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ORIGINAL ARTICLE

# Evaluation of Cardiac Remodeling After Surgical Closure of Atrial Septal Defect in Different Age Groups

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## ABSTRACT

***Background & objective:*** Cardiac remodeling manifested clinically as changes in size, shape and function of the heart. The extent of remodeling depends on initial morphological changes. So the time at which the surgical correction of atrial septal defect (ASD) done is important. Apparently surgical outcome and remodeling is better at earlier age in comparison to adult age. The aim of this study was to find whether surgical correction of ASD is beneficial at younger age (up to 18 years) in comparison to adult age (above 18 years).

***Methods:*** This prospective cohort study was carried out on a total of 70 patients who underwent surgical closure of atrial septal defect over a period of twenty three months (23) months (from February 2013 to December 2014) in the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka. The recruited patients were divided into two groups – Group-A (comprised of ≤ 18 years old patients) and Group-B (comprised of >18 years old patients) 35 patients in each. Condition of the heart was evaluated preoperatively by echocardiography and the result was compared with postoperative echocardiographic findings at follow-ups after 1 and 3 months after surgery.

***Results:*** The comparison of echocardiographic parameters between baseline (preoperative) and those at 1 and 3 months after surgery in Group-A demonstrated that statistically significant remodeling occurred after 1st month ($p < 0.001$) and it further improved at 3 months. In Group-B the comparison of echo parameters between baseline and at 1 month revealed that all the parameters responded significantly indicating that remodeling occurred well after 1 month. But the same parameters when compared between baseline and at months after repair revealed insignificant differences in all the parameters, except PWT indicating that remodeling that occurred at month 1 regressed at 3 months interval. Cardiac remodeling occurred in both groups, but the degree of remodeling between patients of early age (Group-A) and late age (Group-B) revealed that ASD repair at early age responded well with respect to all the echocardiographic variables of remodeling.

***Conclusion:*** Cardiac remodeling occurs after surgical closure of atrial septal defect. But the degree of remodeling is better if the closure is done at earlier age (at or below 18 years).

***Key words:*** Atrial Septal Defect, Cardiac Remodeling, Surgical Closure, Age etc.

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## INTRODUCTION:

An Atrial Septal Defect (ASD) represents a communication between the left and right atrium leading to left to right shunt. It makes up about 10% of all congenital heart diseases after delivery and up to 30–40% of heart defects diagnosed in patients aged over 40 years.[1] The progression of this congenital defect to congestive cardiac failure follows the onset of pulmonary hypertension, arrhythmias, respiratory infections, and other cardiovascular disease. Hence, the defect is usually discovered when a patient presents with dyspnoea or palpitations or occasionally on routine medical examination.[2] About 75% of adult patients with atrial septal defect show signs or symptoms of the disease in the third or fourth decade of life. Closure of most atrial septal defects is still the treatment of choice in children & young adults, because of the low surgical risk and good long-term outcome. Surgical management of atrial septal defect became a clinical reality in the 1940s. However, the beneficial result of closure in adults over 40 years of age remains controversial, primarily because, incomplete information exists regarding the natural history and the variables associated with survival beyond this age.[3]

Cardiac remodeling may be defined as genome expression, molecular, cellular and interstitial changes that are manifested clinically as changes in size, shape and function of the heart after cardiac injury. The myocyte is the major cardiac cell involved in the remodeling process. Other components involved are interstitium, fibroblasts, collagen and coronary vasculature. Relevant processes include in the remodeling are ischemia, cell necrosis & apoptosis.[4] Pathologic remodeling may occur with pressure overload (e.g., aortic stenosis, hypertension), volume overload (e.g., atrial septal defect, valvular regurgitation), or following cardiac injury (e.g., myocardial infarction). In each of these settings, remodeling may reveal transition from an apparently compensatory process to a maladaptive one.[2]

Measures to assess LV remodeling include heart size, shape and mass, ejection fraction, end-diastolic and end-systolic volumes and peak force of contraction. Although direct measurement of the size and shape of the heart might appear to be the most logical method of assessing the extent of remodeling, technical factors and differences of interpretation lead to variation in the results. For example, only 38% of hypertensive patients with anatomic LV hypertrophy showed LV hypertrophy when assessed on M-mode echocardiography.[4] The extent of cardiac remodeling after surgical correction depends on initial morphological changes attributed to the disease process itself. So the age at which surgical corrections are made have important bearings on the remodeling process itself.

## METHODS:

This prospective cohort study was carried out on a total of 70 patients (ranging from 5 – 50 years) who underwent surgical closure of atrial septal defect over a period of twenty three months (February 2013 to December 2014) in the Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka. Informed written consent was taken from each patient before enrollment. Patients with isolated ASD (Septum primum, Septum secondum, Sinous Venosus type of ASD) were included. However, patients of ASD with associated lesion, systemic disease such as end stage renal disease, hepatic failure, respiratory failure and ASD with Eisenmenger's syndrome were excluded. Detailed history, clinical examination & relevant investigation reports of all patients were recorded on the data-sheet. The patients were divided into two groups – Group-A (comprised of ≤ 18 years old patients) & Group-B (comprised of >18 years old patients) 35 patients in each group. Condition of the heart was evaluated preoperatively by echocardiography and the result was compared with postoperative echocardiographic findings at follow-ups after 1 and 3 months of surgery. The echocardiographic variables used to evaluate the cardiac remodeling (morphological and functional outcome of heart) were LA (Left Atrium), IVST (Interventricular Septal Thickness), PWT (Posterior Wall Thickness), LVIDd (Left Ventricular Internal Diameter at End-Diastole), LVIDs (Left

Ventricular Internal Diameter At End-Systole), EF (Ejection Fraction), FS (Fractional Shortening).

All patients underwent median sternotomy followed by surgical closure of ASD. All statistical analyses were performed using SPSS 22.0 statistical package. While continuous data were expressed as mean ± SD & were compared between groups using Unpaired t-Test, qualitative data presented as frequency (percentage) and were compared between groups using Chi-square ($\chi^2$) Test. All analyses were done at 5% level of significance and p-value < 0.05 was considered significant.

## RESULT:

The mean ages of the patients of Group-A and Group-B were 12.1 ± 3.4 and 30.7 ± 6.8 years respectively. Of the 35 patients in Group-A 22(62.9%) were male and 13(37.1%) were female, while in Group-B, out of 35 patients, 18(51.4%) were male and 17(48.6%) female. Majorities of the ASDs in Group-A (71.4%) and Group-B (80%) were septum secondum followed by septum primum and sinous venosus defect. The groups were almost identical in terms of type ASDs (p = 0.700) (Table I).

Table II shows mean diameter of LA, IVST, PWT, LVIDd, LVIDs, EF, FS at preoperative period and at 1 and 3 months following ASD repair. The comparison of these echocardiographic parameters between preoperative findings versus findings at 1 and 3 months revealed that statistically significant remodeling occurred after surgical correction (p < 0.001). In Group-B the comparison between preoperative findings versus findings at 1 month demonstrated that all the parameters responded significantly. But the same parameters when compared between baseline and at 3 months after repair revealed insignificant differences in all the parameters except in PWT (Table III). Table IV shows the mean changes in LA diameter, LVIDd, LVIDs, IVST, PWT, EF, FS from preoperative period to 3 months between Group-A and Group-B. Comparison of degree of remodeling between Group-A and Group-B at 3 months revealed that Group-A responded well in all the variables of remodeling.

**Table I. Comparison of type of type of ASDs between the two study groups**

| Baseline characteristics* | Group | | p-value |
|---|---|---|---|
| | Group-A (n = 35) | Group-B (n = 35) | |
| Sex | | | |
| Male | 22(62.9) | 18(51.4) | 0.334 |
| Female | 13(37.1) | 17(48.6) | |
| Types of ASD | | | |
| Septum Secondum | 25(71.4) | 28(80.0) | |
| Septum Primum | 6(17.1) | 4(11.4) | 0.700 |
| Sinous Venosus | 4(11.4) | 3(8.5) | |

Figures in the parentheses denote corresponding percentage. *Data were analyzed using **Chi-square** ($\chi^2$) **Test** and were presented as **n(%).**

**Table II. Comparison of echocardiographic findings at preoperative, after 1 month and 3 months of operation in Group-A**

| Echo Variables | Group-A | | | Statistical Analysis (p-value) | |
|---|---|---|---|---|---|
| | Preoperative | At 1 month | At 3 month | Preoperative vs. at 1 month | Preoperative vs. at 1 month |
| LA (mm) | 30.43±2.59 | 31.40±2.72 | 29.20±4.14 | <0.001* | 0.062ns |
| IVST (mm) | 8.83±1.42 | 9.89±1.37 | 8.54±1.74 | <0.001* | 0.086 ns |
| PWT (mm) | 9.06±1.30 | 10.26±1.40 | 8.97±1.25 | <0.001* | 0.032* |
| LVIDd (mm) | 47.29±2.54 | 48.46±2.67 | 46.86±2.83 | <0.001* | 0.062 ns |
| LVIDs (mm) | 33.20±2.21 | 34.37±2.21 | 32.74±2.83 | <0.001* | 0.081 ns |
| EF (%) | 65.00±3.13 | 64.14±3.97 | 65.31±7.12 | <0.013* | 0.758 ns |
| FS (%) | 29.37±2.12 | 41.64±4.65 | 30.17±4.84 | <0.001* | 0.268 ns |

*Data were analyzed using **Unpaired t-Test** and were presented as **mean ± SD.**

**Table III. Comparison of echocardiographic findings at preoperative, after 1 month and 3 months of operation in Group-B**

| Echo Variables | Group-B | | | Statistical Analysis (p-value) | |
|---|---|---|---|---|---|
| | Preoperative | At 1 month | At 3 month | Preoperative vs. at 1 month | Preoperative vs. at 1 month |
| LA (mm) | 30.43±2.59 | 31.40±2.72 | 29.20±4.14 | <0.001* | 0.062ns |
| IVST (mm) | 8.83±1.42 | 9.89±1.37 | 8.54±1.74 | <0.001* | 0.086 ns |
| PWT (mm) | 9.06±1.30 | 10.26±1.40 | 8.97±1.25 | <0.001* | 0.032* |
| LVIDd (mm) | 47.29±2.54 | 48.46±2.67 | 46.86±2.83 | <0.001* | 0.062 ns |
| LVIDs (mm) | 33.20±2.21 | 34.37±2.21 | 32.74±2.83 | <0.001* | 0.081 ns |
| EF (%) | 65.00±3.13 | 64.14±3.97 | 65.31±7.12 | 0.013* | 0.758 ns |
| FS (%) | 29.37±2.12 | 41.64±4.65 | 30.17±4.84 | <0.001* | 0.268 ns |

*Data were analyzed using **Unpaired t-Test** and were presented as **mean ± SD.**

**Table IV. Comparison of degree of remodeling in two study group at 3 months of follow up (n=70)**

| Variables | Group | | t-value | p-value |
|---|---|---|---|---|
| | Group-A (n = 35) | Group-B (n = 35) | | |
| LA (mm) | -2.09±0.88 | -1.23±2.17 | -1.30 | 0.033* |
| LVIDd (mm) | -4.20±1.53 | -0.43±1.31 | -11.07 | < 0.001* |
| LVIDs(mm) | -4.17±1.40 | -0.46±1.50 | -10.69 | < 0.001* |
| IVST(mm) | -1.97±0.95 | -0.29±0.96 | -7.38 | < 0.001* |
| PWT(mm) | -1.89±0.96 | -0.09±0.28 | -10.60 | < 0.001* |
| EF(%) | 5.40±2.68 | 0.31±6.00 | 4.58 | < 0.001* |
| FS(%) | 3.43±1.87 | 0.80±4.21 | 3.38 | 0.001* |

Figures in the parentheses denote corresponding percentage. *Data were analyzed using **Chi-square** ($\chi^2$) **Test** and were presented as **n(%).**

## DISCUSSION:

The comparison of echocardiographic parameters between baseline (preoperative) and those at 1 & 3 months after surgery in Group-A demonstrated that statistically significant remodeling occurred after 1st month ($p < 0.001$) & it further improved at 3 months. In Group-B the comparison of echo parameters between baseline and at 1 month revealed that all the parameters responded significantly indicating that remodeling occurred well after 1 month. But the same parameters when compared between baseline and at 3 months after repair revealed insignificant differences in all the parameters, except in PWT indicating that remodeling that occurred at month 1 regressed at 3 months interval.

In a retrospective study, Oliver et al[6] examined the outcome of early and late surgical repair of ASD in adults, as compared with the natural evolution of unoperated patients. Their study population comprised of 280 patients (mean age 40 ± 18 years, with youngest and the oldest patients) with non-restrictive ASD: 102 patients underwent surgery before the age of 25 years, 90 patients underwent surgery after the age of 25 years, and 88 unoperated patients were older than 25 years at the time of study.

In Group-A the mean diameter of left atrium at preoperative period was 28.3 ± 4.0 mm which increased to 35.5 ± 3.3 mm after 1st month and then decreased to 26.2 ± 3.9 mm after 3rd month of postoperative period and in Group-B, the mean diameter of left atrium at preoperative period was 30.4 ± 2.6 mm which increased to 31.4 ± 2.7 mm after 1st month and decreased to 29.2 ± 4.1 mm after 3rd month of postoperative period. LA size increased in the first month probably due to oedema, myocardial ishchaemia and effect of cardiopulmonary bypass. This finding of LA dimension is consistent with finding of Roberts et al[5]. They concluded that there was marked LA enlargement in patients with ASDs, suggesting that in addition to the known volume overload with resultant stretch of the right atrium, there is chronic stretch of the LA. Second, there were structural changes within the LA with loss of functioning myocardium. But according to Oliver et al[6], the size of the left atrium is much smaller in patients who undergo surgery before the age of 25 years than in those who undergo surgery after the age of 25 and in those who do not undergo surgery. The contribution of volume overload to the increase in size of the left atrium does not appear to be important, as those patients who underwent closure of the ASD after the age of 25 years had the same or even greater left atrial size than the patients who did not undergo surgery. In group A, the interventricular septal thickness at preoperative period was 8.5 ± 1.2 mm which increased to 10.4 ± 0.8 mm after 1st month and decreased to 6.5 ± 1.4 mm after 3rd month of postoperative period and in group B, the interventricular septal thickness at preoperative period was 8.8 ± 1.4 mm which increased to 9.9 ± 1.4 mm after 1st month and decreased to 8.5 ± 1.7 mm after 3rd month of postoperative period.

In group A, the posterior wall thickness at preoperative period was 8.11 ± 1.59 mm which increased to 9.6 ± 1.5 mm after 1st month and decreased to 6.2 ± 1.8 mm after 3rd month of postoperative period and in group B, the PWT at baseline was 9.1 ± 1.3 mm which increased to 10.2 ± 1.4 mm after 1st month and decreased to 8.9 ± 1.2 mm 3rd month after repair. The LVIDd at preoperative period was 41.3 ± 3.2 mm which changed to 45.9 ± 3.2 and 37.1 ± 3.6 mm after 1st and 3rd month postoperatively respectively, while the same parameter in Group-B, the LVIDd at preoperative

period was 47.3 ± 2.5 mm which enlarged to 48.4 ± 2.7mm after 1st month and decreased to 46.8 ± 2.8 mm after 3rd month postoperatively. At first month of postoperative period LVIDd probably increased due to postoperative myocardial ishchaemia, and oedematous changes resulting from manipulation of the heart. Komar et al[7] showed that LVIDd reduces insignificantly from baseline value, 49.9 to 47.3 mm at 1st month, 45.9 mm at 6 month. According to Thilén et al[8] the left ventricle increased significantly in size after closure, whether measured as an area or as a dimension (LVIDD). However, closure did not affect left atrial size. Komar et al[7] observed that LVIDs increases from baseline value, 35.4 to 38.5 mm at 1st month and then reduces to 36.5 mm at 6 months with no significant changes from baseline to 6 months.

In group A, the ejection fraction at preoperative period was 62.9 ± 2.6 percent which decreased to 53.4 ±10.9 percent after 1st month and increased to 68.4 ± 3.8 percent after 3rd month postoperatively and in Group-B, the ejection fraction at preoperative period was 65.0 ± 3.1 percent which decreased to 64.1 ± 3.9 percent after 1st month & increased to 65.3 ± 7.1 percent after 3rd month postoperatively. According to Komar et al[7] EF reduces from 60.4% at baseline to 59.4% at 1st month postoperatively but again increases at 6 month postoperatively. The fractional shortening in Group-A at preoperative period was 28.5 ± 1.9 percent which decreased to 22.9 ± 1.9 percent after 1st month and to 31.9 ± 278 percent after 3rd month of repair. The same variable in Group-B, at preoperative period was 29.3 ± 2.1 percent which increased to 41.6 ± 5.6 percent after 1st month and again decreased to 30.2 ± 4.8 percent after 3rd month of postoperative period compared to its preoperative figure.

In group A, the comparison between preoperative findings versus 1 month and preoperative versus 3 months was statistically significant in case of LA, IVST, PWT, LVIDd, LVIDs, EF and FS. In group B, the comparison between preoperative findings versus 1 month was statistically significant in case of LA, IVST, PWT, LVIDd, LVIDs, EF and in FS. But the comparison between preoperative findings versus 3 months was insignificant in case of LA, IVST, LVIDd, LVIDs, EF and in FS. Comparison of degree of remodeling between patients of early age (Group-A) and late age (Group-B) revealed that ASD repair at early age respond well with respect to all the echocardiographic variables of remodeling.

## CONCLUSION:

This study observed that cardiac remodeling occurs after surgical closure of atrial septal defect at any age but the degree of remodeling was better patients less than 18 years, compared to that in 18 or more than 18 years old.

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