

Impact of transcatheter aortic valve implantation on the left ventricular mass

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Abstract

Background: Aortic stenosis (AS) induces pressure overload of the left ventricle (LV) and results in left ventricular hypertrophy. The remodeling of the LV in patients with AS is a complex process including structural and functional disturbances. After aortic valve replacement, reverse remodeling of LV begins. The aim of this study was to evaluate the impact of transcatheter aortic valve implantation (TAVI) on LV mass (LVM) in early and mid-term follow-ups after the procedure.

Methods and Results: We enrolled consecutive 75 patients who underwent successful TAVI. Transthoracic echocardiography was performed prior to TAVI and at hospital discharge, in the 1st month and 6th month of the follow-ups. The mean LV ejection fraction improved significantly after TAVI ($54.2 \pm 15.0\%$ to $57.3 \pm 11.7\%$, $p < 0.001$). There were no significant changes between the baseline and discharge mean LVM and LVM index values (LVMI; $p = 0.1$). However, LVMI decreased significantly in the 1st month of follow-up compared to baseline (123.3 ± 20.3 to 127.9 ± 21.3 g/m², respectively, $p < 0.001$). Also, significant regression of LVM was observed at the 1st month of follow-up compared to baseline (228.3 ± 33.5 g vs. 236.5 ± 34.2 g, respectively, $p < 0.001$). Furthermore, the significant regression in both of LVM and LVMI continued at 1st and 6th months of the follow-ups ($p < 0.001$).

Conclusions: A significant regression of LVM was observed after TAVI. These changes may have prognostic value in patients with severe AS. (Cardiol J 2015; 22, 6: 645–650)

Key words: aortic valve stenosis, TAVI, left ventricular mass

Introduction

Degenerative aortic valve stenosis (AS) is the most common valvular heart disease in the elderly population and it has an increasing prevalence with age [1–3]. AS induces pressure overload of the left ventricle (LV) and results in left ventricular hypertrophy (LVH). Myocyte degeneration and fibrosis have major roles in the pathophysiology of hypertrophic remodeling. LVH caused by AS is associated with systolic and diastolic dysfunction

of the LV which are the recognized risk factors of cardiac morbidity and mortality [3]. Transcatheter aortic valve implantation (TAVI) has been proven to be a promising therapy for high risk or inoperable patients with AS [4].

Left ventricular remodeling in patients with AS is a complex process including structural and functional disturbances. After aortic valve replacement (AVR), reverse remodeling of the LV begins. This way, LV volume and mass regress, LV systolic and diastolic function improves. This

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process seemed to be important for prognosis and symptomatic improvement after open surgery [5, 6]. The early- and late-term effects of TAVI on LV mass (LVM) and volume regression and LV diastolic dysfunction have controversial data in the literature. The aim of this study was to evaluate the impact of TAVI on LVM in early and mid-term follow-ups.

Methods

Patients

We consecutively recruited 75 patients who underwent TAVI using balloon-expandable Edwards Sapien XT (Edwards Lifesciences, Irvine, CA, USA) prostheses between July 2011 and July 2013. The study population included symptomatic patients with severe AS (mean gradient ≥ 40 mm Hg and/or aortic valve area [AVA] < 1 cm² or indexed AVA ≤ 0.6 cm²/m²) and inoperable or at high risk for surgical AVR (s-AVR) due to co-morbid conditions. The exclusion criteria were as follows: any contraindications to anticoagulant and/or antiplatelet agents, life expectancy with or without AVR < 12 months, non-calcified valve, history of AVR, severe aortic or mitral regurgitation, severe renal insufficiency, coagulopathy or bleeding diathesis and abdominal aortic aneurysm. Before the procedure, all patients underwent transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), multislice computed tomography (MSCT) and coronary angiography. Pretreatment operative risk was assessed by the Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons (STS) score.

All patients were informed before the procedure, and the study was approved by our hospital's ethics committee.

Transthoracic echocardiography

All patients underwent TTE (IE33 echocardiography system, Philips Medical Systems, Eindhoven, the Netherlands) with an experienced operator. TTE Doppler and 2-dimensional images were obtained from parasternal short and long axis, apical 4-chamber, and subcostal 4-chamber views. TTE was reviewed to assess the valve morphology, valvular anatomy, aortic annulus diameter, ventricular function, and pericardium. It was performed prior to TAVI and at hospital discharge, in the 1st month and 6th months of the follow-ups.

The Doppler echocardiographic measurements included LV end-diastolic volume, LV ejection fraction (LVEF) calculated with the modified Simpson's

method, transvalvular pressure gradient determined by the Bernoulli formula, and AVA calculated by the continuity equation. Patients with low flow and low gradient AS underwent dobutamine stress echocardiography in order to determine the exact severity of AS and LV contractile reserve. LVM was calculated with the formula as follows: $LVM = 0.8 \times (1.04 \times [(LVEDD + LVPWTd + LVSWTd)^3 + (LVEDD)^3]) + 0.6$ g [7], where LVEDD is left ventricular end diastolic diameter; LVPWTd — left ventricular posterior wall thickness diameter, and LVSWTd — left ventricular septal wall thickness diameter. LVM index (LVMI) was determined by using the formula, LVM/body surface area [g/m²]. LVH was defined as LVMI > 95 g/m² for women and LVMI > 115 g/m² for men. All echocardiographic parameters were evaluated according to guidelines of the American Society of Echocardiography [8].

Transcatheter aortic valve implantation

TAVI was performed at the catheterization laboratory with fluoroscopy using conventional technique. Seventy-two (96%) through femoral artery and 3 (4%) patients through subclavian artery received a balloon expandable Edwards Sapien XT (Edwards Lifesciences, Irvine, CA, USA) aortic valve. The sizes of the valves used were 23 mm, 26 mm and 29 mm. It was decided with combined multimodal imaging methods like TTE, TEE and MCST.

Statistical analysis

All analyses were performed using SPSS version 19.0 (IBM Corporation, Armonk, NY). Continuous variables are presented as mean, standard deviation (SD) and were compared by means of a 2-sided students T-test. Categorical data were expressed as frequency (percentages) and compared using the χ^2 and Fisher's exact tests. Echocardiographic data obtained at baseline; discharge, 1st month and 6th month were compared by repeated measures ANOVA. Continuous variables were compared between patients before and after TAVI using the paired Student's t-test (for normally distributed variables) or the Wilcoxon test (for not-normally distributed variables). Significance was accepted as $p < 0.05$.

Results

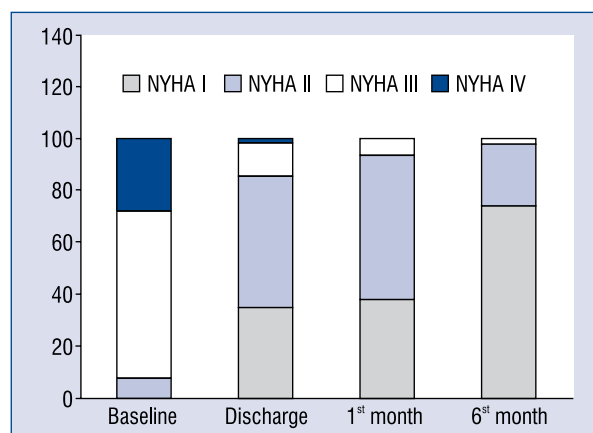
Patients

Demographic and clinical characteristics of the study population were presented in Table 1. The mean age of the patients was 77.8 ± 7.8 years. Thirty-eight point seven percent of the patients

Table 1. Basal characteristics and procedural features.

Patient characteristics	All patients (n = 75)
Male/female	38.7%/61.3%
Age [year]	77.8 ± 7.8
Body mass index [kg/m ²]	27.6 ± 5.2
NYHA II	8%
NYHA III	64%
NYHA IV	28%
STS	7.4 ± 5.6
SURTAVI:	
Low risk	9.3%
Moderate risk	33.3%
High risk	57.3%
EuroScore [%]	21.8 ± 16.5
Associated comorbid conditions	
Coronary artery disease	72.0%
Hypertension	81.3%
Diabetes mellitus	26.7%
Hyperlipidemia	45.3%
Smoker	20.0%
COPD:	
Mild	44.0%
Moderate	30.7%
Severe	22.7%
Peripheral arterial disease	30.7%
Atrial fibrillation	28.0%
Echocardiographic variables	
LVEDD [cm]	4.67 ± 0.7
LVESD [cm]	3.05 ± 0.9
IVS (cm)	1.33 ± 0.2
Posterior wall thickness [cm]	1.27 ± 0.1
Maximal gradient [mm Hg]	87.5 ± 23.2
Mean gradient [mm Hg]	53.3 ± 14.8
Aortic valve area [cm ²]	0.6 ± 0.1
LVEF [%]	54.2 ± 15.1
Peak SPAP [mm Hg]	47.2 ± 14.4
Aortic regurgitation:	
Mild	54.6%
Moderate	5.3%
Severe	1.3%
Mitral regurgitation:	
Mild	56.0%
Moderate	6.7%
Severe	1.3%
Femoral vascular closure	85.5%
Local anesthesia	80%
Valve diameter [mm]:	
23	40%
26	33%
29	2%
Contrast used [cc]	201.5 ± 55.7
Duration of discharge after procedure [day]	7.3 ± 5.3

NYHA — New York Heart Association; STS — Society of Thoracic Surgeons, COPD — chronic obstructive pulmonary disease; LVEDD — left ventricular end diastolic diameter; LVESD — left ventricular end systolic diameter; IVS — interventricular septum thickness; LVEF — left ventricular ejection fraction; SPAP — systolic pulmonary artery pressure


Figure 1. Changing functional capacity after transcatheter aortic valve implantation; NYHA — New York Heart Association.

were male, whereas 61.3% were female. According to New York Heart Association classification, 93% of the patients were in functional class III and IV (Fig. 1). Past history revealed coronary artery disease in 70%, hypertension in 82%, diabetes mellitus in 27%, and peripheral artery disease in 34% of the patients. The STS score of the patients was $7.3 \pm 5.2\%$ and mean logistic EuroSCORE was $21.8 \pm 16.5\%$. According to the SURTAVI risk model, 90.6% of patients were in the moderate and high risk groups.

Transcatheter aortic valve implantation

TAVI was performed with conventional technique under general (42 patients) and local anesthesia (33 patients). Acute procedural success rate was 100%. In all subjects, balloon-expandable Edwards Sapien XT (Edwards Lifesciences, Irvine, CA, USA) valve was deployed through femoral (72 patients) and subclavian artery (3 patients) route. Three valve sizes of 23 mm, 26 mm and 29 mm were available. Patients were heparinized during the procedure to achieve an activated clotting time of 250–300 s and all procedures were performed successfully. For access site closure, vascular closure devices were used in 72 patients while surgical closure was used in the remaining patients. Stable patients were discharged from the hospital and follow-ups at 1st and 6th months were planned. During the follow-ups, routine physical examinations, TTE and functional capacities were evaluated.

TAVI was performed by a 100% procedural success rate. However, a second valve has been required in 2 patients, first due to the lower locali-

Table 2. Changing left ventricular mass after transcatheter aortic valve implantation.

	P			P		
	Baseline	Discharge	1 st month	6 th month	Baseline vs. 1 st month	Baseline vs. 6 th month
LVEDD [cm]	4.67 ± 0.7	4.60 ± 0.6	4.57 ± 0.6	4.50 ± 0.5	0.018	0.192
LVEDS [cm]	3.05 ± 0.9	2.95 ± 0.8	2.90 ± 0.7	2.77 ± 0.5	0.034	0.419
IVS [cm]	1.33 ± 0.2	1.32 ± 0.2	1.29 ± 0.1	1.27 ± 0.1	0.669	0.034
PW [cm]	1.27 ± 0.1	1.26 ± 0.1	1.25 ± 0.1	1.20 ± 0.1	0.904	0.040
LVM [g]	236.5 ± 34.2	233.5 ± 34.8	228.3 ± 33.5	216.9 ± 22.9	0.102	0.002
LVMI [g/m ²]	127.9 ± 21.3	126.3 ± 22.2	123.3 ± 20.3	116.5 ± 14.7	0.129	0.001
LVEF [%]	54.2 ± 15.0	57.3 ± 11.7	59.5 ± 8.4	61.1 ± 6.7	< 0.001	0.002

LVEDD — left ventricular end diastolic diameter; LVEDS — left ventricular end systolic diameter; IVS — interventricular septum thickness; PW — posterior wall thickness; LVM — left ventricular mass; LVMI — left ventricular mass index; LVEF — left ventricular ejection fraction

zation and second due to valve embolization. After the procedure, totally 5 in-hospital mortalities were recognized because of the right ventricular rupture due to rapid pacing (in 2 patients), LV rupture due to wire in the LV, postoperative bleeding via supra-aortic approach and left main coronary artery obstruction due to the shift of aortic cusp calcification.

Transthoracic echocardiography results before and after the procedure

Transthoracic echocardiographic parameters at baseline and during follow-ups were shown in Table 2. Clinical follow-ups of all patients were done in our hospital. All patients had severe AS with a mean AVA of 0.62 ± 0.17 cm² and average mean aortic valve gradient of 53.3 ± 14.8 mm Hg. Mean baseline LVEF was 54.2 ± 15.1%.

Significant hemodynamic improvement has been observed after TAVI. Mean transvalvular aortic valve gradient decreased significantly from 53.3 ± 14.8 mm Hg to 9.22 ± 3.33 mm Hg, (p < 0.001). Also, a statistically significant increase was observed in LVEF compared to baseline at discharge, and in the 1st and 6th months of follow-ups (54.2 ± 15.0% vs. 57.3 ± 11.7% vs. 59.5 ± 8.4% vs. 61.1 ± 6.7%, respectively, p < 0.001). Both LVM and LVMI values decreased at discharge compared with baseline, but these did not reach statistical significance with value of p = 0.10 and p = 0.12, respectively. At 1st month, LVM (228.3 ± 22.9 g vs. 236.5 ± 34.2 g, respectively, p < 0.001) and LVMI (123.3 ± 20.3 g/m² vs 127.9 ± 21.3 g/m², respectively, p < 0.001) reduced significantly compared with baseline and also these regressions continued and reached the statistical significance at the 6th month of follow-up (p < 0.001) (Table 2, Fig. 2). During the 6th month of the follow-up, it was detected that diastolic diameter of LV posterior wall thickness regressed significantly from 1.27 ± 0.1 mm to 1.20 ± 0.1 mm (p < 0.001) in addition to interventricular septum diastolic wall thickness which regressed from 1.33 ± 0.1 mm to 1.27 ± 0.1 mm (p = 0.01).

Echocardiographic follow-ups were achieved in 95% and 85% of patients at 1st month and 6th month, respectively. A statistically significant improvement has been monitored in valve functions (mean gradient, AVA) at discharge and follow-ups after TAVI. There was no severe paravalvular aortic regurgitation in any patients after TAVI and at follow-ups. Only 4 (3.8%) patients required permanent pacemaker because of complete atrioventricular block. The length of mean hospital stay was 7.3 ± 5.3 days.

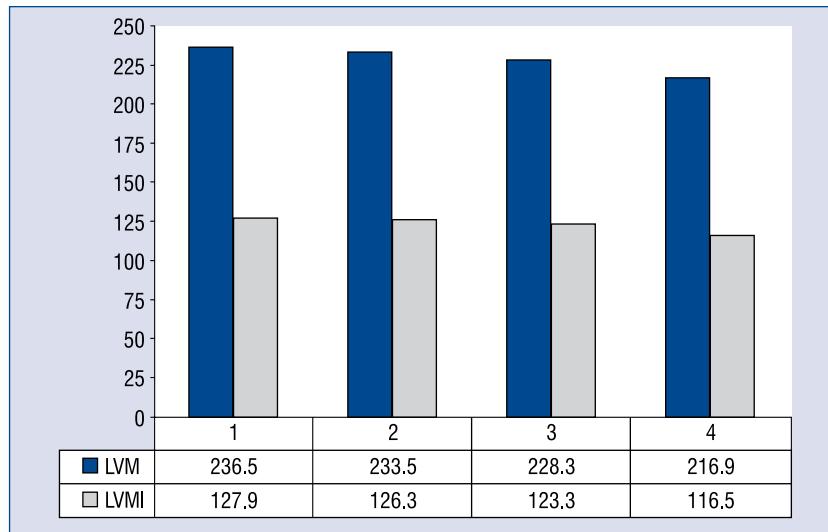


Figure 2. Changing left ventricular mass (LVM) and left ventricular mass index (LVMI) with transcatheter aortic valve implantation.

Discussion

Degenerative AS is one of the most common acquired valvular heart diseases. The mortality rate, especially in older patients, related to severe AS is high. The excessive pressure overload induced by AS results in LVH which in turn leads to an increased risk of heart failure, cerebrovascular accident and sudden cardiac death [9]. Therefore, the prognosis of patients with symptomatic AS accompanying severe LVH is worse.

Increase in LVM is an independent risk factor for adverse cardiovascular events and mortality [10, 11]. LVMI is an index used in the evaluation of LVH. It is known that, LVMI decreases with the reduction of LV afterload after s-AVR and as a result, improvement in myocardial ischemia, functional capacity and long-term prognosis is observed [12, 13]. The regression in LVMI after s-AVR is believed to be more important than valvular gradient as a prognostic factor [14–16]. The rate and magnitude of regression in LVMI can also be used as a distinctive parameter for reverse cardiac remodeling [17]. The decline of LVMI after s-AVR can differ depending on variables such as patient’s age, prosthesis size, valvular gradient, patient-prosthesis mismatch and surgical method. The long-term outcomes have been demonstrated to be better in patients showing rapid regression in LVH after surgery compared to others. In a vast majority of study, it was demonstrated that the regression of LVM after s-AVR is chiefly observed in the 1st year and, generally, the final measurement of regression

in LVM is accepted to be reached approximately in the first 6 months of follow-ups [16, 18–20].

In our study, we assessed the regression of LVH with the help of LVMI measured by echocardiography at discharge and in the 1st and 6th months after TAVI. LVMI was observed to be decreased significantly at 1st month after the procedure and during the clinical follow-ups compared to baseline values. Therefore, it can be propounded that the regression in LVMI and thus LVH after TAVI commences earlier and sustains during the clinical follow-ups compared to conventional s-AVR and thus will be able to reach the final values earlier. Here if we compare the conventional surgery with TAVI, we can observe that, due to the cardiopulmonary bypass, the early stage of hemodynamic effects depending on myocardial ischemia, myocardial edema and ischemia-reperfusion injury can be worse in the surgical method. The impaired diastolic functions depending on these causes can be associated with peri-operative adverse outcomes, especially in older patients [21, 22]. In a study comparing the TAVI and s-AVR in patients with AS, performed by Guarracino et al. [22], acute improvement observed in diastolic functions after TAVI had not been detected after s-AVR. They explained this by the impediment of the reduction in afterload due to the cardioplegia and cardiopulmonary bypass after s-AVR [22]. Gonçalves et al. [23] have showed the reduction of LV end-diastolic pressure with an invasive method just a minute after TAVI and detected this without any change in echocardiographic E/É’ratio [23].

Impaired LV diastolic function is an independent risk factor for early- and late-term mortality in patients with AS after s-AVR. AS leads to an increase in LV myocyte mass and additionally interstitial fibrosis. The regression of interstitial fibrosis can last long and normalization of diastolic functions can take a long time.

TAVI is performed in the older patients with high surgical risk and multiple co-morbid clinical conditions. Due to the early favorable hemodynamic effects and the retrieval of patients from cardiopulmonary bypass, it is believed to be superior compared with s-AVR. As it is shown in our study, the decrease in LVMI, which is the indicator of LVH in the early period and follow-ups after TAVI, can imply the usefulness and reliability of TAVI in patients with older age and co-morbid diseases.

Limitations of the study

The main limitation of our study was a small number of patients. The main reason of limited number of patients included into this study is the rarity of patients with AS convenient for TAVI. Therefore, larger scale studies are needed to confirm the beneficial effect of TAVI on LVH. The second issue is, although all echocardiographic examinations were performed by an experienced single operator, LVM measurement might be affected by some potential errors.

Conclusions

Our study demonstrated that TAVI is associated with a significant improvement on LVMI which is associated with LVH both in early period and follow-ups. TAVI is comparable to s-AVR in terms of LV reverse remodeling and superior to it due to the early favorable hemodynamic effects and the retrieval of patients from cardiopulmonary by-pass. TAVI significantly reduces the trans-aortic gradients and increases LVEF at discharge, and in the 1st and 6th months of follow-ups as well.

Conflict of interest: None declared

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