EARLY LEFT VENTRICULAR REMODELING AFTER AORTIC VALVE REPLACEMENT

Naseem Ahmad , Ahmad Shahbaz, Abdul Ghaffar, Zafar Tufail, Abdul Waheed, Jawad Sajid Khan
Department of Cardiac Surgery, Punjab Institute of Cardiology, Lahore, Pakistan.

Background: Aortic valve disease is associated with eccentric or concentric left ventricular (LV) hypertrophy and changes in the LV mass. The relationship between LV mass and function and the effect of LV remodeling after aortic valve replacement (AVR), in patients with aortic valve disease needs evaluation, that is largely unknown in our population. The aim of this study was to evaluate the effect of AVR on LV remodeling, in patients with aortic valve disease. **Methods:** Fifty patients with aortic valve disease were studied using transthoracic echocardiography to assess LV mass before AVR and compared with early postoperative changes in the LV dimensions and function. LV mass was studied preoperatively and before discharge in 50 consecutive patients undergoing isolated aortic valve replacement. **Results:** Out of fifty patients, 47(94%) were male and 03(6%) were female. Mean age of the patients was 40.42 years. 22 (44%) had isolated aortic stenosis (AS), 16 (32%) patients had isolated aortic regurgitation (AR) and 12 (24%) patients had mixed aortic valve disease (MAVD). 02 (4%) patients died. LV mass regression was studied in all the patients. In group A, with aortic stenosis, LV regressed to 69.88 gm (mean) with maximum of 156.88 gms and minimum of 0.00 gms (SD 43.67 gms, p value = 0.001). In group B, with aortic regurgitation, LV mass regressed to 203.96 gms (mean) with maximum 453.79 gms and minimum of 45.65 gms (SD 95.33, p value = <0.001). In group C, with mixed aortic valve disease, postoperatively LV mass regressed to 122.94 gms (mean) with minimum 9.57 and maximum of 224.75 gms (SD 69.53, p value = 0.524). **Conclusion:** There was significant early LV mass regression after aortic valve replacement in patients with pre existing aortic valve disease. However, it was noticed that LV mass regressed in all patients except no significant changes in LV wall thickness (hypertrophy).

Keywords: Aortic valve replacements; Left ventricular mass regression; Left ventricular function.

INTRODUCTION

Aortic valve disease is associated with eccentric or concentric left ventricular (LV) hypertrophy and changes in the left ventricle function.[1] Severe aortic regurgitation (AR) causes volume overload with an increase in the LV end-diastolic volume and eccentric hypertrophy, but may not change the ratio of ventricular wall thickness to cavity radius.[2] In severe aortic stenosis (AS), concentric ventricular hypertrophy occurs without increasing end-diastolic dimension until late in the disease process, thus increasing the ventricular wall thickness to cavity radius ratio.[3]

Patients with LV hypertrophy are at a risk of cardiac morbidity and mortality and is associated with systolic and/or diastolic dysfunction.[4] Diastolic function improves gradually and may normalize completely long after aortic valve replacement (AVR).[5] Early, after AVR, patients with aortic valve stenosis, show a decrease in both Left Ventricular Mass Index and Left Ventricular Mass Index / Left Ventricular End Diastolic Volume Index and an improvement in diastolic filling, whereas in patients with aortic regurgitation, Left Ventricular Mass Index decreases less rapidly than Left Ventricular End Diastolic Volume Index , causing concentric remodeling of the left ventricle, most likely explaining the observed deterioration of diastolic filling in these patients. [5]

The overall goal of AVR is to alleviate the pressure and volume overload on the left ventricle allowing myocardial remodeling and regression of left ventricular mass. The left ventricular geometrical shape also influences the outcome of AVR.[6]

The clinical impact of left ventricular mass regression is not as well understood, despite its widespread acceptance as a measure of outcome after aortic valve surgery. Considerable LV hypertrophy sometimes remains after AVR for AS.[7] For this issue, most previous studies have focused solely on transprosthetic pressure gradient, although true problem is not the pressure gradient itself but an elevated LV pressure.[8] The prognostic implications of LV mass regression after aortic valve surgery have not been rigorously studied, but logic would suggest that poor LV mass regression is associated with poor clinical outcome.[9]

Echocardiography is performed to assess the LV dimensions and function. Echocardiography is a noninvasive, highly reproducible method for accurate measurement of LV mass and LV volume.[10] In the present study we assessed the relationship between LV dimensions and function in patients with either severe aortic valve stenosis or severe aortic regurgitation, before and early after AVR.

MATERIALS AND METHODS

Fifty consecutive patients, with aortic valve disease (AS, AR, MAVD), undergoing isolated AVR at the Cardiac Surgery Department, Punjab Institute of Cardiology, Lahore, Pakistan, between June 1, 2006 and December 31, 2006, were evaluated prospectively. All clinical and echocardiography data describing this population were collected prospectively.

Median sternotomy was performed under general anesthesia and cardiopulmonary bypass was instituted with ascending aortic and two-stage single atrial cannulation. Moderate hemodilution and mild systemic hypothermia (>28°C) were used. A LV vent was inserted through the right superior pulmonary vein in selected patients. Myocardial protection was initiated with a dose of high-potassium blood cardioplegia through the ascending aortic root to induce cardiac arrest. This was followed by continuous antegrade cardioplegia directly into each coronary ostium. A transverse aortotomy was performed above the aortic annulus. The native aortic valve was excised completely and the annulus, aorta, and anterior leaflet of the mitral valve were extensively debrided of calcium when it was present. All mechanical valves were implanted using interrupted mattress and pledgeted 2-0 ethibond stitches. All pledgets were placed in the subannular position. Aortotomy was closed with prolene stitches.

All patients underwent transthoracic echocardiography week before operation and before discharge after AVR. LV mass were measured preoperatively. Only LV mass was measured in the early postoperative period. All patients had complete preoperative and postoperative measurements of LV mass, thus allowing paired analysis of the results.

A VIVID 3 Samsung sync Mater 795 MB was used for echocardiographic assessment. The examination included 2-dimensional, 2-dimensional derived M-mode, continuous wave and pulsed Doppler, and color Doppler studies. Standard left parasternal, apical, right parasternal, subcostal, and suprasternal views were obtained in a step-by-step successive pattern of interrogation.

LV mass was calculated from 2-dimensional derived M-mode measurements. The postoperative measurements were made without knowledge of the preoperative values.

Postoperative LV mass regression was pre-specified as the primary outcome. In this study, Paired sample "t" test was used to observe the extent of LV mass regression in these patients postoperatively. Continuous data in the text and tables are presented as mean ± standard deviation.

RESULTS

Out of fifty patients 47(94%) were male and 03(6%) were female.

Table 1. Sex distribution

Sex	Frequency	Percent
Male	47	94.0
Female	3	6.0
Total	50	100.0

Mean age of the patients was 40.42 ± 17.8 years with a range of 18 -80 years. In males age was 41.1 years ± 17.6 and in females 30.3 ± 21.4years.

Twenty two patients (44 %) were with isolated AS, 16 (32 %)patients were with isolated AR and 12 (24 %) patients had MAVD.

Table 2. Distribution of case by type of lesion

Disease	Frequency	Percent
AS	22	44.0
AR	16	32.0
MAVD	12	24.0
Total	50	100.0

Prosthetic, Saint Jude (St. Jude) mechanical disc valves were used for replacement. Out of fifty patients, one patient (2%) received 19mm, seven patients (14%) received 21 mm, fifteen patients (30%) received 23mm, fourteen patients (28 %) received 25mm, ten patients (20%) received 27 mm, while three patients (6%) received 29mm valve.

Table 3: Distribution of cases by size of valve used

Valve size (mm)	Frequency	Percent
19	1	2.0
21	7	14.0
23	15	30.0
25	14	28.0
27	10	20.0
29	3	6.0
Total	50	100.0

Mean cardiopulmonary bypass time was 105 minutes and mean aortic X clamp time was 62 minutes (Table 4). Two patients (4%) died; one developed acute renal failure, post operatively and the other developed low cardiac out put syndrome and multiple organ failure.

Table 4. Distribution of cases by duration of surgical procedures

Procedure	n	Range (Minutes)	Mean± SD (Minutes)
Cardiopulmonary Bypass time	50	54 - 336	105.4± 53.2
Aortic cross Clamp time	50	33 -120	62.5 ± 22.3

LV mass regression was studied in all the patients (Tables 5 & 6).

In group A (AS), mean pre-operative LV mass was 335.84 gm with minimum of 197.54 gms and maximum of 768.12 gms (with SD of 127.994). LV mass regressed to 281.40 gm (mean) with maximum of 727.56 gms and minimum of 124.95 gms (SD 131.93 gms). p value for this group was 0.001. Paired sample t-test shows that there is a significant difference between pre LV mass and post mass of stenosis patients with p value .01 at 5% level of significance.

In group B (AR), pre operative mean left ventricular mass was 573.37 gms with minimum of 295.05 gms with maximum of 818.07 gms (SD 135.20). In this group left ventricular mass regressed to 369.41 gms (mean) with maximum 727.56 gms and minimum of 124.95 gms (SD 131.92). p value for this group was 0.001. Paired sample t test shows that there is a significant difference between pre LV mass and postoperative LV mass of regurgitation patients with p value 0.001 at 5% level of significance.

In group C (MAVD), preoperative left ventricular mass was 338.57 with minimum 127.92 gms and maximum 536.93 gms (SD 132.58 gms). Postoperatively this group showed left ventricular mass of 311.38 gms (mean) with minimum 128.63 and maximum of 608.12 gms (SD 127.92). p value was 0.524. Paired sample t test shows that there is no significant difference between preoperative LV mass and postoperative LV mass of MAVD patients with p value 0.524 at 95 % confidence level.

Table 5. Distribution of cases by change in LV mass

Group	N	Preoperative (Gms) Range Mean ± SD	Regression Post operative (Gms) Range Mean ± SD	
A	22	197.5–768.1 335.8±128.0	125.0–727.6 281.4±132.0	0.01
B	16	295.0–818.1 573.4±135.2	125.0–727.6 369.4± 131.9	0.001
C	12	127.9–536.9 338.6 ±132.6	128.6–608.1 311.4 ±127.9	0.52
Total	50			

Table 6. Distribution of cases by change in LV mass with regard to type of basic lesion.

Group	N	Reduction in LV Mass	
		Range	Mean± S.D.
AS	22	0.0-156.9	69.9 ± 43.67
AR	16	45.6-453.8	204.0 ± 95.33
MAVD	12	9.6-224.8	122.9 ± 69.5

DISCUSSION

AVR reduces symptoms, increases long-term survival, and improves the quality of life in patients with aortic valve disease. LV hypertrophy regresses after AVR, but LV mass does not return to normal levels.[11] The time course of the regression of LV hypertrophy after AVR is controversial. The earliest documented evidence of consistent LV mass regression after AVR has varied between 06 weeks[12] and 01 year.[13] The earliest time at which LV mass regression is possible after AVR was the focus of this study.

In this study, we have observed the changes in the LV mass during initial days before their discharge from hospital (5 to 10 days). Per operative and early post operative echocardiography was done to observe the changes in the LV mass.

Hypertrophy is characterized by a concentric increase in muscle mass to preserve a normal relation between systolic wall stress and ejection fraction.[14] Regression of LV hypertrophy after AVR is an important end point. All prosthetic valves are relatively stenotic because the valve sewing ring and stents reduce the effective orifice area. After AVR, transvalvular gradients often remain elevated, and the LV hypertrophy does not resolve completely.[3] Ghali and associates[15] demonstrated that patients with even moderate LV hypertrophy had a greater risk of death from any cause even after adjustment for age, sex, coronary artery disease, and hypertension. Concerns about the long-term effects of residual hypertrophy after AVR have been raised by various investigators. Late deaths AVR are often caused by sudden cardiac arrest, arrhythmias, and congestive heart failure.[16] These late events may be caused by or influenced by LV hypertrophy. LV mass regression after aortic valve replacement may be an important and underestimated determinant of long-term outcome.

Echocardiographic mass measurements are noninvasive and reproducible estimates of the extent of LV hypertrophy. M-mode echocardiography has been shown to correlate well with contrast left ventriculography for LV mass measurement.

LV mass reflects the severity of AS, is positively correlated with peak aortic valve gradients, and has been used to confirm at least partial regression of hypertrophy after AVR. The extent and time course of LV mass regression after valve replacement remain controversial. Kurnik and colleagues[17], using ultrafast computed tomography, reported 27% regression of LV mass at 4 months after AVR and a total of 36% regression at 8 months. Henry and associates[18] demonstrated a 16% mass reduction at 6 months after AVR for AS, with no further changes at 1 year. They observed that most of the regression occurred within the

first month after operation. We have concluded in this study that there is significant LV mass regression of 10 days of operation. The amount of mass regression actually may have been underestimated. Monrad and associates[11] assessed 11 patients after AVR for AS and demonstrated that LV mass regressed from 158 ± 33 g/m2 preoperatively to 114 ± 27 g/m2 at 18 ± 6 months postoperatively, compared with 85 ± 9 g/m2 for control patients. Mass regression after AVR is dependent on host factors. Persistence of myocardial collagen fibrosis may account for some of the incomplete regression. Age, sex, hypertension, coronary artery disease, LV function, and diabetes may be determinants of LV mass.

Venco A and colleagues reported in their study of non-invasive assessment of LV function after correction of severe AR that after AVR, there was an early reduction in end-diastolic dimension, within 2 days, from 7-0 $\pm$ 0-8 cm to 5-7 $\pm$ 1-0 cm (p less than 0.001).[12]

Collinson J and colleagues[13] studied the effect of AVR on LV function. 47 patients who received either a stentless or stented valve for isolated AR were included in their study. All patients had evidence of pre-existing LV dysfunction (end-systolic dimension (ESD) >50 mm). They described that preoperatively. The end-diastolic dimension fell from 75 $\pm$ 10 mm to 61 $\pm$ 10 mm postoperatively and to 52 $\pm$ 10 mm at follow up in the stentless group ($p < 0.001$), and ESD fell from 54 $\pm$ 10 mm to 36 $\pm$ 8 mm at follow up ($p < 0.001$). There were no significant early changes in patients who received stented valves, though LV dimensions fell at follow up. They observed that in the stentless group, LV mass fell from 366 $\pm$ 104g to 276 $\pm$ 68g postoperatively and to 219 $\pm$ 79g at follow up ($p < 0.001$); there was no postoperative change in the stented group, though a late reduction occurred, from 349 $\pm$ 51g preoperatively to 265 $\pm$ 61g at follow up ($p = 0.06$). For patients with AR and LV dysfunction, AVR with stentless prosthesis offers early reductions in LV dimensions, improved LV function, and regression of LV mass.

74 patients with severe aortic valve stenosis were divided into 2 groups according to LV ejection fraction (EF): Group 1 with EF > 50% (n = 40); Group 2 with EF < or = 50% (n = 34). Furthermore, patients were differentiated into a group A without (n = 53) and a group B with AR (< or = II degrees, n = 21). All patients were examined by transthoracic echocardiography before and 1 month after surgery. There was a significant decrease of LV end diastolic and end systolic volume indices following AVR in group 2 and group B. Patients with preoperatively lower EF (group 2) showed an increase in LV ejection fraction from 39 $\pm$ 10% before AVR to 47 $\pm$ 11% after AVR ($p < 0.001$), whereas patients with preoperative normal EF (group 1) showed a significant decrease in EF (from 62 $\pm$ 8% to 57 $\pm$ 10%, $p < 0.05$). Also patients with combined aortic valve disease before AVR had an increase of EF after surgery (from 45 $\pm$ 14% to 56 $\pm$ 14%, $p < 0.03$). There were significant decreases of interventricular septum thickness and LV posterior wall thickness in group 1 and group A, whereas a significant decrease of LV end diastolic diameter index was noted only in group B. Patients with impaired LV function or combined aortic valve disease showed a significant improvement of left ventricular systolic function after AVR, while patients with normal LV function presented a slight decrease of EF. There was a significant regression of left ventricular muscle mass in all groups independent of the left ventricular functional status.

Lamb HJ and colleagues[5] reported that early after AVR, patients with AS show a decrease in both LVMI and LVMI/LVEDVI and an improvement in diastolic filling, whereas in patients with AR, LVMI decreases less rapidly than LVEDVI, causing concentric remodeling of the LV, most likely explaining the observed deterioration of diastolic filling in these patients.

Changes in LV mass and function up to 10 years after AVR for AS were highly predictable. Poor outcomes were related to preoperative excessive hypertrophy and indices of underlying irreversible myocardial disease and further compromised by hypertension and, to a lesser extent, coronary artery disease. The hemodynamic function of the aortic prosthetic valve did not seem to play a role.

This study showed changes in the LV mass in different groups with AS, AR and MAVD.

In group A, with AS, LV mass regressed to 69.88 gm (mean) with maximum of 156.88 gms and minimum of 0.00 gms (SD 43.67 gms). p value for this group was 0.001.

In group B, with AR, LV mass regressed to 203.96 gms (mean) with maximum 453.79 gms and minimum of 45.65 gms (SD 95.33). p value for this group was 0.000.

In group C, with MAVD, postoperatively, LV mass was regressed to 122.94 gms (mean) with minimum 9.57 and maximum of 224.75 gms (SD 69.53). p value was 0.524.

In this study, we have demonstrated that LV mass regression begins early after AVR. We have shown the extent of LV mass regression in early postoperative period.

CONCLUSION

There is significant early LV mass regression after AVR in patients with pre existing aortic valve disease. However it is noticed that LV mass regressed

in all patients except no significant changes in LV wall thickness (hypertrophy).

REFERENCES

1. Natsuaki M, Itoh T, Okazaki Y, Ishida H, Hamada M, Rikitake K et al. Evaluation of postope rative cardiac function and long-term results in patients after aortic valve replacement for aortic valve d isease with increas ed left ventricular mass. Jpn J Thorac Cardiovasc Surg 2000; 48(1):30-8
2. Bilal MBY, Rafi HBB, Sultan J, Shafi BBB, Abbasi SA, Hussain A et al. 12 year's experience of A ortic Valve Replacement for Aortic Regurgitation. Pak J Cardiol 2004; 15(1):36-43
3. Lund O, Erlandsen M, Dørup I, Emmertsen K, Fløe C, Jensen FT. Predictable changes in left ventricular mass and function during ten years after valve r eplacement for aortic stenosis. J Heart Valve Dis. 2004; 13(3):357-68.
4. Sharma UC, Barenbrug P, Pokharel S, Dassen WR, Pinto YM, Maessen JG. Systematic review of the outcome of aortic valve replacement in patients with aortic stenosis. Ann Thorac Surg 2004; 78(1):90-5.
5. Lamb HJ, Beyerbacht HP, de Roos A, van der L aarse A, Vliegen HW, Leujes F et al. Left ventricular remodeling early after aortic valve repla cement: differential effects on diastolic function in aortic valve s tenosis and aortic regurgitation. J Am Coll Cardiol 2002;40(12):2182-8.
6. Ikonomidis I, Tsoukas A, Parthenakis F, Gournizakis A, Kassimatis A, Rallidis L et al. Four year follow up of aortic valve replacement for isolated aortic stenosis: a link betwe en reduction in pressure overload, regression of left ventricular hypertrophy, and diastolic function Heart 2001; 86:309-16.
7. Lund O, Erlandsen M. Changes in left ventricular function and mass during serial investi gations after valve replacement for aortic stenosis. J Heart Valve Dis 2000; 9:583-93.
8. Imanaka K, Kohmoto O, Nishimura S, Yokote Y, Kyo S. Impact of postoperative blood pressure control on regression of left ventricular mass follo wing valve replacement for aortic stenosis. Eur J Cardiothorac Surg 2005; 27(6):994-9.
9. Hafizullah M, Rehman A, Hassan MU, Taqweem A. Optimal time for operation in Aortic Regurgitation. J Postgrad Med Inst 2002:16(2):178-82
10. Karpuz H, Koldas L, Ayan F, Hacioglu Y. Short -Term Regression of Left Ventricular Mass After Aortic Valve Replacement in Aortic Stenosis With Left Ventricular Concentric Hypertrophy. J Clin Basic Cardiol 2002; 5: 101.
11. Monrad ES, Hess OM, Murakami T , Nonogi H, Corin WJ, Krayenbuehl HP. Time course of re gression of left ventricular hypertrophy after aortic valve replacement. Circulation 1988; 77(6):1345–55
12. Venco A, St John Sutton MG, Gibson DG, Brown DJ. Non-invasive assessment of left ve ntricular function after correction of severe aortic regurg itation. Br Heart J 1976; 38(12):1324-31.
13. Collinson J, Flather M, Pepper JR, Henein M. Effects of valve replacement on left ventricular function in patients with aortic regurgitation and sever e ventricular disease. J Heart Valve Dis 2004; 13(5):722-8.
14. Rao L, Mohr-Kahaly S, Geil S, Dahm M, Meyer J. Left ventricular remodeling after a ortic valve replacement. Z Kardiol 1999;88(4):283-9.
15. Ghali JK, Liao Y, Simmons B, C astaner A, Cao G, Cooper RS. The prognostic role of lef t ventricular hypertrophy in patients with or without coron ary artery disease. Ann Intern Med 1992;117(10):831–6.
16. He GW, Grunkemeier GL, Gately HL, Furnary AP, Starr A. Up to thirty-year survival after aortic valve replacement in the small aortic root. Ann Thorac Surg 1995;59(5):1056–62
17. Kurnik PB, Innerfield M, Wachs press JD, Eldredge WJ, Waxman HL. Left ventricular mass regression after aortic valve replacement measured by ultrafast compute d tomography. Am Heart J 1990;120(4):919–27
18. Henry WL, Bonow RO, Borer JS, Kent KM, Ware JH, Redwood DR et al. Evaluation of aortic valve replacement in patients with valvular aortic stenosis. Circulation 1980; 61(4):814–25.

Address for correspondence: Dr. Ahmad Shahbaz, In charge, Department of Research & CME, Punjab Institute of Cardiology, Lahore.