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The Impact of Transcatheter Atrial Septal Defect Closure on Ventricular Repolarization Parameters in Children: Results from a 15-Year Single-Center Tertiary Care Experience

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Abstract

Objectives: Atrial and ventricular arrhythmias can be observed in children after transcatheter atrial septal defect (ASD) closure. This study investigated ventricular repolarization parameters, which are considered to indicate an increased risk of arrhythmias in patients with transcatheter ASD closure.

Materials and Methods: The study included 225 patients aged 0-18 years who underwent transcatheter ASD closure at a tertiary medical school university hospital between 2005 and 2020. Heart rate, Pmax, Pmin, Pdispersion, QTmax, QTmin, QTdispersion, QTcmax, QTcmin, QTcdispersion, Tp-e interval, Tp-e/QT, and Tp-e/QTc values were calculated electronically in 12-lead electrocardiographies (ECGs) taken before the procedure and at 24 h, 1, 6, and 12 months after the procedure.

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Results: Of the 225 patients who underwent transcatheter closure, 144 (64%) were female and 81 (36%) were male. The mean age at angiography was 9.2±4.1 years, and the mean weight was 29.6±14.3 kg. Statistically significant differences were observed in the Tp-e interval and Tp-e/QTc values measured before transcatheter closure compared with those measured after closure (p=0.028; p=0.032), while no significant differences were found between the two groups in terms of other ECG parameters. A negative correlation was found between P and QT dispersion measured before transcatheter closure and after closure (r=-0.408; p=0.041).

Conclusion: Changes in ventricular repolarization parameters were observed in children after transcatheter ASD closure. QT dispersion, Tp-e interval, and Tp-e/QTc ratios, which are sensitive indicators of ventricular arrhythmias, were significant in the post-closure group. Therefore, careful evaluation of these parameters, which are markers for predicting ventricular arrhythmias before and after ASD closure, will serve as a warning for potentially fatal arrhythmias of vital importance in the long term. Each patient undergoing transcatheter ASD closure should be monitored with a 12-lead ECG for atrial and ventricular depolarization and repolarization parameters, and annual 24-hour Holter ECG monitoring should be performed to detect arrhythmias.

Keywords: Atrial septal defect, transcatheter closure, electrocardiography, ventricular repolarization, pediatric

Introduction

Atrial septal defect (ASD) is one of the most common congenital heart diseases[1]. This defect has been closed surgically for many years. In particular, for secondum-type ASDs suitable for transcatheter closure, patient comfort, absence of surgical scarring, and shorter hospital stays have replaced surgical treatment[2]. In the past decade, secondum ASDs have been closed percutaneously using various devices[3]. Hemodynamically significant large defects can be closed transcatheters, even in infancy, in appropriate cases[4]. In ASDs, right ventricular hypertrophy findings on electrocardiography (ECG) due to right ventricular dilation and an incomplete right bundle branch block pattern associated with prolonged depolarization time can be observed. This situation leads to long-term negative effects on left heart size and function. To prevent the development of arrhythmias, it is recommended that ASDs diagnosed in childhood and causing significant volume load in right heart cavities be closed, if possible, before school age[5,6].

Increased atrial distension and volume load due to congenital electrophysiological changes in the sinus node or conduction system play a role in the development of sinus node dysfunction and atrial tachycardia[7]. In the myocardium continuously exposed to volume loading, stress spreads to tissues in the cardiac conduction system, causing delayed intraventricular conduction. In addition, the degeneration of cardiac cells, including fibrosis secondary to myocardial remodeling, leads to the pathological modification of myocardial repolarization. Because of these changes in the left ventricle, arrhythmogenic values can occur in P wave and QT measurements. Delayed cardiac repolarization increases susceptibility to arrhythmias[8-10]. The presence of arrhythmia episodes in patients undergoing transcatheter closure has also been demonstrated in many studies[11,12].

In previous studies, it has been shown that some ventricular repolarization parameters such as the QT interval, corrected QT (QTc) interval, QT and QTc dispersions (QTd, QTcd), T peak-end (Tp-e), and Tp-e/QT ratio indicate susceptibility to ventricular arrhythmias[13-15]. There are limited studies in the literature regarding ventricular repolarization parameters, which are accepted to increase the risk of ventricular arrhythmias in children with ASDs and evaluated RR and Qt variability, and in those with VSD[16,17].

This study investigated ventricular repolarization parameters, which are considered to indicate an increased risk of arrhythmias in patients with transcatheter ASD closure.

Materials and Methods

Between January 2005 and January 2020, 225 patients aged 0-18 who underwent transcatheter ASD closure at the Department of Pediatric Cardiology, Dokuz Eylül University Faculty of Medicine were included. The medical records of the patients were evaluated retrospectively. Patients with concomitant congenital cardiac abnormalities and those with incomplete data were excluded from the study. This study was approved by the Ethics Committee of Dokuz Eylül University Faculty of Medicine, in accordance with the Declaration of Helsinki (dated: 15/02/2021, approval no: 2021/05-19).

In the transcatheter closure procedure, the Amplatzer Duct Occluder II device was used for all patients. Twelve-lead ECGs taken before closure, at 24 h, and 1, 6, and 12 months after the procedure were evaluated. Heart rate, Pmax, Pmin, Pdispersion, QTmax, QTmin, QTdispersion, QTcmax, QTcmin, QTc dispersion, Tp-e interval, Tp-e/QT, and Tp-e/QTc were calculated electronically. Data were analyzed using IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) statistical software package. The normal distribution of numerical variables was evaluated using the Shapiro-Wilk normality test. The homogeneity of variances was assessed using the Levene test. Independent two-sample t-tests were used for intergroup comparisons of variables with a normal distribution. The relationship between ECG variables before and after the transcatheter closure procedure was assessed using Pearson correlation analysis. A p-value of <0.05 was considered statistically significant.

Results

Of the 225 patients who underwent transcatheter closure, 144 (64%) were female and 81 (36%) were male. The mean age at angiography was 9.2±4.1 years, and the mean weight was 29.6±14.3 kg. When evaluated according to the World Health Organization Z-score for body weight, it was calculated as -0.2±1.09 standard deviation score. In all cases, transesophageal echocardiography was routinely performed during the closure procedure, and the measured defect diameter varied between 8 and 21 mm, with a mean of 12.2±3.9 mm. The mean pulmonary artery pressure calculated during catheterization was 14.3±3.2 mmHg, and the mean Qp/Q ratio was 1.86±0.48. The mean follow-up period was 5.8±3.1 (1.9-14.2) years (Table 1).

In all 225 patients, sinus rhythm was observed in the ECGs taken before the procedure. First-degree atrioventricular (AV) block was observed in three patients. In the control ECGs taken 24 h after the procedure, all patients were found to be in sinus rhythm. Ectopic atrial arrhythmia was detected in only six of our cases; two were observed temporarily, and the remaining four were assessed as AV node conduction abnormalities (Table 2). No new arrhythmias developed in the early period. The control ECGs of the cases were taken at median values of 5.6 (3.2-15.1) years.

The Tp-e interval and Tp-e/QTc values measured before the transcatheter closure procedure were found to

Table 1. Demographic and angiographic data of the patients

Gender, n (%) Men Girl	 144 (64.0) 81 (36.0)
Age (years) (mean ± SD) (max-min)	7.2±4.2 (3.5-17.0)
Weight SDS (mean ± SD)	-0.2±1.13
BMI SDS (mean ± SD)	2.57±0.42
Defect size (mean ± SD)	12.2±4.2 7 (8.0-21)
PAP (mean ± SD)	14.3±3.2
Qp/Qs (mean ± SD)	1.86±0.48
Procedure success n (%)	225 (100)
Follow-up duration (years) Mean (min.-max.)	5.8±3.1 (1.9-14.2)

SD: Standard deviation, min.-max.: Minimum-maximum

Table 2. Rhythm abnormalities during the procedure

	Patients (%)
Temporary AV complete block	1 (0.44)
Supraventricular tachycardia	3 (1.3)
I. AV blok	8 (3.5)
Atrial flutter	0
Nodal rhythm	6 (2.6)
Complete right branch block	2 (0.88)

AV: Atrioventricular

be statistically significant compared with those after the closure (p=0.028; p=0.032). In contrast, no significant difference was observed between the two groups regarding other ECG parameters (p>0.05) (Table 3).

A negative correlation was found between pre-transcatheter closure P dispersion and post-closure QT dispersion (r=-0.408; p=0.041) (Table 4).

Table 3. Comparison of ECG parameters before and after transcatheter closure in patients

	Before	After	Statistics	
	Mean ± SD	Mean ± SD	T	p-value
Heart rate	85.1±13.6	82.2±12.4	0.588	0.476
Pmax	0.13±0.025	0.142±0.025	1.64	0.082
Pmin	0.042±0.007	0.064±0.021	3.024	0.007
Pdispersion	0.075±0.029	0.072±0.025	0.561	0.577
QTmax	0.402±0.034	0.405±0.022	0.596	0.554
QTmin	0.328±0.032	0.326±0.029	0.746	0.459
QTdispersion	0.085±0.016	0.081±0.021	0.372	0.711
QTcmax	0.482±0.036	0.487±0.030	0.471	0.640
QTcmin	0.383±0.033	0.384±0.043	0.367	0.715
QTcdispersion	0.133±0.161	0.096±0.034	1.117	0.269
Tp-einterval	0.042±0.004	0.048±0.015	2.520	**0.028**
Tp-e/QT	0.126±0.012	0.158±0.050	2.221	0.062
Te-p/QTc	0.105±0.010	0.110±0.043	2.012	**0.032**

SD: Standard deviation; t: independent two-sample t-test

Table 4. Correlations between ECG parameters before and after transcatheter closure

	Before		After	
	r	p	r	p
Heart rate	-0.144	0.492	-0.324	0.114
Pmax	0.132	0.528	-0.111	0.597
Pmin	0.034	0.874	-0.090	0.668
Pdispersion	**-0.408**	**0.041**	0.205	0.327
QTmax	0.122	0.795	0.081	0.700
QTmin	-0.052	0.973	-0.061	0.772
QTdispersion	-0.006	0.825	**-0.483**	**0.014**
QTcmax	0.023	0.057	0.64	0.021
QTcmin	-0.309	0.132	0.543	0.021
QTcdispersion	0.006	0.977	0.168	0.422
Tp-einterval	-0.008	0.970	-0.083	0.692
Tp-e/QT	0.002	0.992	-0.067	0.751
Te-p/QTc	0.101	0.633	0.088	0.676

r: Pearson correlation coefficient

Discussion

In patients undergoing transcatheter ASD closure, echocardiographic evaluation of device position, residual shunt presence, and complications (erosion, embolization, etc.) should be performed within the first 24 h following device implantation. Due to the rare risk of blockage reported with the use of large devices, a 12-lead ECG should be taken for each patient after the procedure[18]. Post-procedure follow-up should be performed at 1, 6, and 12 months and then every 1-2 years for atrial arrhythmias. At each check-up, patients should be evaluated by physical examination, ECG, and echocardiography. Although ECGs with normal or right-axis deviation along with right bundle branch block are considered indicative of ASD, electrophysiological studies have claimed that there is no true electrical delay and that the block is mostly due to volume load[19].

In 25 pediatric patients with transcatheter ASD closure, Pmax and P-wave dispersion (PWD) parameters were evaluated before and after the closure procedure, and it was found that the closure significantly reduced Pmax and PWD[20]. P-wave dispersion is an electrocardiographic marker that reveals the heterogeneity of electrical conduction in both atria[21]. The usability of P-wave duration and PWD in predicting paroxysmal idiopathic atrial fibrillation (AF) has been demonstrated in adult electrophysiological studies. Intra-atrial conduction delay leads to an increase in P-wave duration and PWD, predisposing patients to AF. P-wave dispersion of 40 ms has been reported as a risk factor for AF[22,23]. In a meta-analysis investigating AF development after transcatheter ASD closure in adults, it was noted that AF was less frequent in the early period after closure, whereas the rate increased in older patients[24]. Changes in the atrium before the closure procedure in children with large ASDs may predispose them to AF later in life[14]. In our study, PWD in the preclosure group was statistically significant compared with that in the postclosure group. Close monitoring of these children for AF development potential in adult life may be beneficial in terms of morbidity and mortality.

The following ASD closure, the development of ventricular arrhythmia was observed. This is because the device causes changes in the heart anatomy, leading to ventricular irritation. In addition, the electrical activity of the heart may change after ASD closure, increasing the risk of ventricular arrhythmia[12]. Non-invasive parameters indicating increased propensity for ventricular arrhythmias include QT, QTc intervals, and QT and QTc dispersions. Prolongations in QT and QTc values indicate an extended ventricular repolarization, whereas increased QT and QTc dispersion values indicate that ventricular repolarization is not homogenous, and the propensity for ventricular arrhythmias is increased[25,26]. In our study, QT dispersion was statistically significant in the post-closure group compared with the pre-closure group.

In addition to QT and QTc dispersions, the Tp-e interval and Tp-e/QT ratio, which are ECG markers of ventricular transmural repolarization dispersion, have been used recently as relatively newer indicators. Experimental studies have shown that the earliest repolarization occurs in epicardial cells, which is reflected as a T-wave peak in surface ECG. The end of the T wave (Tend) represents the mid-myocardial action potential's reflection on the surface ECG[27,28].

Consequently, the Tp-e interval represents the transmural repolarization dispersion. Studies have shown that prolonged Tp-e duration is associated with mortality in cases of Brugada syndrome, long QT syndrome, and hypertrophic cardiomyopathy[29,30]. In addition to the Tp-e interval, the Tpe/QT and Tp-e/QTc ratios have been found to be associated with ventricular arrhythmias and sudden cardiac death[26]. In our study, the Tp-e interval and Tp-e/QTc ratios were found to be statistically significant in the post-closure group.

Study Limitations

Possible limitations of this study are that our results may be limited to our population and therefore have limited applicability to the general population. To confirm these results, it is necessary to conduct a long-term follow-up of the patients in the study and further studies with the new data to be obtained.

Conclusion

In conclusion, changes in ventricular repolarization parameters were observed in children after transcatheter ASD closure. However, the clinical significance of these changes and their relationship with ventricular arrhythmia risk have not been fully determined. In our study, although there was no significant difference between the pre- and post-closure groups in terms of ECG parameters indicating susceptibility to ventricular arrhythmias, such as QT, QTc duration, and QTc dispersion, the QT dispersion, Tp-e interval, and Tp-e/QTc ratios, which have been shown to be more sensitive in detecting ventricular arrhythmias in previous studies, were significant in the post-closure group. The risk of fatal arrhythmias in children after transcatheter ASD closure is very low, but it can lead to serious consequences[31]. Therefore, careful evaluation of these parameters, which are markers for predicting ventricular arrhythmias before and after ASD closure, will be a warning for potentially life-threatening fatal arrhythmias in the long term. Each patient undergoing transcatheter ASD closure should be monitored with a 12-lead ECG for atrial and ventricular depolarization and repolarization parameters, and annual 24-hour Holter ECG monitoring should be performed to detect arrhythmias.

Ethics

Ethics Committee Approval: The study was approved by the ethics committee of Dokuz Eylül University Faculty of Medicine, in accordance with the Declaration of Helsinki (dated: 15/02/2021, approval no: 2021/05-19).

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: Kır M, Ünal N, Concept: Yıldız K, Design: Yıldız K, Data Collection and/or Processing: Armağan C, Genç HZ, Çeliktepe V, Analysis and/or Interpretation: Bardak H, Bayam YS, Literature Search: Ercan Bozyer H, Bayam YS, Writing: Yıldız K.

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