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EFFECTS OF ACCESSORY PATHWAY CATHETER ABLATION ON LEFT VENTRICULAR FUNCTION IN PATIENTS WITH DYSSYNCHRONY-INDUCED CARDIOMYOPATHY ASSOCIATED WITH PRE-EXCITATION SYNDROME

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Aim. To evaluate the effect of radiofrequency ablation (RFA) of accessory pathways on left ventricle (LV) function in patients with Wolff-Parkinson-White (WPW) syndrome and preexitation-induced dyssynchrony cardiomyopathy.

Methods. The study included 22 patients with registered preexitation on the ECG and signs of dyssynchronous cardiomyopathy according to echocardiography (Echo): asynchronous movement of interventricular septum, ejection fraction (EF) decrease and/or global longitudinal strain of the left ventricle (GLS LV), heart chamber increase. The average age of patients at the time of RFA of the accessory pathways - 11 years [8;14].

Results. A regular normalization of the QRS complex width was observed after RFA ($p = 0.0002$). To assess reverse LV remodeling, all patients underwent Echo on day 3 after RFA. In patients with an initially reduced LVEF, its increase was noted. In patients with initial dilatation and an increase in LV volume, normalization of these indicators was noted. However, dynamics of LVEF and its volume was not statistically significant in the early postoperative period. According to Speckle-tracking Echo during medical check-up, complete normalization of longitudinal deformation was observed in 13 patients (59%), this indicator improvement - in 7 patients (31.8%). The average GLS LV before RFA was -17.25 [-16.4; -19], after RFA - -21.5 [-19; -24] ($p = 0.0001$).

Conclusion. Reverse remodeling and restoration of LV function after RFA of accessory pathways indicates a cause-and-effect relationship between the accessory pathways functioning and dyssynchronous cardiomyopathy development. Therefore, patients with signs of preexitation-induced dyssynchronous cardiomyopathy are indicated for RFA of accessory pathways, regardless of age and tachycardia paroxysms.

Key words: Wolff-Parkinson-White syndrome; accessory pathways; dyssynchrony; cardiomyopathy; radiofrequency ablation; children; ejection fraction; global longitudinal strain

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Patients with Wolff-Parkinson-White (WPW) pattern on electrocardiogram (ECG) sometimes demonstrate left ventricular (LV) dilatation and dysfunction on echocardiography (Echo). This is due to the electrical and mechanical eccentric activation of the ventricles directly through the accessory atrioventricular pathways (AP), resulting in early activation of the basal portions of the interventricular septum (IVS) with relatively synchronous activation of the rest of the myocardium. In these situations, the abnormal motion of the IVS resembles the pattern observed in left bundle branch block. The consequence of these processes is the development of hypotrophy of the IVS which begins to function like an aneurysm, leading to the formation of segmental dyskinesia. These changes lead to pathological remodeling of LV, its dysfunction and development of preexcitation induced cardiomyopathy (PIC), mimicking idiopathic dilated cardiomyopathy [1-3]. As a rule, the formation of paradoxical interventricular conduction is observed in patients with the most pronounced pre-excitation on ECG and right septal or right lateral localization of the AP but it can also be associated with other localizations of AP [1-7].

It is important to realize that this problem resolves in most cases after radiofrequency ablation (RFA) of the AP indicating a direct role of eccentric myocardial activation in the development of paradoxical interventricular conduction by dilatation phenotype. AP RFA leads to mechanical and electrical resynchronization and normalization of LV function [1-8].

METHODS

Patient characteristics

The study included 22 patients with registered pre-excitation according to ECG, accompanied by signs

of PIC (decreased ejection fraction, increased volumes of heart chambers, and/or decreased global longitudinal LV deformation) according to Echo. All patients were under evaluation and treatment at our center from 2013 to 2023. Mean age at the time of initial hospitalization: 11 years [7;14] (range 9 months to 17 years).

Inclusion criteria for the study:

- presence of WPW pattern on ECG (WPW phenomenon or syndrome) accompanied by signs of PIC (decreased ejection fraction, increased heart chamber volumes, and/or decreased global longitudinal LV deformation) according to Echo;
- absence of registered continuous recurrent tachycardia according to ECG Holter monitoring (HM), which could be the cause of cardiomyopathy with dilated phenotype;
- absence of laboratory signs of inflammation and myocardial damage;
- absence of acute illnesses and exacerbation of chronic diseases;
- no congenital heart defects.

Before hospitalization, 7 patients were seen in other clinics with a principal diagnosis of dilated cardiomyopathy and a concomitant diagnosis of WPW phenomenon. These patients received therapy appropriate to the underlying disease, consisting in most cases of angiotensin-converting enzyme inhibitor, beta-adrenoblocker, diuretics and other drugs (digoxin, spironolactone, cardiometabolic therapy). In all patients, therapy had no significant clinical effect.

All patients underwent routine diagnostic screening including determination of markers of myocardial inflammation and damage (LDH, CPK, CPK-MB, CPK-MB mass, troponin I), ECG with assessment of QRS width, HM, Echo with assessment of size, heart chamber volumes and LV contractile function and Speckle-tracking Echo with assessment of LV global longitudinal strain (LV GLS). All patients underwent intracardiac electrophysiologic study (EPS) and AP RFA. Mean age at the time of surgery: 11 years [8;14] (Figure 1). ECG, HM, Echo, and Speckle-tracking Echo were performed on day 3 after AP RFA to assess the effectiveness of the performed surgical intervention and dynamic monitoring of the parameters.

Study methods

In each clinical case, patients underwent detailed analysis of electrocardiogram by ECG recording in 12 leads at a recording speed of 50 mm/s according to the generally accepted protocol. The values obtained from the world's major population-based ECG screenings in children were taken as the «normal» ECG values [9].

HM with assessment of rhythm variability was performed using the Schiller 300 daily ECG monitoring system according to the generally accepted methodology. The results were analyzed according to a standard protocol [10].

To assess intracardiac hemodynamics in children with arrhythmias, M- and B-mode Echo and Doppler ultrasonography were performed. Affinity 70cv ultrasound systems (Philips, the Netherlands) were used to assess intracardiac hemodynamics. Standard methods and positions according to the recommendations of the American Society of Echocardiography [11] were used to measure the main sizes and volumes of heart chambers, indicators of intracardiac hemodynamics. In addition to standard measurements of chamber volumes, the deviation of atrial volumes and LV end-diastolic volume from individually predicted anthropometric norms, expressed as a percentage, was as-

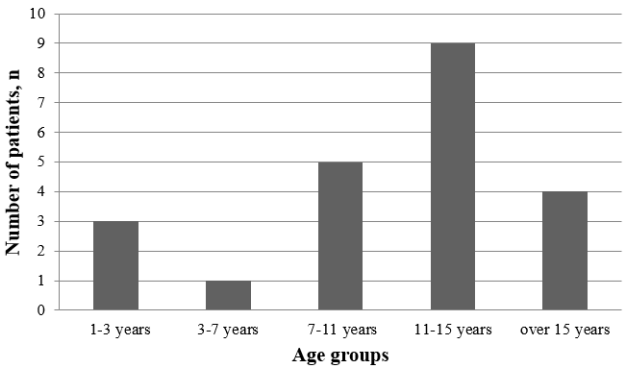

Fig. 1. Division of patients by age groups at the time of intracardiac electrophysiologic study and radiofrequency ablation of the extra atrial-ventricular junction.

Table 1.

Clinical and demographic characteristics of patients

Total number of patients, n	22
Male gender, n (%)	12 (54.5)
Female gender, n (%)	11 (45.5)
Age of primary hospitalization, years (Me [Q1; Q3])	11 [7;14]
Age of RFA, years (Me [Q 1; Q3])	11 [8;14]
Body weight at the time of RFA, kg (Me [Q1; Q3])	42 [23; 60]
Manifesting pre-exertion, n (%)	16 (72.7)
Intermittent pre-exposure, n (%)	6 (27.3)
HF I FC NYHA, n (%)	20 (91)
HF II FC NYHA classification, n (%)	2 (9)
Diseases of the nervous system, n (%)	5 (23.8)
Nutritional and metabolic disorders, n (%)	3 (14.3)
Visual organ diseases, n (%)	3 (14.3)
Diseases of the musculoskeletal system, n (%)	2 (9.5)
Diseases of ENT organs, n (%)	2 (9.5)
Endocrine diseases, n (%)	2 (9.5)
Blood system diseases, n (%)	2 (9.5)
Diseases of the genitourinary system, n (%)	1 (4.8)
Digestive diseases, n (%)	1 (4.8)
Asymptomatic patients, n (%)	15 (68%)
Patients with history of palpitations, n (%)	7 (32%)
Patients treated for HF, n (%)	7 (32%)

Note: RFA, radiofrequency ablation; HF, heart failure; FC, functional class, ENT, ear, nose, throat.

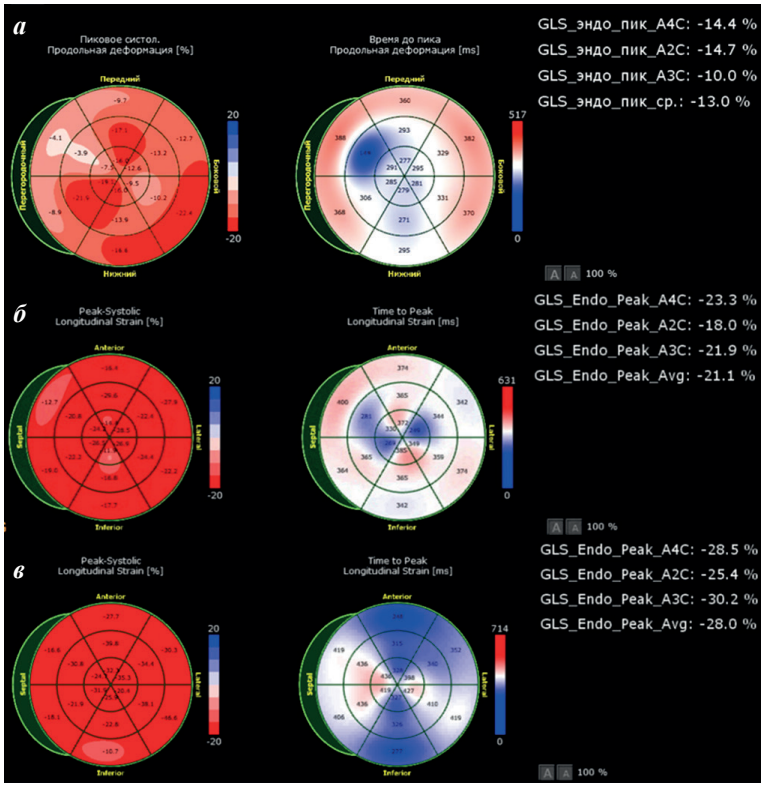

Fig. 2. Assessment of left ventricular global longitudinal strain (LV GLS) by Speckle-tracking echocardiography: a, age 9 months at enrollment; b, 2 years after the ablation procedure; 2 years 9 months after the ablation procedure. A polar map with regional strain values and LV GLS values calculated from 18 segments is presented. Significant reduction in longitudinal deformity in basal, middle segments of the anteroposterior region at initial admission.

Table 2.

Electrophysiologic and echocardiographic characterization of patients before ablation procedure

QRS duration, ms (Me [Q1; Q3])	100 [100;120]
Right-sided AP, n (%)	19 (79.2%)
anterior localization, n (%)	1 (4.2%)
anteroseptal localization, n (%)	9 (37.5%)
anterolateral localization, n (%)	1 (4.2%)
lateral localization, n (%)	3 (12.5%)
posterior septal localization, n (%)	5 (20.8%)
Left-sided AP, n (%)	5 (20.8%)
anterior localization, n (%)	1 (4.2%)
lateral localization, n (%)	3 (12.5%)
posterior septal localization, n (%)	1 (4.2%)
LVEDV, ml (Me [Q1; Q3])	79 [50; 88]
LVEF, %* (Me [Q1; Q3])	115.5 [103; 124]
LVEDVI, ml/m^2 (Me [Q1; Q3])	57.2 [52; 61.39]
LVEF, % (Me [Q1; Q3])	62 [52; 64]
LV GLS, % (Me [Q1; Q3])	-17.25 [-16.4; -19]

Note hereinafter: AP - additional atrial-ventricular junction; LVEDV - left ventricular end-diastolic volume; * - percentage expression of the parameter from the individual predicted norm; LVEDVI - left ventricular end-diastolic volume index; LVEF - Simpson left ventricular ejection fraction; LV GLS - left ventricular global strain.

sessed. This approach is associated with age and anthropometric heterogeneity of patients, as well as for dynamic assessment of echocardiography parameters due to the increase in heart size with changes in age and anthropometric data. These indices were determined automatically in the software application «Child Heart» [12].

To assess LV wall deformation, all patients underwent Echo examination using Speckle-tracking Echo and measurement of LV GLS according to the recommendations of the European Society of Cardiology, European Association of Cardiovascular Imaging Techniques (EACVI) and American Society of Echocardiography (ASE) [13]. The advantages of Speckle-tracking echocardiography include the possibility of non-Doppler, angle-independent and objective quantitative assessment of myocardial deformation and LV systolic and diastolic function, due to which not only visual but also quantitative assessment of LV myocardial contractility is possible [14, 15]. Decreased global LV longitudinal strain (GLS LV) detected by Speckle-tracking Echo has a higher sensitivity with respect to LV dysfunction than ejection fraction (EF) and allows to detect «subclinical» myocardial contractility abnormalities that cannot be detected by standard Echo protocol [2, 14, 16].

Intracardiac electrophysiologic study and RFA were performed using electrophysiologic complexes Elkart II (Electropulse, Tomsk, Russia) and BARD (LabSystem™ PRO EP Recording System, Bard Electrophysiology Division, United States). All children underwent intervention against the background of balanced total intravenous anesthesia, which was provided by constant infusion of 1% propofol at a dose of 7-10 mg/kg/h and 0.005% fentanyl 5-7 mcg/kg/h. The right femoral vein was punctured according to the Seldinger method; in case of left-sided AP location, sometimes additional femoral artery puncture was required, then diagnostic and ablation electrodes were performed. Conducting and electrode placement were performed under fluoroscopic control. Radiofrequency applications were applied with temperature and power values of 60 ˚C and 40 W, respectively. The absence of inducibility of tachycardia, ante- and retrograde conduction over the AP for 30 minutes was considered the immediate effect of ablation.

Statistical analysis

Statistical processing of the obtained data was performed using STATISTICA 10 program. Qualitative data are presented as absolute and relative values of n (%). Quantitative data are presented as median and interquartile range (Me [Q 25; 75]). Differences between two dependent samples of quantitative trait

measurements, were calculated using the Wilcoxon T-test. The critical level of significance for testing statistical hypotheses in this study was taken as 0.05 (p - achieved level of significance).

RESULTS

Table 1 presents the clinical and demographic characteristics of the examined children. At the initial admission, 2 children had decreased tolerance to physical activity, rapid fatigue, which was considered as manifestations of heart failure functional class II (NYHA). Failure to thrive was noted in 4 children. Among these patients, there were 3 children of preschool and primary school age (6 to 11 years) and 1 infant (2 years 3 months). Fifteen patients were asymptomatic, while seven patients reported episodes of palpitations. In symptomatic patients, tachycardia attacks lasted from several minutes to several hours and occurred with a frequency ranging from once a month to once a year.

In ECG analysis, QRS complex dilation due to preexcitation occurred in 14 patients (63.6%). According to Echo data, 5 patients (22.7%) had dilatation and increased LV volume, 9 patients (41%) had decreased LV contractile function. All patients had intraventricular dyssynchrony and decreased LV GLS according to Speckle-tracking Echo. Two patients were admitted to our department for repeat RFA, after this procedure (as well as catheter cryodestruction) had been performed unsuccessfully in other clinics.

Clinical example

The patient was first admitted to our department at the age of 9 months, with signs of heart failure (increased sweating at rest and at exercise, decreased appetite) and significant changes in Echo parameters: dilatation and spherification of LV (end-diastolic volume 35 ml (274% of normal), end-diastolic index 93.01 ml/m^2) and atria, decreased LVEF (B mode) up to 34%. Taking into account the low physical development indicators at the time of hospitalization (body weight 7.9 kg), making it difficult to perform RFA, it was decided to continue drug therapy (captopril, carvedilol, spironolactone) with further dynamic monitoring of the patient. At the age of 2 years, when the patient reached a weight of 16 kg, she underwent successful AP RFA. In the early postoperative period, we observed only partial improvement in Echo parameters (reduction of intraventricular dyssynchrony from 132 ms to 118 ms, increase in LVEF (B mode) from 51% to 56% and LV GLS from -16% to -19%), but dilatation and spherification of the LV cavity and atrial enlargement persisted. The patient was continued to be followed up dynamically. 2 years after RFA (Figure 2), we observed complete normalization of Echo parameters: end-diastolic volume 45 ml (106% of normal, z score 0.4), end-diastolic index 49.85 ml/m^2, atria not enlarged, PV (B mode) 65%, LV GLS -26%, no intraventricular dyssynchrony (82 ms).

In 17 patients (77,3%) only the right-sided localization of AP was diagnosed during EPS, in two patients right-sided and left-sided AP functioned simultaneously (9,1%) and in 3 more cases (13,6%) AP had only left-sided localization. The electrophysiologic and Echo characteristics of the patients are presented in Table 2.

All patients underwent successful AP RFA. The indicators of the effectiveness of the surgical treatment were the absence of tachycardia recurrence during control stimulation and the absence of signs of ventricular preexcitation on ECG. No complications related to the RFA procedure were noted in the early postoperative period. After RFA, there was a consistent normalization of QRS complex width (p=0.0002). To assess LV reverse remodeling, all patients underwent Echo on the 3rd day after RFA (Table 3). In patients with initially decreased LVEF there was its increase, in patients with initial dilatation and increased LV volume there was a normalization of these parameters, but this dynamics was not statistically signifi-

Table 3.

Dynamics of electrocardiographic and echocardiographic data before and after the ablation procedure

Indicator	Befor FRA	After FRA	p
QRS, ms (Me [Q1; Q3])	100 [100;120]	70 [60;100]	<0,001
LVEDV, ml (Me [Q1; Q3])	115,5 [103; 124]	112 [101; 131]	0,073
LVEDVI, ml/m^2 (Me [Q1;Q3])	57,2 [52; 61,39]	55,3 [51,1; 60,7]	0,064
LVEF, % (Me [Q1; Q3])	62 [52; 64]	60 [51; 64]	0,426
LV GLS, % (Me [Q1; Q3])	-17,25 [-16,4; -19]	-21,5 [-19; -24]	<0,001

Note: RFA - radiofrequency ablation

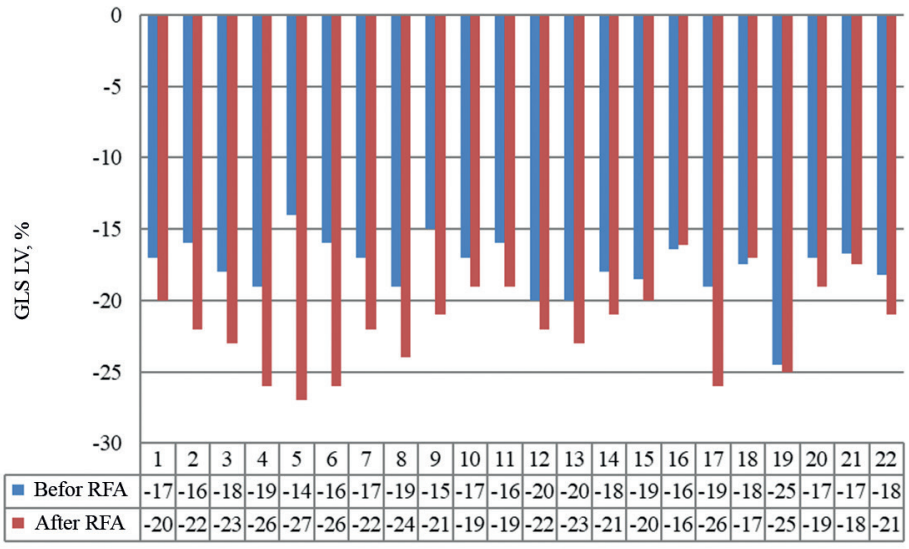

Fig. 3. Dynamics of values of global longitudinal deformation of the left ventricle according to Speckle-tracking echocardiography in patients before and after ablation procedure.

cant in the early postoperative period. As a result of control examination we observed complete normalization of longitudinal deformation according to Speckle-tracking Echo in 13 patients (59%), improvement of this index in 7 patients (31.8%) (Fig. 3). The mean longitudinal strain before RFA was -17.25 [-16.4; -19] and after RFA was -21.5 [-19; -24] (p=0.0001).

DISCUSSION OF FINDINGS

Thus, our study demonstrates that predominantly in patients with right-sided localization of AP there may be formation of segmental dyssynchrony with development of LV dilatation and dysfunction. The presence of left-sided localizations of AP accompanied by PIC in our patients is also consistent with the literature data [2].

The literature describes the use of drug resynchronization therapy (amiodarone, flecainamide, propafenone) in WPW syndrome as an alternative method of introducing young children until the patient reaches optimal physical developmental milestones for RFA. However, drug therapy, cannot eliminate AP and in the future such patients need to undergo AP ablation [17-21]. In 2014, a case of successful RFA was described in a four-month-old patient with WPW syndrome who had no paroxysms of supraventricular tachycardia, but after birth there was a rapid progression of left ventricular dysfunction and the development of heart failure, and therapy with amiodarone had no positive effect [22].

The causal relationship between AP function and the development of PIC is a relatively new topic that continues to evolve at present. Thus, by 2013, only 48 descriptions of such clinical cases had been accumulated [3]. Some authors of publications emphasize that there are no precise data on the prevalence of PIC in WPW syndrome, because a part of patients underwent successful RFA, often even before the development of dyssynchrony, while another part of patients is observed with the diagnosis of dilated cardiomyopathy [2-4, 23]. Thus, according to F.J.Zimmerman et al. 17% of patients on the waiting list for heart transplantation with a diagnosis of dilated cardiomyopathy are diagnosed with arrhythmogenic cardiomyopathy during detailed examination [24].

In most cases, PIC develops in asymptomatic patients, that is, in the absence of paroxysms of supraventricular tachycardia. These data are in agreement with the results of our study, where 68% of patients had no paroxysms of tachycardia in the history and according to HM. Sometimes rapid progression of ventricular dysfunction develops in young patients immediately after birth [3, 7]. In the 2022 publication, 122 clinical cases of patients with pre-exertion and signs of PIC were analyzed. The authors noted that the development of pre-exertion-associated cardiomyopathy was more frequently observed in children, especially infants and young children [1].

It is important to realize that this problem resolves in the majority of cases after AP RFA and indicates a direct role of eccentric myocardial activation in the development of PIC by dilatation phenotype. The recovery of cardiac function after AP RFA occurs in different time periods: from several days, to several years [1, 3, 25]. According to the literature, there are cases when it took more than 3 years to restore LV function. Factors that correlate with the time and degree of LV function recovery after RFA include the degree of baseline LV dysfunction as well as patient age (older than 6 years). Accordingly, in children older than 6 years of age with severe heart failure, sometimes there is only partial recovery of LV function after RFA [1, 7].

Nowadays, there is no unanimity in the medical community regarding the choice of treatment between drug therapy and catheter ablations, especially in the age group of children under 5 years of age [26-31]. To date, asymptomatic WPW syndrome has not been considered as an indication for RFA in domestic pediatric cardiology practice. However, reports demonstrating improvement in ventricular function after RFA in patients with asymptomatic WPW and dyssynchrony have contributed to the revision of the indications for RFA and the transformation of Class IIB to IIA [32], including in children with body weight less than 15 kg.

As a result of control examination in the early postoperative period, we observed significant improvement of global longitudinal LV deformation according to Speckle-tracking Echo, but incomplete normalization of LV volume and ejection fraction. However, our study has a limitation due to the lack of prospective follow-up results.

CONCLUSION

Reversible remodeling and recovery of LV function after AP RFA suggests a causal relationship between AP function and the development of PIC. All patients with symptomatic and asymptomatic WPW syndrome require detailed evaluation using Speckle-tracking Echo to rule out «subclinical» myocardial contractility abnormalities that cannot be detected by standard Echo protocol. According to the literature and our experience, patients with signs of PIC associated with preexcitation are indicated to undergo AP RFA regardless of age and the presence of symptoms in the form of paroxysms of tachycardia.

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