93.5% of patients in SG.

We performed multivariate logistic regression analysis of laboratory predictors of myocarditis, the model included TnT, Tnl, CPK-MB, CRP, de Ritis coefficient and LDH-1/LDH-2. Variables demonstrating statistical significance ($p < 0.05$) in univariate analysis, including perinatal history, individual biomarkers (Tnl, CK-MB, LDH, AST/ALT ratio), and specific imaging features, were entered into a multivariable logistic regression model using backward stepwise elimination. Variables exhibiting high multicollinearity (e.g., Tnl vs. TnT, $r = 0.91$) were excluded to ensure model stability, yielding five final independent predictors. After preliminary calculations and rejection of factors with insignificant influence, we identified independent predictors of myocarditis (Table 2).

To verify the predictive value of the developed model, the Goodness-of-Fit criteria of its final version were

evaluated. Analysis of the 2-Log-Likelihood parameter, which characterizes the measure of model inconsistency with the observed data, showed a decrease in the value down to 68.42, indicating high accuracy of approximation and minimization of residual prediction errors.

The statistical significance of the model as a whole was confirmed by the Omnibus Tests of Model Coefficients (Omnibus Tests of Model Coefficients) in which $\chi^2 = 21.87$ at $p < 0.001$, which allows us to reject the null hypothesis and argue that the included set of predictors (ECHO, X-ray and laboratory markers) has a statistically significantly better predictive ability compared to constant model.

The proportion of variance explained was estimated using the pseudo-coefficient of determination of Nagelkerke R^2 , which was 0.874. This indicates that the final mathematical model describes 87.4% variability in the probability of developing a pathological process in the study sample. Such a high value of the coefficient of determination confirms the exceptional predictive power of the selected risk factors and the adequacy of the model for clinical use.

After that, we built a prognostic model of the development of myocarditis in children against the background of AVRI, based on the coefficients, a risk scale was built (0–17 points). Point values for the prognostic scale were derived directly from the regression coefficients (β) of the multivariate logistic regression model (Table 2) using standard weight normalization. The threshold ≥ 9 points provides sensitivity of 94.6% and specificity of 96.1% (Table 3).

To assess the discriminant ability of the model, we also conducted a ROC analysis of the prognostic model: AUC = 0.981 (95%CI 0.967–0.995; $p < 0.001$) with an optimal cut-off point of 9 points, which demonstrates sensitivity of 94.6%, specificity of 96.1%, positive predictive value of 96.4%, and negative predictive value of 94.1%. Although individual markers exhibit

Table 3

Prognostic risk scale for myocarditis in children

Таблица 3

Прогностическая шкала риска миокардита у детей

Indicator	Points
TnT > 34 pg/mL	6
CRP > 20 mg/L	5
LVEF < 55%	4
Sinus tachycardia + ST-T	3
≥ 3 AVRI per year	2

age-dependent sensitivity variations, the cumulative multi-marker scoring threshold (≥ 9 points) effectively mitigates these differences, maintaining high diagnostic accuracy across all age subgroups.

Thus, based on the statistical data presented, independent predictors of myocarditis in children aged 1-14 years are as follows:

1. Increase in serum troponin levels (TnT above 34 pg/ml);
2. Serum CRP above 20 mg/l;
3. LV EF reduction below 55%;
4. Combination of sinus tachycardia and ST-T changes on ECG; and
5. Frequent AVRI (3 or more episodes in the previous year).

The combination of these five signs allows – with a probability of 98.1% – diagnosing myocarditis at an early stage and can be recommended for implementation in pediatric practice.

Stratified analysis by three age subgroups (1-3 years, 4-7 years, and 8-14 years) revealed significant differences in the sensitivity and informativity of diagnostic markers of myocarditis.

In subgroup I of SG of children aged 1-3 years ($n = 65$), myocarditis was most severe and often subclinical. The analysis sensitivity of serum troponin concentration reached 98.5%, ECG 84.6%, and ECHO 95.4%. The earliest markers were sinus tachycardia (92.3%) and pericardial effusion (38.5%). Radiographic cardiomegaly was reported in 69.2% of patients. Laboratory parameters of inflammation (CRP) were maximally expressed (on average 62.4 ± 38.1 mg/l).

In subgroup II (4–7-year-olds) of SG ($n = 28$), the sensitivity of the analysis of serum troponin levels decreased to 89.3%, however, the significance of ECG signs (conduction abnormalities: 28.6%, ST-T changes: 67.9%) and ECHO signs increased: LVEF $< 55\%$ was detected in 60.7%, LV GPA $> -15\%$ was stated in 53.6%. Mean CRP was 42.8 ± 26.4 mg/l.

In subgroup III of SG, in children aged 8–14 years ($n = 19$), myocarditis was more often manifested by arrhythmias (ventricular ectopy in 36.8%, 1 stage AV block in 31.6%) and QTc prolongation (26.3%). Troponin sensitivity was 84.2%, ECHO 89.5%. Mean TnT and TnI were lower (78.6 ± 54.2 pg/ml and 92.4 ± 68.3 pg/ml, respectively), CRP was 36.2 ± 22.7 mg/l.

Thus, in young children, the leading markers are troponins and ECHO signs of dysfunction; in middle and older age, the role of ECGs (arrhythmias, repolarization disorders) increases.

Conclusions.

Development of AVRI -associated myocarditis in children is not directly dependent on age or gender, but is significantly linked to anamnestic risk factors, including high prior AVRI frequency (≥ 3 episodes/year, OR = 2.51), lack of vaccination against influenza (OR = 2.28), and adverse perinatal history.

Diagnostic markers of myocardial injury demonstrate age – dependent characteristics: in children aged 1-3 years, systemic biochemical markers (troponins, CRP) and echocardiographic signs of dysfunction predominate, whereas in children older than 7 years,

ECG abnormalities (arrhythmias and repolarization changes) play a primary role.

Independent predictors of myocarditis in children are: TnT > 34 pg/mL, CRP > 20 mg/L, LVEF $< 55\%$, combination of sinus tachycardia with ST-T changes, and frequent AVRI (≥ 3 episodes/year).

The proposed risk stratification model (AUC = 0.981; threshold ≥ 9 points) demonstrates high diagnostic accuracy (sensitivity 94.6%, specificity 96.1%) and enables early identification of high – risk patients in pediatric practice.

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