International Journal of Cardiology 167 (2013) 1450–1455

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Severity of aortic stenosis predicts early post-operative normalization of left atrial size and function detected by myocardial strain

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ARTICLE INFO

Article history:
Received 27 December 2011
Received in revised form 18 March 2012
Accepted 8 April 2012
Available online 4 May 2012

Keywords:
Aortic stenosis
Speckle tracking echocardiography
Aortic valve replacement

ABSTRACT

Background: Aortic stenosis (AS) causes significant disturbances in left ventricular (LV) and left atrial (LA) function irrespective of the extent of myocardial hypertrophy which associates the increased afterload. We hypothesize that aortic valve replacement (AVR) and removal of LV outflow tract obstruction should result in LA size and function recovery, even partial, and were set to study this in a group of patients with AVR for AS.

Methods: Peak atrial longitudinal strain (PALS) was evaluated in 43 patients with severe isolated AS and normal EF (56.6 ± 3.8%) and no obstructive coronary artery disease candidates for AVR, pre-operatively and then 40 days and 3 months after surgery. Results were compared with those from 34 age- and gender-matched healthy controls.

Results: LVEF remained unchanged and LV mass regressed after AVR. Global PALS was reduced pre-operatively and increased 40 days after surgery ($p = 0.002$) and showed only a slight further increase at 3 months follow-up ($p < 0.0001$). Indexed LA volume was increased before surgery, but significantly fell 40 days after surgery ($p < 0.0001$) and showed only a slight further reduction after 3 months ($p < 0.0001$). Trans-aortic mean gradient change after surgery was the only independent predictor of the recovery of LA size and function.

Conclusions: AVR reverses LA abnormalities and regains normal atrial function, a behavior which is directly related to the severity of pre-operative LV outflow tract obstruction. Early identification of LA size enlargement and functional disturbances might contribute to better patient's recruitment for AVR.

1. Introduction

Aortic stenosis (AS) causes significant disturbances in left ventricular (LV) function irrespective of the extent of myocardial hypertrophy which associates the increased afterload [1,2]. In patients with maintained ejection fraction (EF), LV subendocardial function as shown by long axis function is often abnormal in AS, even in the absence of additional coronary artery disease. Aortic valve replacement (AVR) results in significant recovery of LV function [3–5], although residual abnormalities may remain [6,7]. Furthermore, recent studies have shown that the extent of irreversible LV dysfunction in the form of reduced myocardial strain rate reserve correlate with the impaired exercise capacity these patients have after AVR [8].

Along with LV dysfunction, it is well known that AS is associated with higher incidence of atrial arrhythmia when compared with age matched controls suggesting a direct relationship between the two [9]. Indeed, studies have shown that AS results in left atrial (LA) enlargement and disturbed atrial mechanical function [10]. Furthermore, it seems that such abnormalities of atrial size and function are related to the extent of rise of afterload irrespective of the degree of myocardial hypertrophy [11]. We hypothesis that AVR and removal of LV outflow tract obstruction should result in LA size and function recovery, even if partial, and were set to study this in a group of patients with AVR for AS.

2. Methods

2.1. Study population

We studied 43 consecutive patients (age 71.5 ± 9.7 years, 16 females) with severe isolated AS, based on a mean aortic gradient > 50 mm Hg and/or aortic valve area < 1.0 cm^2, referred to Le Scotte Hospital, University of Siena, for conventional surgical AVR [12].

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doi:10.1016/j.ijcard.2012.04.057

Patient's demographic details are listed in Table 1. Exclusion criteria were: atrial fibrillation, flutter, or other major arrhythmias; high-degree atrioventricular block, reduced LV EF (<50%); coronary artery disease in the form of, angina, acute coronary syndrome, coronary revascularization, segmental wall motion abnormalities, >50% narrowing in one of the epicardial coronary arteries on the pre-operative angiogram, previous cardiac surgery; coexisting valve disease or signs of pulmonary hypertension (defined as right ventricular-right atrial peak pressure drop > 40 mm Hg). Echocardiographic studies were performed the day before AVR then 40 days and 3 months postoperatively. Pre-operative data were compared with those from 34 normal controls (age 65.9 ± 11.6 years, 37% females), non of whom had a cardiac condition or history of any systemic disease, e.g. hypertension or diabetes (Table 2).

2.2. Echocardiographic examination

All echocardiographic examinations were performed according to the recommendations of the American and European Society of Echocardiography [13,14]. We used a commercially available echocardiograph (Vivid 7, GE Medical Systems, Horten, Norway) equipped with a 2.5-MHz probe, and a one-lead ECG was continuously displayed. LV internal diameters at end-systole and end-diastole (LV ESD and LV EDD, respectively) were measured from the left parasternal cross-sectional recording of the minor axis. Likewise interventricular septum and posterior wall thicknesses (IVST and PWT, respectively), were measured at end-diastole from the same M-mode recording. LV EF was calculated from the apical views using the biplane modified Simpson method. LV mass (LVM, in grams) was calculated according to the Penn formula [15]

$$LVM = 1.04[(LVIDd + PWTd + IVSTd)3–LVIDd]–13.6\ g,$$

where LVIDd is LV end-diastolic internal diameter; PWTd, diastolic posterior wall thickness; and IVSTd, diastolic interventricular septal thickness. LVM was subsequently indexed to body surface area (BSA). Aortic valve area (AVA) was calculated using the standard continuity equation with the velocity–time integral ratio of the pulsed wave Doppler of the LV outflow tract velocities and continuous wave Doppler velocities across the aortic valve. Peak flow velocity across the valve was determined from the apical view where the highest peak velocity could be obtained by placing the continuous-wave Doppler cursor as parallel as possible to the flow across the aortic valve. Peak and mean aortic gradients were calculated using the simplified Bernoulli equation [12,16]. Trans-aortic mean gradient change was defined as the percentage change of pressure drop from preoperative and 40 days follow-up.

2.2.1. Longitudial LV function

Mitral annular plane systolic excursion (MAPSE) was measured using the standard M-mode technique with the cursor placed at the lateral angle of the annulus from the apical 4-chamber view, using the zoom function [17]. Pulsed tissue Doppler imaging (TDI) was used to measure peak systolic (S′), early diastolic (E′), and late diastolic (A′) annular velocities by placing a 5-mm sample volume at the basal part of the lateral LV wall [18]. Particular care was given to adjust filter and gain settings at the minimal level in order to obtain the maximum signal-to-noise ratio. LV long-axis length at end-diastole was obtained by averaging the distances from the central point of the mitral annular plane to the apical subendocardium measured in the 4- and 2-chamber views [19].

2.2.2. LV longitudinal myocardial function

LV myocardial function was studied using longitudinal speckle tracking echocardiography (STE) analysis performed from the apical long axis, 4- and 2-chamber views, using a frame rate of 60–80 frames/s. Peak LV longitudinal strain was defined as the peak negative value on the strain curve during the entire cardiac cycle. LV cavity was traced manually from the innermost endocardial edge at end-systole, and the software automatically defined the longitudinal strain throughout the cardiac cycle. Longitudinal strain was analyzed in the apical long axis view where the closure of the aortic valve is defined. The time interval between the R wave and aortic valve closure was measured and used as a time reference. The automated algorithm provided the longitudinal peak systolic strain (LPSS) value for each LV segment from a 17-segment model polar plot, with the average value of LPSS for each apical view [20].

2.2.3. LV diastolic function

Pulsed-wave Doppler velocities of LV filling were recorded from the apical 4-chamber view, by placing the sample volume at the level of the tips of the mitral valve leaflets and the center of the forward LV filling jet. Early (E) and late (A) diastolic LV filling velocities were registered and E/A ratio calculated. E wave deceleration time was also measured as previously described [14]. LV filling pattern was considered 'restrictive' when E/A ratio was > 2.0, E-wave deceleration time < 140 ms, and the left atrium dilated, > 40 mm in diameter. Raised E/E′ was also taken as a marker of raised filling pressures [21].

2.3. LA structure and function

LA area and volume were measured using the biplane method of disks (modified Simpson's rule), in the apical 4- and 2-chamber view at end-systole (maximum LA size), and a mean value of area and volume was obtained [13]. LA mean area and volume were subsequently indexed BSA.

LA myocardial function was studied using STE performed from the apical 4- and 2-chamber views of the conventional 2D gray scale images during a brief breath hold and with a stable ECG recording. Care was taken to obtain true apical images using standard anatomic landmarks to avoid foreshortening the LA, therefore allowing a clear delineation of the atrial endocardial border. We also avoided visualization of the LA appendage in the apical 2-chamber view in order to minimize its potential effect on LA strain measurements. Three consecutive heart cycles were recorded and averaged, using a frame rate of 60–80 frames/s. Analysis of the acquired data was made off-line using a single experienced and independent echocardiographer, not directly involved in the image acquisition or patient's management, using a commercially available semi-automated 2D strain software (EchoPac, GE, USA). As previously described [22], LA endocardial border was manually traced in both the 4 and 2 chamber views, thus delineating a region of interest (ROI), consisting of 6 segments. After the segmental tracking quality analysis and manual adjustment of the ROI, the longitudinal strain curves were generated by the software for each atrial segment. Peak atrial longitudinal strain (PALS), measured at the end of the reservoir phase, was calculated by averaging

Table 1
Pre-operative clinical data.

Variable	Patients (mean ± SD)
HR (beats/min)	69.19 ± 9.73
NYHA class (1,2,3,4)	(0,34,9,0)
ECC (min)	132.68 ± 34.31
OT (min)	108.36 ± 29.18
Diabetes (%)	13.4
Smoker (%)	18.4
Hypertension (%)	72.9
Stroke (%)	4.5
Euroscore (%)	4.1 ± 2.5

Data are presented as mean ± standard deviation.
HR, heart rate; NYHA, New York Heart Association; ECC, extra corporal circulation time; OT, occlusion cross-clamping time.

Table 2
Comparison between controls and patients before AVR.

	Controls (n = 34)	Patients (n = 43)	P-value
Age	65.9 ± 11.6	71.5 ± 9.7	0.51
Gender (% female)	37.0	38.46	0.87
Height (cm)	171.8 ± 8.2	165.75 ± 7.46	0.31
Weight (kg)	69.5 ± 9.9	71.27 ± 12.13	0.26
Systolic blood pressure (mm Hg)	121.2 ± 11.1	137.44 ± 12.8	0.34
Diastolic blood pressure (mm Hg)	79.3 ± 5.6	76.31 ± 6.9	0.52
LA area (cm^2)	17.3 ± 4.0	23.52 ± 4.23	0.001
Indexed LA area (cm^2/m^2)	10.61 ± 2.13	13.33 ± 2.5	0.001
LA volume (ml)	50.3 ± 13.83	80.86 ± 24.03	<0.0001
Indexed LA volume (ml/m^2)	30.68 ± 7.55	45.84 ± 14.16	<0.0001
LV EDD (mm)	45.4 ± 5.3	49.07 ± 5	0.01
LV ESD (mm)	28.3 ± 4.9	31.32 ± 5.14	0.001
IVST, mm	8.71 ± 1.58	13.63 ± 1.3	<0.0001
PWT, mm	8.18 ± 1.48	12.78 ± 1.2	<0.0001
LV EF(%)	59.1 ± 7.3	56.6 ± 3.8	0.27
LV mass (g)	149.8 ± 26.4	265.54 ± 48.29	<0.0001
Indexed LV mass (g/m^2)	83.7 ± 26.4	149.72 ± 28.88	<0.0001
Global LV LS, %	−19.85 ± 2.07	−15.76 ± 3.63	0.002
Global PALS (%)	40.4 ± 6.5	19.69 ± 4.17	<0.0001
Global PACS (%)	16.3 ± 3.7	11.52 ± 3.65	<0.0001
LV filling variables			
E, m/s	0.63 ± 0.14	0.76 ± 0.24	0.13
A, m/s	0.75 ± 0.19	1.08 ± 0.31	0.02
E/A	1.19 ± 0.41	0.74 ± 0.32	0.001
Longitudinal function			
S′ (m/s)	0.09 ± 0.023	0.07 ± 0.016	0.01
E′ (m/s)	0.12 ± 0.046	0.07 ± 0.020	<0.0001
A′ (m/s)	0.10 ± 0.031	0.11 ± 0.022	0.34
E/E′	6.17 ± 1.87	12.37 ± 5.18	0.001
MAPSE	14.36 ± 2.05	11.48 ± 1.96	0.007

Data presented as mean ± standard deviation.
LA, left atrial; LV, left ventricular; EDD, end-diastole diameter; ESD, end-systolic diameter; IVST, interventricular septum thicknesses; PWT, posterior wall thicknesses; LS, longitudinal strain; PALS, peak atrial longitudinal strain; PACS, peak atrial contraction strain; E, early diastolic peak flow velocity; A, late diastolic peak flow velocity; S′, peak systolic mitral annulus velocity; E′, peak early diastolic mitral annular velocity; A′, peak late diastolic mitral annulus velocity; MAPSE, mitral annular plane systolic excursion.