Original Article

Early Myocardial Remodeling after Aortic Valve Replacement

Deshbandhu Sharma, Sudhir Mehta[1], Rajnish Pathania[1]

Department of CTVS, Dr. RPGMC, Tanda, Himachal Pradesh, [1]Department of CTVS, IGMC, Shimla, Himachal Pradesh, India

ORCID:

Deshbandhu Sharma: 0000000193067367

Sudhir Mehta: 0000-0002-1028-732X

Rajnish Pathania: 0000-0002-2585-2846

Abstract

Background: Aortic valve disease leads to eccentric or concentric left ventricular (LV) hypertrophy and changes in the left ventricle function. The goal of aortic valve replacement (AVR) is to alleviate the pressure and volume overload on the left ventricle, allowing myocardial remodeling and regression of LV mass. **Objectives:** The objective of this study was to assess early LV remodeling in patients with severe aortic valve stenosis and/or moderate-to-severe aortic regurgitation after AVR. **Materials and Methods:** This prospective study was conducted in the department of cardiovascular and thoracic surgery between January 2015 and February 2016. All patients undergoing AVR exclusively over 1 year were included in the study. Patients were assessed at 1 week, 6 weeks, 3 months, and 6 months after AVR by transthoracic echocardiography. Peak and mean pressure gradients across aortic valve, LV ejection fraction, fractional shortening, LV dimensions, and LV mass along with other parameters were measured in the pre- and postoperative period. **Results:** A total of 33 patients with different lesions who underwent AVR were evaluated. All but one child (aged 12 years) were adults with a median age of 52 years ± 14.6 years including 21 males and 12 females. The LV mass index (LVMI) regression occurred over time in all cases. Mean LVMI decreased to 149.20 ± 53.7 g/m^2 at 1 week and 120.8 ± 45.49 g/m^2 at 6 weeks of AVR from its baseline value of 180.8 ± 58.9 g/m^2 ($P < 0.001$). Six patients who were followed up to 1 year had mean LVMI 122.46 ± 50.0 g/m^2. **Conclusion:** Marked reduction in LV mass was discerned after AVR as early as 1 week and further reduction continued up to 6 weeks; however, regression thereafter was not statistically significant.

Keywords: Aortic regurgitation, aortic stenosis, aortic valve replacement, left ventricular mass regression

Introduction

Aortic valve disease is associated with eccentric or concentric left ventricular (LV) hypertrophy and changes in the left ventricle function.[1] It is a beneficial adaptation that compensates for high intracavitary pressure and allows wall stress and the ejection fraction to remain within the normal range.[2] Initially, both the cardiac output and ejection fraction are maintained within normal limits. However, when wall stress exceeds the compensatory mechanism, then LV function starts declining. The overall goal of AVR is to alleviate the pressure and volume overload on the left ventricle, allowing myocardial remodeling and regression of LV mass. The time course and earliest evidence of significant LV remodeling in the form of LV mass regression, changes in end-systolic and diastolic dimensions, LV ejection fraction, and transaortic gradients across aortic valve are controversial. The present study was conducted to ascertain the time course and extent of early LV remodeling in the form of LV mass, dimensions, transvalvular gradients, and function using transthoracic echocardiography (TTE) after AVR in the early postoperative period.

Materials and Methods

This prospective study was conducted in the department of cardiovascular and thoracic surgery between January 2015 and February 2016. The study was approved by the institutional

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Address for correspondence: Dr. Sudhir Mehta, Department of CTVS, IGMC, Shimla, Himachal Pradesh, India. E-mail: sudheermehta09@gmail.com

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ethics committee. All consecutive patients of all age groups undergoing aortic valve replacement (AVR) for aortic stenosis and/or aortic insufficiency over 1 year were included in the study. All patients provided signed informed consent. Patients receiving a prosthetic valve at any other location besides AVR and significant coronary artery disease were excluded. Detailed history including demographic profile, NYHA class, nature of valvular disease, and routine preoperative investigations of all cases was done and recorded. Every patient underwent TTE within a week before the operation. Type of valvular lesion, peak and mean pressure gradients, LV dimensions, fractional shortening, ejection fraction, and indexed LV mass were measured. All operations were performed under standard cardiopulmonary bypass. Native aortic valve was excised completely, and prosthetic valve was implanted at the annular position using interrupted sutures.

All patients underwent TTE after AVR at 1 week, 6 weeks, 3 months, and 6 months. Parameters such as improvement in functional class, peak and mean pressure gradients across aortic valve, LV ejection fraction, fractional shortening, LV dimensions, and LV mass were measured in the postoperative period. LV mass was calculated using an S5-1 transducer on Philips iE33 echocardiography machine according to the American Society recommendations. The examination included two-dimensional derived M-mode, continuous wave and pulse Doppler and color Doppler studies. All echocardiographic measurements were done by a single experienced cardiologist.

Ethical statement

The study protocol was approved by the Local Ethics committee. Patient Consent Declaration was obtained from the patients. The study was conducted in accordance with the Helsinki Declaration.

Statistical analysis

Postoperative measured parameters were analyzed statistically using standard statistical methods and software (SPSS Inc., Chicago, IL, USA, version 15.0 for windows). All values were expressed as mean ± standard deviation. LV mass index (LVMI) regression, improvement in LV dimensions, and improvement in ejection fraction were assessed using paired *t*-test. $P < 0.05$ was considered significant.

Results

We evaluated various echocardiographic parameters preoperatively and after AVR. A total of 33 patients with different lesions who underwent AVR were recruited. Thirty patients were followed up to 6 months. Two patients were lost to follow-up after 1 week and one patient after 6 weeks. No perioperative death occurred.

All, except one (child aged 12 years), were adults. Thirty-two patients were above 18 years of age (maximum age 70 years) with median age 52 years ± 14.6 years [Table 1].

Preoperatively, one patient was NYHA IV, 18 NYHA III, and 14 NYHA II. There was significant improvement ($P < 0.05$) in NYHA class at 6 weeks with 5 patients NYHA III, 18 NYHA II, and 8 NYHA I. Angina was present in 10 (30.4%) and syncope in 16 (51%) cases which improved postoperatively.

Left ventricular end-diastolic dimension

LV end-diastolic dimension improved significantly ($P < 0.001$) from preoperative mean value of 50.24 ± 13.17 mm to 42.21 ± 12.35 mm at 1 week, 36.66 ± 12.9 mm at 6 weeks, 38.06 ± 7.30 at 3 months, and 37.79 ± 7.70 at 6 months. Reduction continued significantly up to 6 months in respect to values at 1 week.

Fractional shortening

There was no significant change in fractional shortening (FS) after AVR till 6 weeks but a significant change in FS at 3 months with *P* value <0.05 and 6 months $P < 0.01$.

Left ventricular ejection fraction

Seven (21%) patients had preoperative LV ejection fraction (LVEF) <50%, out of which 6 showed improvement. There was no improvement in LVEF in immediate postoperative period. It took 6 months for LVEF to have significant improvement ($P < 0.05$), but no significant difference was seen, when AS and mixed groups were compared to each other.

Mean left ventricular mass index

LVMI decreased to 149.20 + 53.7 g/m^2 at 1 week of AVR from its baseline value of 180.8 ± 58.9 g/m^2 ($P < 0.001$) and further reduced to 120.8 ± 45.49 g/m^2 at 6 weeks. The reduction was noticed as early as 1 week (17%) after surgery. This regression continued further at 6 weeks (30.1%), 3 months (32.7%), and at 6 months (43.3%). The maximum reduction was noticed at

Table 1: Demographic data

Parameter	Number
Total number of patients	33
Age (years)	
Mean	50.33±14.6
Range	12-70
Gender	
Males	21
Females	12
Type of lesion	
Aortic aortic stenosis	19
Aortic regurgitation	4
Mixed lesion (patients)	10
Types of valves used (patients)	
Mechanical valves	13
Bioprosthetic valves	20
Size of valves	
Minimum (mm)	19
Maximum (mm)	28
Mean	21.8±2.29
Mean EOAI of the valves used	1.36±0.76 (3 cases had patient prosthesis mismatch with EOAI=0.81)
Mean cardiopulmonary bypass time (min)	128.9±33.24 (range 84-196)

EOAI: Effective orifice area index

6 weeks compared to baseline and insignificant thereafter till 6 months if compared to 6 weeks postoperatively [Figure 1]. LVMI regression occurred over time in all cases. There were 19 patients of AS, 4 of AR, and 10 AS ± AR. As AR group had just 4 patients, this group was not statistically comparable to other groups (AS and mixed). Mean LVMI preoperatively in AS group was 160.75 gm/m^2 and 190.23 g/m^2 in mixed group, which reduced significantly to 79.5 gm/m^2 in AS group (50.5%) and 131.25 g/m^2 in mixed group (31.0%) at 6 months and difference in reduction in both groups was also significant.

The comparative changes in different echocardiographic parameters are shown in Table 2 and Figure 2.

Peak systolic gradient of 76.75 ± 26.57 mmHg baseline (preoperative) reduced to 17.48 ± 8.17 at 1 week, 16.73 ± 9.0 at 6 weeks, 16.70 ± 7.35 at 3 months, and 16.10 ± 7.34 at 6 months postoperatively, showing a significant reduction with $P < 0.001$.

Mean systolic gradient in preoperative period was 46.09 ± 18.84 mmHg (range 11–89 mmHg) which reduced to 8.60 ± 4.6 at 1 week, 8.06 ± 4.84 at 6 weeks, 8.20 ± 3.97 at 3 months, and 8.0 ± 4.0 at 6 months.

Discussion

There is a reduction in the degree of hemodynamic stress faced by the left ventricle after AVR as the stenotic or regurgitant valve is replaced with a prosthetic valve.[3] AVR reduces symptoms, increases long-term survival, and improves the quality of life in patients with aortic valve disease.[4] The LV changes can be assessed by various methods such as echocardiography, cardiac catheterization, ultrafast computed tomography, and magnetic resonance imaging.[2,5] Echocardiography is a noninvasive method of LV mass measurement and is the most widely used technique. It provides reproducible results of the extent of LV hypertrophy and its measurements as accurate as obtained from other invasive and expensive modalities.[6-9] In this study, TTE was used for assessing the changes in LV functions, dimensions, and LV mass in patients with chronic aortic valve disease.

LV end-diastolic and end-systolic volumes decrease after AVR which leads to an increase in the end-systolic pressure–volume ratio, implying an improvement in contractile performance. This results in an improvement in LV function and the functional class of the patient improves with time.[10] In this study, both LV end-diastolic and end-systolic volumes have been found to decrease significantly over 6 weeks from preoperative mean value and minimal thereafter up to 6 months. These findings are consistent with the reports in the literature which have attributed these results to an immediate decrease in LV preload and afterload following AVR.[10]

AVR decreases LV pressure and volume overload, subsequently leading to adaptation and remodeling, with regression of hypertrophy and LV mass. Ejection fraction, therefore, would be expected to improve after AVR in patients with reduced preoperative ejection fraction. Those who do not improve probably have fixed myocardial damage preoperatively due to long-standing chronic aortic valve disease. Subsequent survival has been found to be better in patients with an early improvement in ejection fraction than in patients without an improvement in ejection fraction.[10,11] A significant improvement in postoperative LV ejection fraction of 6 out of 7 patients, who had preoperative LVEF <50%, was noted in the present study. LV mass is the most important parameter in assessing LV remodeling after AVR. The LV hypertrophy

Table 2: Echocardiographic (mean) parameters pre- and postoperative

Parameter	Preoperative	1 week	6 weeks	3 months	6 months
LVED	49.83	42.16	38.06	37	35.13
LVES	31.43	25.83	24.26	23.36	22.8
LVEF	62.63	61.1	63.96	65.9	68.26
FS	37.83	37.2	34.06	38.63	38.83
LVMI	172.68	138.29	120.81	116.05	110.9
MSG	46.2	9	8.06	8.2	8
PSG	75.6	23.7	16.7	16.7	16.2

LVED: Left ventricular end-diastolic dimension, LVES: Left ventricular end-systolic dimension, LVEF: Left ventricular ejection fraction, FS: Fractional shortening, LVMI: Mean left ventricular mass index, MSG: Mean systolic gradient, PSG: Peak systolic gradient

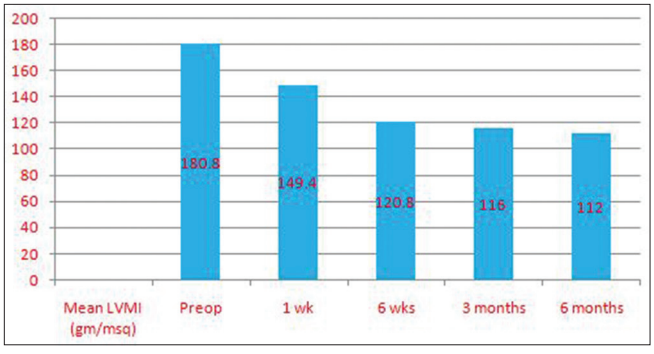

Figure 1: Regression of left ventricular mass over 6 months

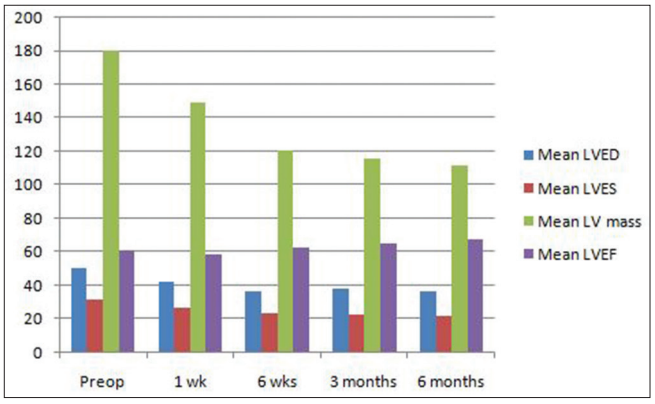

Figure 2: Comparison of improvement mean left ventricular end-diastolic dimension (LVED), left ventricular end-systolic dimension (LVES), LV mass, and left ventricular ejection fraction

in chronic aortic valve disease is mainly due to the increase in size of myofibrils and increase in connective tissue contents.[12] The accepted upper limit of normal LVMI derived by various modalities is 125 gm/m^2.[13,14] The LV hypertrophy is an independent predictor of mortality and morbidity in patients with aortic valve disease. It is associated with a higher incidence of decreased coronary flow reserve, congestive heart failure, ventricular arrhythmias, and sudden cardiac death.[2]

LV hypertrophy regresses after AVR, but it never returns to baseline values because some amount of transvalvular gradient remains across prosthetic valves because the valve sewing ring and stents reduce the effective orifice area.[3,15,16] Despite these prosthetic valves being somewhat stenotic, there is an immediate significant decrease in transvalvular gradient and aortic valve becomes competent, which results in a significant decrease in LV mass.[12] In the present study, LV mass regression was noticed in all cases regardless of type and size of prosthetic valve used. Amarrelle *et al.*[17] and Bech-Hanssen *et al.*[18] observed a significant reduction in LVMI despite effective orifice area of a prosthetic valve being <0.65 cm^2/m^2 and <0.85 cm^2/m^2, respectively. However, contrary to these studies, various workers have demonstrated that increased gradient across prosthetic aortic valve results in an increased LV afterload in the patients having effective orifice area <0.8 cm^2/m^2. This results in the persistence of LV hypertrophy and therefore, higher incidence of mortality and morbidity.[19-21] In the present study, only three patients had effective orifice area <0.85 cm^2/m^2 (0.81 cm^2/m^2). All these showed significant LV mass reduction and improvement in LVEF despite patient prosthesis mismatch; however, this small number is insufficient to make any inference. The extent and time course of LV mass regression after AVR is still a matter of debate. Earliest documented evidence has been a 10% decrease in LV mass within 4.9 ± 2.4 days of surgery by Christakis *et al.*[2] They further concluded that the amount of mass regression actually may have been underestimated, as there may be substantial edema in myocardial tissue in early period after AVR. Sutton *et al.*[22] examined 16 patients by echocardiography and documented a 30% regression of LV mass in 42 ± 7 days, thus confirming that the majority of mass regression occurs early after AVR. Henry *et al.*[23] demonstrated a 16% mass reduction at 6 months after AVR, with no further changes at 1 year. However, Panidis *et al.*[24] using echocardiography demonstrated a nonsignificant regression at <6 months and a significant 34% regression at >6 months of AVR. In the present study, the reduction in LVMI to BSA was noticed as early as 1 week (17%) after surgery. This regression continued further at 6 weeks (30.1%), 3 months (32.7%), and at 6 months (43.3%). The maximum reduction was noticed at 6 weeks and insignificant thereafter till 6 months. These findings are consistent with studies reporting early LV mass regression.

Limitations

Only four patients with isolated severe AR, so exclusive response to the particular lesion was difficult to define with this sample size and require larger study groups. No drug treatment was taken into consideration that could have affected loading conditions pre- and postoperatively.

Conclusion

Significant LV mass reduction after AVR was noticed as early as 1 week and continued up to 6 weeks; however, reduction thereafter was not significant. More LV mass regression was noticed in severe AS group as compared to mix lesion group when compared. Ejection fraction took 6 months to improve noticeably. LV dimensions and transaortic gradients improved significantly as early as 1 week after AVR.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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