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Impact of moderate coronary atherosclerosis on long-term left ventricular remodeling after aortic valve replacement

Jose Antonio Linares Vicente, Isaac Lacambra Blasco, Pilar Portero Perez, Borja Simo Sanchez, Maria Rosario Ortas Nadal, Jose Ramón Ruiz Arroyo, Mariano González Carretero, Alfonso Del Rio Ligorit

Department of Cardiology, Lozano Blesa University Clinic Hospital, Zaragoza, Spain

Abstract

Background: *The role of coronary atherosclerosis (CA+) in ventricular remodeling after aortic valve replacement (AVR) for isolated aortic stenosis (AS) is not well defined. We sought to evaluate the impact of not revascularized moderate coronary atherosclerosis in long-term left ventricular (LV) remodeling after AVR.*

Methods: *We assessed by coronariography the coronary artery disease in 66 patients referred for AVR and evaluated morphological and functional LV data by echocardiography both preoperatively and postoperatively (3 ± 1.2 years).*

Results: *In patients without coronary atherosclerosis, hypertrophy regression was more intense and the absolute reverse remodeling was higher in LV mass index (–55.8 ± 36 g/m² vs –28.4 ± 34 g/m², p = 0.004), reduction of LV dimensions (LV end-diastolic diameter [LVEDD]: –4.1 ± 7.4 mm vs –2.2 ± 8.3 mm, p = 0.04), and regression of wall thickness (interventricular septum [IVS]: –3.3 ± 2.6 mm vs –1.6 ± 2.2 mm, p = 0.01; and posterior wall thickness [PWT]: –2.1 ± 2.1 mm vs 0.6 ± 2.1 mm, p = 0.012).*

Conclusions: *After AVR for AS, not revascularized moderate coronary atherosclerosis determines a long-term lesser degree of LV hypertrophy regression and a worse absolute reverse remodeling of LV mass index, LVEDD, IVS and PWT.* (Cardiol J 2011; 18, 3: 277–281)

Key words: aortic stenosis, valve replacement, ventricular remodeling

Introduction

Aortic stenosis (AS) determines left myocardial hypertrophy due to chronic systolic pressure overload. Prosthetic aortic valve replacement (AVR) for isolated AS determines a marked left ventricular mass index (LVMI) decrease, with reduction of dimensions and wall thickening of the left ventricle [1]. The role of coronary atherosclerosis in this ventricular remodeling has not been properly established. We aimed to evaluate the impact of moderate non-revascularized coronary atherosclerosis in long-term LV remodeling after AVR for AS.

Methods

The study population consisted of consecutive survivors referred for AVR for isolated AS with no

Address for correspondence: Dr. Jose Antonio Linares Vicente, Department of Cardiology, Lozano Blesa University Clinic Hospital, HCU Lozano Blesa, Avda, San Juan Bosco, 15, 50009 Zaragoza, Spain, tel: 0034620140664, e-mail: joselinares1979@hotmail.com

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Table 1. Baseline characteristics of patients.

	CA–	CA+	P
Age	66.7 ± 9.6	69.1 ± 7.2	0.3
Body surface area [m^2]	1.7 ± 0.1	1.8 ± 0.1	0.16
Hypertension	10 (23.8%)	5 (20.8%)	0.78
Dyslipidemia	8 (19%)	6 (25%)	0.56
Diabetes mellitus	4 (9.5%)	5 (20.8%)	0.19
Smoking	6 (14.3%)	6 (25%)	0.27
Number of vessels diseased:			
1	0 (0%)	13 (54.2%)	
2	0 (0%)	7 (29.2%)	
3	0 (0%)	4 (16.7%)	
LVMI [g/m^2]	161.5 ± 49.4	148.6 ± 31	0.25
LVEF (%)	57 ± 11	59 ± 14	0.6
Systolic dysfunction	8 (19%)	4 (16.7%)	0.8
Peak gradient [mm Hg]	92 ± 25	93 ± 22	0.92
Medium gradient [mm Hg]	58 ± 18	58 ± 11	0.88

CA– — absence angiographic coronary stenosis; CA+ — moderate coronary atherosclerosis; LVMI — left ventricular mass index; LVEF — left ventricular ejection fraction

coronary artery bypass grafts (CABG) performed during the surgical intervention (absence of angiographic coronary stenosis or not severe coronary stenosis). Each patient underwent standard coronarography before surgery. The absence of angiographic coronary stenosis (CA–) was defined as smooth and regular walls in three vessels. Moderate coronary atherosclerosis (CA+) was defined as the presence of ≥ one vessel with stenosis ≥ 40% and < 80% by quantitative coronary angiography. Patients with a history of myocardial infarction (MI) were excluded. CABG during AVR was decided jointly by a cardiologist and a surgeon, depending on coronary stenosis severity. All surgical interventions were performed by the same surgical team at another hospital.

At basal characterization, hypertension, dyslipidemia and diabetes mellitus were defined as specific chronic pharmacological medical treatment for these pathologies. Smoking was defined as an active smoker or one who had stopped during the previous ten years.

All patients underwent Doppler echocardiography preoperatively and were re-evaluated three years after surgery (mean 36.5 ± 14 months). All echocardiographic studies were performed by the same experienced work team using the same equipment (Philips Envisor). Echocardiographic end-diastolic (LVEDD) and end-systolic (LVESD) measurements of LV dimensions, interventricular septal thickness (IVS) and posterior wall thickness (PWT) were obtained in millimeters, according to the Guidelines of the American Society of Echocardiography [2]. LVMI was calculated according to body surface area [m^2] as described by Devereux [3]. Left ventricular ejection fraction (LVEF) was estimated by Teicholz method [2], and systolic dysfunction was defined as LVEF < 50%. Reverse remodeling was calculated by arithmetic subtraction between the preoperative and postoperative measurements.

The study was approved by the local bioethical committee and all patients gave their informed consent.

Statistical analysis

Statistical analysis was performed using computer data (SPSS 13.0 software). Values are expressed as mean ± standard deviation for continous variables, and percentages for qualitative variables. Paired and independent comparisons between preoperative and postoperative studies were performed using the two tailed Student-t test. Qualitative comparisons were performed using the χ^2 test. The level of significance was established at $p < 0.05$

Results

A total of 66 patients were enrolled (aged 67.6 ± ± 8.8 years, 44 male): 42 in group CA– and 24 in group CA+. Both groups of patients presented similar basal characteristics (Table 1): age at surgery (66.7 ± 9.6 years in CA– *vs* 69.1 ± 7.2 years in CA+, p = 0.3); body surface area (1.7 ± 0.1 m^2 *vs*

Table 2. Changes in left ventricular morphology from preoperative to postoperative measurements in both groups (regression of wall thickness and reduction of left ventricular dimensions) and differences in remodeling between them.

	CA–			CA+		
	Pre	Post	P	Pre	Post	P
LVEDD [mm]	52.3 ± 7.6	48 ± 5.9	< 0.001	52.4 ± 7.9	50.9 ± 5.2	0.42
remodeling		–4.1 ± 7.4			–2.2 ± 8.3	0.04
LVESD [mm]	34.1 ± 8.2	30 ± 5.3	0.001	33.8 ± 9.2	31.3 ± 4.3	0.19
remodeling		–3.7 ± 7.3			–3.2 ± 8.8	0.79
IVS [mm]	13.4 ± 2.9	10.2 ± 2.2	< 0.001	12.4 ± 2.1	10.1 ± 2.1	0.003
remodeling		–3.3 ± 2.6			–1.6 ± 2.2	0.01
PWT [mm]	12.6 ± 1.7	10.7 ± 2.4	< 0.001	11.9 ± 1.9	11.1 ± 1.2	0.12
remodeling		–2.1 ± 2.1			–0.6 ± 2.1	0.012
LVMI [g/m^2]	161.5 ± 49.4	108.9 ± 28.3	< 0.001	148.6 ± 31	120.8 ± 28.4	0.001
remodeling		–55.8 ± 36			–28.4 ± 34	0.004
LVEF (%)	57.6 ± 11.1	63.3 ± 8.2	0.001	59.1 ± 13.4	62.5 ± 9.5	0.26
remodeling		+5.3 + 9.4			+4.4 + 14.5	0.74

CA– — absence of angiographic coronary stenosis; CA+ — moderate coronary atherosclerosis; Pre — preoperative; Post — postoperative; LVEDD — end-diastolic left ventricular dimension; LVESD — end-systolic left ventricular dimension; IVS — interventricular septum thickness; PWT — posterior wall thickness; LVMI — left ventricular mass index; LVEF — left ventricular ejection fraction

1.8 ± 0.1 m^2, p = 0.16); prevalence of hypertension (23.8% *vs* 20.8%, p = 0.78); LVMI (161.5 ± 49.4 g/m^2 *vs* 148.6 ± 31 g/m^2, p = 0.25); LVEF (57 ± 11% *vs* 59 ± 13%, p = 0.6); systolic dysfunction (19% *vs* 16.7%, p = 0.8) and transvalvular aortic gradients (peak gradient: 92 ± 25 mm Hg *vs* 93 ± 22 mm Hg, p = 0.92, medium gradient: 58 ± 18 mm Hg *vs* 58 ± ± 11 mm Hg, p = 0.88). CA+ was more frequent in men than in women (47.7% *vs* 13.6%; p = 0.007; RR 3.5; 95%CI 1.17–10.4). Besides moderate stenosis in other vessels, three patients presented 70–80% stenosis by QCA [4], but in distal segments or small branches not suitable for CABG (one patient in a distal right posterolateral branch, and two patients in distal marginal obtuse branches with diffuse atheroesclerosis and vessel size reduction in distal segments).

Mechanical prostheses were implanted in similar ratios in both groups (61.9% in CA– *vs* 56.5% in CA+, p = 0.67). After AVR transvalvular aortic gradients did not differ (peak gradient: 27 ± 12 mm Hg *vs* 23 ± 8 mm Hg, p = 0.15; medium gradient: 15 ± 7 mm Hg *vs* 13 ± 3 mm Hg, p = 0.14).

Changes in LV morphology from preoperative to postoperative measurements are displayed in Table 2. In the CA– group, all the echocardiographic parameters evaluated decreased between the preoperative and the postoperative study (except for a LVEF increase), but in the CA+ group only IVS and LVMI changed significantly. The differences in absolute reverse remodeling in LVEDD, IVS, PWT achieved statistical significance between both groups. LVMI suffered a noticeable drop in both groups, but there was a remarkable difference in its absolute reverse remodeling (–55.8 ± 36 g/m^2 *vs* –28.4 ± 34 g/m^2, p = 0.004, Fig. 1). LVEF increased significantly in CA–, but there were no differences between both groups.

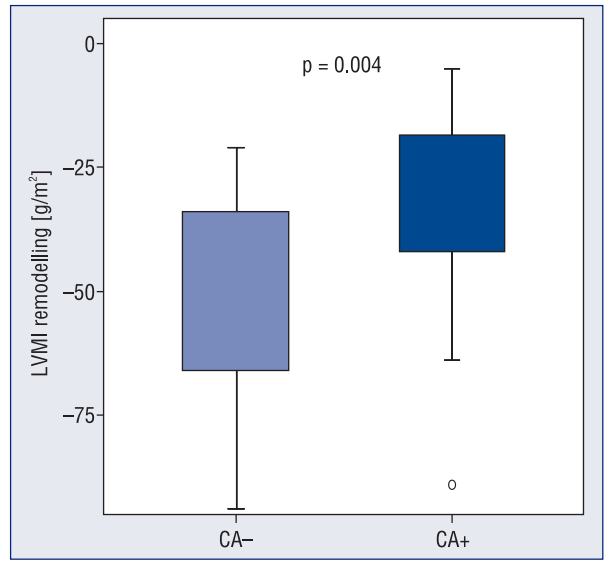

Figure 1. Differences in left ventricular mass index (LVMI) absolute reverse remodeling between CA– and CA+.

Discussion

Left ventricular pressure overload due to aortic valve stenosis leads to a marked myocardial hypertrophy. AVR immediately reduces this pressure overload, conditioning a decrease in wall tension and a reverse LV remodeling with LVMI regression due to ventricular dimensions and myocardial thickness reduction, well known during the first 12 months [1, 4, 5] and sustained many years after surgery [6, 7]. The role of coronary atherosclerosis in this reverse ventricular remodeling is not well defined in the literature. Some authors have said that severe myocardial hypertrophy in patients with severe AS can promote coronary microcirculatory function abnormalities [8], reduction of diastolic perfusion, and increase of systolic impedance to coronary flow due to perivascular compression [9]. Improving diastolic perfusion while reducing perivascular compression due to pressure overload drop after AVR is the main mechanism to improve myocardial blood flow and restore the coronary vasodilatation reserve [10], reducing the tissular ischemia and facilitating molecular mechanisms (inactivation of metaloproteinases that promote interstitial fibrosis) [11] that determine the reverse ventricular remodeling.

Biedermann et al. [12] described specifically how, one year after AVR, in patients with CA+ the left ventricular hypertrophy (LVH) regressed more slowly. But in that study, patients with moderate coronary stenosis, as well as patients who received CABG, were included in group CA+. These revascularized patients (CABG) could have equalized their risk with CA– patients. We aimed to study the specific role of moderate atherosclerosis, and its coronary flow disturbance impact, on long-term LVH regression. Our results concur with those published by Biedermann et al. [12], with a significant reduction in LVMI at three years in both groups: in our sample, reduction in LVMI is progressive and remains throughout in both groups, but it is significantly more intense in CA– than in CA+, probably because of a longer follow-up time (one year *vs* three years), and the different imaging technique used (cardiac magnetic resonance).

In the same way, observed changes in LV dimensions and wall thickness (LVEDD, LVESD and PWT) were more intense in the CA– group, and the absolute drop in measurements of LVEDD, PWT and IVS were significantly higher in CA– than in CA+, a fact that suggests poorer ventricular conditioning or reverse remodeling in the presence of non-revascularized moderate coronary atherosclerosis. With respect to LVEF, our results also agree with those described in the literature, with a similar improvement during long-term follow-up independently of the degree of coronary atherosclerosis.

Although in our study there were more males than females in the CA+ group, many studies have described the absence of gender influence on LVH regression after AVR for AS [12, 13], so we do not consider this basal difference in the groups studied could have influenced the final results.

Hypertension is the only cardiovascular risk factor considered as a potential mechanism to delay or avoid the long-term LV mass regression after AVR: in a ten year follow-up study, it was the only independent factor of LVH after surgery [13]. In our study, this cardiovascular risk factor presented the same prevalence in both groups, so we can expect that the results have not been influenced by it. Further studies with a longer follow-up would be necessary to see if advancing age could increase the prevalence of hypertension and determine different results, or reinforce those we present.

Except in cases with severely impaired LVEF, our echocardiographic study protocol for aortic stenosis did not include the assessment of aortic valve area by continuity equation. Due to the low prevalence of systolic dysfunction in our sample, we did not evaluate patient-prosthesis missmatch (PPM) in our study. PPM seems to play an outstanding role in LV mass regression after aortic valve replacement. As has been recently demonstrated with the clinical outcome and mortality of these patients [14], PPM is only relevant in LVMI evolution after AVR in the presence of systolic dysfunction prior to surgery [15]. It is only in this subgroup of patients that PPM seems to determine an incomplete LVMI regression. Some authors have suggested that this may not be so relevant in LV remodeling after AVR for AS [16, 17]. The low and similar prevalence of systolic dysfunction between both groups in our sample, as well as the absence of severely elevated transvalvular gradients after surgery, could suggest a poor influence of possible cases of PPM in our results.

Clinical implications

Although LVH late after AVR for AS is associated with an increased morbidity (impaired exercise capacity, a higher New York Heart Association dyspnoea class, a tendency for more frequent chest pain), it has not been related to increased mortality [18]. Because of this, and the fact that LVEF (the main surveillance predictor in patients after AVR for AS) is a parameter that remains stable irrespec-

tive of the degree of coronary atherosclerosis [11], it is possible that in cases of moderate coronary stenosis, not performing CABG during the AVR could be a reasonable strategy, thereby reducing surgical off-pump, cardioplegia and cross-clamp times, and so lowering intraoperative risk and mortality. After AVR and LVMI regression (improvement in coronary flow and microcirculation) these moderate coronary stenosis could be re-evaluated and ischemia-driven revascularized by percutaneous coronary intervention if necessary.

Conclusions

After AVR for AS, non-revascularized moderate coronary atherosclerosis determines a long--term lesser degree of LVH regression and a worse absolute reverse remodeling of LVMI, LVEDD, IVS and PWT.

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