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Original Article

Early and six-month assessment of bi-ventricular functions following surgical closure of atrial septal defect

Rajesh Vijayvergiya [a,*], *Jiten Singh* [b], *Sandeep S. Rana* [b], *Ranjan Shetty* [a], *Bhagwant R. Mittal* [c]

[a] *Associate Professor, Department of Cardiology, Advanced Cardiac Centre, Post Graduate Institute of Medical Education & Research, Sector 12, Chandigarh 160 012, India*
[b] *Cardio-thoracic Surgery, Advanced Cardiac Centre, Post Graduate Institute of Medical Education & Research, Chandigarh, India*
[c] *Nuclear Medicine, Advanced Cardiac Centre, Post Graduate Institute of Medical Education & Research, Chandigarh, India*

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ABSTRACT

Background: The effect of surgical closure of atrial septal defect (ASD) on biventricular functions is not well studied. We studied effect of surgical closure of ASD on bi-ventricular functions.

Methods: Patients undergoing surgical closure of ASD from December 2007 to June 2009 had 3 sequential echocardiograms examination: pre-procedure, post surgery at 1-month and at 6-month of follow up. Pulse Doppler velocities across mitral and tricuspid valves were measured as peak early diastolic (E wave) and peak late diastolic (A wave). Tissue Doppler velocities across lateral wall of both right ventricle (RV) and left ventricle (LV) were measured as peak early diastolic (E′), peak late diastolic (A′), and peak systolic (S′) wave. Radionuclide angiography was performed to assess RV and LV ejection fraction at baseline and at 1-month follow up.

Results: The mean age of 20 enrolled patients was 21.85 ± 10.9 years; 8 females & 12 males. Trans-tricuspid flow velocities significantly decreased following surgery at one and 6-month ($p < 0.005$). There was no significant change in trans-mitral flow velocities at one and 6-months. Tricuspid and mitral E/A ratio and E/E′ ratio also had an insignificant change following surgery. There was no significant change in LV ejection fraction as assessed by echocardiography ($p = 0.132$) and radionuclide scan ($p = 0.143$). Right ventricular ejection fraction had a significant improvement at 1-month of follow up ($p = 0.005$).

Conclusions: There was a significant improvement in RV systolic function and an insignificant change in RV and LV diastolic functions following surgical closure of ASD.

* *Corresponding author*. Tel.: +91 172 275 6512; fax: +91 172 274 4401.
E-mail address: rajeshvijay999@hotmail.com (R. Vijayvergiya).
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1. Introduction

Atrial septal defect (ASD) accounts for 25–30% of congenital heart defects, which are diagnosed during adulthood.[1] Most individuals with isolated ASD become symptomatic in third or fourth decade of life.[2] It can cause right ventricular dysfunction, pulmonary artery hypertension, atrial arrhythmias, thrombo-embolism and stroke. Its closure is recommended to avoid these late complications.[2] Echocardiography is the best imaging modality for diagnosis and hemodynamic evaluation of ASD. Nuclear imaging with Equilibrium Radionuclide Ventriculography (ERNV) using 99mTc-pertechnetate provides an accurate measurement of bi-ventricular systolic functions in congenital heart disease. In the present study, we prospectively enrolled patients subjected for surgical repair of ASD and studied (i) bi-ventricle systolic and diastolic functions by assessing mitral and tricuspid valve pulsed wave and tissue Doppler velocities (DTI) at baseline, and post operatively at 1 and 6-month, following surgery. (ii) Right and left ventricular ejection fraction using ERNV at baseline and at 1-month, following surgery.

2. Methods

Twenty consecutive patients of isolated ASD subjected for surgery from December 2007 to June 2009 were enrolled in the study. All patients underwent detailed trans-thoracic echocardiography examination (3.5 MHz transducer, *Vivid System Five, GE Vingmed, Horten, Norway*) before, 1-month later and 6-months after surgery. Bi-ventricular ejection fraction was calculated using ERNV at baseline and 1-month after surgery. The study was approved by institutional ethical committee.

2.1. Echocardiographic measurements

Atrial septal defect was measured in apical 4-chamber and sub-costal view. Electrocardiography gated pulse wave Doppler velocities such as peak inflow velocities at early (E) and late (A) diastole were measured across mitral and tricuspid valves. Doppler tissue velocities in early diastole (E′), late diastole (A′) and peak systolic (S′) wave were measured by the spectral mode of the myocardial Doppler imaging (5 MHz) in two positions: (1) the basal right ventricle (RV) free-wall – tricuspid annular junction, and (2) the basal left ventricle (LV) free-wall – mitral annular junction. The standard para-sternal long-axis view just below the tip of the mitral valve leaflets was used for M-mode measurements. Left ventricle ejection fraction was measured by modified Simpson's method in apical 4-chamber view. The RV dimension was measured at mid level of ventricle at end-diastole, in apical RV focused four-chamber view. An RV dimension of $\geq$35 mm was considered for RV dilatation as per American Society of Echocardiography guidelines.[3]

2.2. Radionuclide study

Radionuclide angiography was performed according to American Society for Nuclear Cardiology recommendation.[4] Electrocardiogram gated Multigated Radionuclide Angiography (MUGA) was performed in each patient after labeling their red blood cells in vivo. Initially, an intra-venous dose of 2–3 mg Stannous Pyrophosphate was given. Twenty minutes later, a dose of 0.2 mCi (7.4 MBq)/kg body weight, maximum dose of 20 mCi (740 MBq) of sodium technetium 99m pertechnetate (Na99mTcO4) was injected. Cardiac imaging was acquired on a single headed SPECT gamma camera (*MPR GE Healthcare Milwaukee, USA*). ERNV studies were acquired on computer using a pixel matrix. Each study was acquired for approximately 5 min, collecting data from 300 to 400 cardiac cycles. The data thus obtained was analyzed to measure RV ejection fraction by first-pass radionuclide angiography (FPRNA) and LV ejection fraction by MUGA. A permission was taken from institute ethics committee for the study.

2.3. Statistical analysis

Statistical analysis was performed using SPSS 15.0 software. After assessment of approximate normal distribution, continuous variables were presented as mean ± 1 SD. The Wilcoxon matched pair test was used to compare baseline, one and six months post surgery variables. Trend for continuous variable over 6 months was assessed using Freidman's test. Ejection fraction of left and right ventricle derived from radionuclide test was compared before and after surgery using the paired t – test. A p value of <0.05 was considered statistically significant.

3. Results

Among 20 patients enrolled in the study, there were 8 females and 12 males. The mean age was 21.85 ± 10.9 years. All patients were in sinus rhythm and had no associated cardiac defects. Seventeen patients had ostium secundum defect and three had sinus venosus defect. Mean size of the defect was 27.10 ± 8.8 mm (Range 12–33 mm). Pericardial patch repair was performed in 18 and direct suturing in 2 patients. There was no peri-operative complication.

Trans-tricuspid flow velocities significantly decreased following surgery. Tricuspid E velocity decreased from 103.35 ± 22.9 cm/s at baseline to 63.55 ± 17.8 cm/s at 1-month and to 63.60 ± 19.4 cm/s at 6-months ($p = 0.001$). Similarly tricuspid A velocity decreased from baseline as 62.75 ± 19.4 cm/s to 42.95 ± 11.1 cm/s at 1-month and to 44.25 ± 11.3 cm/s at 6-months ($p = 0.001$). Tissue Doppler velocities at tricuspid annulus also showed a significant decrease: for E′ wave, 21.39 ± 6.5 to 13.28 ± 5.3 to 3 11.67 ± 4.2 cm/s ($p < 0.001$); for A′ wave 16.40 ± 5.4 to 10.67 ± 4.3 to 8.6 ± 2.73 cm/s ($p < 0.001$); and for S' wave, 17.75 ± 3.5 vs 11.55 ± 4.9 vs 11.60 ± 3.4 cm/s ($p < 0.001$). However, tricuspid inflow velocity ratio such as E/A ratio (1.7 ± 0.63 to 1.5 ± 0.34 to 1.5 ± 0.042, $p = 0.142$) and E/E′ ratio (5.03 ± 1.1 to 5.5 ± 2.7 to 6.19 ± 2.6, $p = 0.086$) showed an insignificant change at follow-up. All these values are described as – at baseline, at 1-month and at 6-month of follow up (Table 1). There was a significant decrease in RV dimension at one and 6-month of follow up following repair (41.30 ± 13.0 to 30.15 ± 8.4 to 24.60 ± 7.9 mm; $p < 0.001$) (Table 1). Right ventricle dilatation

Table 1 – Echocardiographic parameters of patients at baseline, 1 and 6-month post operative period.

Variable	Preoperative	At 1 month follow-up	At 6 month follow-up	*p* Value (pre vs post	*p* Value (post vs 6 months)	*p* Value trend (Freidman's)
Mitral pulse Doppler indices (in cm/sec)						
Peak early diastolic (E)	94.45 ± 21.66	103.75 ± 21.5	102.35 ± 24.8	0.185	0.794	0.247
Peak late diastolic (A)	64.75 ± 15.3	64.05 ± 13.4	65.00 ± 16.8	0.681	0.837	0.549
E/A ratio	1.50 ± 0.34	1.60 ± 0.41	1.60 ± 0.62	0.247	0.823	0.549
Peak early diastolic tissue velocity (E′)	19.69 ± 5.4	17.78 ± 5.5	16.65 ± 4.6	0.104	0.333	0.124
Peak late diastolic tissue velocity (A′)	15.00 ± 13.6	12.43 ± 10.9	9.30 ± 7.8	0.042	0.034	0.001
Peak systolic tissue velocity (S′)	17.94 ± 4.3	15.08 ± 4.1	13.79 ± 3.3	0.073	0.083	0.126
E/E′ (mitral) ratio	5.20 ± 2.2	6.40 ± 2.5	6.70 ± 2.8	0.167	0.502	0.026
Tricuspid pulse Doppler indices (in cm/sec)						
Peak early diastolic (E)	103.35 ± 22.9	63.55 ± 17.8	63.60 ± 12.8	<0.001	0.888	<0.001
Peak late diastolic (A)	62.75 ± 19.4	42.95 ± 11.1	44.25 ± 11.3	0.001	0.837	0.001
E/A ratio	1.7 ± 0.63	1.5 ± 0.34	1.5 ± 0.42	0.108	0.907	0.142
Peak early diastolic tissue velocity (E′)	21.39 ± 6.5	13.28 ± 5.3	11.67 ± 4.2	0.001	0.387	<0.001
Peak late diastolic tissue velocity (A′)	16.40 ± 5.4	10.67 ± 4.3	8.6 ± 2.73	0.001	0.064	<0.001
Peak systolic tissue velocity (S′)	17.75 ± 3.5	11.55 ± 4.9	11.60 ± 3.4	0.002	0.681	<0.001
E/E′(tricuspid) ratio	5.03 ± 1.1	5.53 ± 2.7	6.19 ± 2.6	0.765	0.167	0.086
Other parameters						
RVD (mm)	41.30 ± 13.0	30.15 ± 8.4	24.60 ± 7.9	<0.001	0.003	<0.001
LV EF (Simpsons in %)	64.20 ± 8.5	64.15 ± 6.6	63.80 ± 6.0	0.904	0.856	0.132

Abbreviation:-RVD-right ventricle dimension, LV EF – left ventricle ejection fraction.

with dimension of more than 35 mm was present in 13 (65%) patients at baseline, which decreased to six (30%) patients at 1-month and one (5%) patient at 6-month follow up.

Doppler echocardiography showed insignificant change in trans-mitral flow velocities at one and 6-months of follow up compared to baseline: for mitral E wave – 94.45 ± 21.6 to 103.75 ± 21.5 to 102.35 ± 24.8 cm/s ($p = 0.247$), for mitral A wave – 64.75 ± 15.3 to 64.05 ± 13.4 to 65.00 ± 16.8 cm/s ($p = 0.549$). Tissue Doppler velocities at mitral annulus also showed no significant change at follow up: for E′ wave – 19.69 ± 5.4 to 17.78 to 16.65 ± 4.6 cm/s, ($p = 0.124$); for A′ wave – 15.00 ± 13.6 to 12.43 ± 10.9 to 9.30 ± 7.8 cm/s, ($p = 0.001$); and for S′ wave – 17.94 ± 4.3 to 15.08 ± 4.1 to 13.79 ± 3.3 cm/s, ($p = 0.126$). Mitral inflow velocity ratio as E/A ratio (1.50 ± 0.34 to 1.60 ± 0.41 to 1.60 ± 0.62, $p = 0.549$) and E/E′ ratio (5.20 ± 2.2 to 6.40 ± 2.5 to 6.70 ± 2.8, $p = 0.026$) showed no significant change at follow up (Table 1).

There was no significant change in LV ejection fraction as estimated by echocardiography (64.20 ± 8.5 to 64.15 ± 6.6 to 63.80 ± 6.0%; $p = 0.132$) (Table 1), and MUGA scan (56.78 ± 8.7 to 59.57 ± 7.5% at 1-month follow up; $p = 0.143$) (Table 2). However, RV ejection fraction as assessed by FPRNA had a significant improvement at 1-month of follow up (53.36 ± 9.6 to 61.68 ± 10.5%; $p = 0.005$) (Table 2).

4. Discussion

Atrial septal defect with significant left to right shunt is associated with RV volume overload and increase flow across tricuspid valve, which improves following surgical repair. We have demonstrated a significant decrease in trans-tricuspid diastolic pulse wave and tissue Doppler velocities ($p < 0.001$), following ASD repair. Similar findings have been observed by other authors following surgical and percutaneous device repair of ASD.[5] This decrease in velocities is dependent on RV preload, which decreases following ASD repair. The change in inflow velocities is demonstrable as early as 6-days or as late as 5-years following surgery.[5,6] We demonstrated the change in velocities at 1 and 6-months of follow up. An insignificant change in tricuspid E/A ratio (1.7 ± 0.63 to 1.5 ± 0.34 to 1.5 ± 0.42; $p = 0.142$), and in tricuspid E/E′ ratio (5.03 ± 1.1 to 5.53 ± 2.7 to 6.19 ± 2.6; $p = 0.086$) suggest a relatively preserved filling pressure and RV diastolic function following surgery. Dhillon R, et al[7] had demonstrated that both RV systolic and diastolic functions are impaired following surgical closure but remained preserved following device closure of ASD. There was a favorable RV remodeling following surgery as evident by significant decrease in RV end diastolic dimension as 41.30 ± 13.0 to 30.15 ± 8.4 to 24.60 ± 7.9 mm; $p < 0.001$. Regression of dilated RV has been reported by various authors.[8–12] It is a continuous process extending till 6–18 months following repair.[13] A higher RV dimension at baseline

Table 2 – Bi-ventricular systolic function assessment at baseline and at 1-month post operative period by radionuclide study.

Variable	Preoperative	Postoperative (1 month)	*p* Value
RV EF (%)	53.36 ± 9.6	61.68 ± 10.5	0.005
LV EF (%)	56.78 ± 8.7	59.57 ± 7.5	0.143

Abbreviation:- RV EF – Right ventricle ejection fraction, LV EF – left ventricle ejection fraction.

and an advanced age adversely affect the remodeling process.[2] Ours is the first study to demonstrate RV systolic function assessment by radionuclide scanning in post-operative patients of ASD. Radionuclide technique is a better imaging modality, compared to 2-D echocardiography for assessment of right ventricle systolic function.[14] A good correlation is already been demonstrated between radionuclide scanning v/s cardiac magnetic resonance (CMR) and 3-D echocardiography.[15] We demonstrated a significant improvement in RV ejection fraction as 53.36 ± 9.6 to $61.68 \pm 10.5\%$; $p = 0.005$, at 1-month follow-up. Schoen et al,[16] demonstrated significant improvement in RV ejection fraction following trans-catheter closure of ASD at 6 and 12-months of follow up, as assessed by magnetic resonance imaging. In contrast, Fang F et al,[17] demonstrated an insignificant decrease in RV ejection fraction as 51 ± 14 to $46 \pm 15\%$, $p = 0.052$, at 3 months of follow up following device closure of ASD.

We did not find a significant change in trans-mitral pulse Doppler velocities and E/A ratio following surgery, similar to other's observation.[5,18,19] An insignificant change in mitral E/A ratio as 1.50 ± 0.34 to 1.60 ± 0.41 to 1.60 ± 0.62, [$p = 0.549$], is suggestive of unchanged LV diastolic function following surgery. The mitral annular tissue Doppler velocities showed an insignificant decrease in E' wave as 19.69 ± 5.4 to 17.78 ± 5.5 to 16.65 ± 4.6 cm/s,[$p = 0.124$] and a significant decrease in A′ wave as 15.00 ± 13.6 to 12.43 ± 10.9 to 9.30 ± 7.8 cm/s, [$p = 0.001$]. Various authors have demonstrated an increase,[20] or decrease[21] or no change[22,23] in trans-mitral tissue Doppler velocities following ASD repair. An insignificant change in mitral E/E′ ratio as 5.20 ± 2.2 to 6.40 ± 2.5 to 6.70 ± 2.8 [$p = 0.026$], suggest unchanged filling pressure and LV diastolic function following surgery. Zilberman MV et al[24] demonstrated that LV diastolic dysfunction is insignificantly more in surgical group in comparison to device group. Left ventricular ejection fraction as assessed by echocardiography and radionuclide scanning remained the same after surgery. Various authors have reported no significant change in LV ejection fraction after intervention, as assessed by echocardiography.[18,25,26] A small sample size, shorter duration of follow up and non-comparison with healthy controls are few of the limitation of our study. Strain and strain rate assessment by two or three dimensional speckle-tracking echocardiography could have provide subtle changes in right and left ventricular functions, however this method was not used in present study.[27,28]

In conclusion, we found an improvement in RV systolic function, and unchanged diastolic functions of both RV and LV following surgical closure of ASD. Left ventricular systolic function was unaffected by surgery. A favorable RV remodeling was observed even till 6-months, following surgery.

Conflicts of interest

All authors have none to declare.

Author's contribution

All the authors were actively involved in management of patients, included in the study. Authors Singh J, Rana SS performed surgery; Vijayvergiya R, Shetty R preformed echocardiography; and Mittal BR performed nuclear imaging of patients. Vijayvergiya R and Singh J were actively involved in manuscript writing.

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