Holter Electrocardiography Findings and P-Wave Dispersion in Pediatric Patients with Transcatheter Closure of Atrial Septal Defects

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Background: This study aimed to determine the frequency of postintervention arrhythmia and factors associated with the development of arrhythmia, including the correlation between arrhythmia and P-wave dispersion, and the effects of the latter on transcatheter closure of atrial septal defects (ASDs).

Methods: Holter ECG recordings were performed before and after the intervention and 6 and 12 months later in 47 of the 59 patients who had undergone transcatheter ASD closure and once in the healthy control subjects.

Results: A statistically significant correlation was identified between the patients' arrhythmia grade according to Lown's system and each of the following: the number of defects, the size of the atrioventricular valve rim, the presence of an atrial septal aneurysm.

Conclusion: The frequency of arrhythmia increases after transcatheter ASD closure, gradually decreases within the next year, and is most frequently of a benign nature. Lown's arrhythmia grading of patients occluded with either the Amplatzer septal occluder (ASO) or the Cardio-O-Fix septal occluder (CSO) were compared, and the arrhythmia frequency was higher with the latter. One day after the intervention, the P maximum (P_{max}) and the P dispersion (P_{dis}) values were not increased but in fact slightly reduced in patients occluded with either ASO or CSO. An improvement in the electrical system resulting from early anatomical and mechanical healing following transcatheter ASD occlusion may explain the reduction in the P_{max} and P_{dis} values.

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Holter ECG; p-wave dispersion; children; atrial septal defect; transcatheter closure

Transcatheter atrial septal defect (ASD) occlusion has been applied for approximately 40 years, and its use has accelerated in the last 15 following the development of better performing devices. Large defects are corrected with classical or minimally invasive surgery, but those with a rim of adequate size are percutaneously occluded when possible.^{1,2} Published reports indicate that electrocardiographic complications, such as atrial arrhythmias and reversible or permanent atrioventricular (AV) block, are increased in children

following transcatheter ASD closure.^{3–6} In adult patients, who undergo transcatheter occlusion of ASDs, several factors have been observed to influence the development of atrial tachycardias, such as the size of the device and the presence of atrial septal aneurysms (ASAs).⁷ The fast pathway of the AV node proceeds along the anterior margin of an ostium secundum ASD. The superior margin contains Bachmann's bundle, the primary pathway of interatrial conduction. The installation of the occlusion device may cause squeezing

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or wounding of these two pathways, causing conduction defects.^{8,9}

Irregular or slow atrial conduction is known to cause an increase in P-wave durations.^{10,11} Studies in children with ostium secundum ASDs found significantly increased Pdispersion (P_{dis}) and Pmaximum (P_{max}) values.¹² Several reports indicated that a lengthening of P-wave duration and an increase in P_{dis} are risk factors for atrial fibrillation.^{13–16}

The objective of this study was to determine the frequency of postintervention arrhythmias and factors for developing an arrhythmia, including the correlation between arrhythmias and other parameters, and to study the effects on the latter on transcatheter closure of ASDs.

METHODS

The study population consisted of pediatric patients who had undergone transcatheter closure of ASDs between April 2010 and January 2013 at the Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Center and Research Hospital Pediatric Cardiology Clinic in Istanbul and a control group of healthy subjects. Control group selected as age-gender matched ASD patients. This was designed as a prospective study. Subjects who refused to sign the informed consent form, patients with device embolization, and those in whom the device did not entirely fit the septum were excluded from the study. The study was approved by the Medical Investigation Ethical Committee of the Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Center and Research Hospital. All the patients and the control subjects provided written informed consent.

Electrocardiography

The patients hospitalized for transcatheter ASD closure underwent electrocardiography (ECG) on the day of admission and twice daily in the postoperative period, whereas the control subjects only underwent one recording, using a 12-lead ECG device (GE Healthcare, MAC 1600, Lewis Center, OH, USA). The rhythms of the patients and the control subjects were evaluated on a standard ECG, and the basic rhythm was defined on the days before and after the intervention. The ECG findings were compared to normal values for the appropriate age groups.¹⁷ The P_{max} , P_{min} , and P_{dis}

durations and the RR interval were calculated. The P-wave duration was defined as the distance from the P-wave starting point on the isoelectric line and the point where the wave ended. It was measured for three consecutive beats on each derivation, and the average was calculated. P_{dis} was defined as the difference between the longest and the shortest P distances.¹⁶ The P waves were measured by four investigators unaware of the subjects' individual data. Two separate measurements were performed on each recording by the same observer. All the measurements were performed on a MUSE-Citrix ECG system (Citrix, Santa Clara, CA) with 100% magnification.

Holter ECG

A three-channel Holter ECG (CardioNavigator Plus Impresario, 3.07.0158, Delmar Reynolds; Paris, France) was recorded on admission and on the day after the intervention in the ASD patients and once in the control subjects. The 24-hour recordings of the patients were performed in the hospital with the patients in the supine position. They were repeated 6 months and 12 months after discharge. The recordings were evaluated for supraventricular premature beats (SVPB), supraventricular tachycardia (SVT), ventricular premature beats, ventricular tachycardia, and AV block with pauses.

Atrial arrhythmias were classified according to Lown's system as follows: Grade 0: no SVPB Grade 1: unifocal SVPBs Grade 2: more than 10 unifocal SVPBs per hour, Grade 3: multifocal SVPBs, Grade 4: coupled SVPBs, Grade 5: paroxysmal atrial tachycardia, atrial fibrillation, or atrial flutter, Grade 6: multifocal atrial tachycardia.¹⁸

Statistical Analysis

The statistical evaluation of the data was performed using the SPSS for Windows, Version 15.0 software package (SPSS Inc, Chicago, IL). The categorical variables were compared using the chi-square test, and continuous variables were compared with the Mann-Whitney *U* test. The correlations between grading of arrhythmias according to Lown's classification and other parameters were measured by Pearson's correlation coefficient. To compare the repeated measurements of the ASD patients before and after the occlusion with the device, Wilcoxon's signed-rank test was applied.

Table 1. Demographic Characteristics of the Patient and Control Groups

	Patient Group	Control Group	P Value
Number	59	30	
Girl/boy	38/21	21/9	0.662
Age (year)	9.9 ± 6.1	10.4 ± 5.3	0.660
Height (cm)	131.4 ± 24.1	132.50 ± 15.9	0.824
Weight (kg)	32.2 ± 18.3	32.83 ± 13	0.886
Body mass index(kg/m ²)	17 ± 3.3	17.7 ± 3.2	0.333

A P value <0.05 was accepted as statistically significant.

RESULTS

Patient Group

The study included 59 patients who underwent ASD occlusion. The demographic characteristics of the subjects are summarized in Table 1. Fifty patients were diagnosed with ASD, six with a patent foramen ovale, and three with multiple ASDs at the time of defect closure. The closure was performed using an Amplatzer septal occluder (ASO, AGA Medical Corp., Golden Valley, MN) in 28 cases, a Cardio-O-Fix septal occluder (CSO, Starway Medical Technology Inc., Beijing, China) in 24 cases, and other occlusion devices for defects other than ASDs.

Control Group

The control group contained 30 healthy subjects. No significant difference was between the patient and the control group with regard to age, sex, body weight, or body mass index (BMI; Table 1).

Holter ECG recordings were performed before and after the intervention and 6 and 12 months later in 47 of the 59 patients who had undergone transcatheter ASD closure. The demographic, structural, and hemodynamic characteristics of the patients whose Holter ECG recordings were evaluated are summarized in Tables 1 and 2, and the distribution of arrhythmias in the patients' Holter recordings is shown in Table 3. Patients' Lown arrhythmia degree 0, 1, 2, 3, 4, 5, 6 to ratio were seen as 34%, 12.7%, 10.6%, 0%, 42.5%, 0%, 0%, respectively. Score sum of atrial arrhythmias in the all Holter recordings according to Lown's classification was showed in Table 4. The Q_p/Q_s ratio and device diameter were calculated as 2.11 ± 0.43 , 19.08 ± 4.26 mm, respectively. There was a statistically significant correlation between the

Table 2. Demographic, Structural, and Hemodynamic Characteristics of the Patients Whose Holter ECG Recordings Were Evaluated

	Mean ± SD
Age (year)	9.9 ± 6.8
Gender (girl/boy)	28/19
Height (cm)	131.2 ± 25.9
Weight (kg)	32.4 ± 19.6
BMI (kg/m ²)	17.2 ± 3.5
MPAB (mmHg)	20.8 ± 4.4
Q_p/Q_s ratio	2.1 ± 0.4
Stretched diameter of ASD (mm)	16.8 ± 3.8
Device defect ratio	1.3 ± 1.4
Device diameter (mm)	19 ± 4.2
Device/height ratio (mm/cm)	0.16 ± 0.12

BMI = body mass index; MPAP = mean pulmonary artery pressure; Q_p/Q_s ratio = pulmonary to systemic blood flow ratio; ASD = atrial septal defect; SD = standard deviation.

patients' arrhythmia grades according to Lown's classification and each of the following: the number of defects, the size of the AV valve rim, the presence of an ASA. (P value = 0.033, 0.029, and 0.046, respectively). No statistically significant correlations were detected between the arrhythmia grade according to Lown's classification and any of the other parameters (Table 5). However, a statistically significant difference was established between Lown's arrhythmia grading in Holter ECG of 17 patients closed with ASO and 24 patients closed with CSO (P = 0.012). Arrhythmias were more frequent in the cases occluded by CSO (Table 4). CSO was used in the only patient showing sustained SVT, and the patient in whom an AV block of the first degree was diagnosed had undergone occlusion with the ASO device (Table 3).

The ECG measurements ($P_{\max}$, P_{dis} , $P_{\min}$, PR, and RR distances) of the patient group taken on the days preceding and following the intervention are compared to the ECG of the control group in Table 6. The preintervention $P_{\max}$ and P_{dis} values are significantly higher in the ASD patients than in

Table 3. Distribution of Arrhythmias in the Patients' Holter Recordings

	Initial Holter (n:47)	Day After the Intervention (n:47)	Holter at 6 Month (n:47)	Holter at 12 Month (n:47)
Normal	44	16	38	43
Rare SVPB	3	11	7	3
Nonsustained SVT		20		
Sustained SVT		0	1 (with CSO)	
1. degree AV block		0	1 (with ASO)	1

SVT = supraventricular tachycardia; SVPB = supraventricular premature beat; rare SVPB = <2% SVPB; nonsustained SVT = <30 seconds; sustained SVT = >30 seconds duration; CSO = Cardio-O-Fix septal occluder; ASO = Amplatzer septal occluder.

Table 4. Score Sum of Atrial Arrhythmias in the all Holter Recordings According to Lown's Classification

Patients	Initial	Day After the Intervention	Holter at 6 Month	Holter at 12 Month
Sum of Lown's classification score	3	96	11	6
CSO	3	78	11	2
ASO	0	18	0	4

CSO = Cardio-O-Fix septal occluder; ASO = Amplatzer septal occluder.

the controls (91.40 ± 11.94 vs 98.87 ± 11.84 ms, respectively, $P = 0.008$; 37.20 ± 13.37 vs 41.80 ± 9.31 ms, respectively, $P = 0.002$). Although the pre-procedure $P_{\min}$, PR, and RR values were increased in the ASD patients compared to the control group, no statistical significance was determined (P values 0.29, 0.53, and 0.51, respectively). In the ASD patients, the postintervention $P_{\max}$, P_{dis} , PR, and RR values were significantly higher than in the control group (respectively, 91.40 ± 11.94 vs 97.61 ± 15.14 ms, 37.20 ± 13.37 vs 41.10 ± 13.38 ms, 140.60 ± 23.30 vs 153.84 ± 30.30 ms, and 616.96 ± 151.57 vs 719.00 ± 154.89 ms; all with $p < 0.05$). There was no statistical significance detected for the difference in $P_{\min}$. Although the $P_{\max}$, $P_{\min}$, and P_{dis} values had regressed in the patients on the day following the intervention, the decrease was not statistically significant (respective P values 0.445, 0.820, and 0.449). Similarly, the PR interval values showed a slight increase 1 day after the intervention, but the increase was not statistically significant ($P = 0.651$). The RR distance was lengthened, with statistical significance, compared to its preintervention value (719 ± 154.89 vs 636.41 ± 117.99 ms, $P = 0.002$; Table 6).

DISCUSSION

Transcatheter closure of secundum ASDs is a safe and feasible procedure. However, recent

studies on arrhythmias following occlusion have shown an increase in the frequency of cardiac dysrhythmia in pediatric patients examined by Holter recordings before and after the ASD closure procedure, although such an event remains rare and benign in character.^{3,19,20} The frequency of symptomatic tachycardia had been indicated as 1.3% (9/708) by Szkutnik et al. This study reported symptomatic tachyarrhythmia in four patients between 2 weeks and 4 months after the procedure. During the entire year following the intervention, only one of seven patients who received antiarrhythmic treatment showed a recurrence. Two of these patients were children (aged 3.5 and 8 years), and the other six were adults. The same study found a link between the use of a large device and tachyarrhythmia in two patients. In our study, 47 of the patients who underwent transcatheter ASD closure had a Holter ECG recorded. Nonsustained SVTs were seen postprocedure in 20 patients. Rare SVPBs were observed in 11 other patients, and 16 patients had a normal Holter recording. Follow-up recordings 6 months after the procedure revealed rare SVPBs in seven patients, de novo sustained SVT at a rate of 250–280/minute in one patient occluded by CSO, and 38 unremarkable ECGs. The 12-month follow-up revealed rare SVPBs in three patients, with the rest being unremarkable. No atrial fibrillation was observed in our patients. Based on this study, it appears that the arrhythmia frequency increases after

Table 5. Correlation Analysis Results between Postprocedure Arrhythmia Grades and Other Parameters

Variables	Grading of Arrhythmias According to Lown's Classification	
	R	P
Age (year)	0.001	0.996
Weight (kg)	0.192	0.196
Height (cm)	0.188	0.205
BMI (kg/m ²)	0.222	0.133
Device size (mm)	0.06	0.682
Defect number	0.318	0.033
TSD (mm)	0.239	0.119
AVV rim (mm)	0.337	0.029
PM rim (mm)	0.070	0.683
SVC rim (mm)	0.255	0.099
IVC rim (mm)	0.150	0.337
Ao rim (mm)	0.181	0.234
ASA	0.292	0.046
MPAB (mmHg)	0.147	0.413
Q _p /Q _s ratio	0.005	0.977
Device/defect	0.149	0.323
Device/height (mm/cm)	0.214	0.163
Device/TSD	0.231	0.142
IVC rim/TSD	0.014	0.931
SVC rim/TSD	0.115	0.475
AVV rim/TSD	0.048	0.768
Ao rim/TSD	0.130	0.413
PM rim/TSD	0.034	0.848
IVC rim/device	0.168	0.293
SVC rim/device	0.283	0.073
AVV rim/device	0.227	0.160
Ao rim/device	0.161	0.302
PM rim/device	0.141	0.426
IVC rim/defect	0.001	0.998
SVC rim/defect	0.089	0.578
AVV rim/defect	0.100	0.539
Ao rim/defect	0.092	0.563
PM rim/defect	0.052	0.769

BMI = body mass index; AVV rim = size of the atrioventricular (AV) valve rim; IVC rim = size of the inferior vena cava rim; SVC rim = size of the superior vena cava rim; PM rim = size of the posteromedial rim; Ao rim = size of the aortic rim; TSD = total septal diameter; Device/defect = Device size/defect diameter; ASA = presence of an atrial septal aneurysm (ASA); Q_p/Q_s ratio = pulmonary to systemic blood flow ratio; MPAP = mean pulmonary artery pressure.

transcatheter ASD closure, gradually decreases within the following year, and is most frequently of a benign nature. These findings are consistent with earlier studies.^{3,19,20} However, when considering the published data in addition to our study, one should not forget that an SVT may arise anytime after the procedure. Thus, Holter ECG follow-up should be performed in patients during a period

of approximately 1 year following the procedure. The mean pulmonary artery pressure (PAP) in our patients was 20 mmHg, the pulmonary to systemic blood flow (Q_p/Q_s) ratio was 2.11, the device/body size ratio for all the patients was 0.16 (<0.2), and a device >19 mm was used in 22 patients. Published studies have indicated that the frequency of arrhythmias increases with a high mean PAP, a device >19 mm, a device/body size ratio >0.2, and a high Q_p/Q_s ratio.²¹ In contrast to earlier reports, our study failed to detect a correlation between the frequency of arrhythmias and the mean PAP, device size, device/body size ratio, or Q_p/Q_s ratio. In addition, there was no correlation between the arrhythmia frequency and any of the other parameters examined in our study (i.e., age, height, weight, BMI, total septum length, device/defect ratio, and rim size or ratios of rim to total septum length, rim to defect, and rim to device size). A study by Janion et al. found an increase in P_{dis} and atrial arrhythmias in ASA patients with a left-to-right shunt.²² We found a statistically significant correlation of arrhythmia grading according to Lown's classification with the number of ASDs, the presence of ASAs, and the size of the plain AV valve rim. In our study, a large AV valve rim, the presence of ASAs, and the number of ASDs were associated with an increased incidence of arrhythmias.

AV block, which is generally observed during or following the procedure, has been reported as being temporary and reversible. Nonetheless, the installation of a pacemaker because of complete AV block has been reported in single case reports.^{3,-5,19,23} Suda et al. opined that their more frequent observations of arrhythmias associated with device insertion compared with other authors is because of using an ASO device >19 mm, a device/body size ratio >0.2, and an important left-to-right shunt (Q_p/Q_s > 2.5).²¹ These observations were not reproduced by Szkutnik et al. in a study of two patients or in our study.⁴ Conduction abnormalities following the placement of an ASO device may be because of topical edema, progressive cicatrization, pressure on the AV node, and/or friction between the tissue and the device.^{5,19,23} None of our patients had an AV block during the procedure or one day after it. A single patient exhibited a first-grade AV block at the 6-month and 12-month follow-ups. This patient remains under observation. Repeated Holter ECG follow-up did not show any case of second- or

Table 6. ECG Measurements of the Patient Group Taken on the Days Preceding and Following the Procedure

	Control	Initial P ⁰	Day After the Intervention P ¹	P ²
P _{max} ^a	91.40 ± 11.94	98.87 ± 11.84	97.61 ± 15.14	0.445
P value		0.008	<0.05	
P _{min} ^a	54.90 ± 7.13	57.01 ± 11.14	56.48 ± 11.93	0.820
P value		0.29	>0.05	
P _{dis} ^a	37.20 ± 13.37	41.80 ± 9.31	41.10 ± 13.38	0.449
P value		0.02	<0.05	
PR length ^a	140.60 ± 23.30	150.30 ± 20.43	153.84 ± 30.30	0.651
P value		0.53	<0.05	
RR length ^a	616.96 ± 151.57	636.41 ± 117.99	719.00 ± 154.89	0.002
P value		0.51	<0.05	

P_{max}: Pmaximum, P_{min}: Pminimum, P_{dis}: P dispersion; ^amiliseconds.

P⁰: P value between the values before procedure in patient and control groups. P¹: P values between the values one day after the procedure in patient and control group. P²: P values between the values before and 1 day after the procedure in patients.

third-grade AV block. Considering the published reports and our study, a prolonged follow-up of patients' Holter ECG recordings may be worth recommending.

Studies have found that the incidence of atrial fibrillation reaches 16% following surgical repair and approximately 14% after transcatheter closure using ASO.²⁴⁻²⁶ The incidence of de novo atrial fibrillation is very probably increased by the use of large devices. Large devices cause stretching of the septum, which, in turn, may lead to changes in the electrical activity of the atrium.^{27,28} The measurement of the longest P-wave duration provides an indicator of the effect of the device on electrical homogeneity following device-mediated occlusion of secundum ASD.²⁹ An increase in P_{max} and P_{dis} values in comparison to healthy controls has been reported in patients who underwent surgery for various congenital heart defects. A correlation between atrial tachycardia and either P_{max} or P_{dis} has been established in patients with Fallot's tetralogy following complete repair with the Fontan procedure; such a correlation was not found, however, in patients undergoing Senning's operation.^{16,30,31} We could not evaluate the correlation between arrhythmia and the P_{max} or P_{dis} values in this study because these values were not increased postprocedure. In a study comparing ASO and a Figulla septal occluder (FSO), Paç et al. found increased P_{dis} and P_{max} values in both groups, and these were more pronounced in the ASO patients. P_{dis} was significantly reduced postprocedure in the FSO group. There was no such difference between the two device groups in terms of postocclusion arrhythmia.²⁹ In this study, the P_{max} and P_{dis} values were not increased

one day after the intervention using either ASO or CSO. When the Lown's arrhythmia grades of 17 patients occluded with ASO were compared to those of 24 patients receiving CSO, the latter had a higher frequency of arrhythmias. Such a difference may be related to the different tissue structures of the devices. The lack of P_{max} and P_{dis} increases in our study may be because of the low average age of the patients and, consequently, minor right atrial hypertrophy and volume of connective and fat tissue, with a higher importance of muscle. This may also explain the smaller increase in the atrial conduction time.³² The average diameter of the devices used in the study by Paç et al. was 17.1 mm compared to about 19 mm in ours. The respective device to body size ratios were 1.5 and 1.31. The lack of P-wave prolongation in our study may be because of measuring the P-wave values 1 day after the procedure (i.e., in the early period). The increase in the P_{max} and P_{dis} in our ASD patients compared to the healthy controls is consistent with the published literature.¹² A study conducted in adult patients showed that electrical and mechanical changes in the atrial myocardium following ASD occlusion with ASO were reversible, with a reduction of P_{max} and P_{dis} values. Electrical healing following transcatheter ASD closure was linked to anatomical and mechanical normalization.³³ These results are compatible with ours and may explain the P_{max} and P_{dis} reduction. Some studies, such as the study by Paç et al., have reported a slowing of abnormal conduction as a response to the early atrial depolarization resulting from acute stretching. The inflammation within the atrial myocardial tissue caused by a foreign body reaction

to the device increases atrial conduction disorders. The percutaneous closure of ASDs may, in the short term, lead to favorable changes in the atrial electrogeometry.²⁹ According to a study by Başpınar et al., preprocedure and postprocedure $P_{\max}$, P_{dis} , and $P_{\min}$ values were similar between patients who had undergone transcatheter occlusion or open surgery. A comparison of the P_{dis} duration between the two groups failed to show a statistically significant difference. However, the P_{dis} showed less of a difference in an open surgery group compared with the basic measurements.³⁴ These findings explain how foreign body reactions and mechanical factors may increase P_{dis} in the longer term. In this study, the P_{dis} did not show an increase because it was measured in the early postocclusion period.

Limitations

One limitation of this study is its inability to study the correlations of tachycardia with $P_{\max}$ and P_{dis} , as the latter were not increased. Additional limitations are the lack of $P_{\max}$ and P_{dis} measurements using standard ECGs at the 6-month and 12-month follow-up because of technical reasons and the lack of Holter ECG recordings in our first patients because such recordings have only commenced recently in the hospital.

CONCLUSIONS

The frequency of arrhythmias appears to increase after transcatheter ASD closure and to gradually decrease within the next year. They are most frequently of a benign nature. No correlation was detected between the frequency of arrhythmias and the mean PAP, size of the device, device/body size ratio, or Q_p/Q_s ratio. The size of the AV valve rim, the presence of ASAs, and the number of ASDs increased the incidence of arrhythmias. Comparison of the Lown's arrhythmia grading of patients occluded with either ASO or CSO suggested that the frequency of arrhythmias was higher with the latter. Such a difference may be related to the different tissue structure of the devices. The $P_{\max}$ and P_{dis} in the ECGs of the ASD patients increased compared to the healthy controls. One day after the intervention, the $P_{\max}$ and P_{dis} values were slightly reduced rather than increased in the patients occluded with either ASO or CSO. Page: 10

An improvement in the electrical system resulting from early anatomical and mechanical healing following transcatheter ASD occlusion may explain the reduction in the $P_{\max}$ and P_{dis} values.

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