

# Immediate recovery of the left atrial and left ventricular diastolic function after transcatheter aortic valve implantation: A transesophageal echocardiography study

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## Abstract

**Background:** Chronic increased afterload due to severe aortic stenosis (AS) results in compensatory concentric left ventricular (LV) hypertrophy and LV dysfunction. These in turn cause remodeling of the left heart. The aim of this study was to investigate the acute effect of transcatheter aortic valve implantation (TAVI) on left atrial (LA) mechanics and LV diastolic function.

**Methods:** The study consisted of a total of 35 consecutive patients (mean age was  $77.7 \pm 5.0$  years, 25 female) undergoing TAVI. All TAVI procedures have been performed under the transesophageal echocardiography (TEE) guidance. Before and 24 h after TAVI, all patients underwent transthoracic echocardiography (TTE) and mitral inflow velocities with pulsed-wave (PW) Doppler including early filling wave (E), late diastolic filling wave (A), and E/A ratio were obtained. LV diastolic function was also explored by pulsed tissue Doppler imaging (TDI). Early (E') and late (A') diastolic annular velocities, E'/A' ratio and E/E' ratio were obtained. In addition, during the procedure before and minutes after the valve implantation, the left atrial appendage-peak antegrade flow velocity (LAA-PAFV) was measured and recorded with TEE.

**Results:** Compared with baseline, the mean mitral E, septal E' and E'/A' ratio increased significantly after TAVI. In addition, the LAA-PAFV increased significantly within minutes of TAVI ( $32.45 \pm 10.7$  cm/s vs.  $47.6 \pm 12.6$  cm/s,  $p < 0.001$ ).

**Conclusions:** TAVI improves LV diastolic function and LA performance immediately. (Cardiol J 2016; 23, 4: 449–455)

**Key words:** transcatheter aortic valve implantation, aortic valve stenosis, diastolic dysfunction, left atrial appendage function

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## Introduction

Aortic stenosis (AS) is the most commonly encountered valvular heart disease requiring surgery [1]. The raised pressure overload caused by AS, on left ventricle (LV) results in significant structural and functional changes, and affects the left atrium (LA) even before symptom development [2, 3]. Transcatheter aortic valve implantation (TAVI) has emerged as a promising alternative to surgical aortic valve replacement for patients with severe AS and prohibitive or high surgical risk [4]. Several studies have already shown the immediate almost complete normalization in afterload and a significant decrease in pressure gradient, between the aorta and the LV, as well as clinical improvement at short-term follow-ups after TAVI [5, 6]. However, so far, its acute impact on LA mechanics and LV diastolic function has not been demonstrated with the help of intra-procedural transesophageal echocardiography (TEE).

In this study, the authors' objective was to determine the acute effect of TAVI on LV diastolic function and LA performance, immediately after deployment of aortic bioprosthesis.

## Methods

### Patients

We prospectively enrolled 35 consecutive patients with severe symptomatic AS who underwent TAVI under TEE guidance in our clinic between July 2011 and March 2012. Operative risk of all patients was calculated based on Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) [7] and the Society of Thoracic Surgeon (STS) score [8], and/or clinical judgement. Written informed consent of each patient was obtained and the Ethics Committee of our hospital approved the study. The decision to proceed with TAVI was made by a multidisciplinary heart team including invasive cardiologists, cardiovascular surgeons, radiologists, and anesthesiologists. Before the procedure, transthoracic echocardiography (TTE), TEE and multi-slice computed tomography (MSCT) of the subjects were performed to evaluate the convenience and technique of TAVI.

### Transthoracic echocardiography and Doppler measurements

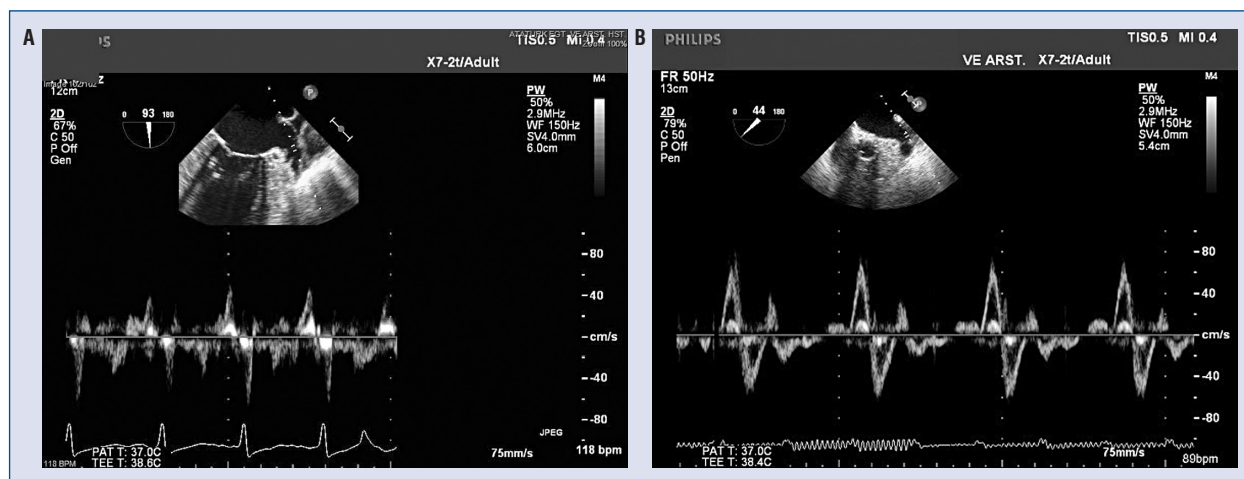
All patients underwent a comprehensive conventional TTE with 2-dimensional (2D), M-mode and Doppler assessment (IE33 echocardiography system, Philips Medical Systems, Eindhoven, the Neth-

erlands) before the TAVI procedure. For all measurements, 3 beats in patients with sinus rhythm and 5 beats in patients with atrial fibrillation (AF) were stored and off-line processed. All echocardiographic data were analyzed at the end of the data collection. Mean transvalvular gradient was calculated with Bernoulli formula and aortic valve area was measured by the continuity equation. Severe AS was defined as a mean transaortic pressure gradient  $> 40$  mm Hg or aortic valve area  $< 1$  cm<sup>2</sup> [9]. LV ejection fraction was calculated from apical views using the biplane Simpson's method. LV mass (LVM) was calculated by Devereux formula [10] and LVM index (LVMI) was calculated by dividing LVM by body surface area using Mosteller formula [11]. LV hypertrophy was defined as LVMI  $> 95$  g/m<sup>2</sup> for women and LVMI  $> 115$  g/m<sup>2</sup> for men. LA enlargement was determined by LA volume that was estimated by biplane 2D echocardiography using the modified Simpson's rule [12]. Normal LA volume indexed to body surface area was defined as  $< 34$  mL/m<sup>2</sup> and LA enlargement was considered over this value.

To assess LV diastolic function from the beginning to the end of the procedure, modified American Society of Echocardiography recommendations with the use of the tissue Doppler parameters were used [13]. Pulsed-wave (PW) Doppler was performed in the apical 4-chamber view to obtain mitral inflow velocities to assess LV diastolic function. A 1-mm to 3-mm sample volume was placed between mitral leaflet tips during diastole, as recommended [13]. Measurements of mitral inflow included the peak of early filling wave (E), late diastolic filling wave (A) and the E/A ratio were obtained. LV diastolic function was also explored by pulsed tissue Doppler imaging (TDI), placing the sample volume at the level of mitral lateral and septal annulus from the apical 4-chamber view [14]. Early (E') and late (A') diastolic annular velocities were obtained. The E'/A' ratio was used as load-independent marker of LV diastolic relaxation [15]. The A and A' waves could not be obtained in patients with AF. Therefore E/A, E'/A', and septal A' were measured in 25 patients. The E/E' ratio was also obtained as a reliable index of LV filling pressures [16].

### Transcatheter aortic valve implantation

Transcatheter aortic valve implantation was performed at the catheterization laboratory with fluoroscopy and TEE guidance and all under general anesthesia using conventional technique. Thirty-four (97%) patients through femoral artery and



**Figure 1.** Left atrial appendage peak antegrade flow velocity measured during the procedure before (A) and minutes after (B) transcatheter aortic valve implantation with help of transesophageal echocardiography.

1 (3%) patient through subclavian artery received a balloon expandable Edwards SAPIEN (Edwards Lifesciences, Irvine, CA, USA) aortic valve. The sizes of the valves used were 23 mm and 26 mm and it was decided with combined multimodal imaging methods like TTE, TEE and MCST.

### Transesophageal echocardiography measurements

During the procedure, left atrial appendage-peak antegrade flow velocity (LAA-PAFV) with TEE (IE33 echocardiography system, X7-2t probe, 7 MHz, Philips Medical Systems, Eindhoven, the Netherlands) was measured and recorded. TEE was performed just before the intervention and it was repeated few minutes after the valve deployment ( $4.8 \pm 1.7$  min) to compare between TEE results before and after TAVI. PW spectral Doppler was recorded in mid-esophageal basal short-axis view at aortic valve level ( $30\text{--}60^\circ$ ) to assess the LAA-PAFV which was calculated by placing PW Doppler cursor in the LAA 2 mm from its orifice (Fig. 1). In sinus rhythm, LAA-PAFV was calculated as the average of the 3 highest velocities, whereas in patients with AF, the average of 5 cardiac cycles was used.

After the valve implantation, the presence of complications like cardiac effusion or tamponade, aortic regurgitation, valve displacement, LV wall motion abnormalities, and mitral valve injury were described [17]. Data expected to interfere with diastolic function parameters like systolic or diastolic blood pressure, heart rate, and hemoglobin level were assessed before the procedure and few minutes after the valve deployment.

### Statistical analysis

Statistics were calculated using SPSS version 19.0 (IBM Corporation, Armonk, NY). Categorical variables were expressed as percentages and continuous variables as mean (standard deviation). A multivariate covariance analysis was also performed to evaluate the influence of potential confounders on main outcome variables. A probability value of  $p < 0.05$  was considered statistically significant.

## Results

### Baseline characteristics

The baseline characteristic features of the patients were presented in Table 1. Of the consecutive 35 study patients, 25 (71.4%) were female. The mean age was  $77.7 \pm 5.0$  years. The mean body mass index was  $30.0 \pm 10.6$  kg/m<sup>2</sup>. Twenty-eight point six percent of patients had AF and 42% of patients had chronic renal failure (defined as glomerular filtration rate  $< 60$  mL/min/1.73 m<sup>2</sup>) before the procedure. Also, pulmonary hypertension (defined as systolic pulmonary artery pressure  $> 40$  mm Hg) was present in 48% of patients. According to the New York Heart Association classification, 74.3% of patients were in functional class III. The valve was successfully deployed in all patients.

### Conventional transthoracic and transesophageal echocardiography

All standard echocardiographic findings were shown in Table 2. After the valve deployment, the peak and mean transaortic systolic gradients, effective orifice area, and LV ejection fraction improved

**Table 1.** Baseline characteristic features of the patients.

Variables	N = 35
Age [years]	77.7 ± 5.0
Female	71.4%
Body mass index [kg/m <sup>2</sup> ]	30.0 ± 10.6
Logistic EuroSCORE [%]	18.1 ± 13.7
STS score [%]	7.0 ± 3.7
Hypertension	80%
Diabetes mellitus	25.7%
Dyslipidemia	45.7%
Coronary artery disease	68.6%
Previous PCI	20%
Prior CABG	28.6%
Atrial fibrillation	28.6%
NYHA functional class:	
I	None
II	14.3%
III	74.3%
IV	11.4%
COPD	55.9%
Renal impairment	42%
Creatinine [mg/dL]	1.0 ± 0.41
Pulmonary hypertension	48%
LA enlargement	82.8%
LV hypertrophy	71.4%
Diastolic dysfunction*:	
Grade I	34.3%
Grade II	20.0%
Grade III	45.7%

\*Grading concerns only the patients with sinus rhythm; CABG — coronary artery bypass grafting; COPD — chronic obstructive pulmonary disease; EuroSCORE — European System for Cardiac Operative Risk Evaluation; LA — left atrial; LV — left ventricular; NYHA — New York Heart Association; PCI — percutaneous coronary intervention; STS — Society of Thoracic Surgeons

significantly. There were no statistically significant differences between the baseline examination and the examination after TAVI regarding LVMI, A wave, E/A ratio, septal A', and E/E' ratio. However, the parameters indicating early diastolic LV filling improved significantly: mean E (1.0 ± 0.38 m/s vs. 1.2 ± 0.34 m/s, respectively, p = 0.003) and septal E' (5.4 ± 1.7 cm/s vs. 6.9 ± 2.4 cm/s, respectively, p = 0.001) increased. Furthermore, the load-independent marker of ventricular diastolic relaxation, E'/A' ratio increased significantly as well (0.76 ± 0.21 vs. 1.02 ± 0.42, respectively, p < 0.001).

When we analyzed the LAA-PAFV measured during the procedure with the help of TEE before

and minutes after TAVI, we realized that it has been significantly improved after valve deployment (32.45 ± 10.7 cm/s vs. 47.6 ± 12.61 cm/s, respectively, p < 0.001). In order to assess the influence of potential confounders on main outcome variables, a multivariate covariance analysis was performed. We found a significant increase in the E wave and LAA-PAFV in the study population (Table 3).

## Discussion

In long-standing severe AS, a time-related structural and histologic remodeling occurs both in the LV, LA, and thereafter in the LAA. LV diastolic dysfunction caused by AS is well established [18, 19] and is related with LA dilatation which is assumed an indicator of severity and chronicity of diastolic dysfunction, as well as the magnitude of LA pressure rise [20–22]. During the diastolic period of left heart, the LA is directly exposed to LV pressure through the open mitral valve, thus it is affected by the chronic pressure rise resulting in increased LV filling pressures [23]. Therefore, many studies to date have come to the conclusion that the state of LA reflects the diastolic function of the LV [24, 25]. LA dysfunction in AS has been shown to predict mortality, indirectly enforcing the significance of raised LA pressure on the clinical outcome of patients with AS [26].

Decreased velocities of LAA in patients with AS can be observed in the presence of elevated LA pressure [27]. In addition, conditions that increase the LV filling pressure like AS impairs LAA flow [28]. Likewise, in patients with disturbed diastolic function, increasing LV end-diastolic pressure and LA pressure give rise to decrease in antegrade flow velocities of LAA [29]. Due to this fact, the loss of contractile elements of LAA may result in its reduced mechanical function which could be expressed in low LAA flow velocity profile. Various studies have proven LAA-PAFV to be a valuable means by which the structure and function of the LA may be predicted. More specifically, the studies have claimed that larger LA and LAA sizes are associated with lower LAA flow velocity [30]. TEE is the most widely used method for the evaluation of the LAA morphology and flow patterns within it. Therefore, in this study, we have used intra-procedural TEE to assess LAA-PAFV and we observed a significant increase in LAA-PAFV minutes after TAVI. Thus, we concluded that TAVI improves LA performance and this in turn improves LV diastolic function immediately.



**Table 2.** Conventional echocardiographic results before and after the procedure (n = 35).

Variables	Baseline	After TAVI	P
<b>Transthoracic echocardiographic variables</b>			
Aortic valve			
Maximum systolic gradient [mm Hg]	87.2 ± 20.3	18.2 ± 4.3	< 0.001
Mean systolic gradient [mm Hg]	54.1 ± 15.1	9.1 ± 2.4	< 0.001
Effective orifice area [cm <sup>2</sup> ]	0.62 ± 0.16	2.0 ± 0.28	< 0.001
Left ventricular ejection fraction [%]	54.4 ± 12.7	57.5 ± 9.6	0.039
Left ventricular mass index [g/m <sup>2</sup> ]	137.9 ± 34.5	138.4 ± 28.5	0.881
Degree of mitral regurgitation [%]:			NS
Mild	68.6	84.4	
Moderate	28.6	15.6	
Severe	2.9	None	
E [m/s]	1.0 ± 0.38	1.2 ± 0.34	0.003
A† [m/s]	0.91 ± 0.36	0.92 ± 0.4	0.491
E/A† ratio	1.19 ± 0.6	1.2 ± 0.6	0.815
Septal E' [cm/s]	5.4 ± 1.7	6.9 ± 2.4	0.001
Septal A'† [cm/s]	7.1 ± 3.8	6.7 ± 3.2	0.641
E'/A'† ratio	0.76 ± 0.21	1.02 ± 0.42	< 0.001
E/E' ratio	20.1 ± 8.1	20.9 ± 7.5	0.718
<b>Transesophageal echocardiographic variables</b>			
Degree of aortic regurgitation [%]:			NS
Absent or mild	77.2	94.3	
Medium	20	5.7	
Severe	2.8	None	
Mean LAA-PAF [cm/s]	32.45 ± 10.7	47.6 ± 12.6	< 0.001

†Evaluated only in patients with sinus rhythm; A — atrial flow velocity; A' — peak late diastolic velocity; E — mitral peak early diastolic velocity; E' — peak early diastolic velocity; LAA-PAF — left atrial appendage peak antegrade flow

**Table 3.** Covariance multivariate analysis of clinical parameters during the procedure (n = 35).

Variables	Baseline <sup>a</sup>	Minutes after TAVI <sup>a</sup>	Difference of means (95% CI)	P
E wave [m/s]	1.00 (0.88; 1.12)	1.09 (0.9; 1.2)	0.09 (−0.17; 0.03)	< 0.001 <sup>b</sup>
LAA-PAF [cm/s]	32.4 (28.7; 36.1)	47.6 (43.2; 51.9)	15.2 (−18.4; −11.7)	< 0.001 <sup>b</sup>
E/A ratio	1.19 (0.91; 1.47)	1.24 (0.9; 1.5)	0.05 (−0.38; 0.30)	0.143
Septal E' [cm/s]	0.052 (0.048; 0.057)	0.053 (0.050; 0.057)	0.001 (−0.006; 0.003)	0.052
E/E' ratio	20.1 (17.3; 22.9)	20.9 (18.3; 23.6)	0.08 (−3.35; 2.33)	0.718
E'/A' ratio	0.76 (0.68; 0.84)	1.02 (0.93; 1.12)	0.26 (−0.32; −0.14)	< 0.001

<sup>a</sup>Data presented as adjusted mean (95% confidence interval); <sup>b</sup>Univariate — none of the confounder had a significant effect on the mean E wave and mean LAA-PAF variation during the procedure; LAA-PAF — left atrial appendix-peak antegrade flow

After TAVI, almost complete normalization of LV afterload occurs without significant variability among patients [5, 6]. Normalization of LV diastolic function [31] and benefit in ejection fraction, volumes, and hypertrophy are observed at long-term follow-up [32]. Gotzmann et al. [33]

have determined improvement in diastolic function at 6-month follow-up in patients undergoing TAVI with CoreValve prosthesis.

The significant increase in LV E, E', and E'/A' ratio observed 24 h after TAVI and also significant increase in LAA-PAFV minutes after TAVI may

imply an immediate improvement of LV diastolic function in our study. The increase in maximum E velocity may be explained by alterations in preload or in LV relaxation. The augmented LA-LV pressure during early diastole and the augmented E wave, are the consequence of an ameliorated LV relaxation, in response to immediate, complete and sustained afterload release.

Bauer et al. [34] demonstrated an increase in E' and A' measured by pulsed TDI in LV septal wall but no difference in LV diastolic function measured by blood flow Doppler echocardiography when they examined the patients 24 h post-procedurally. After TAVI, our patients showed significant increases in effective orifice area and marked decreases in transvalvular pressure gradients, equivalent to a reduction in LV afterload [35]. In addition, E and E' increased significantly after TAVI. These results are consistent with previously published data from Gonçalves et al. [35] and Guarracino et al. [36], who measured LV relaxation parameters within minutes of TAVI.

Our main findings were those of immediate improvement of LV diastolic function and increase in LA hemodynamics in the minutes of valve deployment. TAVI gives rise to a unique opportunity regarding the assessment of LV diastolic function immediately after afterload release and the observed improvement is in concert with the expectations from the Frank-Starling law.

This study is, to the best of our knowledge, the first to examine the early recovery of LV diastolic function and LA performance after TAVI through comprehensive interpretation of echocardiographic findings including LAA-PAFV with TEE. We observed that after the release of chronic pressure overload with TAVI, an immediate improvement has occurred in diastolic function of the left heart. Our results shed light on the direct relationship between the mechanical function of LAA, LA and LV diastolic function in patients with severe AS.

### Limitations of the study

The main limitation of our study is the limited number of patients. The reason for relatively small number of the patients conducted into our study is that we performed TAVI only to the first 35 patients with TEE. After that, due to no need for TEE guidance, other patients underwent TAVI without it.

### Conclusions

From these results we concluded that LA and LAA functions decrease in patients with severe AS and LV diastolic dysfunction. TAVI results in

early recovery of LA performance and LV diastolic function immediately after relieving LV afterload. An acute rise in LAA peak antegrade flow velocity is associated with improvement of LA mechanics and LV diastolic function. However, whether our results are persistent or transient is unknown and they should be evaluated with large scale studies.

**Conflict of interest:** None declared

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