Left Ventricular Functional Recovery and Remodeling in Low-Flow Low-Gradient Severe Aortic Stenosis after Transcatheter Aortic Valve Implantation

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Background: Speckle-tracking-derived global longitudinal strain (GLS) is a more sensitive method of detecting left ventricular (LV) functional recovery after transcatheter aortic valve implantation (TAVI) in patients with severe aortic stenosis. However, it remains unknown whether LV function improves in patients with low-flow, low-gradient severe aortic stenosis (LFLGSAS) after TAVI. The aim of the present was to evaluate LV functional recovery and remodeling after TAVI in patients with LFLGSAS.

Methods: Sixty-eight patients (57% men; mean age, 79.1 ± 7.1 years) with LFLGSAS treated with TAVI were evaluated. LV function and remodeling were investigated before TAVI and at 6 and 12 months after TAVI. All echocardiographic data were prospectively collected, and GLS was retrospectively analyzed.

Results: Among patients with LFLGSAS, 35 (52%) had low LV ejection fraction (LVEF) (<50%), and 33 (48%) had preserved LVEF (≥50%). The low-LVEF group had significantly more impaired GLS than the group with preserved LVEF (−8.3 ± 2.6% vs −13.3 ± 3.5%, $P < .001$). LV systolic function improved after TAVI in both groups. Although in the group of patients with low LVEF, all functional parameters improved, in the group of patients with preserved LVEF, only strain-derived parameters significantly improved. There were significant decreases in absolute LV wall thickness and relative wall thickness and a trend toward decreased LV mass index in both LVEF groups. LV volumes decreased significantly in those with low LVEF but not in those with preserved LVEF. Baseline GLS but not LVEF group was independently associated to GLS improvement at 12 months after TAVI.

Conclusions: Patients with LFLGSAS with low and preserved LVEF had a significant improvement in LV function after TAVI, as assessed by GLS. Absolute and relative LV wall thickness decreased in both groups of patients, but only those with low LVEF had reductions in LV volumes. (J Am Soc Echocardiogr 2014;■:■-■.)

Keywords: Aortic valve stenosis, Low-flow low-gradient, Speckle-tracking, Strain, Transcatheter aortic valve implantation

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The prevalence of low-flow, low-gradient severe aortic stenosis (LFLGSAS) among patients referred for aortic valve replacement is relatively high. Pooled data from the Placement of Aortic Transcatheter Valves (PARTNER) trials (including the inoperable and high-risk cohorts) showed a prevalence of 29% of LFLGSAS.[1] Transcatheter aortic valve implantation (TAVI) in this group of patients leads to a better prognosis than medical treatment.[1-3] The associated factors that may determine improved outcomes remain unknown. Probably improvements in left ventricular (LV) mechanics and remodeling after relief of pressure overload may influence positively the prognosis of the patients. However, changes in LV function and remodeling after TAVI in this particular group of patients have not been investigated. In addition, it remains unknown when exactly these changes do occur, either early after reducing the pressure overload or later at follow-up.

LV ejection fraction (LVEF) is the most frequently used parameter to assess LV function, although it may not be sensitive enough to detect significant improvement in LV mechanics after TAVI, particularly in the subgroup of patients with LFLGSAS and preserved LVEF. Recently, it has been suggested that speckle-tracking-derived

Abbreviations

AVA = Aortic valve area

BSA = Body surface area

CI = Confidence interval

GLS = Global longitudinal strain

GLSr = Global longitudinal strain rate

LFLGSAS = Low-flow, low-gradient severe aortic stenosis

LV = Left ventricular

LVEF = Left ventricular ejection fraction

LVMi = Left ventricular mass index

PARTNER = Placement of Aortic Transcatheter Valves

global longitudinal strain (GLS) is a more sensitive method than LVEF in detecting LV myocardial recovery after TAVI.[4,5] Therefore, the aim of the present evaluation was to characterize LV functional recovery, estimated by LVEF and GLS, and LV remodeling, estimated by LV mass and volumes, after TAVI in patients with LFLGSAS, with special focus on subpopulations with reduced LVEFs (<50%), known as "classical LFLGSAS," and preserved LVEFs (≥50%), known as "paradoxical LFLGSAS," according to the guidelines of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery.[6] In addition, the time course of these changes was investigated.

METHODS

Patients

From a cohort of 253 patients with symptomatic severe aortic stenosis who underwent TAVI at the Leiden University Medical Center, 68 patients (27%) were identified as having LFLGSAS according the baseline Doppler echocardiographic estimation of aortic valve area (AVA) index (≤0.6 cm^2/m^2), mean pressure gradient across the aortic valve (≤40 mm Hg) and stroke volume index (≤35 mL/m^2).[6,7] LV remodeling and functional recovery were evaluated at follow-up after successful TAVI. LV mass index (LVMi) and indexed LV volumes were measured at baseline and at 6 and 12 months after TAVI. In addition, LVEF and speckle-tracking-derived GLS and global longitudinal strain rate (GLSr) were assessed. Further analysis by dividing the population into low-LVEF (<50%) and preserved-LVEF (≥50%) groups at baseline was performed. Patients who had high-gradient aortic stenosis, patients who underwent "valve-in-valve" procedures, and patients who had more than mild aortic regurgitation before TAVI were excluded from the analysis. For this retrospective evaluation, the institutional review board waived the requirement for patients' written informed consent.

TAVI Procedure

TAVI was performed at the catheterization laboratory under general anesthesia and the 23-, 26-, or 29-mm Edwards SAPIEN and SAPIEN XT (Edwards Lifesciences, Irvine, CA) or the 26-, 29-, or 31-mm Medtronic CoreValve (Medtronic, Minneapolis, MN) was implanted. The preferred approach was transfemoral. The transapical approach was used in patients with unfavorable iliofemoral anatomy or in patients in whom 29-mm Edwards SAPIEN XT valves were implanted.[8] A successful TAVI procedure was defined as the implantation of a well-functioning valve in the aortic annulus, without intraprocedural death.[9]

Two-Dimensional Transthoracic Echocardiography

Transthoracic echocardiography was performed before TAVI and at 6 and 12 months after TAVI using a commercially available ultrasound system (Vivid 7 and Vivid E9; GE Vingmed Ultrasound AS, Horten, Norway) equipped with 3.5-MHz or M5S transducers. Two-dimensional grayscale images and color, continuous-wave, and pulsed-wave Doppler data were acquired from the parasternal, apical, and subcostal acoustic windows. Data were stored digitally and analyzed offline on a dedicated workstation (EchoPAC version 112.0.1; GE Vingmed Ultrasound AS).

Aortic stenosis severity was quantified by measuring the maximum velocity through the aortic valve using continuous-wave Doppler. The mean pressure gradient was estimated using the modified Bernoulli equation.[10] The LV outflow tract was measured on two-dimensional transthoracic echocardiography, and subsequently, AVA was calculated using the continuity equation and indexed to body surface area (BSA).[10] Energy loss index was calculated as $[(AVA \times A_A)/(A_A - AVA)]/BSA$, where A_A is aortic cross-sectional area at the level of the sinotubular junction.[10,11] LV dimensions were measured in the parasternal long-axis view on two-dimensional grayscale images. LV mass was then estimated according to the formula of Lang *et al.*[12] $(0.8 \times \{1.04[(\text{LV end-diastolic diameter} + \text{posterior wall thickness in diastole} + \text{septal wall thickness in diastole})^3 - (\text{LV end-diastolic diameter})^3]\} + 0.6\ g)$ and indexed to BSA. Relative wall thickness ([2 × posterior wall thickness in diastole]/LV end-diastolic diameter)[13] and the ratio of LV mass to LV end-diastolic volume were then estimated.[13] LV end-diastolic and end-systolic volumes were calculated from the apical four- and two-chamber views and then indexed to BSA.[12] LVEF was derived using the biplane Simpson method.[12] Stroke volume was calculated by multiplying the LV outflow tract cross-sectional area by the velocity-time integral derived from the pulsed-wave Doppler recordings acquired at the LV outflow tract. Cardiac output was estimated by multiplying stroke volume by heart rate and cardiac index by indexing cardiac output for BSA.[7] Prosthesis-patient mismatch was defined as AVA index ≤ 0.85 cm^2/m^2.[14]

Two-Dimensional Speckle-Tracking Echocardiography

LV systolic function was assessed using two-dimensional speckle-tracking echocardiography–derived GLS and GLSr. To estimate GLS, the three-, four-, and two-chamber apical views were optimized to achieve a frame rate of ≥40 frames/sec, recorded in two-dimensional grayscale and then analyzed offline on a workstation with commercially available software (EchoPAC version 112.0.1). Aortic valve closure timing was first defined at the apical LV long-axis view, and the LV endocardial border was then traced at each apical view at an end-systolic frame. A region of interest was automatically defined and adapted not to extend beyond the epicardial border. Finally, GLS and GLSr were calculated as the average of all three apical views. GLS was expressed as a percentage and GLSr per second. Two representative examples of GLS evaluation at the three time points (before TAVI and 6 and 12 months after TAVI) for a patient with a low LVEF and a patient with a preserved LVEF are presented in Figure 1 and Figure 2, respectively.

Statistical Analysis

Statistical analyses were performed using SPSS version 20 (SPSS, Inc, Chicago, IL). All categorical values are expressed as frequency (percentage) and continuous variables as mean ± SD. Continuous variables were compared between the two groups at baseline using Student's *t* test or the Mann-Whitney *U* test, as appropriate, and categorical variables using χ^2 tests.

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