

Short-term effects of transcatheter aortic valve implantation on left atrial appendage function

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Abstract

Background: *The beneficial effects of the transcatheter aortic valve implantation (TAVI) on echocardiographic parameters including left atrial (LA) and left ventricular (LV) functions were described by previous studies. The aim of this study was to analyze the effects of TAVI on left atrial appendage (LAA) function assessed by transthoracic and transesophageal echocardiography.*

Methods: *Fifty-five patients with severe symptomatic aortic stenosis were included in this prospective study. LAA early and late emptying velocities, LAA filling velocity, peak early diastolic (E_M), late diastolic (A_M), and systolic (S_M) velocities were measured with pulsed wave Doppler and tissue Doppler imaging, and E/E_m ratio was calculated before and 7.1 ± 2.8 days after TAVI. A subgroup analysis was performed in accordance with the left ventricular ejection fraction (LVEF) of the patients and the severity of their LV diastolic dysfunction.*

Results: *Although the post-procedure peaks and mean gradients of the patients decreased significantly, the LVEF increased significantly in those who had low LVEF before the procedure. The post-procedure E/E_m ratio decreased significantly ($p < 0.001$). The post-procedural LAA mean filling velocity and E_M velocity were significantly higher than the pre-procedural filling velocity ($p < 0.001$, $p = 0.002$, respectively). In the subgroup analysis, the post-procedural LAA filling velocity, early and late LAA emptying velocities, in addition to the mean velocity of the E_M , A_M , and S_M were significantly higher than before the procedure in patients with LVEF of $< 50\%$ and E/E_m ratios of > 15 .*

Conclusions: *LAA function improved soon after the TAVI procedure, especially in patients with low LVEF and marked LV diastolic dysfunction. (Cardiol J 2015; 22, 5: 527–534)*

Key words: transcatheter aortic valve implantation, left atrial appendage, echocardiography

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Introduction

Aortic stenosis (AS) leads to severe left ventricular (LV) hypertrophy and impaired relaxation of the LV, resulting in LV diastolic dysfunction [1]. In advanced-stage AS, the contractile functions of myocardial cells are reduced and LV systolic functions are impaired. The subsequent chronic pressure and volume overload into the LV adversely affect the functions of the left atrial (LA) and the LA appendage (LAA) [2, 3].

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative method of surgical aortic valve replacement for symptomatic patients with severe AS and with very high or prohibitive operative risks [4]. Recent studies that used speckle-tracking echocardiography reported an improvement in some LA functions after TAVI in high-risk AS patients [5–7]. Although the beneficial effect of TAVI on clinical and echocardiographic hemodynamic parameters is well known, there are no data in the literature regarding the effect of this procedure on LAA functions. In this study, the functions of the LAA were compared before and approximately 1 week after the TAVI procedure pulsed wave (PW) Doppler and the tissue Doppler imaging (TDI) with transesophageal echocardiography (TEE) technique.

Methods

Study design and patient selection: This study enrolled 78 consecutive patients from January 2011 to December 2014 who had symptomatic aortic valve stenosis New York Heart Association (NYHA) functional class \geq II and documented calcific aortic valve stenosis, with an initial aortic valve area (AVA) of $< 1.0 \text{ cm}^2$ (or an AVA index of $< 0.6 \text{ cm}^2/\text{m}^2$) and a mean pressure gradient of $> 40 \text{ mm Hg}$ or a jet velocity of $> 4 \text{ m/s}$, as measured by transthoracic echocardiography (TTE). The patients were deemed high risk based on the Society of Thoracic Surgery (STS) score of $\geq 10\%$, a logistic EuroSCORE of $\geq 20\%$, or agreement by a multidisciplinary heart team that frailty and/or coexisting comorbidities would be associated with a high surgical risk [8, 9]. The study's exclusion criteria were the following: a congenital unicuspid or bicuspid aortic valve, an acute myocardial infarction, a transient ischemic attack, or a stroke within previous 6 months. Additional exclusion criteria were any permanent neurological defects, severe renal insufficiency, a pre-existing prosthetic heart valve or a prosthetic ring in any position, more

than moderate ($> 3+$) mitral regurgitation or aortic regurgitation, untreated clinically significant coronary artery disease and a documented LV ejection fraction (LVEF) below 30%. In patients with a thrombus or severe spontaneous echo contrast ($> 2+$) in the LAA, which is a contraindication for the TAVI procedure, were excluded from this study. After the initial evaluation, 23 subjects were excluded from further analysis. Finally, 55 patients were included in the study. Patient demographics and medical history were obtained by the attending physicians. The Edwards Sapien XT transcatheter aortic valve system (Edwards Life Sciences, Irvine, CA, US) was used in all cases, with the patients under general anesthesia. The study complied with the Declaration of Helsinki, and the trial protocol was approved by the Institutional Ethics Committee of the hospital.

Echocardiographic study

All the patients underwent TTE and TEE (General Electric Vivid 7 GE Vingmed Ultrasound AS, Horten, Norway) before the procedure and again the first week after TAVI, according to the recommendations of the American Society of Echocardiography [10–11]. Two independent experienced physicians who were blinded to the patients' clinical characteristics performed all the echocardiographic measurements. The patients' blood pressure was measured prior to all of the procedures.

TTE parameters

LV systolic function was assessed by calculating the patients' LVEF with 4-chamber Simpson's method. LV diastolic performance was evaluated using PW Doppler and TDI. The LV diastolic inflow velocities were obtained from the apical 4-chamber view by placing the sample volume at the level of the mitral valve tip. Peak early diastolic flow (E) and peak atrial filling flow velocities (A) were measured. TDI of the velocities of longitudinal mitral annular motion were recorded at the septal and lateral mitral annular borders, the average of the results obtained. The early diastolic (E_m), and late diastolic (A_m) Doppler tissue velocities of the mitral annulus were measured, and the ratio of mitral inflow E velocity to tissue Doppler (E/E_m) for both septal and lateral walls was calculated, the average of the results was obtained.

TEE parameters

All the patients were instructed not to take water or food for at least 4 h. The patients' oro-

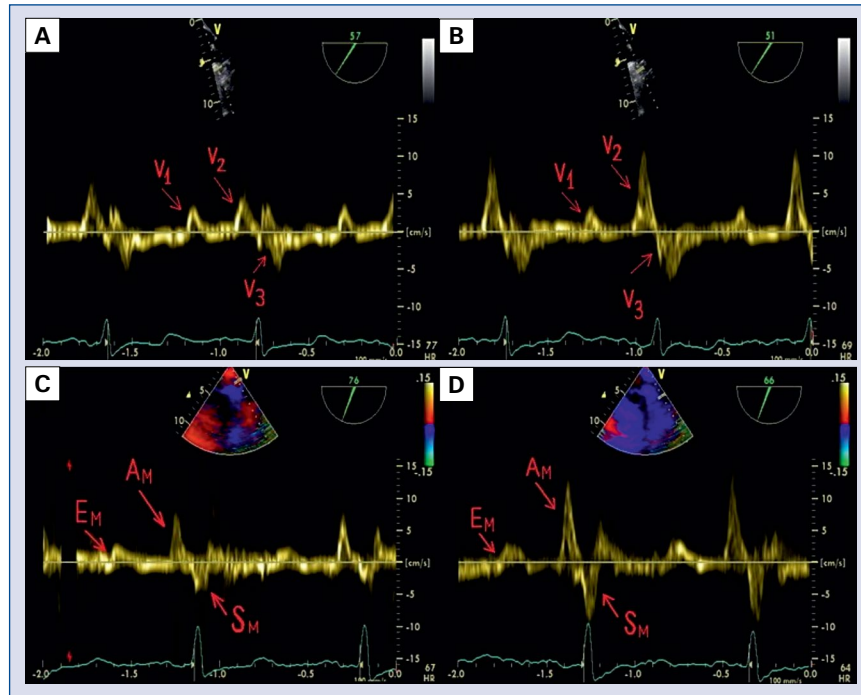


Figure 1. Effect of transcatheter aortic valve implantation on left atrial appendage Doppler velocities: before (A), after (B) and Doppler tissue velocities: before (C), after (D).

pharynx was anesthetized with a topical lidocaine 10% spray. Sedation with midazolam was used if needed. TEE was performed with a 5 MHz multiplane transesophageal probe. The LAA was visualized in the mid-esophageal 2-chamber view by rotation of the imaging sector from 50° to 90°. The LAA emptying and filling flow velocities were also recorded by PW Doppler, with a 2 × 2 mm sampling volume placed at the one-third proximal position of the LAA cavity. During the assessment of LAA flow, 2 blood flow velocities were evaluated. An early diastolic outflow wave observed before the electrocardiographic P wave was termed V₁. Biphasic waves following V₁ subsequent to the P wave were termed V₂ (late emptying flow velocity) and V₃ (filling flow velocity) (Fig. 1). The peak flow velocities of the V₁, V₂, and V₃ waves were measured.

LAA TDI velocities

In the TDI analysis, the spectral mode of the PW Doppler sample volume of the LAA lateral wall was placed midway between the LAA tip and outlet. In sinus rhythm, 3 distinct velocities were recorded. The first positive wave after the electrocardiographic P wave was termed A_M, followed by a negative wave (S_M), which coincided with LV contraction, and then a positive wave (E_M) during

LV relaxation. A representative illustration of the LAA TDI velocities of a patient pre- and post-TAVI is shown in Figure 1.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation. Categorical variables were expressed as frequencies and/or percentages. The Kolmogorov–Smirnov test was used to evaluate whether the continuous variables were normally distributed. The “paired samples test” was used to compare the before and after TAVI procedure results. A p value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were carried out using the Number Cruncher Statistical System 2007 Statistical Software (Utah, USA).

Results

The baseline characteristics of the study patients are presented in Table 1. The mean age was 77.3 ± 6.9 years, and 36 (65%) patients were female. The mean logistic EuroSCORE and STS score were 27.5 ± 14.2 and 12.3 ± 6.6, respectively. Before the TAVI procedure, the diameter of the LA was 43.7 ± 6.0 mm and that of the aortic valve effective orifice area was 0.76 ± 0.17 cm². When systolic blood pressures were compared in

Table 1. Baseline patient characteristics (n = 55).

Variable	Value
Age [years]	77.3 ± 6.9
Female	36 (65%)
Logistic EuroSCORE [%]	27.5 ± 14.2
STS score [%]	12.3 ± 6.6
Body mass index [kg/m ²]	28.0 ± 4.5
Hypertension	39 (70%)
Diabetes	26 (47%)
Coronary artery disease	33 (60%)
Cerebrovascular event	4 (7%)
Smoker	18 (32%)
Creatinine [mg/dL]	1.0 ± 0.7
LDL-C [mg/dL]	111 ± 35
WBC [k/mm ³]	7.0 ± 1.7
HGB [g/dL]	11.8 ± 1.6
LVEF < 50%	21 (39%)
LVDD (E/E _m > 15)	22 (40%)
Effective orifice area [cm ²]	0.76 ± 0.17
LA diameter [mm]	43.7 ± 6.0
Time to echocardiography after implantation [days]	7.1 ± 2.8
Aortic valve prosthesis: — Edwards SAPIEN XT:	
23 mm	18 (32.7%)
26 mm	23 (41.8%)
29 mm	14 (25.5%)
LA diameter [mm]	43.7 ± 6.0
SBP [mm Hg]:	P = 0.106
Before	125 ± 12.3
After	132 ± 13.1

Mean values (standard deviation) and % (n) are reported for continuous and categorical variables; STS — Society of Thoracic Surgery score; LDL-C — low density lipoprotein cholesterol; WBC — white blood cell; HGB — hemoglobin; LVEF — left ventricular ejection fraction; LVDD — left ventricular diastolic dysfunction; LA — left atrium; SBP — systolic blood pressure

terms of before vs. after TAVI procedure, no significant differences were found (before: 125 ± 12.3 mm Hg vs. after: 132 ± 13.1 mm Hg, p = 0.106).

TTE

TTE 2-dimensional and Doppler parameters before and after the procedure are given in Table 2. The mean and peak pressure gradients were significantly reduced after the TAVI procedure (p < 0.001). Moreover, there was no difference between pre- and post-procedural LVEFs in the patients with AS (p = 0.054). However, in the subgroup analysis,

the post-procedural LVEF was higher in the low LVEF group (p = 0.003). The post-procedural means of the E/E_m were also significantly lower compared to the pre-procedural means (p < 0.001).

TEE

The comparison of the TEE PW Doppler and TDI parameters of pre- and post-procedural LAA functions in all the patients is reported in Table 2. Subgroup analyses were performed based on the LVEF (LVEF < 50% and LVEF > 50%) (Table 3) and diastolic dysfunction parameters (E/E_m > 15 and E/E_m < 15) of the patients (Table 4). The post-procedural means of LAA filling velocities were significantly higher compared to the pre-procedural means in all study groups (p < 0.001). When the results of the subgroup analyses of the low and preserved LVEF groups were compared, the post-procedural means of LAA filling velocities were significantly higher compared to the pre-procedural means in both the low and preserved LVEF groups (p = 0.001 and p = 0.021, respectively). In the low LVEF group, the post-procedural means of the LAA early and late emptying velocities were significantly higher compared to the pre-procedural means (p = 0.022 and p = 0.036, respectively). However, the post-procedural means of the LAA early and late emptying velocities were not different from the pre-procedural means in the preserved LVEF group. In the TDI analysis, although the post-procedural velocities of the peak early diastolic (E_M), peak late diastolic (A_M), and peak systolic (S_M) were increased, only the increase in the E_M velocity was significantly higher (p = 0.002). In the subgroup analysis, the post-procedural velocities of E_M, A_M, and S_M were significantly increased in the low LVEF group (Table 3). Despite the increase in the post-procedural velocities of these parameters, there was no significant difference between the pre- and post-procedural velocities in the preserved LVEF group (Table 3). Moreover, the post-procedural means of LAA filling, early and late emptying velocities were significantly higher than the pre-procedural means in the patients with diastolic dysfunction (E/E_m > 15). In the TDI analysis, the post-procedural velocities of E_M, A_M, and S_M were significantly increased in the patients with diastolic dysfunction (E/E_m > 15) (Table 4). However, there was no significant difference in the post-procedural LAA filling and emptying velocities or the LAA tissue Doppler velocities in the patients with preserved diastolic function (E/E_m < 15) (Table 4).

Table 2. Comparison of TTE and TEE variables before and after TAVI.

	Before	After	P
TTE: 2D and Doppler parameters			
LVEF [%]:			
All	53.1 ± 12.3	54.3 ± 10.2	0.054
< 50%	39.4 ± 8.4	43.1 ± 7.2	0.003
> 50%	61.6 ± 3.2	61.2 ± 3.6	0.319
Peak aortic gradient [mm Hg]	84.2 ± 21.7	18.8 ± 9.6	< 0.001
Mean aortic gradient [mm Hg]	52.8 ± 14.3	10.3 ± 5.0	< 0.001
E velocity [cm/s]	95.5 ± 34.3	91.0 ± 32.7	0.230
E _m velocity [cm/s]	7.1 ± 2.1	8.0 ± 2.2	< 0.001
E/E _m	13.7 ± 4.6	11.5 ± 4.1	< 0.001
TEE: Doppler and TDI parameters			
LAA emptying velocity [cm/s]	37.8 ± 16.1	39.5 ± 16.1	0.129
LAA filling velocity [cm/s]	38.8 ± 10.6	42.3 ± 12.0	< 0.001
E _M [cm/s]	7.8 ± 3.8	8.9 ± 4.0	0.002
A _M [cm/s]	14.4 ± 6.1	15.6 ± 6.2	0.065
S _M [cm/s]	13.1 ± 6.0	14.2 ± 6.3	0.091

Mean values (standard deviation) are reported for continuous variables; TTE — transthoracic echocardiography; TEE — transesophageal echocardiography; TAVI — transcatheter aortic valve implantation; LAA — left atrial appendage; TDI — tissue Doppler imaging

Table 3. Comparison of LAA function before and after TAVI by TEE with LVEF.

Parameter	Before	After	P
LVEF > 50%			
LAA emptying velocity [cm/s]	46.0 ± 14.0	46.8 ± 15.8	0.578
LAA filling velocity [cm/s]	43.3 ± 9.9	45.8 ± 11.7	0.021
E _M [cm/s]	9.4 ± 3.5	10.1 ± 3.7	0.182
A _M [cm/s]	16.9 ± 5.4	17.5 ± 6.1	0.533
S _M [cm/s]	16.0 ± 5.7	16.1 ± 6.7	0.865
LVEF < 50%			
LAA emptying velocity [cm/s]	24.6 ± 9.0	27.6 ± 7.2	0.036
LAA filling velocity [cm/s]	31.5 ± 7.4	36.6 ± 10.3	0.001
E _M [cm/s]	5.2 ± 2.6	7.2 ± 3.7	< 0.001
A _M [cm/s]	9.2 ± 3.6	11.8 ± 4.6	0.007
S _M [cm/s]	8.6 ± 2.9	11.0 ± 3.9	< 0.001

Mean values (standard deviation) are reported for continuous variables. LAA — left atrial appendage; TEE — transesophageal echocardiography; TAVI — transcatheter aortic valve implantation; LVEF — left ventricular ejection fraction

Discussion

Previous studies described the beneficial effects of the TAVI procedure on clinical, hemodynamic, and echocardiographic parameters including LA and LV functions, in patients with severe AS [12–15]. However, there are no data in the literature regarding the effects of TAVI on the functions of the LAA. In this study, we used TTE and TEE to

evaluate pre- and post-procedural (7.1 ± 2.8 days) LAA functions. We demonstrated, for the first time, an improvement in LAA functions detected by PW Doppler and TDI approximately 1 week after the TAVI procedure, especially in patients with marked diastolic dysfunction (E/E_m > 15) and a low LVEF (< 50%).

In advanced-stage AS, volume overload, which is caused by a depressed LVEF, impairs LA and

Table 4. Comparison of LAA function before and after TAVI by TEE with E/E_m.

Parameter	Before	After	P
E/E_m > 15			
LAA emptying velocity [cm/s]	30.6 ± 13.4	36.1 ± 16.7	0.001
LAA filling velocity [cm/s]	35.5 ± 9.8	41.7 ± 11.4	< 0.001
E _M [cm/s]	6.6 ± 3.0	9.0 ± 3.7	< 0.001
A _M [cm/s]	11.8 ± 4.9	15.2 ± 6.0	< 0.001
S _M [cm/s]	11.3 ± 5.3	14.3 ± 6.1	< 0.001
E/E_m < 15			
LAA emptying velocity [cm/s]	42.6 ± 16.1	41.8 ± 15.6	0.552
LAA filling velocity [cm/s]	41.0 ± 10.7	42.7 ± 12.5	0.091
E _M [cm/s]	8.6 ± 4.0	8.9 ± 4.2	0.490
A _M [cm/s]	15.9 ± 6.3	15.8 ± 6.4	0.829
S _M [cm/s]	14.4 ± 6.2	14.0 ± 6.5	0.683

Mean values (standard deviation) are reported for continuous variables; LAA — left atrial appendage; TEE — transesophageal echocardiography; TAVI — transcatheter aortic valve implantation

LAA functions. This impairment leads to a decrease in the LAA velocities, the LAA Doppler tissue velocities, and the mechanical functions between the LA–LAA [2, 16, 17]. LV function is an important predictor of LAA velocity. A previous study reported a relationship between a low LVEF and LAA dysfunction. Moreover, reduced LAA velocities in non-valvular atrial fibrillation and LV systolic dysfunction were presented in recent studies [18–20].

Transcatheter valve implantation offers a new treatment modality for patients who have multiple comorbidities that make conventional surgery a high risk [21]. Recent studies reported an improvement in LA functions after the TAVI procedure in high-risk patients with systolic and diastolic dysfunction [5–7]. In the present study, the amelioration of LAA functions soon after the TAVI procedure may have been due to the marked and beneficial effects of the procedure on hemodynamic and echocardiographic parameters.

D’Andrea et al. [5] have recently used speckle-tracking echocardiography to demonstrate an improvement in the LA longitudinal function of patients with severe AS 6 months after they had undergone the TAVI procedure. Spethmann et al. [7] demonstrated that a global and regional LV and LA mechanics improved 12 months after TAVI. LA function was evaluated with speckle-tracking echocardiography in previous TAVI studies [5–7]. To the best of our knowledge, this is the first study to assess LAA functions after TAVI procedure in patients with severe AS. In this study, LAA

filling velocities significantly increased in the post-procedural period. Although LAA emptying velocities were elevated after the TAVI procedure in this population, the increase was significant only in the low LVEF group. Spethmann et al. [6] demonstrated an improvement only in reservoir and conduit functions in the early period after the TAVI procedure. However, their study contained no information on the relationship between reservoir and conduit functions and LVEF. In this study, a significant increase in the post-procedural LAA tissue Doppler velocities in the low LVEF group was detected.

Different studies demonstrated depressed LA or LAA functions due to LV mass, LV outflow tract gradients, and LV diastolic dysfunction [22–24]. Moreover, the functions of LA booster-pump were found to be related to symptoms of severe AS in patients with preserved LVEF [22]. Although the velocities of the E/E_m and E_m have a close relationship with systolic function, recent studies reported that this parameter reflected the functions of the LAA, independent of the LVEF [23–25].

In conclusion, the LA functions as a conduit of LV in early diastole and diastasis phases. Hence, it is affected directly by end-diastolic pressure and diastolic functions of the LV. The LA is also affected directly by compliance and pressure of the LV because it functions as a pump of the LV at the end of diastole [25–27]. In our study, the E/E_m was decreased in the post-procedural period. In the subgroup analysis, the post-procedural LAA filling velocity, LAA emptying velocity, and mean

velocities of the E_M , A_M , and S_M were significantly higher than those during the pre-procedural period in patients with an E/E_m of > 15 . However, this study has not revealed any difference in the post-procedural LAA functions in patients with an E/E_m of < 15 .

As a result of these data, the early increase in the functions of LAA may be due to improved post-procedural hemodynamic parameters, including elevated LVEFs and improved diastolic function, especially in patients with marked systolic and diastolic dysfunction. This improvement may be expected in long-term follow-up of patients with preserved LVEFs and diastolic function, because LA and LV remodeling takes much time.

Limitations of the study

This was a single-center study with a relatively small sample size, both of which limit the power of our research findings. Lack of follow-up of the patients in terms of short- and long-term cardiovascular events and link to the patients outcomes were the most serious weaknesses of our manuscript. Moreover, the lack of long-term follow-up of the echocardiographic parameters was another limitation of the present study. As atrial fibrillation is a common arrhythmia in patients with valvular heart disease, this was not an exclusion criterion. In our study, only 6 patients had chronic atrial fibrillation, and therefore A_{LAA} was not evaluated in these patients.

Conclusions

In this study, we demonstrated that successful TAVI improved the echocardiographic hemodynamic status and increased the LAA Doppler and TDI velocities, which lead to improved regional LAA function in patients with a depressed LVEF, and increased LV diastolic dysfunction. Thus, the relief of AS by TAVI may not only confer hemodynamic benefits resulting in symptomatic improvement, but also have a favorable influence on LA and LAA function.

Conflicts of interest: None declared

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