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Imaging techniques in aortic valve and root surgery

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Chapter 8:

Aortic valve repair versus replacement for aortic regurgitation:
effects on left ventricular remodeling

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Abstract

Background: Left ventricular (LV) reverse remodeling after aortic valve replacement (AVR) for aortic regurgitation (AR) is associated with superior prognosis. The outcomes of valve-sparing aortic root replacement techniques on LV performance have not been compared with LV reverse remodeling in AVR. The present evaluation compared the extent of long-term LV reverse remodeling in patients with aortic root pathology and/or AR who underwent aortic valve repair (AVr) with patients who underwent AVR.

Methods: A total of 226 patients (54.7 ± 14.3 years, 63% male) with AR or aortic root pathology who underwent AVr ($n=135$) or AVR with the Freestyle stentless aortic root bioprosthesis [Medtronic, Inc; Minneapolis, Minnesota] ($n=91$) were included in the present retrospective evaluation. LV volumes and ejection fraction were assessed preoperatively, postoperatively (before hospital discharge) and during follow-up.

Results: Baseline characteristics were comparable between patient groups, except for higher prevalence of bicuspid aortic valve anatomy among AVr patients (38% vs. 16%, $p < 0.001$). In addition, patients undergoing AVr had significantly larger LV end-diastolic and end-systolic volumes than their counterparts. After a median follow-up of 46 months (interquartile range: 17-78 months), both groups of patients showed a significant and sustained reduction in LV end-diastolic and end-systolic volumes, with significantly larger reduction in patients undergoing AVr. Ejection fraction decreased significantly postoperatively and improved later during follow-up similarly in both groups. The incidence of significant AR at long-term follow-up was comparable among groups (AVr: 8% vs. AVR: 7%).

Conclusion: LV reverse remodeling occurs after AVr and AVR, reaching comparable LV volumes and function after a median of 4 years of follow-up.

Introduction

Aortic root pathology is present in 11% of patients with aortic regurgitation (AR).¹ Valve-sparing aortic root remodeling/replacement techniques have emerged as safe and effective techniques providing long-term stable aortic valve function in selected patients.²⁻⁵ In patients who are not suitable for valve-sparing aortic root remodeling/replacement, aortic root replacement with concomitant aortic valve replacement (AVR) using bioprostheses has demonstrated excellent results in terms of long-term outcomes, valve function and left ventricular (LV) function.⁶⁻⁸ In contrast to mitral valve repair and replacement, where the evidence shows that mitral valve repair is associated with superior LV function and remodeling than mitral valve replacement for patients with primary mitral regurgitation,⁹ the outcomes of valve-sparing aortic root remodeling/replacement techniques on LV performance have not been compared with AVR. Accordingly, the aim of the present evaluation was to compare changes in LV dimensions and function in patients with aortic root pathology and/or aortic valve regurgitation who underwent valve-sparing aortic root surgery with patients in whom surgical repair techniques were not feasible and were treated with surgical AVR.

Methods

Patients

From July 1993 to June 2013, 247 adult patients with AR and/or aortic root pathology underwent surgical valve-sparing aortic root reconstruction or surgical AVR using the Freestyle stentless aortic root bioprosthesis (Medtronic, Inc; Minneapolis, Minnesota) at the Leiden University Medical Center. Twenty-one patients were excluded due to lack of echocardiographic data. Patients with concomitant significant mitral or tricuspid valve disease (any grade of mitral or tricuspid stenosis and moderate or severe regurgitation) who were treated during the same surgical intervention were not excluded. Patients with more than mild aortic stenosis were excluded from the present analysis.

Baseline clinical characteristics, EuroSCORE II and surgical procedures were recorded. In addition, LV volumes and function and valvular hemodynamics were assessed with two-dimensional transthoracic echocardiography preoperatively, postoperatively and during follow-up when available. Demographic, clinical, surgical, and echocardiographic data were prospectively collected in the departmental Cardiology Information System (EPD-Vision, Leiden University Medical Center, Leiden, the Netherlands) and retrospectively analyzed. The institutional ethic committee approved this retrospective study and waived the need for individual patient consent.

Patients were divided into two groups: patients undergoing aortic valve repair (AVr) and patients who underwent aortic valve replacement using the Freestyle stentless bioprosthesis (AVR-F). The incidence of recurrent aortic valve regurgitation over time was assessed. In

addition, changes in LV volumes and function over time were assessed and compared between these two groups.

Two-dimensional transthoracic echocardiography

Transthoracic echocardiography was performed at rest with patients in the left decubitus position using commercially available ultrasound systems (Vivid 7, E9 or System 5, General Electric Healthcare, Vingmed, Horten, Norway) equipped with 3.5-MHz or M5S transducers. Two-dimensional, M-mode and Doppler data were acquired at the parasternal, apical, subcostal and supra-sternal views according to current recommendations.¹⁰ The echocardiographic data were digitally stored in cine-loop format and data analysis was retrospectively performed using EchoPac (112.0.1, GE Medical Systems, Horten, Norway). LV end-diastolic (LVEDV) and end-systolic (LVESV) volumes were quantified in the apical 2- and 4-chamber views using Simpson's biplane method and LV ejection fraction (LVEF) was calculated.¹¹ AR grade was assessed using colour, pulsed and continuous wave Doppler recordings and using a multiparametric approach that includes the measurement of the jet width relative to the LV outflow tract width, vena contracta, the pressure half time of the regurgitant flow (if feasible) according to current recommendations.¹⁰ AR was graded as 0 (absent), 1 (mild), 2 (mild-moderate), 3 (moderate-severe) or 4 (severe). Peak and mean aortic valve gradient were obtained from continuous wave Doppler recordings on the apical long-axis of 5-chamber views.

Surgery

After median sternotomy, arterial cannulation was performed in the distal ascending aorta (in elective nondissected pathology and in the absence of dilatation of the distal part of the ascending aorta) or the subclavian or femoral artery (in patients with ascending aorta dissection or dilatation).

For valve-sparing aortic root reconstruction, after resecting the native sinuses of Valsalva, a graft was implanted using the reimplantation technique (modified David procedure) or the remodeling technique (Yacoub technique), as previously described.¹²⁻¹⁴ Concomitant procedures (leaflet triangular resection, leaflet resuspension and plication of the free edge of the leaflet) were performed if needed. In addition, concomitant aortic arch replacement was performed if the luminal diameter at this level was >45 mm or – in cases of dissection – a (re)entry tear was present in the arch.

For AVR using the Freestyle stentless bioprosthesis, the coronary buttons were mobilized and the sinuses of Valsalva and the aortic valve were excised. The bioprosthesis was then implanted, usually with a 120 degrees clockwise rotation, with interrupted sutures at one

plane at the level of the nadir of the sinus. Thereafter the coronary buttons were reattached to the bioprosthesis.¹⁵

Follow-up

Patients underwent transthoracic echocardiography postoperatively before discharge and at follow-up (at the discretion of the treating cardiologist).

Statistical analysis

All data analyses were performed using SPSS software version 20 (SPSS, Chicago, IL). Continuous variables were reported as mean \pm standard deviation or as median and interquartile range (IQR) and categorical variables were reported as numbers and percentages. Differences between patients who underwent AVr and those who underwent AVR-F were analysed using the unpaired Student's *t*-test, Mann-Whitney U test or a chi-square test. Linear mixed model analysis was used to assess the differences in change in LV dimensions and function over time between the two groups. Type of surgery (AVr or AVR-F) and moment of transthoracic echocardiography (preoperative, postoperative or late follow-up) were incorporated in the model as fixed variables as well as the interaction between type of surgery and moment of transthoracic echocardiography. An unstructured covariance matrix was applied. The estimated marginal means \pm standard error of the mean were presented. All statistical tests were two-sided. A *p*-value < 0.05 was considered statistically significant.

Results

A total of 226 patients (mean age 54.7 \pm 14.3 years, 63% men) who underwent aortic root and valve surgery because of aortic regurgitation or aortic root pathology were evaluated. AVr was performed in 135 patients. The remaining 91 patients underwent AVR-F. The clinical characteristics of both groups of patients were comparable (Table 1). In the AVR-F group, the number of patients with bicuspid aortic valve was significantly higher than in the AVr group. There were no differences in number of elective surgeries and the surgical risk was comparable between groups. There were no differences in the number and type of concomitant surgeries performed in both groups. The surgical techniques are summarized in Table 1.

Surgical outcome

There were 5 in-hospital deaths, 2 (1%) in the AVr group and 3 (3%) in the AVR-F group (*p*=0.654). Perioperative complications were comparable between both groups. Postoperative bleeding with cardiac tamponade was treated by pericardiocentesis in 20 (15%) AVr and 9 (10%) AVR-F patients (*p*=0.377) and/or by re-sternotomy in 17 (13%) and 8 (9%) patients,

respectively ($p=0.498$). Thromboembolic complications occurred in 14 (10%) AVr patients and 4 (4%) AVR-F patients ($p=0.169$). Postoperative atrial fibrillation or flutter was present in 47 (35%) AVr and 32 (35%) AVR-F patients ($p=1$).

Table 1. Baseline characteristics.

	AVr (n=135)	AVR-F (n=91)	p-value
Age (years)	54.4 ±13.8	55.2 ±15.0	0.65
Male	83 (61%)	59 (65%)	0.71
Smoking	37 (27%)	18 (20%)	0.30
Diabetes Mellitus	6 (4%)	8 (9%)	0.29
Hypertension	56 (41%)	33 (36%)	0.54
Dyslipidaemia	19 (14%)	20 (22%)	0.09
NYHA functional class			0.47
I	58 (43%)	38 (42%)	
II	45 (33%)	28 (31%)	
III	19 (14%)	14 (15%)	
IV	6 (4%)	9 (10%)	
Creatinine clearance (ml/min)	93.6 ± 34.7	97.2 ± 36.8	0.47
EuroSCORE II (%)	4.3 ± 5.3	5.7 ± 8.9	0.14
Bicuspid aortic valve	22 (16%)	35 (38%)	<0.001
Elective surgery	96 (71%)	64 (70%)	1
Mitral valve surgery	25 (19%)	13 (14%)	0.51
Tricuspid valve surgery	14 (10%)	7 (8%)	0.66
CABG	19 (14%)	12 (13%)	1
Valve-sparing aortic root repair technique			
None	5 (4%)		
Restoration STJ	46 (34%)		
David	68 (50%)		
Yacoub + Hemi-Yacoub	16 (12%)		
Additional aortic cusp repair	21 (16%)		

Data are presented as mean ± standard deviation or as number (percentage). CABG: coronary artery bypass grafting. EuroSCORE: European System for Cardiac Operative Risk Evaluation. NYHA: New York Heart Association; STJ: sinotubular junction

Valvular hemodynamics after AVr versus AVR-F

In the entire cohort, the median echocardiographic follow-up duration was 46 months (IQR: 17 to 78 months). The median echocardiographic follow-up duration was 49 months (IQR: 18 to 76 months) in the AVr group and 34 months (IQR: 12 to 83 months) in the AVR-F group ($p=0.697$). The AR grade over time is displayed in Figure 1. In the AVr group, 44% of the patients had preoperatively grade 3 or 4 AR, compared to 47% in the AVR-F group ($p=0.81$). Immediately after surgery, 99% of the patients in the AVR-F group had grade <2 AR, compared to 83% in AVr group ($p = 0.002$). During follow-up, the percentage of AR grade 3 and 4 was similar between groups (AVr: 8% vs. AVR-F: 7%, $p=1$).

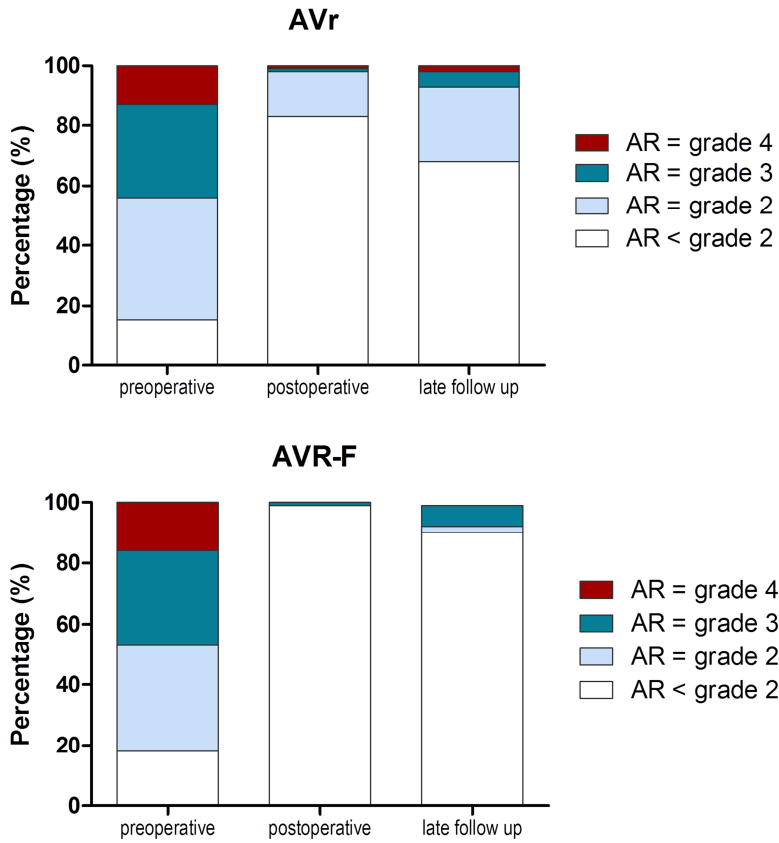


Figure 1. Aortic regurgitation grade over time
 Displayed as percentages per group in AVr and AVR-F. AR: aortic regurgitation.

The peak and mean aortic valve gradients over time are displayed in table 2. The peak aortic valve gradient was preoperatively and postoperatively lower in the AVr group compared to the AVR-F group. At late follow-up, there was no significant difference in peak aortic valve gradient between the two groups. The mean aortic valve gradient in the AVr group remained stable over time. In the AVR-F group, the mean aortic valve gradient was slightly higher before surgery as well as after surgery compared to the AVr group. There was a significant difference in peak and mean gradients over time between the groups ($p=0.002$ and $p=0.005$, respectively).

LV reverse remodeling after AVr versus AVR-F

Table 2 summarizes echocardiographic characteristics of patients undergoing AVr and AVR-F at baseline, immediately postoperatively and during follow-up. Patients treated with AVR-F showed significantly larger LVEDV and LVESV at baseline compared with patients undergoing

Table 2. Echocardiographic characteristics.

	AVr (n=135)	AVR-F (n=91)	p-value
Peak aortic valve gradient (mmHg)			
Preoperative	11.2 ± 0.7	18.9 ± 1.1	<0.001
Postoperative	11.5 ± 0.6	15.1 ± 1.0 *	0.01
Late follow-up	17.9 ± 7.1	14.1 ± 1.6 *	0.83
Mean aortic valve gradient (mmHg)			
Preoperative	6.4 ± 0.4	10.7 ± 0.6	<0.001
Postoperative	6.6 ± 0.3	8.4 ± 0.6 *	0.04
Late follow-up	5.8 ± 0.3	8.2 ± 1.1	0.002
LVEDD (mm)			
Preoperative	53.4 ± 0.9	56.1 ± 1.2	0.20
Postoperative	47.2 ± 0.7 *	48.5 ± 0.9 *	0.61
Late follow-up	49.2 ± 0.8 * [†]	48.7 ± 1.2 *	0.91
LVESD (mm)			
Preoperative	36.1 ± 0.9	37.0 ± 1.2	0.75
Postoperative	34.3 ± 0.8	35.9 ± 1.0	0.41
Late follow-up	33.0 ± 0.9 *	32.2 ± 1.2 * [†]	0.66
LVEDV (ml)			
Preoperative	125.9 ± 4.8	156.5 ± 6.4	0.002
Postoperative	109.9 ± 3.7 *	116.3 ± 4.8 *	0.36
Late follow-up	112.3 ± 4.0 *	117.0 ± 6.6 *	0.65
LVESV (ml)			
Preoperative	59.0 ± 3.4	75.0 ± 4.3	0.045
Postoperative	56.6 ± 3.0	60.1 ± 3.7 *	0.56
Late follow-up	51.0 ± 2.7 *	56.4 ± 4.8 *	0.43
LVEF (%)			
Preoperative	55.1 ± 1.0	54.0 ± 1.0	0.86
Postoperative	50.9 ± 1.0 *	50.9 ± 1.1 *	0.99
Late follow-up	56.5 ± 0.9 [†]	54.8 ± 1.4 [†]	0.34

Data are presented as estimated marginal means ± standard error of the mean. Within groups: * $p < 0.05$ vs preoperative, [†] $p < 0.05$ vs. postoperative. LVEDD: left ventricular end-diastolic diameter, LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESV: left ventricular end-systolic volume.

AVr. However, LVEF was comparable between the two groups. Figure 2 illustrates the changes in LV volumes and function over time. In the AVr-group there was a significant decrease in LVEDV acutely after surgery and remained stable at long-term follow-up. In contrast, LVESV remained unchanged immediately after surgery and reduced significantly at long-term follow-up. LVEF decreased significantly postoperatively but normalized at long-term follow-up. In patients who underwent AVR-F, LVEDV and LVESV showed a significant reduction immediately after surgery and remained stable at long-term follow-up. Similarly to the group of patients undergoing AVr, LVEF decreased significantly after surgery and normalized later during follow-up.

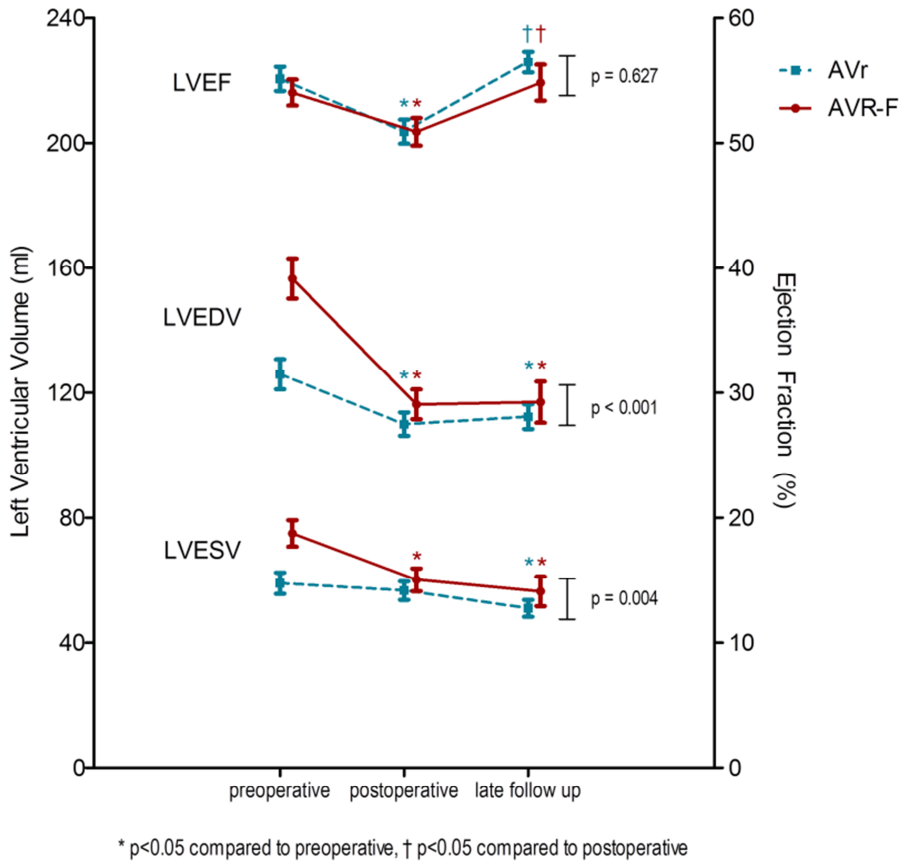


Figure 2. Left ventricular volumes and function over time in AVr compared to AVR-F.

Data are displayed as estimated marginal means \pm standard error of the mean. Group-time interaction p-value is given per variable. LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume.

The change in LVEDV and LVESV was significantly different between groups since the group of patients undergoing AVR-F had significantly larger volumes at baseline compared to the group of patients treated with AVr. In contrast, there were no significant differences in LVEF changes between groups (Figure 2).

Discussion

The present study compared the effect of valve-sparing aortic root reconstruction versus AVR on LV remodeling and function at follow-up. Patients with aortic root pathology and/or AR

who undergo these surgical techniques have long-term freedom of recurrence of AR \geq grade 3 and show favourable LV reverse remodeling with preserved LVEF during follow-up. Chronic significant AR leads to volume and pressure overload of the LV which responds with an increase in LV dimensions to maintain LVEF.¹⁶ If left untreated, the compensatory LV remodeling eventually fails and LVEF decreases. Patients with severe AR and LV dilation or dysfunction have poor survival if they remain under medical treatment and consequently current guidelines recommend surgical aortic valve replacement in case of symptoms, LVEF $<$ 50% or LV end-diastolic diameter $>$ 75 mm or end-systolic diameter $>$ 55mm.¹⁷ The surgical technique to use depends on the anatomical characteristics of the aortic valve and aortic root and the experience of the surgeon. Aortic valve repair techniques have shown good outcomes in selected patients. A systematic review of the outcomes of aortic valve repair pooling data from 2,891 patients undergoing aortic valve repair procedures showed an early mortality of 2.6% and a 5-year survival free from aortic valve reintervention and $>$ grade 2 AR of 92% and 88%, respectively.¹⁸ The late mortality was 1.3%/patient-year.¹⁸ However, these results are derived from centers with high experience in aortic valve repair techniques which are continuously evolving. In addition, previous series have not compared aortic valve repair and replacement in terms of LV performance outcomes. In contrast to mitral valve repair for primary mitral regurgitation, with an overwhelming evidence showing the superior outcomes in terms of LV function and remodeling over mitral valve replacement (particularly without preserving the subvalvular apparatus),⁹ there is a paucity of data on the LV outcomes of aortic valve repair and replacement techniques.

Changes in LV dimensions and function after AVR for significant AR have been reported in several studies.^{19,20} In a series of 40 patients with severe AR, Gentles et al. showed significant decreases in LVEDV and LVESV at 7 ± 2 months after AVR while LVEF remained stable.²⁰ This decrease in LV volumes can be observed acutely after AVR due to an acute correction of the volume overload with the consequent reduction in LVEF. However, at follow-up, this LV reverse remodeling remains with further reduction in LVESV which results in improvement and sometimes normalization of LVEF.^{8,21,22} In 93 patients with severe AR undergoing surgical AVR, Tanoue et al. showed that the LVEF changed from $60.2 \pm 11.0\%$ preoperatively to $51.9 \pm 14.6\%$ directly postoperative and to $57.9 \pm 15.2\%$ at 1 year follow-up.²² This was accompanied by significant reductions in LVEDV and LVESV that were sustained at 1 year follow-up. A few series have described changes in LV volumes and function after valve sparing aortic root reconstruction.^{23,24} In patients undergoing these surgical techniques, the presence of recurrent, significant AR may theoretically halt the LV reverse remodeling process. However, this has not been described. Leshnowar et al. evaluated changes in LV volumes and function in 51 patients undergoing David-V reimplantation technique.²³ The authors reported a significant

decrease in LV end-diastolic and end-systolic diameters during follow-up. Furthermore, LVEF improved from $51 \pm 7\%$ to $57 \pm 6\%$ during a mean follow-up period of 18 months.

The present study provides further insight into this field by comparing changes in LV volumes and function between patients undergoing AVr and patients treated with AVR-F. Both groups of patients showed significant reductions in LVEDV acutely after surgery and remained stable at follow-up. However, LVESV significantly reduced acutely in the group of patients undergoing AVR-F whereas their counterparts showed a further significant LV reverse remodeling at long-term follow-up. This indicates either a different pattern of LV reverse remodeling that may be associated with the surgical technique, or be related to the larger pre-operative volumes in the AVR-F group. Additional studies including larger number of patients are needed to confirm these results. In addition, similarly to previous series, LVEF reduced immediately after surgery but recovered at long-term follow-up.

The results of the present study demonstrate that a durable repair of the aortic valve in patients with AR or aortic root pathology is associated with beneficial LV reverse remodeling and preserved LVEF at follow-up. LV dimensions and function are important prognostic determinants in patients with significant AR and accordingly, current guidelines recommend AVR when significant LV dilatation or reduced LVEF coexist.¹⁷ Similarly to mitral valve repair for primary mitral regurgitation, the possibility of performing a durable aortic valve repair may impact on current guidelines, recommending aortic valve repair in patients with severe AR who do not have yet a significant damage of the left ventricle (LV dilatation or reduced LVEF). Prospective randomized trials comparing a watchful waiting strategy versus aortic valve repair would provide the evidence to this unmet clinical need.

Some limitations should be acknowledged. The present study was retrospective and non-randomized. The surgeon decided intraoperatively whether AVr was feasible. If not, AVR-F was performed, which may have introduced a selection bias. Furthermore systematic preoperative, postoperative and follow-up echocardiography was not available in few patients. In addition, the duration of significant AR before surgery was not recorded. This may have resulted in higher preoperative LV volumes in the AVR-F group which may have the effect of more impressive LV reverse remodeling postoperatively. This study compared the Freestyle stentless aortic root bioprosthesis with a valve sparing technique. Similar results may not occur with stented bioprosthetic or mechanical valves as the replacement technique.

Conclusion

In conclusion, LV reverse remodeling occurs both after aortic valve replacement and repair and comparable LV volumes and function are reached during a median follow-up of 4 years.

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