https://doi.org/10.35336/VA-1358

PROGNOSTIC FACTORS FOR THE EFFECTIVENESS OF CATHETER ABLATION OF FOCAL ATRIAL TACHYCARDIA IN SCHOOL-AGE CHILDREN: DATA FROM A SINGLE-CENTER REGISTRY STUDY

T.S.Kovalchuk[1], R.B.Tatarsky[1], D.Yu.Alekseeva[1], E.N.Mikhailov[1], D.S.Lebedev[1], S.V.Gureev[1], K.A.Chueva[1], O.L.Peregudina[1], D.I.Marapov[2], E.S.Vasichkina[1]

[1]Almazov NMRC, Russia, Saint-Petersburg, 2 Akkuratova str.; [2]Kazan State Medical Academy - branch of the Federal State Budgetary Educational Institution of Further Professional Education "Russian Medical Academy of Continuing Professional Education", Russia, Kazan, 36 Butlerova str.

Aim. To identify factors associated with the effectiveness of radiofrequency catheter ablation (RFA) of focal atrial tachycardia (AT) in school-aged patients in the long-term period.

Methods. The study group consisted of 57 children aged 11 to 17 years 11 months (Me 15.83, IQR 14.63-17.0), who underwent catheter ablation, including repeated, for focal AT in the Almazov National Medical Research Centre from December 2009 until April 2023. We analyzed clinical and demographic data, laboratory data, parameters of tachyarrhythmia, electrophysiological study and RFA. Structural heart diseases were present in 13 children, and idiopathic arrhythmia was present in 44 patients. The criterion for intraoperative effectiveness were the absence of arrhythmia at the end of the waiting period in the X-ray operating room, delayed - within 12 months after the procedure.

Results. Intraoperative effectiveness of RFA was achieved in 51 patients (89.5%), long-term - in 32 patients (56.1%). Based on the data obtained, a prognostic model of the delayed effectiveness of RFA of focal AT in school-age children was developed ($p<0.001$). Predictors included in the model: percentage of arrhythmia during the day (odds ratio (OR): 0.981; 95% confidence interval (CI) 0.962-0.999; p=0.043), presyncope (OR: 0.177; 95% CI 0.035-0.903; p=0.037), number of ectopic foci (OR: 0.289; 95% CI 0.128-0.649; p=0.003), right atrium localization (OR: 0.097; 95% 0.013-0.699; p=0.021). The area under the ROC curve corresponding to the association of the absence of arrhythmia after ablation and the values of the logistic regression function was 0.843±0.54 with 95% CI: 0.738-0.938. The sensitivity was 81.3%, specificity - 76.0%. No significant association with effectiveness of RFA was found between the method of arrhythmia induction and the use of drug sedation.

Conclusion. It was established that factors such as percentage of arrhythmia during the day, the presence of presyncope, the number of ectopic foci and the presence of an ectopic foci in the right atrium had an inverse relationship with the effective outcome of RFA.

Key words: atrial tachycardia; children; radiofrequency catheter ablation; arrhythmia burden; presyncope

Conflict of Interest: none.
Funding: none.
Received: 10.04.2024 **Revision received:** 23.07.2024 **Accepted:** 12.08.2024
Corresponding author: Kovalchuk Tatyana, E-mail: tskovalchuk@yandex.ru

T.S.Kovalchuk - ORCID ID 0000-0002-0842-9560, R.B.Tatarsky - ORCID ID 0000-0001-6752-3306, D.Yu.Alekseeva - ORCID ID 0000-0003-1751-1424, E.N.Mikhailov - ORCID ID 0000-0002-6553-9141, D.S.Lebedev - ORCID ID 0000-0002-2334-1663, S.V.Gureev - ORCID ID 0000-0003-2416-5304, K.A.Chueva - ORCID ID 0000-0002-5027-0565, O.L.Peregudina - ORCID ID 0000-0002-2761-7209, D.I.Marapov - ORCID ID 0000-0003-2583-0599, E.S.Vasichkina - ORCID ID 0000-0001-7336-4102

For citation: Kovalchuk TS, Tatarsky RB, Alekseeva DYu, Mikhailov EN, Lebedev DS, Gureev SV, Chueva KA, Peregudina OL, Marapov DI, Vasichkina ES. Prognostic factors for the effectiveness of catheter ablation of focal atrial tachycardia in school-age children: data from a single-center registry study. *Journal of Arrhythmology.* 2024;31(3): 41-50. https://doi.org/10.35336/VA-1358.

Focal atrial tachycardias (AT) in children are the third most common of all supraventricular tachycardias (SVTs). According to the literature, they account for about 14-25% regardless of age, but the true prevalence is not reliably known because of the high percentage of asymptomatic forms and the likelihood of spontaneous resolution [1, 2]. However, the probability of spontaneous resolution of arrhythmias decreases with the age of the child and is about 25-34% in children over three years of age [3-5]. Given the peculiarities of clinical manifestations, atrial tachycardia is the most frequent cause of arrhythmia associated cardiomyopathy (AAC) in children [6].

It should be acknowledged that, as of the present, no universally accepted algorithm exists for determining the management tactics for patients with ATs. Dynamic monitoring of the natural progression of arrhythmia, along with the utilization of both medical and interventional treatment methods, are considered viable approaches for managing this condition [3, 5, 7, 8]. The effectiveness of drug therapy according to the literature ranges from 50 to 74% and decreases with age [3-5].

In recent decades, radiofrequency catheter ablation (RFA) has seen increased application in pediatric practice and is now regarded as the treatment of choice for patients with hemodynamically significant paroxysms, the development of AAC, or those who are refractory to pharmacological therapy or experience adverse effects from medications. Additionally, RFA may be considered in cases where there is poor adherence to drug therapy [5, 9]. An effective RFA procedure also improves the quality of life of school-aged children [10].

Nevertheless, in cases of atrial heart rhythm disturbances (HRD), data from the European Multicenter Pediatric Catheter Ablation Registry (EUROPA) indicate that RFA was utilized in only 4.9% of instances, with focal AT comprising 2.9% of these cases. This prevalence is notably lower compared to its application in other forms of supraventricular tachycardia [11]. The efficacy of interventional treatment in pediatric ATs is lower than in other types of arrhythmias [8]. According to the findings from the registry, the acute efficacy of radiofrequency catheter ablation (RFA) was reported as 95.6% for all types of arrhythmias. However, for AT specifically, the efficacy was somewhat lower at 80%. Additionally, within one year of follow-up post-RFA, recurrence of arrhythmia was observed in 11% of patients [11].

The aim of our study was to identify factors associated with the efficacy of RFA of focal AT in the distant period in school-aged patients.

METHODS

A database of patients with focal AT who underwent RFA at our Center from December 2009 to April 2023 was analyzed. The inclusion criteria were the patient's age at the time of ablation (from 11 to 18 years), the last RFA performed in the Almazov Federal State Institution of Medical Center. Exclusion criteria were a history of open-heart surgery (3/60, 5%). The study group consisted of 57 children aged 11 to 17 years 11 months (Me 15.83, IQR 14.63-17.0).

Data were collected from patients' electronic health records, outpatient or telemedicine consultation records, and included results from objective examinations, laboratory tests, electrocardiograms (ECG), 24-hour ECG monitoring (Holter monitoring), echocardiography (Echo), endovascular electrophysiological studies (endoEPS), and RFA protocols. Echo parameters were estimated using the Boston Children's Hospital z-score calculator (https://zscore.chboston.org/). AAC was diagnosed in the presence of dilatation of the heart chambers (z-score greater than 2.0) and/or decreased contractility of the left ventricular myocardium.

The presumed localization of the ectopic focus was initially determined based on the morphology of the P wave on the ECG, following the algorithm proposed by P.M. Kistler et al. The precise localization was then confirmed during endovascular electrophysiological studies (endoEPS), by identifying the zone of early activation using electroanatomical mapping techniques [1, 12,

Table 1.

Results of comparative analysis of groups of patients with effective and ineffective radiofrequency ablation in the remote period (quantitative signs, Me [IQR])

Indicators	Groups by RFA outcome		p
	Effective (n=32)	Ineffective (n=25)	
Age of onset of complaints, years	12.0[7.3;14.5]	9.75[7.6;14.9]	0.590
Age at the time of RFA, years	16.1[14.8;16.8]	15.8[14.6;17.1]	0.949
Follow-up period from debut to RFA, months	47[14;73]	60[13;96]	0.568
Echocardiography			
Transverse dimension of the LA, z-score	-0.93[-1.41;-0.49]	-0.76[-1.13;0.3]	0.240
Longitudinal dimension of LA, z-score	-1.42[-1.8;-0.99]	-1.13[-1.67;-0.45]	0.383
LA in parasternal position, z-score	-0.03[-0.58;0.61]	-0.38[-1.01;0.07]	0.307
Transverse dimension of RA, z-score	-1.66[-2.18;-1.19]	-1.5[-2.36;-0.39]	0.473
Longitudinal dimension of RA, z-score	-2.44[-3.25;-2.02]	-1.45[-3.09;-0.91]	0.275
LV EDD, z-score	-0.36[-1.32;-0.08]	-0.7[-1.45;-0.03]	0.825
LVEF, Simpson, %	51.0[47.0;58.0]	52.0[47.5;61.5]	0.886
LVEF, Teicholz, %	63.0[57;70.3]	63.0[60.0;68.5]	0.993
LVEF, Teicholz, % (HRD)	58.0[51.0;60.3]	58.0[56.4;60.5]	0.612
Electrocardiogram for tachycardia			
Arrhythmia density, %	37.7[10.4;91.3]	57.7[8.2;98.0]	0.386
RFA			
Fluoroscopy time, min	10.0[5.5;13.5]	10.0[5.0;13.0]	0.968
Operation time, min	105.0[90;140]	135.5[100;190]	0.127

Notes: hereinafter RFA - radiofrequency ablation; LA - left atrium; RA - right atrium; LV - left ventricle; EF - ejection fraction; HRD - heart rhythm disturbances.

13]. Tachycardias were categorized into right-sided and left-sided tachycardias. Right-sided tachycardias included those originating from ectopic foci located in the right atrial appendage (RAA), the walls of the right atrium, the crista terminalis, the tricuspid valve area, the cavo-tricuspid isthmus, the interatrial septum (IAS) on the right atrial side, or the orifice of the coronary sinus (CS). Left-sided tachycardias encompassed those originating from the left atrial appendage (LAA), the walls of the left atrium, the pulmonary veins, the interatrial septum (IAS) on the left atrial side, the mitral valve area, or the mitral isthmus.

The criteria of antiarrhythmic drug (AAD) ineffectiveness included the presence of paroxysms of tachycardia clinically and/or according to Holter monitoring, in patients with chronic AT – absence of sinus rhythm recovery or persisting HR values above 95‰ for the patient's age, signs of AAC on the background of ongoing therapy [14, 15].

On the 1st to 2nd day following RFA, all patients underwent a 12-lead ECG and Echo to assess myocardial contractility and detect any fluid in the pericardial cavity. From the 2nd to 4th day, patients were subjected to Holter monitoring. If pneumothorax was suspected, chest radiography was performed.

Voluntary informed consents for the examination and RFA procedure were signed by the patients' legal representatives and patients older than 15 years of age.

Prior to RFA, in accordance with standard practice [5], AAD administration was discontinued for at least five half-lives. However, for two patients who experienced persistent symptomatic, hemodynamically significant tachycardia with elevated heart rates, AAD therapy was discontinued only 12 to 16 hours before the procedure. A three-dimensional electroanatomical mapping system was used in all patients: Carto®3 (Biosense Webster, USA) in 55 patients (96.5%) and Rhythmia (Boston Scientific,

Table 2.

Results of comparative analysis of groups of patients with effective and ineffective radiofrequency ablation in the remote period (categorical features)

Indicators	Groups by RFA outcome		p
	Effective (n=32)	Ineffective (n=25)	
Boys, n (%)	24 (75.0)	16 (64.0)	0.37
Complaints			
Heart palpitations, n (%)	20 (62.5)	20 (80.0)	0.152
Dizziness, n (%)	9 (28.1)	11 (44.0)	0.213
Decrease in exercise tolerance, n (%)	9 (28.1)	10 (40.0)	0.345
Weakness*, n (%)	5 (15.6)	11 (44.0)	0.018
Presyncope*, n (%)	4 (12.5)	9 (36.0)	0.036
Electrocardiogram for tachycardia			
Minimum tachycardia cycle duration, ms, M (SD)	368.7±77.9	362.0±84.2	0.824
Tachycardia cycle duration maximal, ms, M (SD)	403.3±82.9	429.7±85.2	0.398
Nature of the arrhythmia			
Paroxysmal, n (%)	9 (28.1)	8 (32.0)	0.751
Permanent-return >50%, n (%)	8 (25.0)	10 (40.0)	0.227
Permanent-return <50%, n (%)	8 (25.0)	2 (8.0)	0.094
Chronic, n (%)	7 (21.9)	5 (20.0)	0.863
Echocardiography			
Structural pathology*, n (%)	4 (12.5)	9 (36.0)	0.036
RFA			
Manipulation-induced AF*, n (%)	9 (28.1)	14 (56.0)	0.033
Induction of AF without HR recovery through AF*, n (%)	4 (12.5)	11 (44.0)	0.01
Right-sided localization*, n (%)	20 (62.5)	22 (88.0)	0.030
Left-sided localization*, n (%)	10 (31.3)	2 (8.0)	0.028
Presence of more than 1 ectopic focus*, n (%)	6 (18.8)	14 (56.0)	0.003
General/combined anesthesia, n (%)	9 (28.1)	8 (32.0)	0.751
Initial HRD, no induction required, n (%)	22 (68.8)	14 (56.0)	0.322
Drug induction of HRD, n (%)	6 (18.8)	8 (32.0)	0.249
Repeated RFA procedures, n (%)	6 (18.8)	4 (16.0)	0.786
Difficulties in induction/mapping, n (%)	3 (9.4)	4 (16.0)	0.450

Notes: * - differences of indicators are statistically significant ($p<0.05$); SR - sinus rhythm; AF - atrial fibrillation.

USA) in 2 (3.5%). The procedure was performed under either local anesthesia (40 patients, 70.2%) or general/combined anesthesia (17 patients, 29.8%).

All patients underwent puncture of the right femoral vein and, if necessary, additionally the right subclavian vein (n=24, 42.1%) or jugular vein (n=1, 1.8%); the diagnostic electrode was placed in the RA and the ablation electrode in the RA. For left-sided foci, access to the LA was performed through an open oval window or IAS puncture under fluoroscopic control with the use of contrast agent. A transseptal intraducer (Preface, Biosense Webster, USA or Agilis™ NxT, St. Jude Medical, USA) was inserted into the LA. Further, the anatomical and activation map of the atrium was constructed, during which the localization of the ectopic focus was determined according to the zone of early activation. In the absence of AT, the protocol involved programmed atrial and ventricular stimulation to determine the effective refractory period and Wenkebach's point. If necessary, incremental atrial stimulation was employed, along with pharmacological provocation using adrenergic agonists or atropine at a dose of 1 mg to facilitate induction.

Ablation was performed using a 3.5-mm open-loop irrigation catheter (NaviStar ThermoCool; Biosense Webster, USA or IntellaNav, Boston Scientific, USA). RFA parameters: power 20-40 W, temperature up to 39 °C, catheter irrigation using a CoolFlow pump (Biosense Webster, USA) at a rate of 17-30 ml/min.

The study evaluated the intraoperative and delayed efficacy of RFA. In patients who underwent repeat surgery, efficacy was assessed according to the last procedure performed. The criterion for intraoperative efficacy was the absence of tachycardia induction at the end of the procedure in the fluoroscopy suite. Delayed efficacy was assessed 12 months post-procedure by evaluating the recurrence of tachycardia. To evaluate the delayed effects of the surgery, standard ECG and 24-hour ECG monitoring were performed at 3, 6, and 12 months. Additionally, if AACs were present, Echo was conducted at these same intervals [16]. The delayed efficacy of radiofrequency catheter ablation, defined as the absence of AT episodes 12 months postoperatively, was assessed as a predictive factor. This was quantified as the odds ratio (OR) within the predictive model.

The present single-center retrospective cohort study was approved by the Ethics Committee of the Almazov NMRC.

Statistical analysis

The methods of parametric and nonparametric analysis were used for statistical processing. Accumulation, correction, systematization of initial information and visualization of the obtained results were carried out in Microsoft Office Excel 2019 spreadsheets. Statistical analysis was performed using IBM SPSS Statistics v.26 program (developer - IBM Corporation, USA).

Quantitative measures were assessed for conformity to a normal distribution using the Shapiro-Wilk criterion or the Kolmogorov-Smirnov criterion. Normally distributed quantitative measures were described by the mean (M) and standard deviation (SD). Scores whose distribution differed from normal were described using median (Me) and interquartile range (IQR). Categorical data were described using absolute values and percentages.

The Student's t-test was used to compare normally distributed quantitative indicators, and the Mann-Whitney U-test was used in the absence of normal distribution. Categorical data were compared using Chi-square or Fisher's exact test. The binary logistic regression method was used to build the prognostic model, with threshold value and prognostic significance indices determined using ROC analysis. For each predictor included in the model, odds ratio (OR) values were calculated. Differences at $p<0.05$ were considered statistically significant.

RESULTS

To identify prognostic factors influencing the efficacy of RFA for focal AT in school-age children, we analyzed data from 57 patients. These patients were categorized into two groups based on the outcome of the procedure: 32 patients in the «effective» RFA group and 25 patients in the «ineffective» RFA group. Intraoperative efficacy of RFA was achieved in 51 patients (89.5%), and long-term efficacy, considering repeated interventions - in 32 patients (56.1%).

Table 3.

Distribution of patients according to the nature and density of arrhythmias

Indicator	n, %
Nature of the arrhythmia	
Paroxysmal	17 (29.8)
Chronic	40 (70.2)
Including permanent	17 (42.5)
Including permanent-return	23 (57.5)
Arrhythmia density	
90-100%	17 (42.5)
50-89%	13 (32.5)
30-49%	4 (10)
≤29%	6 (15)

Table 4.

Patients with structural heart disease

Structural heart pathology	n (%)
Myocarditis	7 (53.8)
Primary genetically determined CMP	
Mutations in the TTN gene	1 (7.7)
Mutations in the TTN and SCNB1 genes	1 (7.7)
Mutations in the MYH6 and BRAF genes	1 (7.7)
CHD without surgical correction	1 (7.7)
Combination of CHD and chronic myocarditis	1 (7.7)
CMP in the structure of neuromuscular pathology (Emery-Dreyfuss myopathy, mutation in the EMD gene)	1 (7.7)
Total	13 (22.8)

Note: CMP - cardiomyopathy; CHD - congenital heart defect.

In 6 patients (10.5%) RFA was initially ineffective: in 4 patients (7%) there were difficulties in arrhythmia mapping (in 2 patients - induction difficulties, in 2 patients - re-induction of atrial fibrillation (AF), requiring repeated electric pulse therapy and medication), in 2 patients (3.5%) - polyphonic nature of HRD, requiring application of many RF interventions. Nineteen patients (33.3%) had arrhythmia recurrence.

A total of 70 RFA procedures were cumulatively performed in the study patients. Of the 57 RFA procedures included in the analysis, 10 were repeat procedures (17.5%): 7 patients (12.3%) had two procedures and 3 (5.3%) had three procedures. Two patients had previously undergone interventional treatment at another Center. The time interval between treatments ranged from 2 weeks to 22 months (Me 6.75 months, IQR 0.5-15 months). Intraoperative efficacy was achieved in all 10 patients; however, 4 patients had arrhythmia recurrence (3 in the first day and 1 patient with paroxysmal AT 11 months after RFA). Thus, final efficacy was achieved in 6 (60%) of them. During the last ablation, AT was initially recorded in 8 patients and drug provocation was required in 2 patients; in the preceding procedure, AT was recorded in 6 and 4 patients, respectively. The localization of the ectopic focus did not differ significantly between the groups. However, during subsequent procedures, additional areas of ectopic activity that required ablation were identified in 4 patients. The clinical and instrumental characteristics and results of comparative analysis of the «effective» and «ineffective» RFA groups are presented in Tables 1, 2.

The distribution of patients according to the clinical and electrophysiologic classification of supraventricular tachycardias in children [1], is presented in Table 3. It should be noted that the term «chronic» does not fully reliably reflect the nature of arrhythmia in patients with persistent-onset tachycardia and arrhythmia representation of less than 50% during the day, we considered it appropriate to divide patients from this group depending on arrhythmia density (arrhythmia representation during the day according to the Holter monitoring) before RFA.

Eight (14%) patients had no complaints; indications for RFA were the development of AAC (n=1), ineffectiveness of AAD with high arrhythmia presentation (n=2), child's desire for sports/professional guidance (n=3), and low adherence to medication (n=2). In 13 patients (22.8%) the presence of structural pathology of the heart was confirmed during standard cardiologic examination (Table 4). In the remaining 44 patients (77.2%), no clear cause of arrhythmia was identified and such arrhythmias were considered «idiopathic». Signs of AAC were detected in 19 patients (33.3%): reduction of left ventricular ejection fraction was noted in 17 (29.8%), left ventricular dilatation - in 5 (8.8%), atrial dilatation - in 2 (3.5%). Heart failure symptoms in patients corresponded to functional class 1-2 (NYHA).

Forty-one patients (71.9%) received 1 to 6 different antiarrhythmic therapy regimens before RFA, using both a single drug at a time and various combinations (beta-blockers + IC class AADs, IC + III class AADs, digoxin + beta-blockers, ivabradine + III class AADs).

During 57 RFA procedures evaluated, 79 ectopic foci were ablated. Right-sided localization occurred in 42 patients (73.7%), left-sided - in 12 patients (21.1%), and in three patients (5.2%) ectopic foci were localized in both atria. More detailed data are presented in Table 5. In 20 patients (35%), mapping revealed more than 1 ectopic focus.

Table 5.

Localization of ectopic foci (n, % of the number of RFA)

Localization of ectopic foci	Total	RFA effective	RFA ineffective
Crista terminalis	22 (38.6)	11 (34.4)	11 (44.0)
Atrial wall	12 (21)	6 (18.8)	6 (24.0)
Coronary sinus	10 (17.5)	8 (22.9)	2 (8.0)
Interatrial septum	9 (15.8)	5 (15.6)	4 (16.0)
Atrial auricles	7 (12.3)	2 (6.3)	5 (20.0)
Valve area	6 (10.5)	1 (3.1)	5 (20.0)
Cavotricuspidal isthmus.	5 (8.8)	3 (9.4)	2 (8.0)
Pulmonary vein area	5 (8.8)	3 (9.4)	2 (8.0)
Isthmus between LSPV and LAA	2 (3.5)	2 (6.3)	0 (0.0)
Mitral isthmus region	1 (1.8)	1 (3.1)	0 (0.0)

Notes: LSPV - left superior pulmonary vein; LAA - left atrial appendage.

Table 6.

Characteristics of predictors of effective radiofrequency ablation outcome

Predictor	OR	95% CI	p-value
Arrhythmia density	0.981	0.962-0.999	0.043
Presyncope complaints	0.177	0.035-0.903	0.037
Number of foci	0.289	0.281-0.649	0.003
Presence of a focus in the RA	0.097	0.013-0.699	0.021

Notes: CI - confidence interval; OR - odds ratio

In the group of patients in whom RFA was ineffective, the prevalence of complaints of weakness (p=0.018) and presyncopal states (p=0.036) and the presence of structural heart pathology (p=0.036) were statistically significant. In patients with left-sided localization of ectopic foci according to endoEPS, RFA was statistically significantly more often effective (p=0.046), while no significant differences were obtained according to the specified localization. The procedure was most often ineffective when more than 1 ectopic focus was present (p=0.003).

No statistically significant difference in RFA efficacy was obtained depending on the characteristics of the procedure (operation time, radiation exposure, fluoroscopy time), type of anesthesia aid, features of induction and mapping of the ectopic focus. Patients in the group of «ineffective» RFA had statistically signifi-

cantly more frequent manipulation-induced AF induction intraoperatively (p=0.033), however, there was no significant association of AF induction with the localization of ectopic focus, polyphonic nature of arrhythmia.

Based on the results of preliminary data analysis, we identified the following potential risk factors for ineffective RFA: the presence of structural heart pathology, high arrhythmia representation according to the Holter monitoring, presence of more than one arrhythmic focus, localization of arrhythmic substrate, induction of AF during RFA, and clinically more severe course of the disease.

When clinical-anamnestic and instrumental data were included in the stepwise regression analysis by the exclusion method, a prognostic model was developed to determine the probability of effective RFA outcome, including 4 independent predictors. The observed dependence is described by Eq:

$p=1 / (1 + e^{-z}) * 100\%$

z=5.4 - 0.02*Xdensityaarhyt - 1.734*Xpresyncope - 1.23*Xfocinum - 2.34*Xrightatriumloc (1)

where p is the probability of effective radiofrequency catheter ablation (RFA) (%), Xdensityaarhyt is the arrhythmia density (%), Xpresyncope is the presence of presyncope (0 = no, 1 = yes), Xfocinum is the number of ectopic foci (1 = one, 2 = two, 3 = three or more), and Xrightatriumloc is the presence of a focus in the right atrium (0 = no, 1 = yes).

The regression model obtained on the training sample is statistically significant (p<0.001). According to the value of the Nijelkerk coefficient of determination, model (1) determines 44.9% of the variance of the probability of developing an effective RFA outcome.

Based on regression coefficient values, arrhythmia density, the presence of presyncope, the presence of a foci in the right atrium, and the number of foci have an inverse relationship with the probability of developing an effective RFA outcome. Thus, the presence of presyncope complaints reduced the odds of effective outcome of RFA by 5.65-fold (OR: 0.177; 95% CI 0.035-0.903; p=0.037), and the presence of a focus in the right atrium by 10.3-fold (OR: 0.097; 95% 0.013-0.699; p=0.021). A 1% increase in arrhythmia representation by the preoperative Holter monitoring data decreased the odds of effective RFA outcome by 1.02-fold (OR: 0.981; 95% CI 0.962-0.999; p=0.043) and 3.46-fold for each arrhythmic substrate if more than 1 ectopic focus was present (OR: 0.289; 95% CI 0.128-0.649; p=0.003). The characteristics of the predictors are presented in Table 6.

The area under the ROC curve corresponding to the relationship between the prediction of effective RFA and the value of the logistic regression function was 0.843±0.54 with 95% CI: 0.738-0.938. The threshold value of the function P (1) at the cut-off point was 0.5. Function values equal to or greater than this value were consistent with the prediction of effective RFA. The ROC curve of the model is shown in Fig. 1. The sensitivity of the method was 81.3% and specificity was 76.0%.

In 1 case (1.8%), complications from vascular puncture (pneumothorax that did not require puncture and drainage) were observed during RFA.

DISCUSSION

AT in children are currently the smallest group of all arrhythmias undergoing interventional treatment. According to our results, in Almazov NMRC the share of AT accounts for about 5.5% of all performed RFA procedures, which is comparable to the data of other large arrhythmological centers.

One of the factors complicating the decision-making process for interventional treatment of AT is subjectivity in determining the ineffectiveness and intolerance of drug therapy, which is based on the opinion of the attending physician and the patient / his/her legal representatives [5]. A special group of patients also includes adolescents involved in professional sports, in whom the presence of clinically significant arrhythmia is a contraindication to admission to training and participation in competitions [16, 17]. These examples demonstrate the need for a way to predict the efficacy of the RFA procedure in pediatric patients with AT.

In our study, we compared groups of school-aged patients according to the efficacy of RFA of focal AT to optimize the algorithm of patient selection for this procedure aimed at improving the effectiveness of the intervention and reducing the number of recurrences. The intraoperative efficacy rate of AT ablation in our study was 89.5%, which is comparable to the literature data, according to which it ranges from 62.5% to 100%. The «ultimate» success rates are 63.6-96.6%, which is slightly higher than the result obtained at our Center [18-25].

It is believed that the efficacy of interventional treatment and complication rates depend on many factors, including the presence of structural heart disease, the nature of arrhythmia, the patient's weight, and the number of radiofrequency exposures [26]. In a study by C.E. Balla et al. (2019), comparing a group with effective RFA to a group with recurrence of focal AT in children and young patients under 30 years of age, no statistically significant

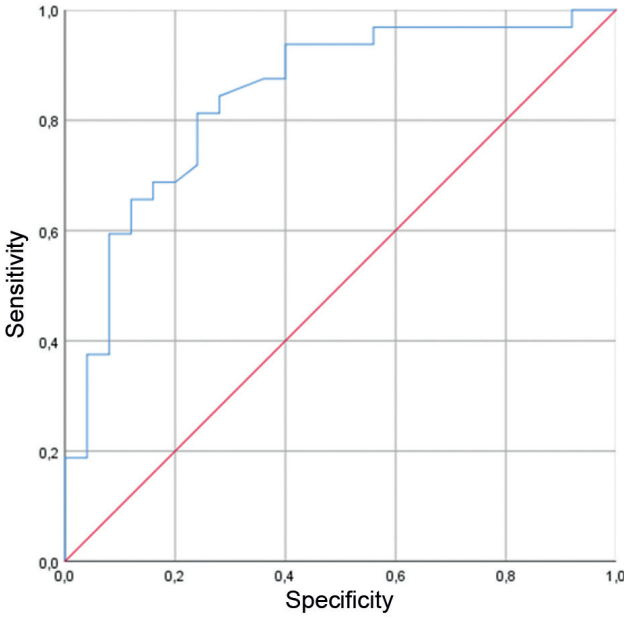

Fig. 1. ROC curve characterizing the dependence of the probability of ineffective radiofrequency ablation on the value of the prognostic model.

differences were found in the localization or number of ectopic foci between the groups [25]. In a literature analysis conducted by S.A. Chen et al. (1998), it was demonstrated that right-sided localization of the ectopic focus is the only independent predictor of RFA efficacy, while the presence of polymorphic tachycardia serves as a predictor of tachycardia recurrence [27]. I. Anguera et al. (2001) also observed that lower intraoperative efficacy rates were associated with patients who had persistent-recurrent forms of AT and those with multiple ectopic foci [28].

Some of the predictors obtained in our study coincide with the data from the literature. Thus, a clinically more severe course, characterized by complaints of weakness, presyncope, the presence of structural heart pathology, more than one ectopic focus, and an ectopic focus located in the right atrium, was significantly associated with the ineffectiveness of interventional treatment. In addition, our study derived a model to predict the long-term efficacy of RFA in children with focal AT by multivariate analysis.

Our results are consistent with the distribution of ectopic foci described previously for adult patients and adolescents [5, 8, 9]. The crista terminalis region was the most frequent (38.6%). In the group of «ineffective» RFA there was some relative quantitative predominance of localization in the region of valves and atrial appendages, however, statistically significant difference of RFA efficiency depending on more precise localization was not obtained, which, probably, can be attributed to the small number of observations.

According to P.C.Lee et al. (2007), two or more sources of ectopic automatism are determined in 20-30% of focal AT cases [29]. In our study, the presence of more than 1 ectopic focus was noted in 20 (35%) patients with a statistically significant predominance in the «ineffective» RFA group. In the studies with the highest intraoperative and long-term efficacy of the ablation procedure, the number of patients with polyphonic arrhythmias was lower and amounted to 3-8.3% [3, 18, 25].

Intraoperative ineffectiveness of RFA may also be related to the difficulty of AT induction and mapping. One reason may be the administration of medication sedation [11, 30]. According to a review of the current literature by G. Vladinov et al. (2018) on the effects of the most used anesthetics for sedation and anesthesia during endoEPS, which included seven studies in children, no association was found between the administration of fentanyl and difficulties in arrhythmia induction. In a study by L.P. Lai et al. (1999), tachycardia ceased in four out of seven children with focal AT following propofol infusion and could not be re-induced with isoproterenol infusion, thereby preventing the performance of RFA. Based on these findings, the researchers concluded that intravenous anesthesia with propofol is suitable for most tachyarrhythmias during RFA, except for focal AT [31, 32]. B.Kast et al (2022) noted that children with focal AT tended to have a lower probability of induction with IV anesthesia compared to inhalation anesthesia (64% vs 88%) [33]. In our study, difficulties in induction and mapping were observed in 7 patients (12.3%), and in 3 of these cases, it led to the absence of an intraoperative effect of ablation (12% of the total number of «ineffective» RFA cases). However, no significant association was found between these induction difficulties, the use of drug sedation, and the overall effectiveness of RFA.

Additional reasons for unsatisfactory results of RFA described in the literature are epicardial location of foci and wide arrhythmogenic field in the atrial wall [11, 18]. Wide arrhythmogenic field according to the data of operation protocols was described in 7 patients (12.3%), 5 of whom had recurrence of tachycardia in the first day after surgery. There were no patients with epicardial localization of foci in the study group. Our study also revealed that patients with «ineffective» RFA more frequently experienced intraoperative induction of AT beats. In our opinion, this may be associated with greater anisotropy of myocardial tissues in this group.

One of the factors for achieving higher cumulative long-term efficacy of RFA is repeated procedures [3, 18, 21]. In our case, the lower percentage of «delayed» efficacy may also be related to patients' and their legal representatives' refusal of repeated RFA procedures and their choice in favor of drug treatment.

A study by C.E.Balla et al (2018) showed that almost all recurrences of focal AT after RFA manifest within 6 months after ablation; however, among our patients, 2 patients developed complaints at 10 and 11 months after ablation, which is in line with the recommendations of experts on 24-hour ECG follow-up also at 12 months after surgery [16, 25].

Predicting the risk of ineffective RFA in patients with focal AT is highly relevant, as identification of predictors of ineffective RFA will allow personalizing the strategy of management of children with this nosology.

Limitations of the study

The limitations of the study include a small sample size, which is primarily justified by the infrequent selection of interventional treatment for the pathology being studied. n addition, the lack of validation of the developed prognostic model prevents us from assessing its performance in clinical practice.

CONCLUSION

The study developed a prognostic model for the delayed efficacy of radiofrequency catheter ablation of focal AT in school-aged children. The model revealed that factors such as arrhythmia density, presence of presyncope, number of ectopic foci, and the presence of an ectopic focus in the right atrium were inversely related to the likelihood of achieving an effective RFA outcome. The use of the proposed model, in conjunction with the evaluation of the clinical presentation of the disease, has the potential to optimize the decision-making algorithm for managing school-age patients with relative indications for interventional treatment of arrhythmias.

REFERENCES

1. Kruchina TK, Egorov DF. Sinus and atrial tachycardias. In Supraventricular tachycardias in children: manifestation, diagnosis, treatment. Saint-Petersburg 2011: 65-112. (In Russ) ISBN 978-5-93339-174-6.

2. Ko JK, Deal BJ, Strasburger JF, Benson DW Jr. Supraventricular tachycardia mechanisms and their age distribution in pediatric patients. *Am J Cardiol*. 1992;69(12): 1028-1032. https://doi.org/10.1016/0002-9149(92)90858-v.
3. Kang KT, Etheridge SP, Kantoch MJ, et al. Current management of focal atrial tachycardia in children: a multicenter experience. *Circ Arrhythm Electrophysiol*. 2014;7(4): 664-670. https://doi.org/10.1161/CIRCEP.113.001423.
4. Salerno JC, Kertesz NJ, Friedman RA, et al. Clinical course of atrial ectopic tachycardia is age-dependent: results and treatment in children < 3 or > or =3 years of age. *J Am Coll Cardiol.* 2004;43(3): 438-444. https://doi.org/10.1016/j.jacc.2003.09.031.
5. Philip Saul J, Kanter RJ, Asirvatham S, et al. PACES/HRS expert consensus statement on the use of catheter ablation in children and patients with congenital heart disease: Developed in partnership with the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American Academy of Pediatrics (AAP), the American Heart Association (AHA), and the Association for European Pediatric and Congenital Cardiology (AEPC). *Heart Rhythm*. 2016;13(6): e251-e289. https://doi.org/10.1016/j.hrthm.2016.02.009.
6. Moore JP, Patel PA, Shannon KM, et al. Predictors of myocardial recovery in pediatric tachycardia-induced cardiomyopathy. *Heart Rhythm*. 2014;11(7): 1163-1169. https://doi.org/10.1016/j.hrthm.2014.04.023.
7. Benatar A, Dewals W. Incessant Ectopic Atrial Tachycardia in the Pediatric Age: Clinical Presentation and Therapeutic Options. *Ann Cardiol Cardiovasc Med*. 2018;2(2): 1016.
8. Brugada J, Katritsis DG, Arbelo E, et al. 2019 ESC Guidelines for the management of patients with supraventricular tachycardiaThe Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC) [published correction appears in Eur Heart J;41(44):4258]. *Eur Heart J*. 2020;41(5): 655-720. https://doi.org/10.1093/eurheartj/ehz467.
9. Brugada J, Blom N, Sarquella-Brugada G, et al. Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement. *Europace*. 2013;15(9): 1337-1382. https://doi.org/10.1093/europace/eut082.
10. Abo-Haded HM. Radiofrequency ablation changes the quality of life of children with supraventricular tachycardias. *Arch Dis Child*. 2015;100(8): 754-757. https://doi.org/10.1136/archdischild-2014-306466.
11. Krause U, Paul T, Bella PD, et al. Pediatric catheter ablation at the beginning of the 21st century: results from the European Multicenter Pediatric Catheter Ablation Registry 'EUROPA'. *Europace*. 2021;23(3): 431-440. https://doi.org/10.1093/europace/euaa325.
12. Kistler PM, Roberts-Thomson KC, Haqqani HM, et al. P-wave morphology in focal atrial tachycardia: development of an algorithm to predict the anatomic site of origin. *J Am Coll Cardiol.* 2006;48(5):1010-1017. https://doi.org/10.1016/j.jacc.2006.03.058.
13. Svintsova LI, Dzhaffarova OYu, Plotnikova IV. Prediction of antiarrhythmic therapy effectiveness in children. *Russian Journal of Cardiology*. 2019;7:75-82 (In Russ). https://doi.org/10.15829/1560-4071-2019-7-75-82.
14. Fleming S, Thompson M, Stevens R, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. Lancet. 2011;377(9770): 1011-1018. https://doi.org/10.1016/S0140-6736(10)62226-X.
15. Konev AV., Jelyakov EG., Ardashev AV. On the issue of standardization of interventional interventions in arrhythmology. In Clinical arrhythmology. Moscow 2009: 1107-1159 (In Russ) ISBN 978-5-98803-198-7.
16. Kovalev IA., Khamnagadaev IA., Svintsova LI., et al. Supraventricular Tachycardia in Children. *Pediatric pharmacology*. 2019;16(3):133-143 (In Russ) https://doi.org/10.15690/pf.v16i3.2024.
17. Boytsov SA, Kolos IP, Lidov PI, et al. National recommendations on the admission of athletes with cardiovascular system deviations to the training and competition process. *Rational Pharmacotherapy in Cardiology*. 2011;7(6): 4-60. (In Russ)].
18. Dieks JK, Müller MJ, Schneider HE, et al. Catheter Ablation of Pediatric Focal Atrial Tachycardia: Ten-Year Experience Using Modern Mapping Systems. *Pediatr Cardiol*. 2016;37(3): 459-464. https://doi.org/10.1007/s00246-015-1299-x.
19. Sahin GT, Kafali HC, Ozturk E, et al. Catheter ablation of focal atrial tachycardia in children using three-dimensional electroanatomic mapping system: a 6-year single-centre experience. *Cardiol Young*. 2021;31(5): 744-750. https://doi.org/10.1017/S1047951120004527.
20. Hiippala A, Happonen JM. Population-based single-center outcome for pediatric catheter ablation of common supraventricular tachycardias. *Pacing Clin Electrophysiol*. 2015;38(1): 115-119. https://doi.org/10.1111/pace.12511.
21. Kubuš P, Vít P, Gebauer RA, et al. Long-term results of paediatric radiofrequency catheter ablation: a population-based study. *Europace*. 2014;16(12): 1808-1813. https://doi.org/10.1093/europace/euu087.
22. Ge H, Li X, Zhang Y, et al. Clinical course and treatment of ectopic atrial tachycardia in 144 children. *Chinese Journal of Pediatrics*. 2015;53(3): 214-219. https://doi.org/ 10.3760/cma.j.issn.0578-1310.2015.03.012.
23. Jiang H, Li XM, Li MT, et al. Clinical characteristics and radiofrequency ablation of focal atrial tachycardia in 125 children. *Chinese Journal of Pediatrics.* 2020;58(11): 900-904. https://doi.org/ 10.3760/cma.j.cn112140-20200308-00199.
24. Ponnusamy SS, Muthu G, Kumar M, et al. Safety, Efficacy, and Intermediate-Term Outcomes of Radiofrequency Catheter Ablation for Pediatric Arrhythmias. *Cureus*. 2020;12(9): e10488. Published 2020 Sep 16. https://doi.org/10.7759/cureus.10488.
25. Balla C, Foresti S, Ali H, et al. Long-term follow-up after radiofrequency ablation of ectopic atrial tachycardia in young patients. *J Arrhythm*. 2019;35(2): 290-295. Published 2019 Mar 7. https://doi.org/10.1002/joa3.12172.
26. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart As-

sociation Task Force on Clinical Practice Guidelines and the Heart Rhythm Society [published correction appears in Circulation. 2016 Sep 13;134(11): e234-5]. *Circulation*. 2016;133(14):e506-e574. https://doi.org/10.1161/CIR.0000000000000311.
27. Chen SA, Tai CT, Chiang CE, Ding YA, Chang MS. Focal atrial tachycardia: reanalysis of the clinical and electrophysiologic characteristics and prediction of successful radiofrequency ablation. *J Cardiovasc Electrophysiol*. 1998;9(4): 355-365. https://doi.org/10.1111/j.1540-8167.1998.tb00924.x
28. Anguera I, Brugada J, Roba M, et al. Outcomes after radiofrequency catheter ablation of atrial tachycardia. *Am J Cardiol*. 2001;87(7):886-890. https://doi.org/10.1016/s0002-9149(00)01531-9.
29. Lee PC, Hwang B, Chen SA, et al. The results of radiofrequency catheter ablation of supraventricular tachycardia in children. *Pacing Clin Electrophysiol*. 2007;30(5):655-661. https://doi.org/10.1111/j.1540-8159.2007.00727.x.
30. Toyohara K, Fukuhara H, Yoshimoto J, et al. Electrophysiologic studies and radiofrequency catheter ablation of ectopic atrial tachycardia in children. *Pediatr Cardiol*. 2011;32(1): 40-46. https://doi.org/10.1007/s00246-010-9809-3.
31. Vladinov G, Fermin L, Longini R. et al. Choosing the anesthetic and sedative drugs for supraventricular tachycardia ablations: A focused review. *Pacing Clin Electrophysiol*. 2018;41(11): 1555-1563. https://doi.org/10.1111/pace.13511.
32. Lai LP, Lin JL, Wu MH, et al. Usefulness of intravenous propofol anesthesia for radiofrequency catheter ablation in patients with tachyarrhythmias: infeasibility for pediatric patients with ectopic atrial tachycardia. *Pacing Clin Electrophysiol*. 1999;22(9): 1358-1364. https://doi.org/10.1111/j.1540-8159.1999.tb00629.x.
33. Kast B, Balmer C, Gass M, et al. Inducibility of atrioventricular nodal reentrant tachycardia and ectopic atrial tachycardia in children under general anesthesia. *Pacing Clin Electrophysiol*. 2022;45(9): 1009-1014. https://doi.org/10.1111/pace.14566.