Enhanced left ventricular mass regression after aortic valve replacement in patients with aortic stenosis is associated with improved long-term survival

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Background: Aortic valve replacement in patients with aortic stenosis is usually followed by regression of left ventricular hypertrophy. More complete resolution of left ventricular hypertrophy is suggested to be associated with superior clinical outcomes; however, its translational impact on long-term survival after aortic valve replacement has not been investigated.

Methods: Demographic, operative, and clinical data were obtained retrospectively through case note review. Transthoracic echocardiography was used to measure left ventricular mass preoperatively and at annual follow-up visits. Patients were classified according to their reduction in left ventricular mass at 1 year after the operation: group 1, less than 25 g; group 2, 25 to 150 g; and group 3, more than 150 g. Kaplan–Meier and multivariable Cox regression were used.

Results: A total of 147 patients were discharged from the hospital after aortic valve replacement for aortic stenosis between 1991 and 2001. Preoperative left ventricular mass was 279 ± 98 g in group 1 ($n = 47$), 347 ± 104 g in group 2 ($n = 62$), and 491 ± 183 g in group 3 ($n = 38$) ($P < .001$). Mean time to last echocardiogram was 6.2 ± 3.2 years. Left ventricular mass at late follow-up was 310 ± 119 g in group 1, 267 ± 107 g in group 2, and 259 ± 96 g in group 3 ($P = .05$). Transvalvular gradients at follow-up were not significantly different among the groups (group 1, 24.8 ± 23 mm Hg; group 2, 21.4 ± 16 mm Hg; group 3, 14.7 ± 9 mm Hg) ($P = .31$). There was no difference in the prevalence of other factors influencing left ventricular mass regression such as ischemic heart disease or hypertension, valve type, or valve size used. Ten-year actuarial survival was not statistically different in patients with enhanced left ventricular mass regression when compared with the log–rank test (group 1, $51\% \pm 9\%$; group 2, $54\% \pm 8\%$; and group 3, $72\% \pm 10\%$) ($P = .26$). After adjustment, left ventricular mass reduction of more than 150 g was demonstrated as an independent predictor of improved long-term survival on multivariate analysis ($P = .02$).

Conclusions: Our study is the first to suggest that enhanced postoperative left ventricular mass regression, specifically in patients undergoing aortic valve replacement for aortic stenosis, may be associated with improved long-term survival. In view of these findings, strategies purported to be associated with superior left ventricular mass regression should be considered when undertaking aortic valve replacement. (J Thorac Cardiovasc Surg 2011;142:285-91)

Aortic valve stenosis (AS) subjects the left ventricle to abnormal loading conditions leading to the development of left ventricular hypertrophy (LVH).¹ A principal aim of the surgical treatment of aortic valve lesions is to restore normal left ventricular (LV) hemodynamics.² Aortic valve replacement (AVR) is usually followed by regression of LVH.^{3,4} This is considered to be advantageous and potentially to be associated with improved clinical outcomes.⁵ However, the

presumed correlation between left ventricular mass (LVM) regression and impaired long-term outcome is based on extrapolation from historical studies, which documented the negative impact of LVH on survival in patients with hypertensive heart disease.⁶⁻⁹ Ventricular hypertrophy secondary to aortic valve disease is a distinct entity from that which occurs in response to essential hypertension.¹⁰ Consequently, presumptions that hypertrophy in these 2 settings will have an equivalent effect on outcome are unfounded. The impact of persistent LVH on long-term clinical outcomes, specifically in a population of patients who have undergone AVR for significant AS, has not been previously investigated. Our aim was to evaluate whether enhanced LVM regression after AVR is correlated with improved long-term survival.

METHODS

This is a retrospective review of a consecutive series of patients who underwent AVR with a stentless bioprosthesis for aortic valve disease

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Abbreviations and Acronyms

AS	= aortic valve stenosis
AVR	= aortic valve replacement
LV	= left ventricular
LVH	= left ventricular hypertrophy
LVM	= left ventricular mass

from January 1991 to January 2001. Patients were not excluded from analysis if they had additional concomitant cardiac procedures.

Bioprosthetic Stentless AVR

The Toronto Stentless Porcine Valve (St Jude Medical, Inc, St Paul, Minn) was the stentless valve used in this series. Allograft valves were also used. An established allograft cryopreservation protocol has been in place at our institution for over 15 years.

Surgical Technique

Operations were performed by a single surgeon (J.P.) The decision to use a biological valve and type of valve selected was left to surgeon–patient preference. In general, allografts were used for redo procedures and in patients of younger age. All procedures were performed with the patient supported by cardiopulmonary bypass with cooling to 28°C. Myocardial protection was undertaken with antegrade and retrograde cold blood cardioplegia. The majority of bioprostheses were implanted in the subcoronary position. With allograft valves, the coronary sinuses were excised but the noncoronary sinus was preserved. The valve was then implanted with separate inflow and outflow suture lines. Interrupted sutures were used for the proximal suture line and continuous for the distal anastomosis. Separate mattress sutures were used to secure the commissures. Allograft valves were also implanted as a free-standing root replacement with reimplantation of the native coronary artery ostia as buttons within the allograft wall.

Data Acquisition

Demographic, clinical, and operative data were obtained from individual patient hospital records. Our follow-up protocol included annual echocardiograms to assess cardiac and allograft valve function. Serial echocardiographic reports were reviewed to document LVM. Mortality was determined using the NHS strategic tracing system (NHS, United Kingdom) and survivors were contacted by telephone for interview. Approval for this study was obtained from Royal Brompton and Harefield and Imperial College Ethics Committee (Ethics number 00-128).

Echocardiographic Details

Patients in our series had annual echocardiographic follow-up at our institution. Transthoracic echocardiography was performed with the Hewlett–Packard Sonos 5000 echocardiograph (Hewlett–Packard, Houston, Tex). Two-dimensional images were obtained with standard apical 5-chamber, parasternal short- and long-axis views. Continuous wave Doppler was used to measure transvalvular gradients. LVM was measured by 2 experienced echocardiographers in all patients before and after AVR. LV volumes in cubic centimeters were measured from apical 4-chamber views using the Simpson rule. In patients in whom the Simpson rule could not be used, the area–length method was used. LVM was then calculated using values obtained for the external (EDVe) and internal (EDVi) end-diastolic volume using the following equation: $LVM = 1.05 (EDVe - EDVi) \text{ g}$.

Clinical Definitions and Follow-up Protocol

Hypertension was defined as a systolic blood pressure greater than 140 mm Hg or a diastolic blood pressure greater than 90 mm Hg. Poor

LV function was defined as an LV ejection fraction of less than or equal to 30%, documented on either left ventriculography or transthoracic echocardiography. The end points of interest were the following: postoperative change in LVM at 1 year of follow-up and actuarial freedom from death. Clinical follow-up data were collected in the immediate postoperative period and subsequently during annual clinic visits. All surviving patients remained on this annual surveillance protocol. The survival commenced at the time of first year and ended at the time of death-event or at last follow-up (censoring). The selection of the time point of 1 year postoperatively was considered as being more clinically important in informing us about patient prognosis. All patients were included on an intention-to-treat basis; thus all attempted procedures, including initial technical procedure failures, were included in the overall analysis.

Statistical Methods

Patients were classified according to their reduction in LVM at 1 year of follow-up: group 1, less than 25 g or increase in LVM from baseline; group 2, 25 to 150 g; group 3, more than 150 g. Data were expressed as mean $\pm$ standard deviation for normally distributed values and median $\pm$ interquartile change when variables were not normally distributed. Normal distribution of each continuous variable was assessed with the Kolmogorov–Smirnov test, and for comparison, analysis of covariance with Bonferroni correction for normally distributed variables was used. For the nonnormally distributed variables, the Kruskal–Wallis test was used to compare groups, and the cutoff value for significance was adjusted for multiple comparison to the value of .01. Categorical variables were shown as percentages. Comparisons for categorical variables were performed with the χ^2 test.

Actuarial outcomes were compared with Kaplan–Meier curves and multivariable Cox proportional hazards regression. A log–rank test was used to determine whether significant differences existed between curves. The proportional hazard assumption was tested for each covariate by 2 methods: first, correlating the corresponding Scaled Schoenfeld Residuals with the rank of time; second, using the procedure “stptest” in Stata (Stata Corporation, College Station, Tex). The linearity assumption for each binary covariate was assessed graphically with Martingale residuals. To elucidate associated causative factors to the outcomes of interest, we performed a multivariable regression analysis. Initially, univariable regression analysis was used to determine all significant confounding variables (covariates). Those associated confounding variables were subsequently included in the multivariable regression model. Statistically ($P \leq 0.2$) or clinically significant causative factors from the univariable analysis were adjusted for (included) in the multivariable model. We also included those variables that were found to have a different distribution among the 3 LVM regression groups and we thought may have been able to influence results. All statistical tests were 2-sided. In all cases, corrections were not made for multiple comparisons. Statistical analysis was performed using SPSS 17.0 (SPSS Inc, Chicago, Ill) and Stata 9.0 (Stata Corporation).

RESULTS

Between January 1, 1991, and January 1, 2001, 153 patients underwent AVR with a homograft or stentless porcine valve. There were 6 (3.9%) postoperative deaths. One hundred forty-seven patients who survived AVR underwent postoperative echocardiography at 1 year to assess the extent of LVM regression. Forty-seven patients had less than 25 g of LVM regression at late follow-up (group 1), in 62 patients LVM regression was between 25 and 150 g (group 2), and in 38 patients LVM regression was greater than 150 g. Patient characteristics according to extent of LVM regression are listed in Table 1.

TABLE 1. Baseline characteristics

Degree of LVM regression	Group 1: < 25 g	Group 2: 25–150 g	Group 3: > 150 g	P value
No.	47 (32)	62 (42)	38 (26)	
Age ≥ 70 y	21 (45)	28 (45)	15 (40)	.84
Female sex, n (%)	15 (32)	18 (29)	12 (32)	.92
Hypercholesterolemia, n (%)	10 (21)	8 (13)	6 (16)	.51
Diabetes, n (%)	5 (11)	3 (5)	2 (5)	.45
Hypertension, n (%)	17 (36)	24 (39)	15 (41)	.92
Serum creatinine ≥ 150 μmol/L	2 (4)	0 (0)	3 (8)	.09
Antihypertensive treatment (ACE inhibitor)	15 (32)	22 (37)	14 (39)	.77
Sinus rhythm	40 (85)	56 (90)	32 (84)	.60
Valve size ≥ 25 mm	22 (47)	31 (50)	19 (50)	.94
Redo AVR	5 (11)	4 (7)	3 (8)	.73
Operative urgency				
Emergency, n (%)	6 (13)	5 (8)	3 (8)	.66
LV function				
LVEF ≤ 30%, n (%)	7 (15)	7 (11)	3 (2)	.60
Preoperative functional status				
Pre NYHA class III/IV, n (%)	27 (57)	31 (50)	20 (53)	.74
Preop echocardiography				
LVEDD, cm (SD)	4.8 (0.97)	5.3 (0.87)	5.8 (1.1)	<.001
LVESD, cm (SD)	3.3 (1.1)	3.5 (0.90)	3.76 (0.88)	.10
LVEF, % (SD)	65 (18)	69 (15)	70 (13)	.24
Transaortic gradient, mm Hg (SD)	69 (24)	74 (21)	71 (13)	.54
LVM, g (SD)	279 (98)	347 (104)	491 (183)	<.001

LVM, Left ventricular mass; ACE, angiotensin-converting enzyme; AVR, aortic valve replacement; LV, left ventricular; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; LVEDD, left ventricular end-diastolic dimension; SD, standard deviation; LVESD, left ventricular end-systolic dimension.

Baseline Characteristics

The mean age of our study population was 65 ± 12 years, consisting of 102 (70%) men. There were no differences between groups with regard to age or sex. Seventy-eight (53%) patients were in New York Heart Association functional class III/IV preoperatively. In total, 147 patients were operated on for aortic stenosis. Fourteen (10%) patients underwent emergency surgery. Twelve (8%) patients in the series were undergoing redo AVR.

Preoperative Echocardiography

Details relating to preoperative echocardiographic measurements are listed in Table 1. Patients in group 3 had significantly larger LV end-diastolic diameter ($P < .001$). There was no difference between groups in end-systolic dimensions, LV ejection fraction, or preoperative transvalvular gradient. LVM was also significantly higher in group 3 patients at baseline ($P < .001$).

TABLE 2. Operative characteristics and postoperative outcomes

Degree of LVM regression	Group 1: < 25 g	Group 2: 25–150 g	Group 3: > 150 g	P value
No.	47 (32)	62 (42)	38 (26)	
Concomitant CABG, n (%)	18 (38)	19 (31)	7 (19)	.16
No. of grafts, n (SD)	0.53 (0.8)	0.53 (0.9)	0.35 (0.8)	.56
Valve type and insertion				
Homograft, n (%)	22 (47)	28 (45)	17 (45)	.98
Valve size, mm (SD)	24.5 (2.6)	24.5 (2.2)	24.8 (2.7)	.75
Subcoronary implant, n (%)	42 (89)	56 (90)	32 (84)	.63
Postoperative functional status				
Postop NYHA class III/IV, n (%)	3 (6)	0 (0)	1 (3)	.13
Postoperative pacemaker	1 (2)	2 (3)	8 (22)	.001
Clinical outcomes				
Anticoagulation, n (%)	3 (6.4)	5 (8)	3 (8)	.54
Thromboembolism, n (%)	0 (0)	2 (3)	1 (3)	.42
Endocarditis, n (%)	1 (2)	1 (2)	0 (0)	.71
Postop echocardiography (last follow-up)				
LVEDD, cm (SD)	5.21 (1.1)	4.95 (0.81)	4.67 (0.6)	.07
LVESD, cm (SD)	3.47	3.24	2.95	.06
LVEF, % (SD)	72.4 (13)	71 (12)	72 (11)	.89
Transaortic gradient, mm Hg (SD)	24.8 (23)	21.4 (16)	14.7 (9)	.31
LVM, g (SD)	310 (119)	267 (107)	259 (96)	.05

CABG, coronary artery bypass grafting; SD, standard deviation; NYHA, New York Heart Association; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LVM, left ventricular mass.

Operative Details

Operative and postoperative data are documented in Table 2. Allograft valves were implanted in 67 (46%) patients. The Toronto Stentless Porcine Valve was implanted in the subcoronary position in 80 (54%) patients. The bioprostheses were implanted using the subcoronary freehand technique in 130 (88%). Seventeen (12%) patients who had an allograft implanted received a freestanding root replacement with reimplantation of the coronary ostia. The mean valve size implanted was 24.6 (2.5) mm with no differences in size among the 3 LVM regression groups. There was no difference among groups in the frequency of concomitant coronary artery bypass grafting or mean number of bypass grafts performed per patient.

Postoperative Echocardiography

Postoperative echocardiographic details are listed in Table 2. There were significant trends of differences in LV end-diastolic diameter ($P = .07$) and a trend for end-systolic dimensions among groups ($P = .06$). Mean time

FIGURE 1. Changes in left ventricular end-diastolic diameter (LVEDD) (A), transvalvular gradient (B), and ejection fraction (EF) (C) during follow-up in patients groups with different degree of left ventricular mass (LVM) regression. The *P* value for the different LVM groups (vertical axis) has been calculated by analysis of covariance and the *P* values for different time points (horizontal axis) are from the Bonferroni test.

to last echocardiogram was 6.2 ± 3.2 years. LVM at late follow-up was 310 ± 119 g in group 1, 267 ± 107 g in group 2, and 259 ± 96 g in group 3 ($P = .05$). Transvalvular gradients at follow-up were not significantly different among groups (group 1, 24.8 ± 23 mm Hg; group 2, 21.4 ± 16 mm Hg; group 3: 14.7 ± 9 mm Hg; $P = .31$). Two patients in group 1, 2 in group 2, and 1 in group 3 demonstrated an increased transvalvular gradient of more than 50 mm Hg, demonstrating degenerative disease of the

replaced valve during follow-up. Changes in LV end-diastolic diameter, transvalvular gradients, and LV ejection fraction during follow-up for the 3 groups of patients are depicted in Figure 1. Patients in group 3 had smaller LV end-diastolic dimensions and lower postoperative transvalvular gradients, although this did not reach statistical significance. Between 1 year and late follow-up, there was a significant increase in transvalvular gradient in all groups (*P* value from Bonferroni test, $P = .01$).

FIGURE 2. Actuarial survival according to left ventricular mass (LVM) reduction at 1 year of follow-up.

Actuarial Survival

The mean time to follow-up was 7.8 (3.1) years. Five-year (group 1, 89% ± 5%; group 2, 93% ± 3%; group 3, 94% ± 4%) and 10-year (group 1, 51% ± 9%; group 2, 54% ± 8%; group 3, 72% ± 10%) actuarial survivals were not significantly greater in patients with enhanced LVM regression: log-rank = 2.68; *df* = 2; *P* = .26 (Figure 2).

Cox Hazard Regression Analysis

The results of univariable analysis are presented in Table 3. Cox proportional hazard survival regression analysis was undertaken to identify independent predictors of late mortality, and results are presented in Table 4. Independent predictors of late mortality were identified as the following: age 70 years or older (*P* = .003), preoperative LVM (*P* < .03), postoperative New York Heart Association class III/IV (*P* < .001), and concomitant coronary artery bypass grafting (*P* < .003). LVM regression greater than 150 g was independently protective against late mortality with a hazard ratio of 0.28 (0.09–0.87)

DISCUSSION

In this retrospective study we investigated whether superior LVM regression after AVR in patients with AS was associated with improved long-term survival. Through analysis of serial echocardiograms, we determined the extent of LVM regression after the first year of follow-up and assessed whether this had an association with late prognosis. Patients with enhanced LVM regression (>150 g) did not demonstrate improved survival on Kaplan–Meier analysis compared with those with less resolution of LVH. However, after adjustment for other confounders, multivariable Cox regression analysis demonstrated that the magnitude

TABLE 3. Predictors of late mortality in univariable analysis

	P value
Age ≥ 70 y	<.001
Concomitant CABG	<.001
Sub-coronary technique	.005
Homograft valve	.01
Antihypertensive treatment (ACE inhibitor)	.03
Postop NYHA class III/IV	.03
Preop NYHA class III/IV	.05
Valve size ≥ 25 mm	.06
Preop LVM	.08
Emergency operation	.12
Hypertension	.21
LVEF ≤ 30%	.23
Diabetes	.26
Redo AVR	.34
Serum creatinine ≥ 150 μmol/L	.50
Sex (male)	.59
Permanent pacemaker	.87
Hypercholesterolemia	.91
Loss of sinus rhythm	.93

CABG, Coronary artery bypass grafting; ACE, angiotensin-converting enzyme; NYHA, New York Heart Association; LVM, left ventricular mass; LVEF, left ventricular ejection fraction; AVR, aortic valve replacement.

of LVM regression was an independent predictor of improved long-term survival.

Concentric LVH develops in patients with AS or systemic hypertension and represents adaptation of LV muscle to excessive intraventricular pressure. Such changes in the shape of the left ventricle allow it to maintain a normal relation between systolic wall stress and ejection fraction. Population studies have identified that LVH is associated with an

TABLE 4. Independent predictors of late mortality on multivariable analysis

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Age ≥ 70 y	.003	2.81	1.41	5.59
Postop NYHA class III/IV	.000	62.84	12.10	326.24
Concomitant CABG	.003	2.64	1.39	5.00
Preop LVM	.036	1.00	1.000	1.01
Preop NYHA class III/IV	.11	1.70	0.87	3.29
Subcoronary implantation	.09	6.59	0.71	61.05
Homograft valve	.24	0.60	0.25	1.410
Serum creatinine ≥ 150 μmol/L	.25	2.48	0.52	11.81
Antihypertensive treatment (ACE inhibitor)	.26	1.43	0.76	2.70
Emergency operation	.43	1.43	0.58	3.53
Postoperative pacemaker	.64	1.29	0.42	3.97
Valve size ≥ 25 mm	.84	0.92	0.42	1.99
LVM < 25 g (reference: group 1)		1.00		
LVM 25–150 g (group 2)	.19	0.61	0.294	1.286
LVM > 150 g (group 3)	.02	0.28	0.09	0.87

Sig., Significance; Exp(B), exponentiation of the B coefficient; CI, confidence interval; NYHA, New York Heart Association; CABG, coronary artery bypass grafting; LVM, left ventricular mass; ACE, angiotensin-converting enzyme.

ACD

increased incidence of myocardial infarction, sudden death, and congestive heart failure.^{6,7,9} Accordingly, LVH is linked to impaired long-term survival compared with age-matched controls.^{7,8} Previous studies evaluating the impact of incomplete regression of ventricular hypertrophy on surgical outcome have been limited by small numbers of patients and a short duration of follow-up.^{11,12} There are minimal data on the impact of persistent LVH on very long-term survival specifically after AVR in patients with AS. A lack of such information has led to extrapolations being made from the observational studies discussed herein. The consensus has been that residual LVH after AVR has a detrimental effect on long-term survival,^{5,13} although some investigators have reported contradictory findings.¹⁴ LVH in the setting of AS has been correlated with a number of adverse effects including abnormal coronary flow reserve and exacerbation of diastolic dysfunction.^{15,16} Consequently, cardiac surgeons and valve manufacturers have concentrated their efforts toward engineering prostheses with optimal hemodynamic performance to facilitate postoperative LVM regression.

LVH is the culmination of a variety of molecular processes in response to chronic pressure overload. It is associated with geometric chamber alterations, changes in ventricular mass, as well as myocardial cellular structure and development of fibrosis.¹⁷ Differences exist in the morphometry of hypertrophy associated with essential hypertension and AS. Strotmann and associates¹⁰ used strain-rate imaging studies of LV long- and short-axis function to demonstrate that despite similar degrees of LV wall thickness, AS and arterial hypertension had different effects on the rate of LV deformation. Consequently, the effect of LVH on outcomes in patients with hypertension cannot be justifiably applied to patients who have been surgically treated for aortic valve disease. In our study, we observed that superior LVM regression may have an independent effect on long-term survival after AVR for AS. We classified patients according to the degree of LVM regression that was observed at 1 year of follow-up. Forty-seven patients lost less than 25 g of their LV muscle mass; survival was poorest in this group, with a 10-year actuarial survival of only $51\% \pm 9\%$. Interestingly, the LVM preoperatively was in fact lower than the follow-up value in this group (preoperative value 279 g vs postoperative value 310 g), with this subset of patients demonstrating an increase in LVM. Sixty-two patients had regression of between 25 and 150 g over follow-up and 38 had a reduction of greater than 150 g. Both of these patient groups were observed to have a net loss of LVM over the long term and had greater survival at 10 years: $54\% \pm 8\%$ and $72\% \pm 10\%$, respectively.

Numerous variables have been suggested to influence postoperative LVM regression. Recent studies have identified preoperative LVM as the most important determinant of postoperative LVM regression,^{18,19} with patients with

a larger preoperative LVM demonstrating the greatest degree of LVM reduction. Other factors such as the type and size of valve implanted, hypertension, residual transaortic gradients, and the presence of ischemic heart disease are thought to have an impact on resolution of LVH. In accordance with these previous reports, preoperative LVM was higher in our study in the group of patients who demonstrated the greatest postoperative reduction in LVM.^{8,19} There were no significant differences between groups in the frequency of coexistent hypertension or the type and size of valve used. The need for concomitant coronary artery bypass grafting was not different between groups. Enhanced LVM regression was also associated with trends of significantly smaller LV end-diastolic dimensions and end-systolic diameter. This suggests that enhanced LVM regression may occur in association with improved LV remodeling after AVR. Transvalvular gradients were lower in group 3, and this may explain the presence of superior resolution of LVH in this group. This may validate the use of strategies aimed at optimizing valvular hemodynamics to promote LVM regression over the longer term. Reduced LVM regression may be secondary to a specific phenotype of LVH and may not necessarily be secondary to an inferior hemodynamic environment after AVR.

The reasons why LVM regression occurs in some individuals and is incomplete in others, despite similar preoperative values of LVM and postoperative hemodynamic and clinical profiles, is uncertain. The presence of increased amounts of myocardial fibrosis has been suggested as one possible factor responsible for this observation.²⁰ The molecular basis of LVM regression after AVR is being elucidated. Walther and associates²¹ used an animal model to study the role of changes in the cardiac extracellular matrix. In a sheep model they observed that LVH induced by aortic banding was associated with a significant increase in extracellular matrix gene expression of matrix metalloproteinases and a number of their tissue inhibitors. Regression of these genes was noted after relief from chronic pressure overload in their model.²¹ Further investigation is necessary to scrutinize the molecular mechanisms responsible for postoperative LVM regression after AVR. In particular, efforts should be directed at understanding why some subsets of patients fail to demonstrate satisfactory LVM regression despite adequate relief of AS and whether specific clinical interventions in this group may be of value in promoting resolution of LVH.

The advent and subsequent evolution of surgical treatment for aortic valve disease has been accompanied by a progressive drive toward engineering prostheses with optimal hemodynamic performance. A major impetus behind these efforts has been the desire to facilitate remodeling of the left ventricle after AVR, principally through resolution of LVH. More recently, this has been invigorated by concerns regarding the generation of patient-prosthesis

mismatch. Patient–prosthesis mismatch refers to circumstances in which a prosthesis is deemed to be too small for a given patient, resulting in a degree of residual impedance to transaortic flow. This entity has been strongly linked with both morbidity and mortality in patients undergoing AVR.^{5,22} One of the major concerns relating to patient–prosthesis mismatch is that it predisposes to incomplete postoperative regression of LVH.⁵ We have demonstrated that patients who have greater LVM regression after AVR may exhibit increased survival at very long-term follow-up. Furthermore, the group of patients who were observed to have the greatest LVM regression was also found to have lower postoperative tranvalvular gradients, although this did not reach statistical significance. A number of strategies can be used to avoid the development of patient–prosthesis mismatch. The use of stentless valves, which are engineered to occupy the smallest possible area within the aortic root, is widely regarded as a means of maximizing the available cross-sectional area for transprosthetic flow. Procedures aimed at enlarging the aortic root represent an alternative method aimed at avoiding patient–prosthesis mismatch and maximizing the size of prosthesis that can be implanted. A number of randomized trials have been undertaken to compare performance of stentless valves with the presumably more hemodynamically “challenged” stented valve. The results have been conflicting, with some demonstrating improved hemodynamic performance and LVM regression after stentless AVR,²³ while others have failed to identify any difference in such outcomes.²⁴ One important conclusion that can be drawn from these studies is that both stented and stentless AVR can be undertaken with minimal morbidity and mortality. Similarly, concomitant aortic root enlargement procedures at the time of AVR can also be performed with a low risk to patients.²⁵ Evidence that superior LVM regression is correlated with greater long-term survival warrants that interventions optimizing hemodynamic performance be used to promote resolution of LVH.

CONCLUSIONS

Enhanced LVM regression at late follow-up in patients undergoing AVR is associated with improved long-term survival. Strategies to optimize postoperative LVM regression should be considered in view of potential prognostic benefit.

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