Predictive Value of Left Ventricular Myocardial Deformation for Left Ventricular Remodeling in Patients With Classical Low-Flow, Low-Gradient Aortic Stenosis Undergoing Transcatheter Aortic Valve Replacement

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Background: Transcatheter aortic valve replacement (TAVR) is an alternative treatment in surgically intermediate- or high-risk patients with classical low-flow, low-gradient (LFLG) aortic stenosis (AS). The objective of this study was to investigate whether two-dimensional (2D) speckle-tracking echocardiography (STE) can predict left ventricular (LV) flow reserve during dobutamine stress echocardiography (DSE) and remodeling after TAVR in patients with LFLG AS.

Methods: Seventy-five symptomatic patients with severe LFLG AS were recruited (mean age, 77.6 ± 8.4 years). Patients underwent a complete clinical evaluation, standard echocardiography, 2D STE, and DSE. Echocardiographic analysis was performed before and 6 months after TAVR using global longitudinal strain (GLS) measured on 2D STE.

Results: All patients received self-expanding transcatheter prosthetic valves. Six months after TAVR, LV GLS (12.8 ± 3.2% vs 16.3 ± 4.2%, $P < .0001$) significantly increased. In a multivariate analysis, LV GLS before TAVR ($P < .0001$) was an independent predictor of LV flow reserve during DSE. By receiver operating characteristic curve analysis, a cutoff value for LV GLS of ≤12% well distinguished patients without significant flow reserve and with lack of positive remodeling after TAVR at follow-up. These results support the hypothesis that myocardial analysis by 2D STE at baseline can be useful for the identification of patients with LFLG AS who would benefit from TAVR.

Conclusions: The results of this study underline the predictive value of LV GLS on flow reserve during DSE and on global LV remodeling after TAVR in patients with LFLG AS. Cutoff values for LV GLS could be used to identify patients responding better to TAVR. (J Am Soc Echocardiogr 2019;32:730-6.)

Keywords: Aortic stenosis, Low flow, Low gradient, Contractile reserve, Two-dimensional strain, Transcatheter aortic valve replacement

Low-flow, low-gradient (LFLG) aortic stenosis (AS) accounts for 5% to 10% of the AS population. Typically, it is more prevalent in men and is often associated with coronary artery disease.[1] The main diagnostic challenge in LFLG AS with low left ventricular (LV) ejection fraction (LVEF) is the distinction between true severe and pseudosevere forms of AS, which is currently made using dobutamine stress echocardiography (DSE). Transcatheter aortic valve replacement (TAVR) has become the recommended therapy for patients with severe symptomatic LFLG AS at high or intermediate surgical risk.[2]

AS induces LV remodeling with progressive myocardial hypertrophy and fibrosis due to increased afterload,[3] and myocardial deformation analysis has been proposed as a reliable tool for the detection of clinical and subclinical regional LV dysfunction.[4] In fact, the conventional measurement of LV contractility using LVEF reflects primarily

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Abbreviations

2D = Two-dimensional

AS = Aortic stenosis

DSE = Dobutamine stress echocardiography

GLS = Global longitudinal strain

LAVI = Left atrial volume index

LFLG = Low-flow, low-gradient

LV = Left ventricular

LVEF = Left ventricular ejection fraction

LVMI = Left ventricular mass index

NYHA = New York Heart Association

STE = Speckle-tracking echocardiography

TAVR = Transcatheter aortic valve replacement

radial function, but this parameter is extremely load dependent and therefore less useful in patients with AS. Conversely, longitudinal strain imaging may add further information to LV functional assessment and longitudinal contraction.[4]

The aim of this study was therefore to investigate whether speckle-tracking echocardiography can predict both LV flow reserve and LV reverse remodeling after TAVR in patients presenting with LFLG AS.

METHODS

Study Population

In our prospectively study, a total of 75 symptomatic patients (New York Heart Association [NYHA] functional class ≥ II) with severe LFLG AS, considered to be at increased risk for undergoing surgical aortic valve replacement, were enrolled in two groups: at Monaldi Hospital and at Cava dei Tirreni Hospital. The recruitment period lasted from January to May 2017.

Patients included were at more than low risk for surgery with indication for TAVR. Patients were considered to be at increased surgical risk when the European System for Cardiac Operative Risk Evaluation score was ≥10% or the Society of Thoracic Surgeons risk score was ≥4%. A candidate who did not meet these criteria could be included in the study if a heart team, consisting of a surgeon and a cardiologist, concurred that the subject's predicted risk of operative mortality was considered high because of the presence of multiple major organ system compromise.

Exclusion criteria were (1) evidence of an acute myocardial infarction <1 month before TAVR; (2) congenital unicuspid or bicuspid valve; (3) mixed aortic valve disease (AS and aortic regurgitation with predominant aortic regurgitation >3+); (4) preexisting prosthetic heart valve in any position, prosthetic ring, severe mitral annular calcification, and severe (>3+) mitral regurgitation; (5) permanent atrial fibrillation; (6) significant (>50% stenosis) coronary artery disease by coronary angiography; and (7) LVEF ≥ 50%.

Study Protocol

All patients underwent complete clinical and laboratory evaluations. Risk factors, comorbidities, medical therapy, and measurement of cardiac markers were recorded. All patients underwent electrocardiography, standard echocardiography with two-dimensional (2D) STE and multidetector computed tomography to obtain information about valve sizing and arterial access. All patients had classical LFLG AS and underwent DSE before TAVR.

After TAVR, patients were closely monitored in the coronary care unit for ≥24 hours and then in the ward for several days, monitoring hemodynamic status, vascular access, rhythm disturbances, and renal function.

Follow-up at 6 months after TAVR, including clinical evaluation with NYHA functional classification and documentation of possible adverse events, electrocardiography, standard echocardiography, and 2D STE was performed. Valve Academic Research Consortium consensus document definitions were used to determinate clinical end points, such as mortality (cardiovascular or all cause), myocardial infarction (periprocedural or spontaneous), transient ischemic attack or stroke (disabling or not), bleeding complications (life threatening, major, or minor), acute kidney injury (Acute Kidney Injury Network classification stage 1, 2, or 3), vascular complications (major, minor, or percutaneous closure device failure), conduction disturbance, and arrhythmias (new first-degree atrioventricular block, new third-degree atrioventricular block, new left bundle branch block, or new permanent pacemaker implantation).[5,6]

Standard Doppler Echocardiography

Transthoracic echocardiography was performed immediately before and 6 months after TAVR using a commercially available ultrasound system (Vivid E9; GE Ultrasound, Milwaukee, WI) with a variable-frequency phased-array transducer (2.5, 3.5, or 4.0 MHz).

LVEF was calculated from conventional apical two-chamber and four-chamber images using the biplane Simpson technique. LV mass was calculated using the Devereux formula and indexed to body surface area to obtain LV mass index (LVMI). LV hypertrophy was defined as an LVMI > 115 g/m^2 in men and an LVMI > 95 g/m^2 in women. Relative wall thickness was calculated as 2 × LV posterior wall thickness/LV end-diastolic diameter and considered abnormal when >0.42. Relative wall thickness and LVMI were used to assess LV geometry. Left atrial volume index (LAVI) was obtained using the area-length method.[7]

Accurate evaluation of the aortic valve was performed to obtain information about morphology, calcification, and hemodynamic parameters such as jet velocity, mean transaortic gradient, and aortic valve area using the continuity equation.[8]

Severe LFLG AS was defined as aortic valve area < 1.0 cm^2 or an aortic valve index of <0.6 cm^2/m^2 and a low mean transvalvular gradient (<40 mm Hg) with a reduced ejection fraction causing a low-flow state (valve area < 1 cm^2, mean gradient < 40 mm Hg, LVEF < 50%, stroke volume index ≤ 35 mL/m^2).[2] Low-dose DSE was performed in this setting to distinguish truly severe AS from pseudosevere AS, which is defined by an increase to an aortic valve area of >1.0 cm^2 with flow normalization during stress,[2] and to assess LV flow reserve (increased stroke volume >20% compared with baseline).

Two-Dimensional STE

Digital loops with three successive cardiac cycles from the apical four-chamber, two-chamber, and long-axis views were acquired with a frame rate of 50 to 80 frames/sec (mean, 58.4 ± 7.3 frames/sec) to assess global longitudinal strain (GLS) by STE. GLS was quantified using semiautomated function imaging (EchoPAC version 202; GE Vingmed Ultrasound, Horten, Norway). Tracking quality was assessed by the operator and scored by the software with automated function in the region of interest adjusted by correcting the endocardial border or width if deemed necessary. Aortic valve closure was identified using the automated function from the apical long-axis view. GLS was calculated by averaging local strains of all

HIGHLIGHTS

- In patients with classical LFLG AS, there is improvement of LV strain after TAVR.
- Two-dimensional STE can predict LV flow reserve after TAVR in patients with LFLG AS.
- A value for LV GLS of −12% identified patients with lack of remodeling after TAVR.

17 segments and expressed as bull's-eye (Figure 1). If the software did not correctly identify LV wall movement and did not assign a strain value to an LV segment (poor tracking), the operator could repeat the process, readjusting the endocardial tracing, or changing software parameters such as region of interest width and smoothing until a better score was achieved.

Dobutamine Stress Echocardiography

Under continuous electrocardiographic monitoring, dobutamine was infused into a peripheral vein at an incremental regimen of 5 μg/kg body weight per minute every 3 min until a maximum of 20 μg/kg body weight per minute. Systolic blood pressure was taken at baseline and at the end of each stage. End points of the study included increase in stroke volume >20% or <20% (significant flow reserve) compared with basal measurement, increase of mean aortic gradient, new wall motion abnormalities, significant ST-segment changes (i.e., ST-segment depression or elevation ≥1 mm in two contiguous leads), significant symptoms, arrhythmias, or conclusion of the protocol. A 12-lead electrocardiographic recording was taken every minute with pediatric-sized precordial electrodes to maximize the chest area available for echocardiography. Two-dimensional echocardiographic images were continuously recorded from parasternal long-axis, short-axis, and apical four- and two-chamber views using a variable-frequency phased-array transducer (2.5, 3.5, or 4.0 MHz).

Intra- and Interobserver Variability

To reduce measurement errors, three expert echocardiographers performed measurements in all 75 patients and were blinded to patient clinical data and one another's results. The readers were allowed to select the best cardiac cycle, and they were required to repeat measurements at least three times. For the analyses, average values of all echocardiographers measurements were considered. Intraobserver variability was determined by using offline data at different points in time. Interobserver variability was determined by repeating measurements from the same images.

Transcatheter Aortic Valve Replacement

All patients received a CoreValve self-expanding prosthesis (Medtronic, Minneapolis, MN). Valve size was determined on the basis of multidetector row computed tomographic measurements. TAVR was performed using a retrograde transfemoral approach percutaneously or through surgical cut-down. Dual-antiplatelet therapy with aspirin, at a dose of 100 mg/d, and clopidogrel, at a dose of 75 mg/d, was recommended from the night before to 3 months after the procedure, followed by same dose of aspirin or clopidogrel indefinitely, unless there was high risk for bleeding complications.

Statistical Analysis

All analyses were performed by SPSS for Windows release 21.0 (SPSS, Chicago, IL). Variables are presented as mean ± SD. Paired *t* tests were performed to estimate differences between groups. Percentage changes between baseline measurements before TAVR and follow-up measurements after TAVR were calculated as follows: (follow-up value − baseline value)/baseline value × 100. Linear regression analyses and partial correlation test using the Pearson method were done to assess univariate relations. To identify significant independent determinants of LV functional and morphologic measurements before and after TAVR, their individual associations with clinically relevant and echocardiographic variables were assessed using multivariate linear regression analysis. The following variables were included in the analysis: clinical data (age, sex, body mass index,

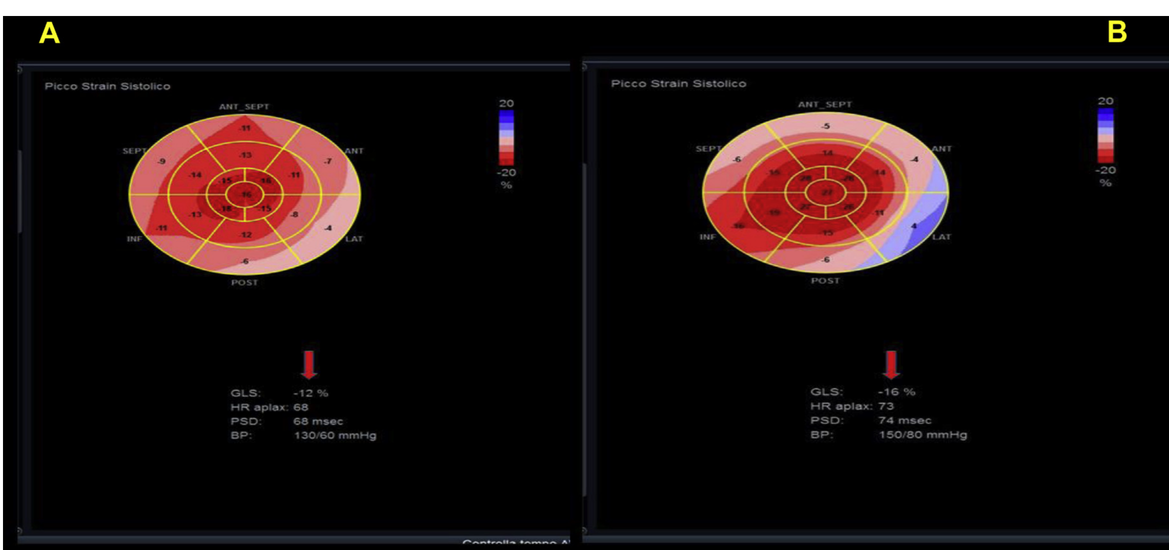

Figure 1 **(A)** GLS in a patient with LFLG AS without flow reserve during DSE. Myocardial deformation (GLS −12%) was severely impaired. **(B)** GLS in a patient with LFLG AS with significant flow reserve during DSE. Myocardial deformation (GLS −16%) was mildly reduced.

Table 1 Clinical and demographic characteristics of the study population (*N* = 75)

Variable	Value
Male/female	45/30
Age (y)	77.6 ± 8.4
BMI (kg/m^2)	27.3 ± 4.5
Logistic EuroSCORE	16.1 ± 6.4
Chronic kidney disease stage ≥ 3	28 (37)
Systolic blood pressure (mm Hg)	135.2 ± 13.1
Diastolic blood pressure (mm Hg)	78.3 ± 9.4
Heart rate (beats/min)	75.3 ± 11.4
COPD	16 (21.3)
Cirrhotic liver disease/esophageal varices	5 (6.6)
Chronic cerebral vasculopathy	10 (13.3)
Arterial hypertension	45 (60)
Diabetes mellitus	23 (30.6)
Smoking or history of smoking	15 (26.6)
Obesity	15 (17.3)
Hyperlipidemia	37 (49.3)
β-blockers	65 (86.7)
ACE inhibitors or angiotensin receptor blockers	60 (77.3)
Mineralocorticoid or aldosterone receptor antagonists	53 (70.6)
Antiplatelet agents/oral anticoagulants	30 (40)/18 (24)
Diuretics	55 (73.3)

ACE, Angiotensin-converting enzyme; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation.
Data are expressed as number (percentage) or as mean ± SD.

mean blood pressure), laboratory measurements (creatine kinase MB mass after TAVR), standard echocardiographic indices (LV volumes, LVMI, Doppler mitral inflow measurements, left atrial diameter), and strain measurements (LV GLS). These variables were selected according to their clinical relevance and potential impact on LV morphology and function. Variable selection was performed in the multivariate linear regression as an interactive stepwise backward elimination method, each time excluding the one variable with the highest *P* value, according to Wald statistics. To decrease the inflation of the type I error rate due to multiple testing, statistical significance was defined as a two-sided *P* value < .01. Receiver operating characteristic curve analysis was performed to select optimal cutoff values of echocardiographic measurements. Reproducibility of strain measurements was determined in all subjects. Intraobserver variability and interobserver variability were examined using the coefficient of variation, defined as the ratio of the SD to the mean, and using Bland-Altman analysis. Coefficients of variation, 95% CIs, and percentage errors are reported.

RESULTS

Baseline Characteristics of Patients

We selected 75 patients with AS (mean age, 77.6 ± 8.4 years) and a mean logistic European System for Cardiac Operative Risk Evaluation score of 16.1 ± 6.4. All patients were symptomatic for angina, dyspnea, or syncope. An overview of the baseline characteristics of the study population is provided in Table 1.

Dobutamine Stress Echocardiographic Parameters

All patients had LGLG AS. During dobutamine stress, 28 patients with AS (37%) did not show significant LV flow reserve (percentage increase in stroke volume < 20% during DSE).

TAVR Procedure

CoreValve size 29 was the valve with the greatest number of implantations (45 patients [60%]); in 18 cases (25%), postdilation was performed. The procedure was carried out through femoral access in 100% of cases. At discharge, most patients (80%) received dual-antiplatelet therapy with aspirin, at a dose of 100 mg/d, and clopidogrel, at a dose of 75 mg/d, for 3 months after the procedure.

Laboratory Evaluation

Mean baseline serum creatinine was 1.2 ± 0.4 mg/dL, and peak creatinine after the procedure was 1.28 ± 0.58 mg/dL. Acute kidney injury was found in 10 patients. Mean creatine kinase MB mass before TAVR was 2.87 ± 2.8 ng/mL, and mean creatine kinase MB mass after the procedure was 9.2 ± 9.3 ng/mL.

Echocardiographic Parameters

Six months after TAVR, patients showed significant reductions of mean transaortic gradient, LV mass, LVMI, and LAVI and an improvement of LVEF. There were no significant changes in LV end-diastolic diameter or pulmonary artery systolic pressure. Aortic paravalvular regurgitation (leak) after TAVR was found in 22 patients (29%), but it did not reach moderate or severe grade (Table 2).

Strain Analysis

LV GLS measured by STE significantly improved after TAVR. Each of the 17 segments analyzed by longitudinal regional strain demonstrated a significant improvements in all basal, mid, and apical segments. As a result, mean LV GLS (baseline, −13.8 ± 4.2%; 6 months after TAVR, −16.2 ± 4.9%; *P* < .0001) significantly improved after TAVR. These improvements in myocardial function were more evident in the subgroup of patients with significant LV flow reserve (Table 2).

Univariate Analyses

Peak creatine kinase MB mass after TAVR (*r* = −0.43, *P* < .0001) and LVMI before TAVR (*r* = −0.48, *P* < .0001) were moderately associated with lower improvement of LV GLS after TAVR.

LV GLS (*r* = −0.71, *P* < .0001) before TAVR appeared to be strongly associated with LV flow reserve (Figure 2).

In addition, LV GLS was moderately correlated with LV end-systolic volume (*r* = 0.53, *P* < .0001) and with LVMI after TAVR (*r* = 0.56, *P* < .0001) and strongly correlated with their percentage change between baseline and follow-up measurements (Figures 3 and 4).

Multivariate Analyses

On multivariate analysis, after adjusting for potential confounders, LV GLS (multiple partial correlation coefficient = 0.6, *P* < .00001) before TAVR was a powerful independent predictor of LV flow reserve

Table 2 Standard echocardiographic and dobutamine stress echocardiographic measurements of the study population at baseline and at 6-month follow-up after TAVR

Variable	LV flow reserve ≥ 20% (*n* = 47)			LV flow reserve < 20% (*n* = 28)		
	Baseline	6 mo	*P*	Baseline	6 mo	*P*
Aortic valve area (cm^2)	0.54 ± 0.21	2.3 ± 0.22	<.00001	0.52 ± 0.31	2.1 ± 0.18	<.00001
LV stroke volume (mL/m^2)	36.4 ± 8.4	45.9 ± 6.7	<.001	33.4 ± 6.4	35.3 ± 4.4	NS
Mean transaortic gradient (mm Hg)	28.4 ± 14.2	12.4 ± 3.8	<.001	24.6 ± 11.4	10.8 ± 4.2	<.001
LVEF (%)	25.3 ± 5.8	42.4 ± 4.5	<.0001	22.4 ± 6.3	23.2 ± 5.4	NS
Interventricular septum (cm)	1.4 ± 0.2	1.1 ± 0.4	<.01	1.4 ± 0.3	1.2 ± 0.4	<.01
Posterior wall (cm)	1.3 ± 1.1	1.1 ± 0.4	<.01	1.4 ± 0.2	1.2 ± 0.3	<.01
LV end-diastolic volume (mL)	166.3 ± 10.2	147.8 ± 6.7	<.001	176.3 ± 11.4	174.4 ± 9.8	NS
LV end-systolic volume (mL)	128.3 ± 4.6	89.9 ± 7.6	<.0001	142.3 ± 11.2	139.4 ± 12.4	NS
LA diameter (mm)	45.4 ± 3.8	41.7 ± 3.3	<.001	46.4 ± 3.9	42.3 ± 3.8	<.01
LAVI (mL/m^2)	41.2 ± 14.3	34.5 ± 12.4	<.001	43.6 ± 16.2	39.2 ± 13.4	<.01
LV mass (g)	263.4 ± 61.3	212.6 ± 51.3	<.0001	282.6 ± 58.3	248.5 ± 65.1	<.001
LVMI (g/m^2)	148.3 ± 22.1	116.3 ± 19.6	<.0001	158.3 ± 22.4	137.3 ± 21.6	<.001
RWT	0.47 ± 0.12	0.43 ± 0.14	<.001	0.50 ± 0.13	0.48 ± 0.11	<.01
LV GLS (%)	−14.5 ± 3.3	−18.4 ± 4.7	<.0001	−10.6 ± 2.1	−12.9 ± 3.9	<.01

LA, Left atrial; *LAVI*, left atrial volume index; *RWT*, relative wall thickness.

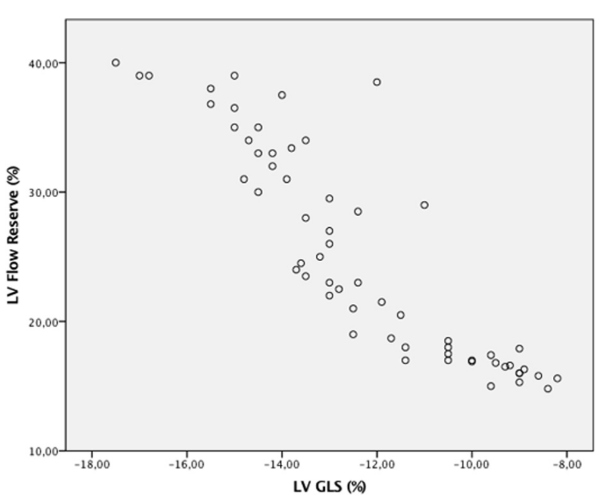

Figure 2 Scatterplot between LV flow reserve and LV GLS in the overall population of LFLG AS.

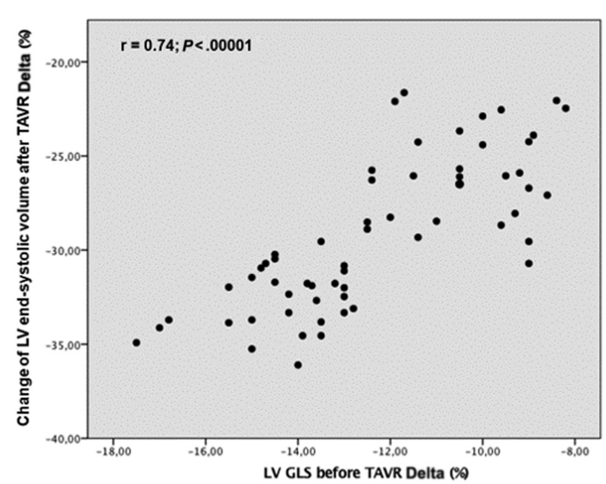

Figure 3 Scatterplot between percentage change in LV end-systolic volume at follow-up and LV GLS at baseline in the overall population of LFLG AS.

during DSE (global $R^2 = 0.8$). Moreover, LV GLS before TAVR was an independent predictor of LV end-systolic volume (correlation coefficient = −0.44, $P < .0001$) and of LVMI (correlation coefficient = −0.41, $P < .0001$) after TAVR. On receiver operating characteristic curve analysis, a cutoff value of LV GLS worse than −12% (sensitivity, 84%; specificity, 93%; area under the curve, 0.92 [95% CI, 0.86–0.99]) identified patients without significant flow reserve and with lack of remodeling after TAVR at follow-up. Finally, LV GLS was also an independent predictor of NYHA functional class at 6-month follow-up (correlation coefficient = −0.46, $P < .001$).

Reproducibility of 2D Speckle-Tracking Echocardiographic Measurements

The intraobserver coefficient of variation for LV GLS was 5.37 (intraclass correlation coefficient = 0.73); on Bland-Altman analysis, LV GLS had a 95% CI of ±1.5 and percentage error of 3.2%. The interobserver coefficient of variation for LV GLS was 7.22 (intraclass correlation coefficient = 0.77); on Bland-Altman analysis, LV GLS had a 95% CI of ±1.7 and percentage error of 3.6%.

Clinical End Points

In the overall population, one patient died because of pneumonia 3 months after TAVR (no procedure- or valve-related death), 10 procedures (13%) were complicated by periprocedural myocardial infarction, and only one patient had a stroke (nondisabling according to the modified Rankin scale). Eleven patients (14%) had bleeding complications, including four major: two intramuscular bleeding with compartment syndrome, one hemopericardium requiring surgery, and one overt bleeding with a drop of hemoglobin level of >3 g/dL according to the definitions of the Valve Academic Research Consortium 2 consensus document.[6] There were 10

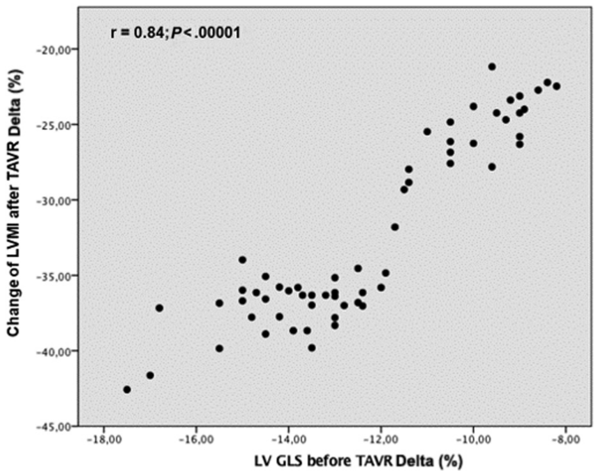

Figure 4 Scatterplot between percentage change in LVMI at follow-up and LV GLS at baseline in the overall population of LFLG AS.

vascular complications (13%): one major (as explained previously), nine minor access-site complications (ruptured access site requiring percutaneous transluminal angioplasty with implantation of stent, distal embolization in superficial femoral artery resolved with local thrombolysis, pseudoaneurysm, and common iliac artery dissection). Fifteen patients (17%) had acute kidney injury. In 17 patients (20%), the procedure was followed immediately by onset of left bundle branch block, and three of these patients (4%) required permanent pacemaker implantation. TAVR resulted in diminished symptoms: at 6-month follow-up, all patients were in NYHA functional class I or II (mean NYHA functional class before TAVR, 3.3 $\pm$ 0.8; mean NYHA functional class after TAVR, 1.3 $\pm$ 0.4; $P < .0001$).

DISCUSSION

Improvement of LV Systolic Function and "Reverse Remodeling" after TAVR in LFLG AS

In a previous study, our group documented significant improvements in global, regional, longitudinal, and radial strain 6 months after TAVR in patients with symptomatic normal-flow, high-gradient AS.[9] These data were also confirmed by other authors.[10,11] Current evidence suggests that afterload is responsible for GLS impairment, so that better GLS in the face of increased LV afterload may be indicative of a relatively compensated myocardial contractile function, whereas worse GLS may correlate with the risk for symptom development, irreversible myocardial damage, and increased myocardial fibrosis.[12] Furthermore, Adda *et al.*[13] previously demonstrated that longitudinal LV dysfunction is particularly severe in patients with LFLG AS. In fact, patients with LFLG AS showed significant worsening in basal longitudinal strain compared with those with normal-flow, high-gradient AS and normal-flow, low-gradient AS.

After aortic valve replacement, changes in LV systolic function are not only related to relief of pressure overload but also associated with LV remodeling. Previously, our group demonstrated LV "reverse remodeling" assessed by 2D STE in patients with severe AS undergoing TAVR.[9] In addition, the Placement of Aortic Transcatheter Valve trial showed a significant reduction in LVMI at 2-year follow-up without significant changes in LV volumes.[14] However, selected data on LV remodeling in patients with LFLG AS after TAVR are very limited. Gotzmann *et al.*[15] demonstrated significant reductions in LVMI in 10 patients with LFLG AS and higher LVEFs at 6 months after TAVR. Kamperidis *et al.*[16] demonstrated that patients with LFLG AS benefit from TAVR, with significant reduction in LV mass and improvement in LV systolic function. These improvements were independent of TAVR access (transfemoral or transapical), baseline LVEF, and LVMI and other clinical variables.

In accordance with such previous research, our study underlined significant LV "reverse remodeling," with a reduction of LVMI and relevant improvement of LVEF and LV GLS, also in a larger population of patients with classical LFLG AS undergoing TAVR. Furthermore, we observed that LAVI was reduced significantly after TAVR. Similarly, in our previous study, we reported that LAVI was smaller and left atrial reservoir function significantly improved after the procedure in patients with classical AS.[9]

Predictive Value of LV 2D Strain on Reverse Remodeling after TAVR in LFLG AS

To the best of our knowledge, this is the first prospective study assessing in patients with LFLG AS the predictive value of 2D STE on LV morphology and function at follow-up after TAVR.

In our population, 2D GLS before TAVR was an independent predictor of LV flow reserve during DSE. Moreover, LV GLS before TAVR was an independent predictor of LV end-systolic volume and of LVMI after TAVR. On receiver operating characteristic curve analysis, a cutoff value for LV GLS of -12% well distinguished patients without significant contractile reserve and with lack of remodeling after TAVR at follow-up.

According to previous reports, GLS is independently associated with mortality in patients with low-LVEF, low-gradient AS,[17] and the measurement of GLS at rest and during DSE may be helpful to enhance risk stratification in low-LVEF, low-gradient AS.[17,18] Our results support the hypothesis that myocardial analysis at baseline could be useful for the identification of patients who would benefit from TAVR, which is pivotal to their well-being and to the correct use of technical and economic resources.

Study Limitations

Limitations of this study include its small sample size and the technical limitations of 2D STE (image resolution). Moreover, another limitation of our study was that the cutoff value was not tested in an independent population to determine its accuracy. Although our results were obtained after implantation of the self-expanding CoreValve, they could be applicable to all types of catheter-based valves. In addition, the data from the present study may not be extrapolated to the overall population of patients with LFLG AS, because of the exclusion of "paradoxical" AS, which eliminated patients with preserved LVEFs from statistical analyses. However, we intentionally selected symptomatic patients with "classical" LFLG AS and normal coronary vessels to examine changes in strain global and regional properties independent of ejection fraction and/or ischemic disease. Additionally, we did not analyze the outcome data in relation to GLS, and the mean follow-up duration was too short. Additional longitudinal studies by strain analyses are warranted to further our understanding of the natural history of LV myocardial deformation and work in patients with AS with either preserved or reduced LVEFs and the possible long-term impact of such changes on outcomes in patients with AS.

CONCLUSION

In the present study, using a selected population of patients with LFLG AS, we documented significant LV "reverse remodeling" and improvement of LV myocardial deformation after TAVR procedure, assessed both by standard methods and by 2D STE. This is the first study to investigate the predictive value of 2D STE on LV flow reserve and LV remodeling in patients with LFLG AS undergoing TAVR. Additional longitudinal studies by strain analyses are warranted to further our understanding of the natural history of myocardial deformation in patients with LFLG AS, the extent of reversibility of LV dysfunction with medical therapy and/or interventional procedures, and the possible long-term impact of such changes on outcomes in patients with LFLG AS.

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