

Effects of surgical atrial septal defect closure operation on the frontal QRS-T angle

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Abstract

Aim: A new marker has been found for ventricular repolarization and depolarization heterogeneity, which is the frontal plane QRS-T [f(QRS-T)] angle between the directions of ventricular depolarization (QRS axis) and repolarization (T axis). Adverse cardiac outcomes can be detected based on observation of the f(QRS-T) angle.

In atrial septal defect (ASD) patients, surgical closure of ASD is safer and more effective than its percutaneous closure with higher popularity in the last two decades. Nevertheless, we have scarce information about the impact of ASD closure on cardiac autonomic function and heart repolarization.

The aim of the study is to investigate the potential effect of ASD operation on the f(QRS-T) angle and cardiac repolarization parameters.

Materials and Methods: In our retrospective study design we sampled a total of 24 patients who underwent ASD closure surgery operation between December 2011 and January 2019. Preoperative and postoperative 6 week ECG parameters including the f(QRS-T) of the patients were compared.

Results: When pre- and postoperative ECG parameters were compared, no statistically significant difference was found in QT interval ($p=0.079$), adjusted QT interval ($p=0.079$), Tpe interval ($p=0.150$) and Tpe/QTc ratio ($p=0.696$). An improvement was found in QRS duration ($p=0.035$), p wave duration ($p<0.001$) and f(QRS)-T angle ($p<0.001$).

Conclusion: In our study, it was observed that surgical ASD closure operation was associated with heart repolarization parameters and improvement in f(QRS-T).

Keywords: Arrhythmia; atrial septal defect; Frontal QRS-T angle

INTRODUCTION

Clinicians routinely use twelve-lead electrocardiogram (ECG) for cardiac examination in daily practice and this method is low cost, noninvasive, fast and available everywhere. A new marker has been found for ventricular repolarization and depolarization heterogeneity, which is the frontal plane QRS-T [f(QRS-T)] angle between the directions of ventricular depolarization (QRS axis) and repolarization (T axis). (1,2). To estimate it using surface electrocardiography (ECG) it is sufficient to subtract the QRS axis from the T axis, which can be simply observed by reviewing the automated reports of many 12-lead ECG devices. The prognostic value of this easily available parameter has been shown in different populations (3-5).

Secundum atrial septal defect (ASD) may be the cause 10% of neonates with congenital heart disease and about 30%-40% of adults with heart disease (6). In the last six decades surgical ASD, which has been used for

six decades, has proven its safety and effectiveness (7). However, we have limited information about the impact of ASD closure surgery on cardiac repolarization and f(QRS-T). We evaluated the effects of ASD closure on cardiac autonomic functions based on the cross-sectional case control study design.

MATERIALS and METHODS

Patients who underwent ASD closure between December 2011 and January 2019 at the Isparta Suleyman Demirel University Faculty of Medicine Research and Training Hospital were included in the study. ASD was diagnosed with both TTE and transesophageal echocardiography followed by cardiac catheterization for confirmation purposes. Single-secundum type ASD was present in each patient (8). Clinical indications for closure of ASD and the inclusion criteria for the study were a significant left- to-right shunt (pulmonary:systemic flow ratio: >1.5) shunt-related symptoms, and/or echocardiographic signs

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of dilatation of the right heart chambers (9). Percutaneous ASD closure could not be performed for a while in our center due to technical restrictions. In addition, most of the cases consist of patients referred to us because percutaneous ASD closure cannot be performed in the outer center

The exclusion criteria were premium ASD, partial anomalous pulmonary venous drainage, pulmonary vascular resistance of >4.6 Wood units, and/or $>2/3$ systemic vascular resistance even after reversibility testing, right-to-left shunt with a peripheral arterial saturation of $<95\%$, associated structural cardiac defect requiring surgery, moderate-severe valvular heart disease, coronary artery disease, and left ventricular ejection fraction (LVEF) $\leq 55\%$ on TTE. Since there may be secondary causes affecting the ECG parameters in secundum type ASD surgery, the membranous ventricular septum and thus the AV node may require intervention, they were not included in the study. Following the exclusion, we made an assessment for the remaining 30 patients in total. Preoperative and postoperative 6-week, the f(QRS-T) measurements of the patients were compared. The local Ethics Committee approved our study protocol (Suleyman Demirel University Faculty of Medicine Clinical Research and Ethics Committee decision date 07.10.2020 number: 302) and all patients included in the study provided written consent. TTE and blood sampling were performed prior to closure, and 24 hours and 6 weeks after the procedure

Electrocardiography

For the patients in the supine position, automatic recording 12-lead ECG was taken at a rate of 50 mm paper per second along with scanning and transferring to a PC for avoidance of errors, and then, the images were magnified by 400% using the Adobe Photoshop software. Two cardiologists, who had no access to the patient data, made ECG measurements of the QT and Tp-e intervals. We excluded the patients with their ECGs including U waves. The average value of three records from one lead was considered in the study. The section of ECG from the beginning of the QRS complex to the end of the T wave was the QT interval which was then adjusted to heart rate using the Bazett formula: $cQT = QT\sqrt{(R-R \text{ interval})}$. Another section from the peak of the T wave to the end of the T wave was defined as the Tp-e interval based on the measurements by precordial leads (10). The ECG device automatically provides the frontal QRS and T-wave axes in papers. We calculated the f(QRS-T) angle by subtracting the absolute values of the frontal plane QRS axis from the frontal plane T axis. The angle difference from 360° was calculated when above 180° (11-14). On the automated ECG reports, the f(QRS-T) angles were eliminated because these indicated the subjectivity in each record. ECG procedures were followed as one prior to surgery and another 6 weeks after.

Echocardiography

We followed the recommendations of the American Society of Echocardiography and used a Vivid 7

instrument (GE Healthcare, Inc. Chicago, IL, USA) and a 2.5 MHz transducer for the echocardiographic examinations. Three representative beats were caught to take measurements, and the average values were calculated. Typically echocardiographic analysis was performed upon 2-dimensional, M-mode, and Doppler flow data. To avoid inter-reader variability, an observer blinded to all clinical reports performed the echo-Doppler studies. There was no internet access to the computer. The examination reports were interpreted by another cardiologist who also did not know the status of the patients. We conducted a correlation analysis to calculate intra-observer variability as well as inter-observer variability ($<5\%$).

Anesthesia and Surgical Procedure

In a form inserted through one radial artery catheter intravenous midazolam (Zolamid®; Defarma, Tekirdag, Turkey) (0.05-0.1 mg/kg) was administered to each patient for monitoring. To induce anesthesia Fentanyl (Talinat®; Vem, Istanbul, Turkey), pentothal (Pental® Sodium, Istanbul, Turkey) and intravenous rocuronium bromide (Curon®, Mustafa Nevzat, Istanbul, Turkey) were used at the doses of 1-2 $\mu\text{g}/\text{kg}$, 5-7 mg/kg and 0.6 mg/kg respectively. An anesthetic device, Primus® (Draeger Medical, Lübeck, Germany) was employed to supply intraoperative mechanical ventilation, and then anesthesia was maintained with administration of midazolam, fentanyl, and rocuronium. Primary closure, pericardial patch, or Gore-Tex (W.L. Gore & Associates, Inc, Flagstaff, Arizona) patch was carried out through a right atriotomy for operational repair following the establishment of general endotracheal anesthesia, cardiopulmonary bypass, and anterograde cardioplegia. After recovery, the patients who were extubated at the intensive care unit were transferred to the general care unit for further convalescence if any, followed by intravenous administration of cefazolin (25 mg/kg) which was performed every 8 hours prophylactically, and then chest tubes were taken off. Each patient was discharged only after an echocardiogram, chest x-ray, and electrocardiogram were performed. For follow-up, we scheduled outpatient evaluation with the surgeon in the second week and with the cardiologist in the sixth week. There were no major complications at the end of the operations performed.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL) was used in the statistical analyses. The numerical variables with normal distribution are presented as mean \pm standard deviation, while those with non-normal distribution are presented as median (interquartile range) values. Number of each group was adjusted as 30 patients. Because we calculated the minimum number of individuals that should be sampled with 90% power and 0.05 Type-I error as at least 27 (R 3.0.1. open source program). The primary effect variable was determined as the QRS angle. 1% change in total f(QRS-T) angle [4.5 degrees on f(QRS-T) plane] was accepted as clinically relevant. Standard deviation

of the primary effect variable was calculated as ± 0.22 . The categorical variables are presented as percentages (%). Kolmogorov-Smirnov test was used for assessment of normal distribution (i.e., $P > 0.05$ for all physiological measurements). One-way analysis of variance (ANOVA) determined the statistical significance of serial ECG parameters from the sequential measurements. In case of violation of the sphericity assumption, the Greenhouse-Geisser adjustment was used in ANOVA. Unpaired t-test was appropriate for two group comparisons of normally distributed variables, and the nonparametric Mann-Whitney U test was used for those of the non-normally distributed ones. Statistical significance was defined as p values < 0.05 .

RESULTS

Among the patient group, the mean age was 35.98 ± 8.07 , the ratio of the female patients was 50.0%, the mean body mass index was 26.91 ± 3.71 , the diabetes rate was 10.0%, the hypertension rate was 10.0%, the smoking rate was 33.3%, the mean ejection fraction was 63.35 ± 3.75 , the mean left atrial diameter was 3.9 ± 1.0 cm, the mean systolic pulmonary artery pressure was 29.8 ± 7.1 mmHg, and the mean atrial septal defect diameter was 1.7 ± 0.9 cm (Table 1).

Table 1. Demographic, echocardiographic and surgical characteristics of the patients

Variables	(n=30)
Age	35.98 ± 8.07
Female n(%)	15 (50.0%)
Body Mass Index, kg/m ²	26.91 ± 3.71
Diabetes Mellitus, n(%)	3 (10.0%)
Hypertension, n(%)	3 (10.0%)
Smoking, n(%)	10 (33.3%)
Left ventricular ejection fraction (%)	63.35 ± 3.75
Left ventricular end diastolic diameter (cm)	4.2 ± 0.4
Left ventricular end systolic diameter (cm)	2.9 ± 0.2
Interventricular septum thickness (mm)	9.0 ± 0.4
Posterior wall thickness (mm)	8.4 ± 0.3
Left atrium diameter (cm)	3.9 ± 1.0
Systolic pulmonary artery pressure, mmHg	29.8 ± 7.1
Atrial septal defect diameter	1.7 ± 0.9
Primary repair	20 (66.6%)
Repair by patch	10 (33.3%)

Data are given as mean \pm standard deviation or percentage [n (%)]

Table 2. Electrocardiographic and echocardiographic features of the groups

Variables	Before surgery	6 weeks after surgery	p value
QRS, ms	110.3 ± 22.3	100.1 ± 15.3	0.035
QT, ms	367.5 ± 31.2	356.3 ± 30.6	0.079
QTc, ms	407.2 ± 23.9	394.9 ± 29.0	0.077
Tpe, ms	81.1 ± 17.7	80.2 ± 9.2	0.150
Tpe/QTc	0.20 ± 0.04	0.20 ± 0.04	0.696
f(QRS)T (°)	76.1 ± 30.5	65.1 ± 14.3	<0.001
P wave, ms	134 ± 24.7	121 ± 21.3	<0.001
Left ventricular ejection fraction (%)	63.35 ± 3.75	62.21 ± 5.33	0.786
Left ventricular end diastolic diameter (cm)	4.2 ± 0.4	4.2 ± 0.5	0.931
Left ventricular end systolic diameter (cm)	2.9 ± 0.2	2.9 ± 0.6	0.876
Systolic pulmonary artery pressure, mmHg	29.8 ± 7.1	27.6 ± 5.1	0.652

Data are given as mean \pm SD, n or median (interquartile range). QTc - corrected QT interval; f(QRS)-T; frontal QRS-T angle

DISCUSSION

Our study was found to be associated with improvement in the cardiac repolarization parameters and f(QRS-T) after ASD operation for the first time in the literature.

It has been shown in previous studies that ECG parameters can be useful in determining the ASD diameter (15). ECG may be normal in young and uncomplicated patients with ASD. However, the classical findings of significant ASD are prolonged PR interval, QRS time, and the presence of incomplete right bundle branch block (16). Ostium primum ASD may show left axis deviation and transmission delay to the atrioventricular node (16). The QRS complex is often slightly prolonged and has a characteristic rSr' or rsR'

patterns that is thought to result from disproportionate thickening of the right ventricular outflow tract, which is the last portion of the ventricle to depolarise (16). Therefore, it may have potential benefits in terms of ASD diagnosis and prognosis in the f(QRS-T) angle.

Due to right-sided volume overload caused by atrial left-to-right shunting both atrial and ventricular stretch may lead to variations in 12-lead ECG from mechano-electrical coupling (17,18). For instance, a dilatation has a risk of higher amplitude, longer duration, and wider dispersion for P waves because of delayed atrial conduction, which are all effective as markers to predict atrial arrhythmias (19,20). RV dilatation may cause prolongation in QRS-

duration, right bundle branch block, and crochetaje (a notch near the apex of the R-wave in the inferior limb leads) (21). Recently, it has been shown for ASD patients that QTc-interval extension may occur due to RV volume overload (22). As achievement criteria, ASD closure may adjust the right-sided volume overload within 24 h and initiate geometric remodeling of the right atrium and ventricle, lasting up to 6–8 weeks following the operation (23,24). In literature there are actually multiple reports on postoperative electrical remodeling (20,25-27).

Similarly, in this study we found that ventricular electrical remodeling is unavailable in the short-term after ASD closure based on the data of QRS duration on the 12-lead ECG, whereas Veldtman et al. reported that RV geometrical remodeling had been cleared within one-month after the surgery (24). The results in our study indicated that the QRS duration shortened in the early follow-up period in the two groups. In clinical assessment the variation seems to be irrelevant; and however, ventricular electrical remodeling may be reflected at further stages within the postoperative period. In a recent study, Rucklova et al. (22) proposed that RV volume overload in ASDs indicates prolongation in repolarization. It was also reported that the QTc-interval was significantly shorter at 6 months after the surgery. In this study it was observed that the numerical shortening of the QTc-interval commenced from the fourth week both in the adult and child patients who underwent the ASD operation.

The angle from the QRS axis and the T axis is defined as the f(QRS-T) angle (11). With this, it can be used as a measure of ECG concordance/discordance: since the QRS-complex and T-wave polarities take equal values in most ECG-leads, a small f(QRS-T) angle represents a concordant ECG while a large, obtuse, QRS-T angle represents a discordant ECG for opposite values. Typically, variations in the QRS-complex or T-wave morphology always exhibit a difference between the QRS and T axes or in the f(QRS-T) angle. In several cases, we may judge that the condition is worsening based on the widened f(QRS-T) angle. It was reported that a greater f(QRS-T) angle is related to sudden cardiac death following acute coronary syndromes (28) and the overall mortality rate in a general population. In this study the patient group showed a narrower preoperative f(QRS-T) angle compared to healthy people (29). We determined that the postoperative f(QRS-T) angle narrowed in the ASD patients. It is more likely that ventricular electrical remodeling takes place on relatively further stages following ASD closure. In the literature, there is no evidence that in ASD patients, a smaller QRS-T angle also reduces the risk of sudden death, arrhythmia or mortality.

LIMITATIONS

This current study had limitations in some respect. Firstly, our sample size was relatively small. Thus, to support our findings further studies are required with larger and more homogeneous patient groups and more complete ECG data. Unfortunately, echocardiographic right ventricular

evaluation could not be performed in many patients in the patient records. Moreover, our study simply targeted ECG records and not the accompanying hemodynamic and morphological data to establish a correlation between electrical and structural reverse remodeling. Finally, we designed a retrospective study, and the long-term follow-up data of the ASD patients were unavailable.

CONCLUSION

In our study, it was observed that the surgical ASD closure operation was associated with heart repolarization parameters and improvement in f(QRS-T). Our study has the potential to shed light on the pathophysiology of ASD and future treatments for it.

Competing interests: The authors declare that they have no competing interest.

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