



Original Research

Diastolic Dysfunction and Health Status Outcomes After Transcatheter Aortic Valve Replacement



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ABSTRACT

Background: Baseline left ventricular diastolic dysfunction (LVDD) is associated with poor health status in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement (TAVR), but health status improvement after TAVR appears similar across all grades of LVDD. Here, we aim to examine the relationship between changes in LVDD severity and health status outcomes following TAVR.

Methods: Patients who underwent TAVR and had evaluable LVDD at both baseline and 1 year in the PARTNER (Placement of Aortic Transcatheter Valves) 2 SAPIEN 3 registries and PARTNER 3 trial were analyzed. LVDD grade was evaluated using echocardiography core lab data and an adapted definition of American Society of Echocardiography guidelines. Health status was assessed using the Kansas City Cardiomyopathy Questionnaire Overall Summary (KCCQ-OS) score. The association between Δ LVDD severity and Δ KCCQ-OS was examined using linear regression models adjusted for baseline KCCQ-OS.

Results: Of 1100 patients, 724 (65.8%), 283 (25.7%), and 93 (8.5%) had grade 0/1, 2, and 3 LVDD at baseline, respectively. At 1 year, LVDD severity was unchanged in 790 (71.8%) patients, improved in 189 (17.2%), and worsened in 121 (11.0%). Among 376 patients with baseline grade 2 or 3 LVDD, 50.3% had improvement in LVDD. In the overall cohort, KCCQ-OS score improved by 21.9 points at 1 year. There was a statistically significant association between change in LVDD severity (improved, unchanged, and worsened) and Δ KCCQ-OS at 1 year ($p = 0.007$).

Conclusions: Change in LVDD grade was associated with change in health status 1 year following TAVR.

ABBREVIATIONS

6MWT, six-minute walk test; AS, aortic stenosis; ASE, American Society of Echocardiography; EACVI, European Association of Cardiovascular Imaging; KCCQ, Kansas City Cardiomyopathy Questionnaire; LV, left ventricle; MR, mitral regurgitation; MS, mitral stenosis; LVDD, left ventricular diastolic dysfunction; TAVR, transcatheter aortic valve replacement; TR, tricuspid regurgitation; STS PROM, Society of Thoracic Surgeons Predictive Risk of Mortality.

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Introduction

As the indications for transcatheter aortic valve replacement (TAVR) expand across the spectrum of operative risk, the pool of patients with severe symptomatic aortic stenosis (AS) eligible for TAVR continues to grow, including younger patients with longer life expectancies. As a result, there is a growing need to better understand predictors of long-term outcomes, one of which is left ventricular diastolic dysfunction (LVDD).

LVDD has been shown to predict poor outcomes in patients with AS,¹ including those undergoing TAVR.²⁻⁵ The presence of LVDD at baseline is associated with increased risks of mortality and cardiovascular hospitalization 1 year following TAVR.²⁻⁴ Conversely, after the elimination of AS-induced afterload following TAVR, improvement in LVDD is associated with a reduction in adverse events at 1 year.^{3,4} While there is accumulating evidence regarding the impact of LVDD on clinical outcomes, there remains a paucity of knowledge about the associations of LVDD before and after TAVR with patients' symptoms, functional status, and quality of life. Health status outcomes are an important endpoint for patient populations considering TAVR.⁶

Previous studies have demonstrated that patients with baseline LVDD have worse health status at the time of TAVR; however, health status improvement after TAVR appears similar across all grades of LVDD.⁷ Whether changes in LVDD are associated with health status recovery after TAVR remains unclear. Accordingly, we evaluated the association between change in LVDD and change in health status following TAVR.

Materials and Methods

Study Population and Echocardiographic Acquisition

Patients enrolled in the PARTNER (Placement of Aortic Transcatheter Valves) 2 SAPIEN 3 registries and the PARTNER 3 trial were included. The design and results of these trials have been previously reported.⁸⁻¹⁰ In brief, these were prospective multicenter studies that enrolled patients with severe symptomatic AS across the surgical risk spectrum, that is, inoperable/high-risk, intermediate-risk, and low-risk. Both trials were approved by the individual site institutional review boards, and written informed consent was provided by all patients. The trials were registered with [ClinicalTrials.gov](https://clinicaltrials.gov): #NCT03222141 (P2 S3 high-risk/inoperable cohort), #NCT03222128 (P2 S3 intermediate-risk cohort), and #NCT02675114 (P3). Patients with severe mitral regurgitation (MR), mitral stenosis (MS) of any severity, or missing data necessary for assessing LVDD grade in this study (e.g., peak E and A velocities) were excluded from the analytic cohort.

Assessment of Diastolic Dysfunction

All echocardiograms were analyzed by independent echocardiography core laboratories in accordance with American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) standards.¹¹ Image acquisition and analysis quality assurance were ensured by the use of a detailed acquisition protocol, intraobserver and interobserver variability testing, and by comprehensive training. LVDD was assessed at baseline and 1-year post-TAVR. The diagnosis and severity of LVDD were examined using definitions adapted from guidelines set forth by ASE/EACVI.¹² The 4 variables required for identifying the presence of LVDD and their abnormal cutoff values are: (1) annular e' velocity (septal e' <7 cm/s or lateral e' <10 cm/s); (2) average E/e' ratio >14; (3) left atrial volume index >34 mL/m²; and (4) peak tricuspid regurgitation (TR) velocity >2.8 m/s.¹² LVDD was considered present if 3 or more variables were abnormal. Grade 0 LVDD or normal diastolic dysfunction was considered present if only one variable was abnormal. The required variables to grade the severity of LVDD were the mitral inflow pattern (E/A ratio) and peak E velocity. Grade 1 LVDD was

defined as an E/A ratio ≤ 0.8 and peak E velocity <50 cm/s. Grade 3 LVDD was defined as an E/A ratio ≥ 2 .

If the E/A ratio was ≤ 0.8 and E > 50 cm/s or E/A ratio was >0.8 but <2, then additional parameters were necessary. To further characterize LVDD severity, 3 recommended variables and their abnormal cutoffs were required: (1) peak TR continuous-wave Doppler velocity >2.8 m/s; (2) E/e' ratio (septal E/e' ratio >15, lateral E/e' ratio >13, or average E/e' ratio >14); and (3) left atrial volume index >34 mL/m². If 2 or 3 of these variables met their cutoff values, grade 2 LVDD was identified. If 0 or 1 of the 3 variables met their cutoff values, grade 1 LVDD was identified. If only 2 variables were available to analyze, 0, 1, and 2 abnormal variables classified LVDD grade as grade 0/1, grade indeterminate, and grade 2, respectively. The indeterminate group was excluded from this analysis. The same methodology was used to assess LVDD at follow-up echocardiograms. Change in LVDD was evaluated between baseline, 30 days, and 1-year post-TAVR. "Improved" LVDD was defined as a decrease of ≥ 1 LVDD grade at 30 days or 1 year. Conversely, "worsened" LVDD was defined as an increase of ≥ 1 LVDD grade at 30 days or 1 year. Otherwise, LVDD was considered "unchanged."

Measurement of Health Status

Patient-level health status was assessed using the 23-item Kansas City Cardiomyopathy Questionnaire (KCCQ) at baseline, 30 days, and 1 year after TAVR. The 23-item KCCQ¹³ is a self-administered questionnaire in patients with heart failure that has been shown to be a reliable and valid instrument in patients with AS.¹⁴ A KCCQ Overall Summary (KCCQ-OS) score is calculated as the average of 5 domain areas: physical limitation, symptom frequency, quality of life, self-efficacy, and social limitation. The range of KCCQ-OS scores is 0 to 100 categorized as very poor (KCCQ-OS < 25), poor (KCCQ-OS 25-49), fair (KCCQ-OS 50-74), and good health status (KCCQ-OS ≥ 75). Changes of 5, 10, and 20 points on the KCCQ-OS indicate a small, moderate, and large change in health status.¹⁵ Six-minute walk test (6MWT) distance (in meters) was analyzed as a secondary measurement of health status at baseline, 30 days, and 1 year after TAVR.

Statistical Analysis

Baseline characteristics and echocardiographic parameters were compared by LVDD grade severity. Continuous variables were compared using analysis of variance, and categorical variables were compared using Fisher exact test. The mean KCCQ-OS at baseline, 30 days, and 1 year following TAVR and the change from baseline at follow-up visit were compared across LVDD grades using analysis of variance. In addition, from baseline to the 1-year time point, we presented the frequencies of different magnitudes of change in KCCQ-OS across the change of LVDD (unchanged, improved, worsened) and across the number of grades changed (i.e., improved 2 grades and worsened 2 grades). Lastly, a linear regression model was used to examine the association between change in LVDD grade and change in KCCQ-OS at 1 year following TAVR. The model was adjusted for baseline KCCQ-OS, age, sex, hypertension, chronic obstructive pulmonary disease, and stroke.

Results

Study Population

Between October 2013 and October 2017, a total of 2253 TAVR patients were enrolled in the PARTNER 2 SAPIEN 3 registries and PARTNER 3 trial. Of these, 593 patients were excluded from analysis for the following reasons: severe MR (n = 17), MS (n = 155), and missing data (e.g., missing E/A ratio; n = 421). Baseline LVDD grade was evaluated in 1660 patients; LVDD grade was indeterminate in 85 patients who were excluded from analysis. Between baseline and 1 year, 475 patients were also excluded due to missing LVDD grade (n = 117 died; n = 48 exited the study; n = 257 had unevaluable echocardiograms; n = 53 had

indeterminate LVDD grade). The final paired analytic cohort comprised 1100 patients (Figure 1).

Baseline characteristics of the study patients according to LVDD grade are provided in Table 1. According to adapted ASE/EACVI classification, the patients were stratified as LVDD grade 0/1 (n = 724, 65.8%), grade 2 (n = 283, 25.7%), and grade 3 (n = 93, 8.5%). The mean age was 79.8 years, 57.5% were male, the average Society of Thoracic Surgeons Predictive Risk of Mortality (STS PROM) score was 4.9 ± 2.9 , and 65.8% had mild baseline LVDD. Age, race, STS PROM score, and gait speed were the only significant differences in

baseline characteristics between the grades of LVDD. The median duration of follow-up was 1292.4 ± 488.2 days.

Baseline Echocardiographic Parameters

At baseline, higher LVDD grade was associated with larger left atrial volume indices, higher rates of MR or TR, and higher right ventricular systolic pressures ($p < 0.001$). Conversely, higher baseline LVDD grades were associated with smaller aortic valve areas and lower left ventricular ejection fractions ($p < 0.001$) (Table 2).

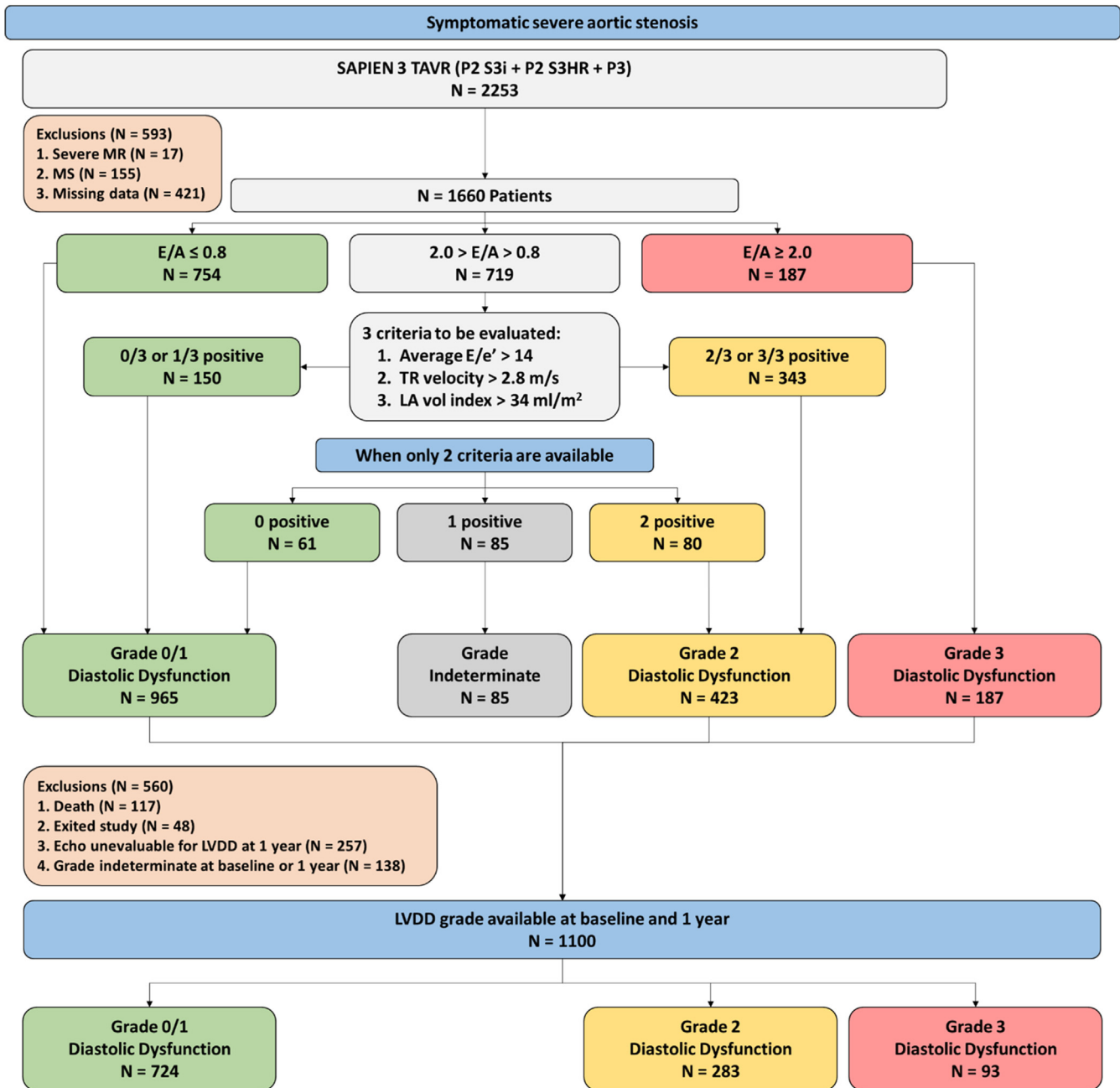


Figure 1. Algorithm for assessment of baseline LVDD. Derivation of the final analytic cohort by LVDD severity. Patients with severe aortic stenosis undergoing TAVR from the PARTNER 2 SAPIEN 3 high- and intermediate-risk registries and PARTNER 3 low-risk trial were assessed for baseline LVDD. LVDD grade was evaluated using echocardiography core lab data and an adapted definition of American Society of Echocardiography guidelines. Patients who had evaluable data at both baseline and 1 year were analyzed.

Abbreviations: LA, left atrium; LVDD, left ventricular diastolic dysfunction; MR, mitral regurgitation; MS, mitral stenosis; PARTNER, Placement of Aortic Transcatheter Valves; TAVR, transcatheter aortic valve replacement; TR, tricuspid regurgitation.

Table 1

Baseline characteristics according to baseline LVDD grade

Characteristics	Grade 0/1 (N = 724)	Grade 2 (N = 283)	Grade 3 (N = 93)	p value*
Age, y	79.3 ± 7.62	80.7 ± 7.31	81.3 ± 7.78	0.0036
Female sex	307/724 (42.4%)	130/283 (45.9%)	30/93 (32.3%)	0.0674
Non-Caucasian	48/724 (6.6%)	34/283 (12.0%)	7/93 (7.5%)	0.0227
STS PROM	4.5 ± 2.83	5.5 ± 2.79	6.1 ± 3.20	<0.0001
HTN	641/724 (88.5%)	255/283 (90.1%)	88/93 (94.6%)	0.1791
Home O ₂	23/437 (5.3%)	12/233 (5.2%)	4/81 (4.9%)	>0.9999
ESRD on HD	49/724 (6.8%)	23/283 (8.1%)	7/93 (7.5%)	0.7090
Stroke	54/724 (7.5%)	23/283 (8.1%)	8/93 (8.6%)	0.8306
Sleep apnea†	45/281 (16.0%)	9/47 (19.1%)	1/9 (11.1%)	0.8827
Gait speed‡				
Normal ≥0.83m/s	284/712 (39.9%)	70/280 (25.0%)	22/92 (23.9%)	<0.0001
Slow 0.5-0.83m/s	224/712 (31.5%)	98/280 (35.0%)	25/92 (27.2%)	
Slowest <0.5m/s	204/712 (28.7%)	112/280 (40.0%)	45/92 (48.9%)	

Values presented as mean ± SD or n/N (%).

Abbreviations: ESRD on HD, end-stage renal disease on hemodialysis; HTN, hypertension; LVDD, left ventricular diastolic dysfunction; STS PROM, Society of Thoracic Surgeons Predictive Risk of Mortality.

* p values were computed by analysis of variance for continuous variables and Fisher exact test for categorical variables.

† Sleep apnea was not collected in the SAPIEN 3 registries.

‡ Gait speed was calculated based on six-minute walk test; slowest group includes those unable to walk.

Change in LVDD at 30 Days and 1 Year Following TAVR

Of 1100 patients who had baseline and 1-year LVDD assessments, 997 also had completed a 30-day LVDD assessment. The changes in LVDD grades between baseline, 30 days, and 1 year are shown in [Supplemental Figure 1](#). At 30 days following TAVR, LVDD severity was unchanged in 709 (71.1%) patients, improved in 177 (17.8%), and worsened in 111 (11.1%) patients. At 1 year, LVDD severity was unchanged in 790 (71.8%) patients, improved in 189 (17.2%), and worsened in 121 (11.0%) patients. Among patients with grade 2 or grade 3 LVDD at baseline, 53.2% had an improvement in LVDD grade at 30 days and 50.3% demonstrated an improvement at 1 year. Out of the 177 patients with improved LVDD from baseline to 30 days, 126 (71.2%) patients showed sustained improvements at 1 year ([Supplemental Table 1](#)). There was no significant interaction between STS PROM and change in LVDD grade.

Association Between Change in LVDD and Health Status

In the overall cohort, the KCCQ-OS score improved by 21.9 points at 1-year follow-up. Changes in KCCQ-OS score from baseline to 30 days and 1 year stratified by baseline LVDD grade are summarized in [Table 3](#). The proportion of patients experiencing different magnitudes of change in KCCQ-OS at 1-year follow-up is shown in [Figure 2](#), stratified according to change in LVDD (unchanged, improved, worsened). In the unadjusted analysis, the mean (95% CI) KCCQ-OS increased by 24.1 (21.1, 27.2) points among patients with improved LVDD; 22.1 (20.6, 23.6) points among patients with unchanged LVDD, and 17.4 (13.5, 21.3) points change in KCCQ-OS at 1-year post-TAVR among patients whose LVDD worsened ($p = 0.0278$). In the adjusted analysis, there was a statistically significant association between change in LVDD severity (improved, unchanged, and worsened) and Δ KCCQ-OS at 1 year ($p = 0.007$). In comparison to unchanged LVDD, worsened LVDD was associated with

Table 2

Comparison of baseline echocardiographic characteristics in patients according to LVDD grade

Characteristics	Grade 0/1 (N = 724)	Grade 2 (N = 283)	Grade 3 (N = 93)	p value*
Mean aortic valve gradient	47.9 ± 13.32	48.6 ± 14.32	44.3 ± 11.44	0.0682
Aortic valve area	0.72 ± 0.172	0.69 ± 0.160	0.65 ± 0.151	<0.0001
LVEF	64.2 ± 11.88	60.2 ± 14.22	53.4 ± 14.43	<0.0001
RVSP	29.1 ± 7.75	37.3 ± 12.82	41.8 ± 12.18	<0.0001
Mitral regurgitation	260/713 (36.5%)	176/282 (62.4%)	73/93 (78.5%)	<0.0001
Mild	243/713 (34.1%)	152/282 (53.9%)	55/93 (59.1%)	NA
Moderate	17/713 (2.4%)	24/282 (8.5%)	18/93 (19.4%)	
Severe	0/713 (0.0%)	0/282 (0.0%)	0/93 (0.0%)	
Aortic regurgitation	35/719 (4.9%)	23/283 (8.1%)	5/93 (5.4%)	0.2691
Moderate	34/719 (4.7%)	23/283 (8.1%)	5/93 (5.4%)	NA
Severe	1/719 (0.1%)	0/283 (0.0%)	0/93 (0.0%)	
Tricuspid regurgitation	5/696 (0.7%)	18/277 (6.5%)	13/92 (14.1%)	<0.0001
Moderate	5/696 (0.7%)	16/277 (5.8%)	9/92 (9.8%)	NA
Severe	0/696 (0.0%)	2/277 (0.7%)	4/92 (4.3%)	
E/A ratio	0.7 ± 0.20	1.1 ± 0.28	2.7 ± 0.57	<0.0001
A, cm/s	109.8 ± 27.24	102.8 ± 27.62	43.1 ± 11.60	<0.0001
E/e' ratio	13.9 ± 5.81	21.4 ± 7.68	20.0 ± 6.81	<0.0001
Average e', cm/s	7.7 ± 1.97	11.1 ± 2.08	11.3 ± 1.93	<0.0001
TR velocity (cm/s)	253.3 ± 35.08	295.9 ± 50.50	317.1 ± 48.74	<0.0001
LAVI (mL/m ²)	35.2 ± 11.16	45.1 ± 11.59	52.6 ± 15.60	<0.0001
LVOT stroke volume	75.8 ± 15.72	76.6 ± 18.33	67.2 ± 16.80	<0.0001

Values presented as (mean ± SD) or n/N (%).

Abbreviations: LAVI, left atrial volume index; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation.

* p values were computed by analysis of variance for continuous variables and Fisher exact test for categorical ones.

Table 3
Comparison of KCCQ according to baseline LVDD grade by analysis of variance

Visit	Grade 0/1 (N = 724)	Grade 2 (N = 283)	Grade 3 (N = 93)	p value
Baseline	61.8 ± 21.88 (711)	57.9 ± 22.74 (277)	56.1 ± 23.82 (90)	0.0096
30 d	80.0 ± 18.50 (718)	78.4 ± 18.91 (280)	76.2 ± 20.16 (89)	0.1342
30 d change from baseline	18.6 ± 19.78 (705)	20.5 ± 21.33 (274)	20.0 ± 21.96 (87)	0.4134
1 y	82.7 ± 18.34 (708)	81.2 ± 18.29 (277)	81.7 ± 17.23 (91)	0.5105
1 y change from baseline	20.9 ± 20.28 (696)	23.3 ± 22.14 (271)	26.3 ± 24.71 (88)	0.0364

Values presented as mean ± SD (N).

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; LVDD, left ventricular diastolic dysfunction.

worsening KCCQ-OS at 1 year (Δ KCCQ-OS -4.0 [95% CI -7.1, -0.9]), whereas the association between improved LVDD and change in KCCQ-OS did not reach statistical significance (Δ KCCQ-OS +1.9 [95% CI -0.6, 4.4]). Sensitivity analyses were performed in which the 85 patients from the indeterminate baseline LVDD group were included as having grade 1 or grade 2 LVDD at baseline, and no significant differences in health status at 30 days and 1 year were observed. The addition of aortic valve mean gradient as a covariate in adjusted analyses did not significantly change these results (Supplemental Table 2).

In unadjusted analyses, 6MWT distance was lower in patients with LVDD at baseline (Table 4). However, in adjusted analyses, the association between change in LVDD at 1 year and change in 6MWT distance did not reach statistical significance ($p = 0.13$).

Discussion

Given that the treatment of AS can improve health status by both directly relieving cardiac outflow gradients and by improving the diastolic function of the left ventricle (LV), we sought to understand the association of the latter with health status improvements after TAVR. The main findings were that: (1) approximately 50% of patients with severe AS and at least moderate (grade 2) LVDD at baseline demonstrated an improvement in LVDD 1 year following TAVR, and (2) change in LVDD at 1 year was associated with differences in the extent of health status improvement after TAVR, that is, improvement in LVDD was associated with greater improvement in health status and worsening LVDD was associated with less improvement in health status. The trend between 6MWT distance and change in LVDD following TAVR was similar to the trend observed between KCCQ-OS and change in LVDD but did not reach statistical significance. This may be because KCCQ-OS is a comprehensive measurement of health status encompassing physical limitation, symptom frequency, quality of life,

self-efficacy, and social limitation whereas 6MWT distance is a measurement of exercise capacity alone. While prior studies have established the significance of improvement in LVDD following TAVR with respect to cardiovascular death and rehospitalization,⁴ these results extend the prior findings to patients' health status—their symptoms, functional status, and quality of life.

In patients with cardiovascular disease, optimization of health status and disease-specific quality of life has been recognized as an important goal of treatment.¹⁶ Using the PARTNER 2 SAPIEN 3 registry, Ong et al.⁴ demonstrated that improvement in LVDD was associated with a larger improvement in KCCQ-OS at 30 days, but health status outcomes at 1 year were not reported. A prior single-center study of 304 patients demonstrated that baseline LVDD grade was inversely associated with baseline health status; however, improvement in LVDD was not associated with 30-day or 1-year health status.⁷ In contrast, the present study reveals a significant association between change in LVDD and change in health status 1 year after TAVR.

There are several potential explanations for these divergent findings. First, the larger sample size in the current study may have allowed for better detection of changes in KCCQ during follow-up. Second, the use of a consortium of core laboratories in a clinical trial cohort may have improved the ability to detect changes in LVDD grade on follow-up and reduced variability in echocardiographic interpretation. Third, the definition of severe AS required for enrollment in trial cohorts may be more strict than what is seen in clinical practice. Irrespective of the exact mechanism for these differences, our findings can be further explained by exploring the pathophysiology of LVDD with severe AS.

Progressive mechanical obstruction due to AS imposed on the LV leads to increased afterload with the eventual development of hypertrophic remodeling and reactive interstitial fibrosis.¹⁷⁻¹⁹ Consequently, impairment in myocardial relaxation and increased cardiomyocyte



Figure 2. Health status change 1-year post-TAVR by change in LVDD severity. Unadjusted change in KCCQ-OS score from baseline to 1 year by patients whose LVDD grade stayed the same (N = 758), improved (N = 185), or worsened (N = 112) from baseline to 1 year. Majority of patients across the LVDD spectrum had an improvement in KCCQ-OS score after TAVR, however, the largest improvement in health status was seen in patients whose LVDD grade also improved.

Abbreviations: KCCQ-OS, Kansas City Cardiomyopathy Questionnaire—Overall Summary; LVDD, left ventricular diastolic dysfunction; TAVR, transcatheter aortic valve replacement.

Table 4
Comparison of 6MWT distance according to baseline LVDD grade by analysis of variance

Visit	Grade 0/1 (N = 724)	Grade 2 (N = 283)	Grade 3 (N = 93)	p value
Baseline (m)	250.3 ± 134.01	207.0 ± 125.84	190.7 ± 121.80	<0.0001
30 d (m)	277.5 ± 133.78	244.2 ± 127.70	234.9 ± 130.20	0.0001
30 d change from baseline (m)	24.4 ± 102.66	37.6 ± 99.10	43.2 ± 128.67	0.0866
1 y (m)	271.7 ± 141.23	235.3 ± 138.29	229.2 ± 127.01	0.0002
1 y change from baseline (m)	18.4 ± 114.95	31.5 ± 128.56	38.0 ± 139.05	0.1621

Values presented as mean ± SD.

6MWT, six-minute walk test; LVDD, left ventricular diastolic dysfunction.

stiffness culminate in the development of LVDD.²⁰ As LVDD progresses, transmittance of elevated end-diastolic pressures to the pulmonary vasculature leads to increased pulmonary capillary pressure which manifests as exertional dyspnea or overt heart failure, the most common symptoms of severe AS.^{21,22} Elimination of AS-associated afterload by TAVR has been shown to induce regression of LV hypertrophy^{23,24} and subsequently improve LVDD.²⁵ To this end, it is plausible that improvement in LVDD following TAVR contributes to improvement in symptomatology, and hence, health status as seen in the present study.

In agreement with previous observations,^{2,4,24} our study demonstrates that LVDD grade may not improve or may even worsen following TAVR in a substantial group of patients. Worsened LVDD was found to be associated with less improvement in health status at 1 year following TAVR. Our study shows that increasing severity of baseline LVDD is associated with worsening echocardiographic changes in cardiac structure and function (ie, left atrial volume, MR, TR, LV ejection fraction) and worsening LV filling and relaxation (i.e., E/A ratio, average e' velocity, TR velocity), indicating progression of disease and compromised cardiac reserve. How these factors impact health status following TAVR is unknown. Despite reduction of afterload with TAVR, there may be slow nonlinear regression of LV hypertrophy^{23,25} and/or sustained myocardial fibrosis^{26,27} that may contribute to the irreversibility of LVDD. Furthermore, particularly in the elderly population, concomitant pathologies contributing to persistent or residual LVDD may be underrecognized, such as hypertension²⁸ or cardiac amyloidosis.²⁹ The nonuniformity of change in LVDD post-TAVR highlights its complex mechanisms and multifactorial etiologies and underscores the need for further diagnostic investigation.

The use of multimodality imaging is essential in the evaluation of cardiac function and structure during follow-up after TAVR.³⁰ Novel echocardiographic parameters such as LV diastolic strain^{31,32} and left atrial strain^{33,34} may offer additional diagnostic and prognostic value in refining LVDD assessment. In a single-center study of 100 patients undergoing TAVR, Sabatino et al.³⁵ found left atrial strain, which is correlated with elevated LV end-diastolic pressures,³³ to be predictive of mortality and heart failure hospitalization. Cardiac magnetic resonance imaging can also provide a direct examination of myocardial fibrosis as measured by extracellular volume and late gadolinium enhancement.^{36,37} Chin et al.¹⁸ demonstrated, in a prospective cohort of 166 AS patients and 37 healthy volunteers, that there was progressive LV decompensation, including worsening LVDD, across stages of fibrosis. Early reversible diffuse myocardial fibrosis, quantified by extracellular volume on T1-mapping, has been found to be associated with LVDD in patients with AS³⁸ and may potentially enhance LVDD assessment post-TAVR. Further studies are needed to determine whether these tools can help inform the assessment of LVDD following TAVR.

Study Limitations

The findings of this study should be interpreted in the light of several potential limitations. First, 51.2% of the initial cohort were excluded due to various reasons such as missing baseline data, MR or MS, unevaluable echocardiogram for LVDD at 1 year, or LVDD indeterminate grade. Consequently, selection bias may have been introduced in our

observational study. The majority of missing E/A data was secondary to the presence of atrial fibrillation. Second, the presence of mitral annular calcification was not collected. Mitral annular calcification is known to influence diastolic assessment leading to falsely elevated transmitral velocities and decreased lateral and posterior annular velocities. We excluded patients with MS to overcome this potential confounding factor. Third, although the importance of myocardial fibrosis in understanding the longitudinal change in LVDD and health status following TAVR, data on myocardial fibrosis were not available for our study. Finally, advanced echo imaging parameters such as left atrial strain and left ventricular global longitudinal strain were not available in this data set and could not be analyzed.

Conclusions

Approximately half of patients with severe AS and \geq moderate LVDD at baseline demonstrated improvement in LVDD 1 year following TAVR. Moreover, improvement in LVDD was associated with greater improvement in patient-level health status. Further investigation is needed with respect to multimodal imaging in the assessment of LVDD after TAVR and clinical management.

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Ethics Statement

The research reported has adhered to the relevant ethical guidelines. The PARTNER 2 S3 Registry and PARTNER 3 Trial protocols were approved by the institutional review boards of participating sites and all patients provided written informed consent.

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Review Statement

Given their roles as editors, Philippe Pibarot, DVM, PhD, Rebecca T. Hahn, MD, Maria Alu, MS, Martin B. Leon, and Michael J. Mack, MD, had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Julius Gardin, MD.

Supplementary Material

Supplemental data for this article can be accessed on the [publisher's website](#).

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