Original Article

# Evaluation of the Ventricular Mechanical Dyssynchrony in Patients with Atrial Septal Defect

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## Abstract

*Background:* There is some evidence indicating improvement in myocardial performance after atrial septal defect closure, either device closure or surgical, but ventricular dyssynchrony has not been evaluated before and after surgical closure. The aim of this study was to evaluate ventricular mechanical dyssynchrony in patients with atrial septal defect before and after surgical closure.

*Methods:* Twenty patients (mean age: 23±11years) with isolated secundum or sinus venosus type atrial septal defect, unsuitable for device closure, were evaluated before and after successful surgical closure. Interventricular and intraventricular dyssynchrony (using 6 basal and 6 mid-segmental models) were determined.

*Results:* A significant reduction in the right atrial and right ventricular dimensions and the tricuspid regurgitation peak gradient was noted after atrial septal defect closure (3.6±0.54 cm versus 4.2±0.7, P=0.009; 3.5±0.29 cm versus 4.3±0.41, P=0.02; and 20.4±10.5 mmHg versus 35.3±6.5, P<0.002; respectively).

There was no significant difference in the maximum difference in time-to-peak systolic velocity and the standard deviation of time-to-peak systolic velocity of the l2 left ventricular myocardial segments in the patients with atrial septal defect before and after surgical closure in comparison with the normal subjects (normal: 26±10.64 ms versus before closure: 21.0±33.9 versus after closure: 27±29.5, both P=0.68) and the left ventricular asynchrony index after atrial septal defect closure (normal: 14.9±8.7 versus before closure: 11.46±8.5 versus after closure: 18.12±13.6, both P=0.2). There was a significant positive relation between the tricuspid regurgitation peak gradient and the left ventricular asynchrony index (r=0.67, P=0.03) and an insignificant negative relation between the left ventricular ejection fraction and the asynchrony index before atrial septal defect closure (r=−0.53, P=0.11). No significant relation was found between the total asynchrony index and the atrial septal defect size, the degree of left-to-right shunt, and the tricuspid regurgitation peak gradient.

*Conclusion:* There was no significant ventricular dyssynchrony in the patients with atrial septal defect before and after surgical closure.

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## Introduction

Atrial septal defects (ASDs) account for approximately 10% of all congenital heart diseases[1] and sometimes result in the development of pulmonary hypertension, atrial arrhythmias, and right heart decompensation.[2] Although

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the transcatheter closure of isolated secundum type ASD has been established as an alternative treatment to surgical closure, surgical closure is required for patients with ostium primum and sinus venosus ASDs, as well as for patients with secundum ASDs whose anatomy is unsuitable for device closure (multiple ASDs, aneurismal septum, and inadequate rims).[3,4] A secundum ASD may be closed primarily with direct sutures or with a patch using the pericardium or synthetic material.

Studies have shown homodynamic and functional improvement in both right and left ventricles after ASD closure, either surgical or transcatheter closure.[5-7] It is generally agreed that the surgical closure of ASD in adulthood is associated with significant mortality benefit.[7] Although there is a positive association between the severity of left ventricular failure and ventricular asynchrony,[8] currently there are no data on left ventricular asynchrony in patients with ASD before and after closure.

In this study, we sought to evaluate the influence of chronic right ventricular (RV) volume overload on ventricular mechanical synchrony in patients with ASD. The first aim of this study was to assess ventricular dyssynchrony in patients with ASD compared with healthy normal subjects and its correlation with left ventricular (LV) systolic function. The second aim of the study was to investigate how ventricular dyssynchrony is influenced by the abolishment of volume overload after ASD closure.

## Methods

Twenty consecutive patients scheduled for ASD closure were prospectively enrolled in the study. The study protocol consisted of tissue Doppler, 2-dimentional (2D), M-mode, and color Doppler echocardiography before and early (one week) after surgical closure. All the patients had a significant left-to-right shunt by color Doppler and considerable RV dilation on 2D echocardiography. Exclusion criteria were any rhythm other than sinus rhythm, primary valvular disease, significant coronary artery disease, or other pathology affecting the left and right ventricular geometry and function. The results were compared with those of 10 normal healthy volunteers (51% men). The volunteers had no history of cardiovascular or systemic diseases and had normal physical examination, electrocardiography, and echocardiography findings. The study was approved by the local medical ethics committee.

Echocardiography was performed in the standard manner using the Vivid 7 digital ultrasound scanner equipment with an ergonomically-designed multi-frequency M3S transthoracic sector transducer and tissue velocity imaging facility. Standard views (apical, parasternal, and subcostal) were used for the evaluation of the chamber size and function. LV volume and ejection fraction (EF) were measured using

a biplane Simpson's method. The examination focused on the measurement of the RV dimensions. From the apical 4-chamber view, the maximal RV inlet diameter at end-diastole at the tip of the tricuspid valve leaflets was measured and indexed to the body surface area.

The atrial septal defect size was measured by transthoracic and corrected by transesophageal echocardiography if it was available.

The LV volumes and EFs were obtained in the apical 4- and 2-chamber views (biplane method).

The magnitude of the left-to-right shunt (QP/QS) was determined using a continuity equation. The LV diastolic function was evaluated by the mitral valve and pulmonary vein flow and tissue Doppler imaging. The degree of mitral regurgitation (MR) and tricuspid regurgitation (TR) was assessed and graded (0-IV) by color Doppler jet area and as the mid-systolic percentage jet area relative to the atrial size in the apical 4-chamber view. The TR peak gradient was assessed by continuous wave Doppler.

To determine intraventricular dyssynchrony, spectral displays of 6 basal and 6 middle LV segments with pulsed wave tissue Doppler imaging (TDI) were obtained in the apical 4-, 3-, and 2-chamber views and stored digitally. In brief, pulsed wave TDI was obtained by placing the sample volume in the middle of each myocardial segment. Gain and filter settings were adjusted as needed to eliminate background noise and to allow for a clear spectral display. The measurements were performed with a sweep of 100 mm/s. Offline analysis of 3 end-expiratory beats was performed, and the results were averaged. The time interval from the onset of the QRS complex to aortic valve opening (Q-AV), time interval from the onset of the QRS complex to pulmonic valve opening (Q-PV), and time interval from the onset of the QRS complex to the peak systolic velocity (TTP) were measured.

The parameters evaluated for intraventricular dyssynchrony were as follows: 1) septum-to-posterior wall mechanical delay (SPWMD), 2) septum-to-lateral wall mechanical delay, 3) maximum difference in time-to-peak systolic velocity of two segments between twelve segments (TS-diff), and 4) total asynchrony index (TS-SD) defined as the standard deviation of TTP of the 12 LV segments (the lower, the better).[9] The mean differences for interobserver and intraobserver variability were 3.5%, 4.3%, and 5.2 % for 2D, Doppler, and TDI data, respectively.

Statistical analysis was done using SPSS 11.5 for Windows. The results are reported as mean±SD for the continuous variables. The comparisons of the echocardiographic variables were tested using a 2-tailed paired t-test. The relation between the changes in systolic function, end-diastolic and systolic volume and area, EF, and asynchrony index were examined with Pearson's correlation coefficient. A p value less than 0.05 was considered statistically significant.

## Results

Twenty patients with a mean age of 23±11 years (40 % men) were enrolled in this study. Successful surgical closure was achieved in all the patients without residual shunts in early (2-3 days) post-operative echocardiography by the color Doppler study.

The baseline characteristics of the patients are presented in Table 1.

Table 1. Baseline characteristics of patients

| | |
|---|---|
| Age (y) (mean±SD) | 23±11 |
| Male/female | 8/12 |
| ASD size (cm) (mean±SD) | 2.3±0.8 |
| QP/QS (mean±SD) | 2.7±0.6 |
| MR severity (0/I) | 11/9 |
| TR severity (0/I/II) | 2/14/3 |

ASD, Atrial septal defect; QP/QS: Pulmonary flow to systemic flow ratio; MR, Mitral regurgitation; TR, Tricuspid regurgitation

TR was present in all the patients (mild versus moderate in 70% and 30%, respectively), which decreased after closure (no TR versus mild in 20% and 70%, respectively). The TR peak gradient decreased significantly after ASD closure (20.4±10.5 mmHg versus 35.3±6.5, P<0.002).

ASD closure resulted in a significant increase in the left ventricular end-diastolic dimension (LVEDD) and left ventricular end-diastolic volume (LVEDV) (3.7±0.23 cm versus 4.4±0.33, P=0.001; 49.7±6.99 ml versus 69.4±13.12, P=0.001; respectively) and an insignificant increase in the left ventricular end-systolic diameter (LVESD), left ventricular end-systolic volume (LVESV), and LA diameter (2.5±0.2 cm versus 2.8±0.2, PV=0.44; 20.5±4.5 ml versus 30.3±7.5, P=0.06; and 3.2±0.34 cm versus 3.4±0.29, P=0.44; respectively).

There was an insignificant decrease in LVEF (53.9±6.9%, versus 55.9±5.6%, P=0.31) and a significant decrease in the RV diameter (3.5±0.2 versus 4.3±0.4 cm, P=0.02) and the

RA diameter (3.6±0.54 cm versus 4.2±0.7, P=0.009) after ASD closure (Table 2).

Table 3 shows a comparison of the hemodynamic data before and after ASD closure.

Both mitral peak early (E) and late (A) diastolic velocities decreased after surgery (90.6±32.3 cm/s versus 92.7±19.6, P=0.67; and 52.5±23.8 cm/s versus 62.0±15.7, P=0.193; respectively). Mitral valve peak E velocity post-ASD closure had a positive relation with the degree of left-to-right shunt (r=0.88) and RV diameter (r=0.73), both P<0.05.

Our results showed that in the patients with ASD, although time-to-peak systolic velocities were within the normal range, these measurements were significantly lower than those in the normal subjects and after these the values returned toward normal (Table 4). Surgical repair also resulted in an insignificant increase in TS-diff and LV asynchrony index (21.0±33.9 msec versus 27±29.5, P=0.6; and 11.46±8.5 ms versus 18.12±13.68, P=0.21; respectively); however, there was no significant LV asynchrony in the patients with ASD before and after surgical closure.

Our multivariate analysis showed a significant negative relation between LVEF and TS-SD after ASD closure (P<0.05), and a significant positive relation between the tricuspid regurgitation peak gradient and LV asynchrony index (r=0.67, P=0.03), but no significant relations were found between the asynchrony index with the size of defect, the degree of the left-to-right shunt, and pulmonary artery pressure (either pre- or post-closure).

## Discussion

Our study is the first one to compare left ventricular asynchrony in ASD patients before and after surgical closure.

The TR gradient and RV diameter decreased significantly after repair, similar to the study of Joseph Shaheen et al.[5]

Table 2. Two-dimensional and M-mode recordings of cardiac chambers pre- and post ASD closure

| | Control (n=10)* I | Pre (n=20)* II | Post (n=20)* III | p (I versus II) | p (II versus III) |
|---|---|---|---|---|---|
| LVEDD (cm) | 4.47±0.45 | 3.7±0.23 | 4.4±0.33 | 0.006 | 0.001 |
| LVESD (cm) | 2.9±0.4 | 2.5±0.21 | 2.84±0.23 | 0.090 | 0.440 |
| LVEDV(ml) | 79.8±24.5 | 49.7±6.99 | 69.4±13.12 | 0.006 | 0.001 |
| LVESV(ml) | 38.1±10.38 | 20.5±4.5 | 30.3±7.5 | 0.001 | 0.060 |
| LVEF (%) | 54.5±3.5 | 55.9±5.6 | 53.9±6.95 | 0.450 | 0.310 |
| LAD (cm) | 3.31±0.2 | 3.2±0.34 | 3.4±0.24 | 0.630 | 0.440 |
| LAA (cm²) | 13±2.5 | 15.2±0.98 | 17.0±1.46 | 0.470 | 0.230 |
| RAD (cm) | 3.1±0.33 | 4.2±0.70 | 3.6±0.54 | 0.001 | 0.009 |
| RAA (cm²) | 12.3±2.97 | 20.3±3.75 | 15.6±3.67 | 0.005 | 0.002 |
| RVD (cm) | 2.9±0.24 | 4.3±0.41 | 3.5±0.29 | 0.001 | 0.020 |

*Data are presented as mean±SD

ASD, Atrial septal defect; LVEDD, Left ventricular end-diastolic diameter; LVESD, Left ventricle end-systolic diameter; LVEDV, Left ventricle end-diastolic volume; LVESV, Left ventricle end-systolic volume; LVEF, Left ventricle ejection fraction; LAD, Left atrial diameter; LAA, Left atrial area; RAD, Right atrial diameter; RAA, Right atrial area; RVD, Right ventricle diameter

Table 3. Comparison of hemodynamic data before and after ASD closure

| | Control (n=10)* I | Pre ASD closure* II | Post ASD closure* III | p (I versus II) | p (II versus III) |
|---|---|---|---|---|---|
| Mitral E wave (cm/s) | 79±11.6 | 92.7±19.6 | 90.6±32.3 | 0.380 | 0.670 |
| Mitral A wave (cm/s) | 51.4±7.3 | 62.0±15.7 | 52.5±23.8 | 0.061 | 0.193 |
| Dec T (ms) | 180±17.4 | 175.88±31.4 | 199.2±19.0 | 0.900 | 0.390 |
| $TVI_{RVOT}$ (cm) | 15.8±4.9 | 26.86±3.2 | 14.0±2.5 | 0.001 | 0.001 |
| $TVI_{LVOT}$ (cm) | 19.15±1.1 | 17.4±2.0 | 19.0±2.3 | 0.048 | 0.760 |
| TR-PG (mmHg) | - | 35.3±6.2 | 20.4±10.5 | - | 0.002 |
| RV Sa (cm/s) | 12.9±1.6 | 16.4±1.7 | 7.1±1.83 | 0.020 | 0.001 |
| TAPSE (cm) | 24±2 | 25.2±3.3 | 14.2±3.4 | 0.410 | 0.001 |

*Data are presented as mean±SD
ASD, Atrial septal defect; Dec T, Deceleration time; $TVI_{RVOT}$, Time velocity integral of right ventricle outflow tract; $TVI_{LVOT}$, Time velocity integral of left ventricle out flow tract; TR-PG, Tricuspid regurgitation peak gradient; TAPSE, Tricuspid annulus peak systolic excursion

Table 4. Tissue Doppler imaging-derived variables

| | Control (n=10)* I | Pre ASD closure (n=20)* II | Post ASD closure (n=20)* III | p (I versus II) | p (II versus III) |
|---|---|---|---|---|---|
| TTP Base Septum (ms) | 119±37.9 | 92.5±21.6 | 115.0±40.6 | 0.006 | 0.090 |
| TTP Mid Septum (ms) | 116±36.9 | 93.5±21.2 | 115.0±40.6 | 0.000 | 0.090 |
| TTP Base Lateral (ms) | 124±20 | 85.0±16.6 | 121.5±32.8 | 0.002 | 0.009 |
| TTP Mid Lateral (ms) | 124±20 | 83.0±18.4 | 120.5±33.7 | 0.001 | 0.010 |
| TTP Base Antero septal (ms) | 121.5±30 | 91.0±18.9 | 115.0±34.3 | 0.000 | 0.093 |
| TTP Mid Antero septal (ms) | 123.5±20 | 91.5±13.9 | 110.0±34.7 | 0.000 | 0.050 |
| TTP Base Posterior (ms) | 114.5±16.6 | 91.0±31.6 | 133.0±34.8 | 0.002 | 0.010 |
| TTP Mid Posterior (ms) | 118.5±16.7 | 90.0±32.9 | 131.0±36.3 | 0.002 | 0.020 |
| TTP Base Anterior (ms) | 123.5±19.4 | 89.5±16.5 | 103.5±36.9 | 0.009 | 0.005 |
| TTP Mid Anterior (ms) | 121.5±19.4 | 88.5±16.5 | 106.5±38.7 | 0.008 | 0.004 |
| TTP Base Inferior (ms) | 140.5±33 | 90.0±20.4 | 130.0±35.2 | 0.000 | 0.005 |
| TTP Mid Inferior (ms) | 141.5±33 | 89.0±22.7 | 130.0±35.2 | 0.000 | 0.004 |
| Q-AV opening (ms) | 69±18 | 64.1±17.9 | 63.8±11.06 | 0.970 | 0.230 |
| Q-PV opening (ms) | 64.7±16.8 | 66.3±17.4 | 79.6±15.8 | 0.680 | 0.460 |
| Q-AVto Q-PV difference(ms) | 9.6±7.6 | 5.2±7.5 | 16.4±16.2 | 0.230 | 0.400 |
| TS-diff (ms) | 26±10.6 | 21.0±33.9 | 27±29.5 | 0.680 | 0.600 |
| TS-SD (ms) | 14.9±8.7 | 11.46±8.5 | 18.12±13.6 | 0.280 | 0.210 |

*Data are presented as mean±SD
TTP, Time to peak systolic velocity; Q-AV, Time interval from Q to aortic valve opening; Q-PV, Time interval from Q to pulmonic valve opening; TS-diff, Maximum difference in time-to-peak systolic velocity in two segments between twelve left ventricle segments; TS-SD, Standard deviation of time-to-peak systolic velocity of l2 left ventricular myocardial segments

The RV contractility as estimated by the tricuspid annular plane systolic excursion (TAPSE) and TDI peak systolic velocity reduced after surgery, which may be due to the less volume overload of the RV, or probably a true reduction in RVEF due to post-cardiopulmonary bypass status and influence of extracorporeal membrane oxygenator and temporary myocardial ischemia during surgical closure.[5,10-12] The remodeling of the RA and RV after ASD closure has also been described in previous studies.[5,13-15] These parameters return to normal values in 90% of surgical patients. However, specifically the systolic function recovers in only 80% of operated patients.[14] The return to normal values depends on the defect size, patient's age, and pulmonary artery pressure.[16] At the same time, no significant increase in systolic function has been found among patients operated on for ASD.[16] The diastolic function among patients with ASD differs comparing to healthy ones. These parameters are altered due to the RV volume overload, significant influence of RV dilation, and paradoxical interventricular movement.[12,16] In our study, the diastolic function improved after ASD closure, which chimes in with the result of a previous study.[14] Given the findings of this study, the fact that LV asynchrony index increased insignificantly after ASD closure may be secondary to the mild decrease in the LV systolic function and delayed contraction mostly in the inferior, posterior and lateral wall segments (Table 4).

The present study is the first in its kind to examine the presence of LV asynchrony in patients with ASD before and after successful surgical closure.

Our study suffers from a few limitations. Firstly, the total number of patients evaluated in the current study is small. Secondly, although we are currently following these patients in order to assess the long-term outcome, the present result represents the early assessment within 2-3 days after surgery.

Further studies with larger populations are needed to assess LV dyssynchrony in patients with ASD before and after either surgical or device closure.

## Conclusion

This study demonstrated a mild increase in TS-diff and LV asynchrony index after ASD closure. Nonetheless, we were not able to find significant ventricular dyssynchrony in the patients with ASD before and after surgical closure. We also found no correlation between ventricular dyssynchrony and the size of defect, the degree of left-to-right shunt, and pulmonary artery pressure. After surgical closure, LVEF was the only independent variable that negatively affected ventricular synchrony.

## Acknowledgment

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