



# Changes in left ventricular function in patients with aortic regurgitation 12 months after transapical transcatheter aortic valve implantation

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## Abstract

Transcatheter aortic valve implantation (TAVI) is an established treatment for high surgical risk aortic stenosis patients; in recent years, it has also been used in patients with pure/dominant aortic regurgitation (AR). This study aimed to determine the impact of transapical TAVI on left ventricle myocardial mechanics in AR patients. Thirty AR patients (70% men; mean age,  $72.8 \pm 4.3$  years) were enrolled. Conventional echocardiography was performed on all patients before and 12 months after TAVI. Three-dimensional speckle tracking was accomplished in 20 AR patients for the evaluation of global longitudinal strain, global circumferential strain, twist, torsion, apical rotation and basal rotation. Preoperative left ventricular ejection fraction (LVEF), global longitudinal strain (GLS), global circumferential strain (GCS), twist, torsion and apical rotation were impaired in AR patients compared with controls. Mean left ventricular (LV) end-diastolic diameter (from  $62.9 \pm 7.3$  to  $52.0 \pm 6.8$  mm,  $p < 0.001$ ), LV end-diastolic volume (from  $199.4 \pm 55.0$  to  $130.1 \pm 48.9$  mL,  $p < 0.001$ ), and LV mass index ( $179.8 \pm 52.2$ – $134.4 \pm 42.5$  g/m<sup>2</sup>,  $p = 0.001$ ) decreased 12 months after TAVI. Interestingly, GLS (from  $-17.2 \pm 3.2$  to  $-18.9 \pm 3.7$ ,  $p = 0.007$ ) and GCS (from  $-23.9 \pm 4.9$  to  $-25.7 \pm 5.0$ ,  $p = 0.008$ ) improved significantly, but LVEF did not significantly improve. In terms of the rotational mechanics, twist, rotation and basal rotation remained almost unchanged, whereas apical rotation (from  $7.4 \pm 4.0$  to  $5.5 \pm 3.9$ ,  $p = 0.009$ ) was significantly impaired after transapical TAVI. Our results indicate that LV function was improved in terms of myocardial deformation but worsened in terms of apical rotation 12 months after TAVI in AR patients. Three-dimensional speckle tracking echocardiography appears to be a sensitive method for detecting subtle cardiac remodeling after TAVI.

**Keywords** Aortic regurgitation · Transcatheter aortic valve implantation · Three-dimensional speckle tracking · Strain

## Introduction

Aortic regurgitation (AR) is a common aortic valvular disease that involves left ventricular (LV) volume overload [1]. Elevated volume load in AR patients leads to increased LV

volume. In addition, myocardial mechanics impairment and LV remodeling occur in these patients [2–5].

Transcatheter aortic valve implantation (TAVI) is a recently established treatment for AS patients with high surgical risk in conventional aortic valve replacement [6, 7]. In recent years, TAVI has also been used in patients with pure/dominant AR with the development of several types of second-generation TAVI devices [8–12], such as the Jena-valve and J-valve. Several studies have shown the recovery of LV function in AS patients after TAVI [13–17]. However, data on LV function changes after TAVI are rare in AR patients.

Three-dimensional speckle tracking (3D STE) functional analysis has been proven to be an accurate and sensitive tool for evaluating LV dysfunction due to aortic valvular disease [2] and the improvement of LV function after TAVI in AS patients [14]. Instead of relying on a geometric model, 3D STE tracks the authentic three-dimensional motion of

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acoustic speckles [18]. Therefore, 3D STE can provide novel deformation parameters, which may improve our pathophysiologic understanding of changes in LV performance after TAVI.

We hypothesized that the LV functional parameters impaired in AR patients who were TAVI candidates would improve after the procedure. Thus, in the present study, we aimed to evaluate AR-related LV dysfunction before TAVI and LV functional changes after transapical TAVI using 3D STE.

## Methods

### Patients

From March 2014 to June 2016, 32 successive patients with AR were admitted for transapical TAVI to our hospital (West China Hospital of Sichuan University). Thirty patients with successfully implanted J-valve prostheses (JC Medical Inc, CA, USA) were enrolled in this study. Conversion to open surgical aortic valve replacement was necessary in two patients because of valve dislocation. For 3D STE analysis, ten patients were excluded due to poor acoustic windows ( $n=6$ ) or atrial fibrillation ( $n=4$ ). Twenty-one healthy patients over 65 years old were included as a control group.

### Transapical TAVI

The inclusion criteria for TAVI were (1) pure/dominant (grade III–IV) AR with vena contracta width  $\geq 0.6$ ; (2) New York Heart Association (NYHA) heart function  $\geq$  II and a logistic European System Operative Risk Evaluation of  $\geq 20\%$  [8]; and (3) no significant dilation of the ascending aorta or aortic sinus ( $< 50$  mm). Transapical TAVI was performed under general anesthesia in a hybrid operation room, and a J-valve (JC Medical Inc, CA, USA) was implanted.

### Echocardiography

Transthoracic echocardiograms were obtained before TAVI and at 12-month follow-ups using a commercially available echocardiographic system (Philips IE 33 and EPIQ 7C, Philips Medical Systems Corporation, MA, USA) equipped with S5-1 (1–5 MHz) and X5-1 (1–5 MHz) transducers. Two-dimensional echocardiographic, Doppler, and Doppler tissue imaging parameters were measured. LV end-diastolic and left ventricular ejection fraction (LVEF) were measured manually using Simpson's biplane method. LV mass (LVM) was assessed according to the formula [19]  $LVM (g) = 0.8 \times 1.04 [(LV \text{ end-diastolic diameter} + \text{posterior wall thickness in diastole} + \text{septal wall thickness in diastole})^3 - (LV \text{ end-diastolic diameter})^3] + 0.6$ , and LV

mass index (LVMI) was calculated by LVM/body surface area (BSA). The severity of AR was determined by vena contracta width, which was measured in the long axis view, apical five-chamber view or apical three-chamber view. 3D echocardiographic full-volume images were acquired according to the European Association of Echocardiography guidelines [20]. Patients were instructed to maintain a left lateral decubitus position and hold their breath during image acquisition. Digital data were saved in DICOM format, and the average frame rate was 20–35 Hz.

### 3D STE analysis

All images were analyzed by a single observer using a Tomtec Imaging System (4D LV-Analysis 3.1, Tomtec Corporation, Germany). First, the cardiac circle with the best image quality was selected. Second, the software automatically aligned the 3D image with standard LAX views (apical four-chamber, apical three-chamber, and apical two-chamber views) and defined the end-diastolic and end-systolic frames. The position of the aortic valve landmark could be adjusted manually to ensure standard LAX views. Mitral annulus and LV apex landmarks were positioned manually. Then, the endocardial border was automatically reconstructed and manually adjusted with the goal of obtaining the best possible tracking in all myocardial segments. Finally, the values of 3D LV global longitudinal strain (GLS), global circumferential strain (GCS), twist, torsion, apical rotation and basal rotation were calculated [21]. Figures 1 and 2 show the GLS and GCS evaluations before and 12 months after TAVI for a representative patient.

Furthermore, 20 randomly selected images of AR patients were reanalyzed 2 weeks later by the same observer for intraobserver assessment and reanalyzed by a second experienced observer for interobserver agreement.

### Statistical analysis

Categorical data were presented as frequencies and percentages. Continuous data were shown as the mean  $\pm$  standard deviation, and normal distributions were examined using the Kolmogorov–Smirnov test. The baseline characteristics of the AR patients and the control group were compared using the Chi square test or Fisher's exact test for categorical data and an independent t-test or Wilcoxon's signed-rank test for continuous variables. A paired t-test or Wilcoxon's signed-rank test was used to analyze the changes in echocardiographic parameters before and after TAVI. Intraobserver and interobserver variability were assessed using intraclass correlation coefficients and the coefficient of variation. All statistical analyses were conducted using SPSS 19.0 software (SPSS, Inc., Chicago, IL), and statistical significance was set at  $p < 0.05$ .

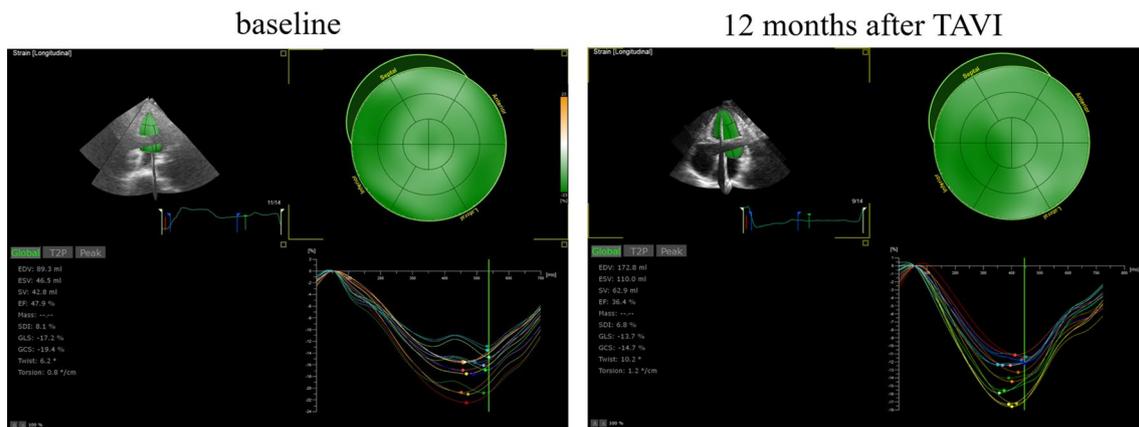


Fig. 1 Pre- versus post-TAVI LV 3D GLS in a representative patient

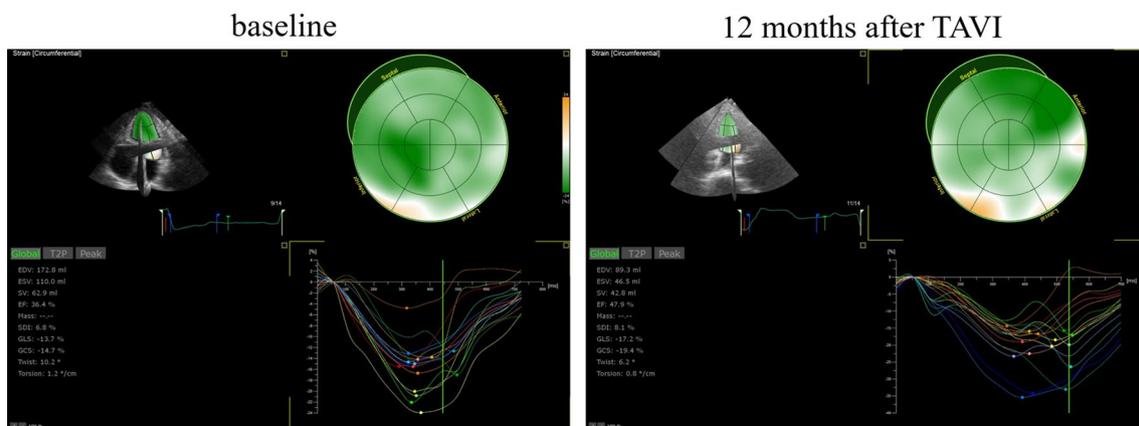


Fig. 2 Pre- versus post-TAVI LV 3D GCS in a representative patient

## Results

### Study population

Baseline characteristics are presented in Table 1. The mean age was  $72.8 \pm 4.3$  years, and 21 patients (70%) were males. The mean logistic European System Operative Risk Evaluation score was  $20.9 \pm 4.8$ . In addition, 29 (96.7%) patients were in functional class III or IV according to the NYHA classification. There are no significant differences between the AR patients and the control group in age, gender, body mass index and diastolic blood pressure. However, systolic blood pressure was significantly higher in the AR group than in the controls. The mean prosthesis size was  $25.3 \pm 1.6$  mm. All patients had tricuspid aortic valve.

### Conventional echocardiography

All transthoracic echocardiographic characteristics are presented in Table 2. LV end-diastolic diameter, LV end-diastolic volume and stroke volume decreased significantly at 12 months, which was accompanied by significant LVMi regression. LVEF, transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity (E/E') ratio and systolic pulmonary artery pressure showed mild enhancement, but this result was not significant. Aortic peak speed and mean gradient presented almost no change 12 months after the procedure. Mild paravalvular regurgitation was observed in three patients (10.0%). Moderate paravalvular regurgitation was found in two patients (6.7%).

**Table 1** Baseline clinical characteristics

Variable	AR (n=30)	AR with 3D image (n=20)	Control (n=21)	<i>p</i>
Age (years)	72.8±4.3	72.7±4.8	71.6±4.8	0.48
Men	21 (70%)	14 (70%)	12	0.52
Body mass index (kg/m <sup>2</sup> )	23.5±3.0	23.4±2.7	23.7±3.5	0.67
Logistic European System for Cardiac Operative Risk Evaluation score (%)	20.9±4.8	21.5±5.0	NA	NA
Arterial hypertension	16 (53.3%)	10 (50%)	NA	NA
Systolic blood pressure (mmHg)	132.45±18.2	137.3±19.7	124.7±16.4	0.009
Diastolic blood pressure (mmHg)	73.7±11.0	72.0±11.9	72.5±10.0	0.85
NYHA class III or IV	29 (96.7%)	18 (90%)	NA	NA
Dyslipidemia	19 (63.3%)	14 (70%)	NA	NA
Coronary artery disease	7 (23.3%)	3 (15%)	NA	NA
Diabetes mellitus	2 (6.7%)	2 (10%)	NA	NA
Cerebral vascular disease	14 (46.7%)	7 (35%)	NA	NA
Chronic lung disease	20 (70.0%)	13 (65%)	NA	NA
Prosthesis size (mm)	25.8±1.3	25.3±1.6	NA	NA

Data are expressed as mean ± SD or as number (percentage)

*p*, AR patients with 3D image versus control group

NA not assessed, NYHA New York Heart Association

**Table 2** Conventional echocardiographic parameters before and after TAVI

Variable	AR (n=30)		<i>p</i> *
	Pre	Post	
Aortic peak speed (m/s)	2.3±0.7	2.3±0.4	0.93
Aortic mean gradient (mmHg)	12.1±7.3	12.2±4.2	0.98
LV end-diastolic diameter (cm)	62.9±7.3	52.0±6.8	<0.001
LV end-diastolic volume	199.4±55.0	130.1±48.9	<0.001
Stroke volume (mL/beat)	110.6±26.4	70.4±20.5	<0.001
LVEF (%)	57.0±10.3	57.6±9.3	0.71
LV mass (g)	305.7±88.7	228.0±69.3	<0.001
LV mass index (g/m <sup>2</sup> )	179.8±52.2	134.4±42.5	0.001
E' (m/s)	0.7±0.3	0.7±0.2	0.48
E/E' ratio	16.0±6.0	14.9±5.5	0.46
Systolic pulmonary artery pressure (mmHg)	24.9±8.1	24.4±7.5	0.36

Data are expressed as mean ± SD

\*Pre-TAVI versus post-TAVI

### 3D STE analysis

A total of 20 patients had standard 3D echocardiographic images for speckle tracking analysis. The data from 3D STE are presented in Table 3. All preoperative 3D STE parameters except basal rotation were markedly reduced in high-risk AR patients compared with the healthy group. No marked development of the 3D ejection fraction (EF) was

**Table 3** 3D speckle-tracking parameters

Variable	Control (n=21)	AR (n=20)		<i>p</i> *
		Pre	Post	
LVEF (%)	61.7±3.0	51.2±8.3 <sup>†</sup>	52.4±7.6	0.08
GLS (%)	21.6±2.2	-17.2±3.2 <sup>†</sup>	-18.9±3.7	0.007
GCS (%)	30.4±2.3	-23.9±4.9 <sup>†</sup>	-25.7±5.0	0.008
Twist (°)	14.8±4.4	11.0±6.2 <sup>†</sup>	10.1±6.1	0.36
Torsion (°/cm)	2.2±0.8	1.4±0.9 <sup>†</sup>	1.3±0.9	0.80
Apical rotation (°)	11.0±4.2	7.4±4.0 <sup>†</sup>	5.5±3.9	0.009
Basal rotation (°)	4.8±2.3	-4.8±3.7	-5.1±3.3	0.66

Data are expressed as mean ± SD

GLS globe longitudinal strain, GCS globe circumferential strain

\*Pre-TAVI versus post-TAVI

<sup>†</sup>*p*<0.05, AR versus control

found 12 months after transapical TAVI. However, GLS and GCS improved significantly in these patients. In terms of the rotational mechanics, twist, rotation and basal rotation remained almost unchanged, whereas apical rotation was significantly impaired after transapical TAVI.

### Intraobserver and interobserver variability

An analysis of intraobserver and interobserver variability established very good agreement between observations (Table 4).

**Table 4** Reproducibility of 3D speckle-tracking parameters

Variable	Intraobserver results		Interobserver results	
	ICC	CV	ICC	CV
EF	0.98	4	0.96	6
GLS	0.96	5	0.90	10
GCS	0.97	4	0.93	8
Twist	0.93	9	0.89	14
Torsion	0.92	8	0.88	15
Apical rotation	0.91	9	0.90	11
Basal rotation	0.94	7	0.92	9

ICC intraclass correlation coefficient, CV coefficient of variation

## Discussion

The present study employed 3D STE functional analysis, which demonstrated that high-risk patients with pure/dominant AR had impaired LV functional parameters that partially improved 12 months after transapical TAVI. In addition, apical rotation was reduced after transapical TAVI. To the best of our knowledge, this is the first study to assess LV functional changes in AR patients who underwent TAVI.

### LV functional changes in AR

In patients with chronic AR, progressive overfilling of the left ventricle causes a gradual increase in LV volume load. A series of changes in LV structure, such as LV myocardial hypertrophy and LV dilation, occur to maintain systolic function and restrict the increase in LV filling pressures. These compensation mechanisms result in a long asymptomatic stage. LVEF is normally preserved in this stage. Nevertheless, the strain parameters highlighted subtle LV functional changes during the compensated phase. Broch et al. [5] found an early compensatory mechanism with a lower GLS but a higher GCS in patients with chronic AR, which maintained the EF at a level comparable to that in healthy patients and athletes. In addition, reduced LV twist and rotation were also found in the same type of patients by Enache et al. [4].

In advanced AR stages, however, it becomes challenging for adequate LV structure changes to catch up with the sustained enlargement of LV volume and increases in filling pressure. Symptoms occur when the compensation mechanism breaks down and LV function deteriorates. LVEF and strain parameters are correspondingly reduced in this phase. Ewe et al. [3] discovered that compared with asymptomatic patients, symptomatic AR patients had significantly impaired multidirectional LV strain. Impairments of GLS and GCS were also observed in AR patients with NYHA functional class I or II by Li et al. [2]. In the present study,

we employed innovative 3D STE, which provided multidirectional strains and torsional parameters simultaneously. 3D STE served as a quick and accurate tool for the assessment of LV function and deformation, with high feasibility and reproducibility [14]. The AR patients who were candidates for transapical TAVI met the standard requirements of surgery, but they had a higher incidence of comorbidities and were of advanced age. However, in terms of mean age, the patients in this study group were younger than the patients in the European and US TAVI registries. Unsurprisingly, in our study, LVEF and strain were impaired in AR patients compared with the healthy group.

### LV functional changes after TAVI

TAVI offers a less invasive approach for treating aortic valvular diseases by breaking up the cascade of deterioration in LV function. However, there are limited data on LV functional recovery in AR patients after TAVI. It is expected that LV volume could be reduced and that LV function could improve after the procedure. LV remodeling and the recovery of myocardial mechanics were found at 12-month follow-ups in the current study.

In accordance with previous studies on surgical aortic valve replacement (SAVR) [22], LV end-diastolic volume diameter, LV end-diastolic volume, and stroke volume decreased after the procedure. Favorable reverse LV remodeling was also found as LVM and LVMi were greatly reduced.

Unlike certain improvements, such as improvements in LV volume, the changes in LV functional parameters in AR patients after surgery are contentious. Regeer et al. [23] detected that LVEF increased after SAVR in both chronic and acute AR patients at 34 months, whereas GLS remained unchanged. Magnetic resonance imaging with tissue-tagging was adopted by Pomerantz et al. [24], who discovered that the LVEF improvements were not significant, whereas the partial regions and global longitudinal and circumferential strain were significantly impaired 28 months after SAVR. Nevertheless, Chen et al. [25] found that GLS and GCS were impaired early after SAVR but improved at 3-month follow-ups in AR patients. Importantly, we found a significant improvement in GLS and GCS 12 months after transapical TAVI, whereas LVEF remained unchanged, which is consistent with the results of Pomerantz et al.

The rotational parameters also showed non-significant improvements in the present study. Unexpectedly, apical rotation worsened after transapical TAVI. Rotation refers to the angle of deformation on a short-axis LV plane and is expressed in degrees. Twist is defined as the net difference between the basal and apical rotation angles, and torsion is calculated by dividing the LV twist by the length of the LV to allow comparability of the LV twist between ventricles of different sizes [26]. Therefore, a possible explanation is

that the scar of the LV apex as a result of the transapical access, even though it is tiny, hindered the recovery of the rotational movement of the LV apex. Meyer et al. [27] found that compared with transfemoral TAVI, apical LV function was reduced at the 3-month follow-up in transapical TAVI AS patients using cardiac magnetic resonance feature tracking. Asthana et al. [28] also found persistently impaired apical longitudinal strain at 1-month follow-up visits using 2D STE. However, torsional parameters were not included in these studies. Our study confirmed that there was no improvement in the twist and torsion parameters 12 months after transapical TAVI, and that there was even a reduction in apical rotation.

## Limitations

There were several limitations in this study. As a second-generation device, J-valve started being used relatively recently, and the number of patients who have received this device is limited. As a result, it is difficult to subdivide these patients according to cardiac function. Future studies are needed to investigate the influence of baseline ventricular function on the relief of myocardial mechanics. In addition, a subset of potentially appropriate patients was excluded from speckle tracking analysis due to poor acoustic windows.

## Conclusions

Our results indicate that LV function was improved in terms of myocardial deformation, but reduced in terms of apical rotation 12 months after TAVI in AR patients. Three-dimensional speckle tracking echocardiography appears to be a sensitive method for detecting subtle cardiac remodeling after TAVI.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The study protocol was approved by the hospital ethics committee.

**Informed consent** Written informed consent was obtained from all participants.

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