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Transcatheter Aortic Valve Replacement Improves Quality of Life and Ventricular Function With Low-Flow/Low-Gradient Aortic Stenosis

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Abstract

Background: D2 aortic stenosis (AS) is the highest risk AS subtype with worse operative and mortality outcomes. This study aimed to investigate the quality of life (QoL) and left ventricular ejection fraction (LVEF) in patients with classic (D2 subtype) low-flow/low-gradient AS who underwent transcatheter aortic valve replacement (TAVR).

Methods: In total, 634 patients with severe AS underwent TAVR at our institution from 2014 to 2020, of whom 76 met criteria for classic D2 AS with reduced LVEF. Echocardiographic and clinical outcomes including mortality, stroke, pacemaker placement (PPM), and readmission at baseline were compared with those at 30 days and 1 year. QoL data were extracted from the Kansas City Cardiomyopathy Questionnaire (KCCQ-12).

Results: The average baseline Society of Thoracic Surgeons risk score for patients with D2 AS was 7.66 ± 6.76. Patients with D2 AS reported improved QoL post-TAVR. The average baseline KCCQ-12 score was 39.5 ± 20, with improvement to 68.9 ± 20.6 at 30 days ($P < .01$) and 74.9 ± 17.5 at 1 year ($P < .01$). Mortality was 0% at 30 days and 18.4% at 1 year. The average baseline LVEF was 36.1 ± 9.4. Left ventricular function improved to 43.5 ± 12.9 ($P < .001$) at 30 days and 46.3 ± 11.2 ($P = .03$) at 1 year. Complications post-TAVR at 30 days included stroke (1.3%) and PPM (11.8%). Patients with D2 AS exhibited higher baseline conduction defects including atrial fibrillation and higher postoperative PPM than those with other subtypes.

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Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics statement and patient consent

This work did not involve the use of human subjects, and institution review board approval was obtained for retrospective database review.

Conclusions: Patients with D2 AS had significantly improved LVEF and QoL following TAVR at 30 days and 1 year. Postoperative rates of new PPM were higher than other subtypes, while stroke, dialysis, and mortality were lower than expected, supporting the benefit of TAVR in this high-risk group.

Keywords

aortic stenosis; transcatheter aortic valve replacement; low-flow/low-gradient; cardiac surgery; quality of life

Introduction

Aortic stenosis (AS) is categorized into 3 subtypes: high-gradient (D1), classic low-flow/low-gradient with reduced ejection fraction (D2), and paradoxical low-flow/low-gradient with normal ejection fraction (D3). Low-flow/low-gradient AS is defined by aortic valve area (AVA) of ≤1.0 cm^2 and mean aortic valve (AV) gradient of <40 mm Hg. There are 2 types of low-flow/low-gradient AS. The classic low-flow/low-gradient (D2) subtype has reduced left ventricular ejection fraction (LVEF) of <50% and low cardiac output. Dobutamine stress echocardiography is recommended to assess flow and contractile reserve. The second subtype, paradoxical low-flow/low-gradient (D3), has a preserved LVEF (≥50%) and stroke volume index (SVI) of <35 mL/m^2.[1,2] Patients with D3 AS have small left ventricular cavities with subsequently reduced stroke volumes. While AV calcium scoring by multidetector computed tomography can confirm the diagnosis, a precise calcium score has not been universally accepted.[3] Pseudosevere AS refers to low-flow/low-gradient AS with low EF that is defined as a condition in which the calculated AVA falsely overestimates the severity of the AS when the AVA is calculated at low flow. In dobutamine stress echocardiography, classic D2 AS reveals an augmentation of mean gradient of >40 mm Hg and AVA <1.0 cm/m^2, whereas pseudosevere AS demonstrates stress mean gradient of <40 mm Hg and stress AVA of >1.0 cm^2. The management of patients with true-severe low-flow/low-gradient AS is particularly challenging as the AVA and AV gradient discrepancies raise questions about the true severity of AS and indications for aortic valve intervention, especially in patients with clinical symptoms and/or reduced LVEF.

Classic low-flow/low-gradient (D2) AS represents 5% to 15% of the AS population and has been associated with poorer outcomes compared with high-gradient (D1) or low-gradient with preserved LVEF (D3).[2,4–7] For patients with D1 AS, the mortality rate exceeds 50% at 2 years without valve replacement. The symptoms of AS include angina, dyspnea, and presyncope/syncope.[8] Conservative management of all patients with severe symptomatic AS has been associated with a poor prognosis, and patients with low-flow/low-gradient AS show worse prognoses. Recent reports have shown that patients with classic low-flow/low-gradient D2 AS carry the highest 1-year and 5-year mortality at 30.5% and 72.9%, respectively, compared with the other 2 subtypes in the absence of surgical intervention.[9] Mortality rates as high as 70% at 2 years have been reported for symptomatic patients with nonoperative management.[5–7,10] Patients with D2 subtype also exhibits significantly worse 1-year rates of mortality and major adverse cardiac and cerebral events following TAVR than those with D1 and D3 subtypes.[11] Consequently, patients with D2 AS are considered

as those with the highest risk subtype for AV intervention due to their reduced LVEF and low-flow cardiac output state.

There have been few studies exploring the quality-of-life (QoL) benefit in patients with D1 high-gradient AS. TAVR has shown significant QoL benefits at 30 days and 1 year for patients with severe D1 AS.[12] Patients with low-flow/low-gradient stenosis (D2 and D3) also experience a 30-day QoL improvement after TAVR.[13,14] However, evidence on QoL outcomes beyond 30 days post-TAVR, particularly for patients with the D2 AS subtype classification, remains scarce. The lack of available QoL and survival benefits for patients with low-flow/low-gradient AS has created uncertainty as to whether these patients should be offered valve intervention. Therefore, the purpose of this study was to examine the benefits of TAVR in terms of QoL and LVEF for patients diagnosed with classic D2 AS, compared with other AS subtypes.

Materials and methods

Data were extracted from the Transcatheter Valve Therapy registry. This study included 634 patients (mean age, 77.3 ± 10.0 years) with severe AS who underwent TAVR between January 2014 and July 2020 at the University of Utah Health in Salt Lake City, Utah. This represents an academic quaternary referral center in the Mountain West of the United States. Patient subgroups were determined by AS subtype (D1, D2, and D3). AS subtype was designated by AV mean gradient, AVA of <1.0 cm/m^2, and LVEF. D1 group was defined as a high-gradient subtype, with AV mean gradient of >40 mm Hg, AVA of <1.0 cm/m^2, and any LVEF value. Patients with D2 AS recorded an AV mean gradient of <40 mm Hg with an LVEF of <50%, and patients with D3 had an AV mean gradient of <40 mm Hg with an LVEF of >50%. Patients with D2 AS underwent confirmatory dobutamine stress echocardiography and/or direct dual pigtail AV gradient with dobutamine challenge at catheterization. D3 AS was confirmed with an SVI of <35 mL/m^2. Patients with an indication of native aortic insufficiency were excluded from the study. We identified 76 of the 634 patients (12%) as D2 AS. Baseline patient characteristics including age, sex, race, New York Heart Association (NYHA) class, Society of Thoracic Surgeons (STS) risk score, prior valve interventions, diabetes, lung diseases, and AV etiology were collected. Echocardiographic outcomes including LVEF, AV mean gradient, AVA, and SVI and clinical outcomes including patient mortality, stroke, pacemaker placement (PPM), length of stay, transfusion, readmission, and reoperation at baseline were compared with those at 30 days and 1 year. Twenty (3.15%) patients were lost to follow-up at 1 year. QoL data were obtained from the Kansas City Cardiomyopathy Questionnaire (KCCQ)-12 at baseline, 30-day postoperatively, and 1 year postoperatively. The KCCQ-12 overall score ranges from 0 to 100; higher scores indicate better QoL. This work was conducted under University of Utah institutional review board (00141428), which was approved on April 26, 2021.

Statistical analysis

Patient baseline characteristics were summarized using standard summary statistics, including frequencies, percentages, and means. One-way analysis of variance (ANOVA) was used to look at global differences among the groups. Post hoc comparisons between

groups for ANOVA were performed using Sidak multiple-comparison adjustment.[15] Paired *t* tests were used to compare baseline and follow-up LVEF and KCCQ scores within TAVR groups. Finally, univariable and multivariable Cox regression models were used to examine the effect of baseline LVEF and KCCQ-12 score on 1-year mortality rates across all patients and within TAVR subtype groups.

Results

Baseline characteristics

Patients with D2 AS had higher STS risk scores than those with D1 and D3 AS. STS risk score by subtype were as follows: D1, 6.60 ± 5.83; D2, 7.66 ± 6.76; and D3, 5.97 ± 4.04. A majority of patients from all subtypes were NYHA class III: D1, 74.5%; D2, 76.3%; and D3, 77.2%. Patients with D2 AS had the highest percentage in the NYHA class IV group with 15.8%, followed by those with D1 (9.5%) and then D3 (4.0%) AS. Patients with D2 AS exhibited significantly higher baseline conduction defects including atrial fibrillation ($P < .001$) and higher permanent PPM ($P < .001$) than other subtypes of AS. Baseline PPM rates by subtype were D1, 8.3%; D2, 27.6%; and D3, 9.6%. Baseline atrial fibrillation presence by subtype was D1, 25.9%; D2, 64.5%; and D3, 36.5%. Furthermore, 6.6% of patients with D2 AS underwent prior implantable cardioverter defibrillator (ICD) placement, which was significantly higher than the D1 and D3 subtypes ($P < .05$) (Table 1).

Echocardiographic data

The D2 subtype showed significant improvement in LVEF post-TAVR (Figure 1). The D2 average baseline LVEF was 36.1 ± 9.4. Left ventricular function improved to 43.5 ± 12.9 ($P < .001$) at 30 days and to 46.3 ± 11.2 ($P = .03$) at 1 year. Patients with D1 and D3 subtype showed no significant improvement in LVEF following TAVR. D2 SVI at baseline (31.4 ± 10.4) improved to 32.5 ± 12.2 at 30 days and 37.8 ± 17.3 at 1 year, although this was not statistically significant (Table 2).

Clinical outcomes

Patients with D2 subtype had the lowest 30-day mortality (compared with D1 subgroup, $P < .05$) and the highest 1-year mortality, which was not statistically significant compared with those with D2 and D3 AS (Figure 2). In-hospital mortality by subtype was as follows: D1, 2.1%; D2, 0%; and D3, 0.4%. The 30-day patient mortality by subtype was as follows: D1, 4.3%; D2, 0%; and D3, 0.4%. The 1-year patient mortality by subtype was as follows: D1, 15.9%; D2, 18.4%; and D3, 12.2% (Table 3). There was no statistically significant difference in postoperative KCCQ-12 overall scores between all 3 subtypes, but all patients reported a significantly improved QoL post-TAVR at 30 days and 1 year when compared with baseline (Figure 3). Patients with D2 AS had the lowest QoL at baseline ($P < .02$). Baseline KCCQ-12 scores by subtype were as follows: D1, 45.3 ± 26.1; D2, 39.5 ± 20.1; and D3, 49.2 ± 25.1. Thirty-day KCCQ-12 scores by subtype were as follows: D1, 73.2 ± 20.4; D2, 68.9 ± 20.6; and D3, 73.4 ± 22. Baseline to 30-day differences were significant across all groups ($P < .001$). One-year KCCQ-12 scores by subtype were as follows: D1, 79.4 ± 18.7; D2, 74.9 ± 17.5; and D3, 76.9 ± 20.3. Baseline to 1-year differences were also significant in all groups ($P < .001$). Complications post-TAVR in D2 subtype at 30 days

included ischemic stroke (1.3%), new ICD (1.3%), and new PPM (11.8%). New ICD and hemorrhagic stroke were both 1.3% at 1 year. Ischemic stroke and new PPM were both zero at 1 year. New onset dialysis, major bleeding, and valve-related readmission rates were zero at 30 days and 1 year for the D2 subtype. In a multivariable analysis controlling for age, sex, and patient clinical history characteristics, a history of percutaneous coronary intervention (PCI) had a significant protective effect against 1-year mortality ($P = .047$). Age, sex, and D subtype status were not predictors of mortality among the 3 subtypes.

Discussion

In this large, single-center study, all patients with AS reported improved QoL following TAVR at 30 days and 1 year. Patients with low-flow/low-gradient (D2 subtype) AS demonstrated significantly improved QoL and a notable increase in LVEF following TAVR at both 30 days and 1 year. Despite reporting the lowest baseline QoL, patients with D2 AS had nearly equivalent QoL improvement compared with those with other subtypes at 1 year. However, the long-term improvements in QoL and LVEF for patients with low-flow/low-gradient AS are not known (Central Illustration).

While several studies have assessed the benefit of TAVR in patients with low-flow/low-gradient AS by hemodynamic and/or QoL data, there are limited data on these outcomes, specifically for the different subtypes. To our knowledge, our study is the first to report improvements in QoL and LVEF specifically in patients with D2 AS because they were compared with those with other D1 and D3 subtypes for a time interval greater than 30 days. Mosleh et al[16] found similar QoL improvements and mortality in patients with D1 versus those with D3 at 1 year. However, they excluded patients with LVEF of <50% (D2 subtype). Ahmed et al[13] evaluated QoL in patients with low-flow AS who underwent TAVR with a median follow-up of 2.4 years and found similar improvements in QoL in all subtypes with no difference in mortality. Only 25 (8%) patients in this study had classic D2 AS, and echocardiographic data were not captured at 1 year. Ribeiro et al[4] evaluated a largest group of 287 patients with D2 low-flow/low-gradient AS from the TOPAS-TAVI registry and found an increase of 8.3% in LVEF at the 1-year follow-up. Mortality was 3.8% at 30 days and 20.1% at 1 year. They excluded patients with D1 and D3 and did not evaluate their QoL.[4] Simone et al[17] investigated QoL outcomes in all D subtypes, similarly finding significant improvement after TAVR; however, data were not collected past 30 days.

In our patient experience, patients with D2 AS had the lowest rates of both valve-related and non–valve-related readmissions at 30 days and 1 year, along with the lowest mortality at 30 days. Despite these findings, patients with D2 exhibited the highest rate of mortality at 1 year at 18.5%. Wagener et al[18] performed a multicenter study from the SwissTAVI registry, similarly finding the highest 1-year mortality rate in the classic low-flow/low-gradient compared with that in the high-flow and paradoxical-flow subgroups. These patients also experience higher all-cause mortality after a 3 years.[18–20] This 1-year mortality reflects lower-than-expected mortality for patients with severe D2 AS who do not undergo TAVR. It is important to note that conservative management of these patients has been associated with a dismal prognosis. Snir et al[9] reported that patients with classic low-flow low-gradient D2 AS with no procedural intervention had the highest 1-year and 5-year mortality compared

with those with D1 and D3 AS at 30.5% and 72.9%, respectively.[9] Once patients develop symptomatic AS, mortality is >50% at 2 years unless valve replacement is performed.[8] Long-term predictors of mortality for patients with low-flow/low-gradient AS include chronic obstructive pulmonary disease, residual moderate to severe mitral regurgitation, and anemia.[4] Medical management of low-flow/low-gradient AS has been associated with late mortality rates of up to 70% at 2 and 3 years. The long-term survival of patients with low-flow/low-gradient AS post-TAVR has not been clearly defined. Fischer-Rasokat et al[21] found that the 1-year mortality for patients with low-flow/low-gradient AS was twice that of patients with high-flow AS after TAVR, at 30.9% versus 16.2% (P =.43). One-year mortality was the highest at 29.5% for patients with D2 post-TAVR, when compared with 12.8% for patients with D1 and 20.1% for patients with D3. The 30-day mortality rate was also the highest in the D2 subtype at 13%.[21] In the TOPAS-TAVI registry, post-TAVR mortality of 39% at 2 years for patients with classic low-flow/low-gradient AS is comparable with that of other early TAVR trials in high-risk to prohibitive-risk patients and comparable with that of other TAVR studies in patients with low-flow/low-gradient AS. In this high-risk patient population, at least half of patients succumbed to noncardiac causes, from other significant comorbidities including pulmonary disease.[4,22,23]

In this study, we observed that patients with D2 AS had the highest prevalence of baseline conduction disturbances and the highest rate of new pacemakers post-TAVR. This aligns with previous multicenter literature assessing mortality and postoperative complications when comparing AS subgroups by flow and gradient characteristics.[18] The higher incidence of atrial fibrillation and baseline bundle branch block in the D2 group likely contributes to these results. Currently, there is little known outcome data regarding preoperative conduction disturbances and pacemaker requirements in patients with AS as they relate to specific subtype status. The most common conduction disturbances after TAVR in all subtypes include high-grade atrioventricular block and new-onset left bundle branch block; however, almost half of these abnormalities improved following TAVR without need for PPM implantation. Preoperative presence of right and left bundle branch block has been associated with PPM implantation and mortality following TAVR.[24] The overall rate of PPM implantation after TAVR with new-generation valves has ranged between 2.3% and 36.1%. A systematic review[25] found that the Medtronic Corevalve/Evolut R valve carries a higher risk (14.7%−26.7%) and the Edwards SAPIEN 3 valve carries a lower risk (4% −24%). In this study, more patients with D2 AS received the Medtronic valve, which may also be a possible explanation for the increased PPM need for that cohort. Sebag et al[26] evaluated the prognostic impact of QRS width in patients with low-flow/low-gradient AS with a 3.1-year follow-up. They found that there was no significant change in QRS duration between baseline and late follow-up and that wider QRS was a strong independent predictor of overall mortality. However, they did not divide the patients into D2 and D3 subtypes. While the rate of PPM implantation after TAVR was highest in the D2 subtype at 11.8%, this falls within known rates of PPM implantation post-TAVR and represents all generations of transcatheter valve implantation from the initiation of our program. Further electrophysiologic studies are warranted to compare the risks of post-TAVR PPM implantation among patients with all subtypes of AS.

In our patient population, patients with D2 AS who underwent TAVR represented only 12% of patients overall (or 76 patients). This is consistent with other reports of patients with all subtypes undergoing TAVR. The incidence of low-flow/low-gradient classic AS has been estimated at 5%−15% of all patients.[4,21,23,27,28] The underrepresentation of these patients in TAVR procedures may be attributed to the diagnostic challenges associated with low-gradient AS because patients may not meet classic echocardiographic criteria for diagnosing for severe AS. Studies have shown that cardiologists most commonly refer patients for TAVR, followed by surgeons and proceduralists completing preoperative workups.[29] Therefore, patients without access to specialists may not be given referrals as frequently. In addition, a large population study of echocardiographic screening have indicated a clinically significant proportion of patients with severe valvular disease go unrecognized.[30] The echo report may not trigger the need for calculation of SVI or dimensionless index, dobutamine stress echocardiography, and/or further diagnostic studies. Many early studies exploring outcomes after TAVR did not identify or include this patient population because patients with mean AV gradients of <40 mm Hg were excluded from initial study inclusion criteria. Consequently, there is a need to expand the diagnostic criteria and educate referring primary care providers regarding the different low-flow/low-gradient subtypes of AS. This further validates the need for structural heart teams and adopting a multidisciplinary heart team approach to diagnosis and treat higher-risk patients with low-flow/low-gradient AS.

In our multivariable analysis controlling for age, sex, and patient clinical history, we discovered a statistically significant protective effect for a history of PCI and 1-year mortality. There was no difference in age, sex, history of dialysis, home oxygen use, pacemaker implantation, and/or peripheral arterial disease. This has not been previously reported in the literature. Patients with D2 AS carry higher rates of comorbidities and decreased LVEFs. This could potentially explain the protective effect of PCI on patient mortality as coronary lesions have been treated with PCI. Further studies are needed to determine the exact history of coronary intervention and its effect on TAVR outcomes in all subtypes.

Study limitations and future directions

We acknowledge the limitations of our study. While this was a retrospective single-center academic valve center experience, we have included all patients with all subtypes of AS since the initiation of our valve program in 2014. The overall numbers of patients with D2 AS are low; however, we do feel that this reflects current literature as to patients with low-flow/low-gradient AS undergoing TAVR. Future directions will include the long-term evaluation of QoL and clinical outcomes in prospective trials looking specifically at patients with low-flow/low-gradient in D2/D3 subtypes. Furthermore, we desire to perform a thorough investigation of perioperative conduction abnormalities to better understand differences in postoperative pacemaker risk because it applies to low-flow/low-gradient AS subtypes.

Conclusions

Patients with D2 AS experienced significantly improved LVEF and improved QoL after TAVR at 30 days and 1 year. The postoperative rates of new PPM were the highest in those with the D2 subtype, while postprocedural stroke, dialysis, bleeding, and mortality were lower than expected. We feel that these findings support the benefit of TAVR in this high-risk group.

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Abbreviations:

AS	aortic stenosis
AV	aortic valve
AVA	aortic valve area
ICD	implantable cardioverter defibrillator
LVEF	left ventricular ejection fraction
PCI	percutaneous cutaneous intervention
PPM	permanent pacemaker
QoL	quality of life
TAVR	transcatheter aortic valve replacement

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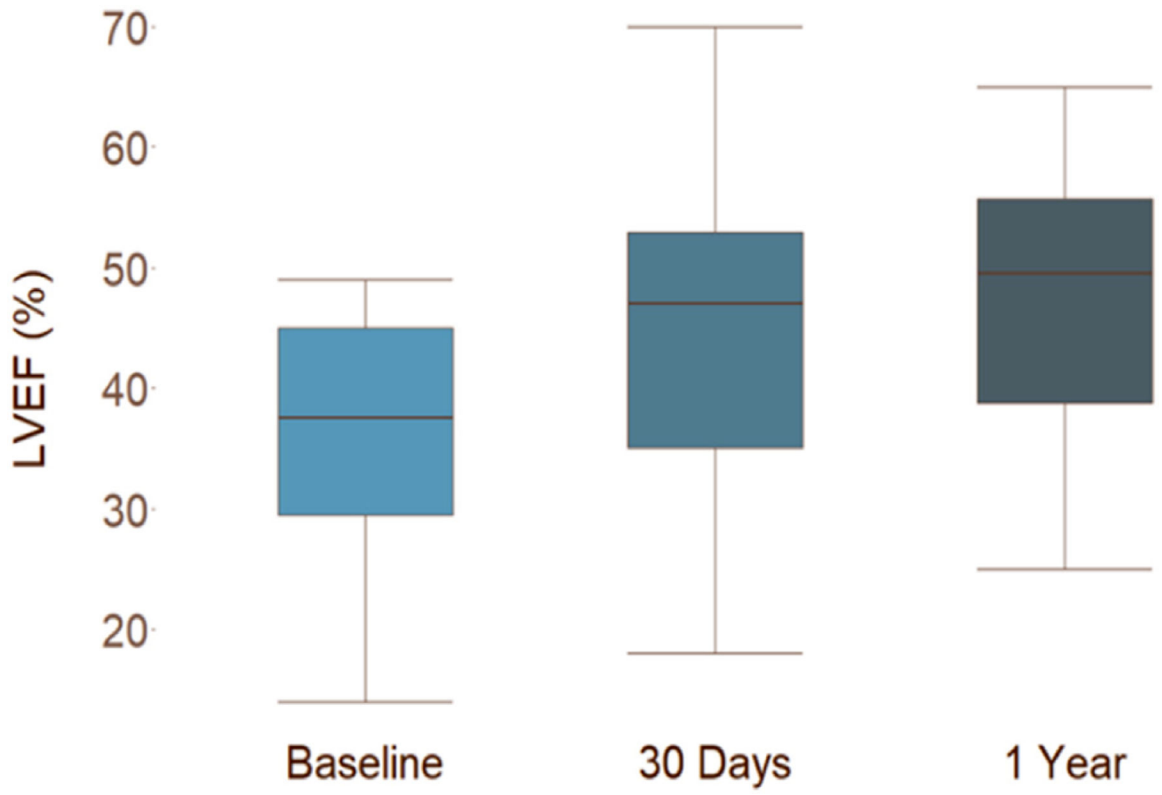


Figure 1. Progression of LVEF in D2 subtype aortic stenosis.

D2 Subtype LVEF (%) shows significant improvement from baseline at 30 days (P <.001) and 1 year (P = .03). D2, classic low-flow/low-gradient aortic stenosis subtype; LVEF, left ventricular ejection fraction.

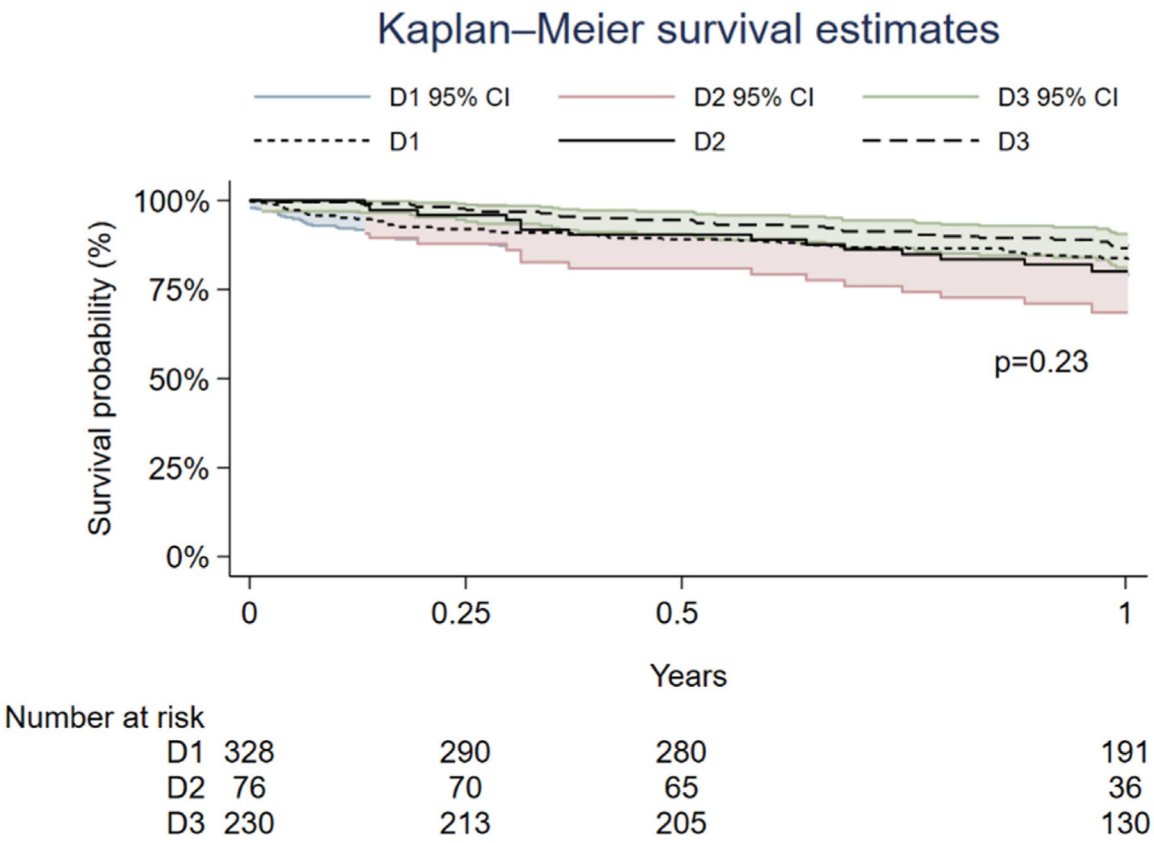


Figure 2. Kaplan–Meier survival curve for aortic stenosis subtypes.

Kaplan–Meier survival estimates posttranscatheter aortic valve replacement (TAVR) by aortic stenosis subtype over 1 year. Patients with D2 aortic stenosis subtype had better 30-day survival but worse 1-year mortality than the other aortic stenosis subtypes.

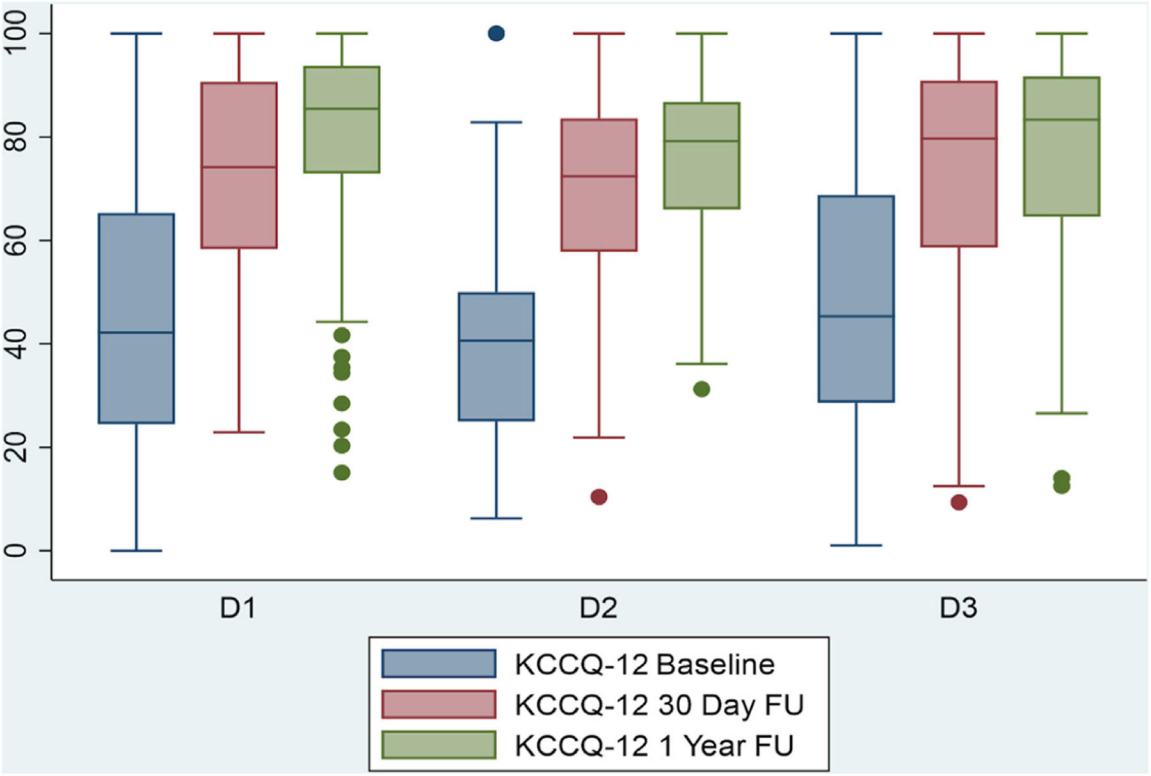
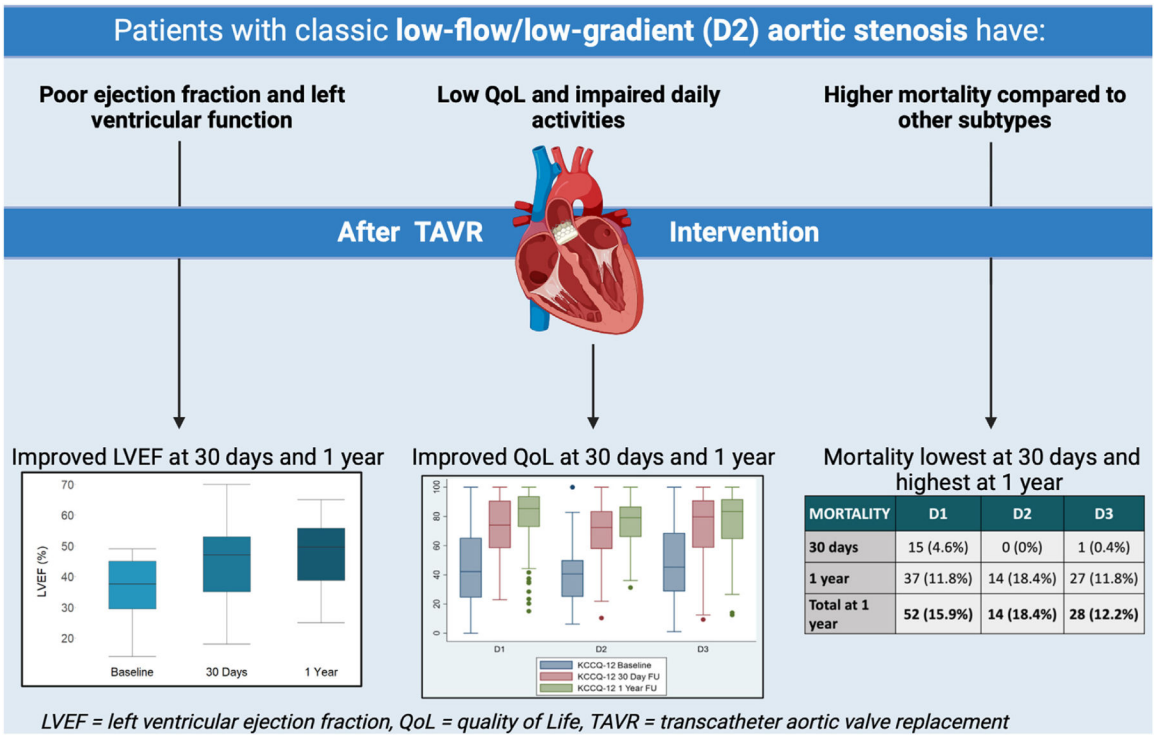


Figure 3. Quality-of-life (QoL) score across aortic stenosis (AS) subtypes.

QoL from Kansas City Cardiomyopathy Questionnaire (KCCQ)-12 overall score by AS subtype shows improvement from baseline at 30 days and 1 year. FU, follow-up.



Central Illustration.

Improved LVEF and QoL for D2 subtype aortic stenosis. This study found that patients who underwent TAVR for low-flow/low-gradient aortic stenosis reported improved QoL at 30 days and 1-year postprocedure. Based on echocardiography, this aortic stenosis subtype cohort also had improved LVEF at 30 days and 1 year. Created with BioRender. LVEF, left ventricular ejection fraction; QoL, quality of life; TAVR, transcatheter aortic valve replacement.

Table 1.

Baseline demographics and characteristics by AS subtype.

	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
Age, y	77.3 ± 10.0	76.6 ± 10.4	79.2 ± 9.6	77.6 ± 9.4	.09
Male sex	396 (62.5)	201 (61.3)[a]	60 (79.0)[b]	135 (58.7)	.004
Race					.80
Caucasian	612 (97.9)	314 (97.2)	72 (98.6)	226 (98.8)	
Asian	2 (0.3)	1 (0.4)	0 (0)	1 (0.4)	
Native American	6 (1.0)	4 (1.2)	1 (1.4)	1 (0.4)	
Pacific Islander	5 (0.8)	4 (1.2)	0 (0)	1 (0.4)	
Hispanic	10 (1.6)	3 (0.9)	2 (2.6)	5 (2.2)	.30
Endocarditis	10 (1.6)	6 (1.8)	1 (1.3)	3 (1.3)	.90
Permanent pacemaker	70 (11.1)	27 (8.3)[a]	21 (27.6)[b]	22 (9.6)	<.001
Previous ICD	17 (2.7)	9 (2.8)	5 (6.6)[b]	3 (1.3)	.05
Previous PCI	199 (31.5)	92 (28.2)	24 (31.6)	83 (36.1)	.15
Previous CABG	112 (17.7)	50 (15.2)	18 (23.7)	44 (19.1)	.17
Previous other cardiac surgery	33 (5.2)	17 (5.2)	5 (6.6)	11 (4.8)	.83
Previous AV procedure	49 (7.7)	24 (7.3)	7 (9.2)	18 (7.8)	.85
Previous AV replacement	38 (6.0)	18 (5.5)	6 (7.9)	14 (6.1)	.73
Previous non-AV procedure	15 (2.4)	7 (2.1)[a]	5 (6.6)[b]	3 (1.3)	.04
Previous stroke	65 (10.3)	30 (9.2)	9 (11.8)	26 (11.3)	.63
Previous TIA	46 (7.3)	23 (7.0)	7 (9.2)	16 (7.0)	.78
Carotid stenosis (not assessed included as none)	76 (12.1)	41 (12.7)	7 (9.5)	28 (12.2)	.75
Peripheral arterial disease	162 (25.6)	85 (26.0)	20 (26.3)	57 (24.8)	.94
Current/recent smoker	39 (6.2)	27 (8.3)	0 (0)	12 (5.2)	.008
Hypertension	554 (87.5)	283 (86.5)	65 (85.5)	206 (89.6)	.49
Diabetes mellitus	263 (41.6)	146 (44.7)	30 (39.5)	87 (37.8)	.25
Dialysis	20 (3.2)	11 (3.4)	3 (4.0)	6 (2.6)	.81
Chronic lung disease					.61
None	397 (63.1)	206 (63.0)	44 (57.9)	147 (65.0)	
Mild	113 (18.0)	56 (17.1)	16 (21.1)	41 (18.1)	

	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
Moderate	80 (12.7)	40 (12.2)	13 (17.1)	27 (12.0)	
Severe	39 (6.2)	25 (7.7)	3 (3.9)	11 (4.9)	
Home oxygen	182 (28.8)	99 (30.3)	22 (29.0)	61 (26.6)	.65
Hostile chest	140 (22.2)	63 (19.3)	23 (30.3)	54 (23.6)	.09
Immunocompromised	80 (12.6)	45 (13.8)	4 (5.3)	31 (13.5)	.10
Previous MI	132 (20.8)	65 (19.8)	21 (27.6)	46 (20.0)	.30
NYHA class					.01
I	11 (1.8)	5 (1.5)	1 (1.3)	5 (2.2)	
II	90 (14.3)	47 (14.5)	5 (6.6)	38 (16.7)	
III	476 (75.7)	242 (74.5)	58 (76.3)	176 (77.2)	
IV	52 (8.3)	31 (9.5)	12 (15.8)	9 (4.0)	
Cardiogenic shock	11 (1.7)	6 (1.8)	3 (4.0)	2 (0.9)	.19
Cardiac arrest	6 (1.0)	5 (1.5)	1 (1.3)	0 (0)	.14
Cardiac procedure within 30 days	90 (14.2)	41 (12.5)	15 (19.7)	34 (14.8)	.26
Porcelain aorta	15 (2.4)	9 (2.7)	0 (0)	6 (2.6)	.43
Atrial fibrillation	218 (34.4)	85 (25.9)[a,c]	49 (64.5)[b]	84 (36.5)	<.001
Conduction defect	245 (38.7)	115 (35.2)	37 (48.7)	93 (40.4)	.07
AV etiology					.42
Degenerative	430 (67.9)	219 (66.8)	56 (73.7)	155 (67.7)	
Primary aortic disease	165 (26.1)	87 (26.5)	15 (19.7)	63 (27.5)	
Supravalvular aortic stenosis	1 (0.2)	1 (0.3)	0 (0)	0 (0)	
Other	37 (5.8)	21 (6.4)	5 (6.6)	12 (4.8)	
Aortic insufficiency					.13
None	140 (22.3)	69 (21.1)	15 (20.0)	56 (24.6)	
Trace/trivial	120 (19.1)	60 (18.3)	14 (18.7)	46 (20.3)	
Mild	272 (43.2)	151 (46.2)	30 (40.0)	91 (40.1)	
Moderate	84 (13.3)	45 (13.8)	14 (18.7)	25 (11.0)	
Severe	13 (2.1)	2 (0.6)	2 (2.6)	9 (4.0)	
Valve morphology					.71
Bicuspid	48 (7.6)	29 (8.9)	5 (6.7)	14 (6.1)	
Tricuspid	579 (91.9)	297 (90.8)	70 (93.3)	212 (93.0)	

	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
Other	4 (0.5)	1 (0.3)	0 (0)	2 (0.9)	
Annular calcification	578 (92.6)	302 (92.6)	70 (94.6)	206 (92.0)	.82
STS risk score	6.50 ± 5.40	6.60 ± 5.83	7.66 ± 6.76	5.97 ± 4.04	.06
TAVR indication					.19
Failed bioprosthetic valve	24 (3.8)	12 (3.7)	2 (2.7)	10 (4.4)	
Mixed AS/AI	11 (1.7)	5 (1.5)	4 (5.3)	2 (0.9)	
Primary AS	597 (94.5)	311 (94.8)	69 (92.0)	217 (94.7)	
Valve manufacturer					.10
Edwards	556 (87.7)	293 (89.3)	61 (80.3)	202 (87.8)	
Medtronic	78 (12.3)	35 (10.7)	15 (19.7)	28 (12.2)	
Valve-in-valve	43 (6.8)	20 (6.1)	6 (7.9)	17 (7.4)	.77

Values are mean ± SD or n (%).

AI, aortic insufficiency; AS, aortic stenosis; AV, aortic valve; CABG, coronary artery bypass graft; ICD, implantable cardioverter defibrillator; MI, myocardial infarction; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement; TIA, transient ischemic attack.

[a] D1 vs D2, $P < .05$.

[b] D2 vs D3, $P < .05$; all analyses performed using Sidak multiple-comparison post hoc tests.

[c] D1 vs D3, $P < .05$.

Table 2.

Quality of life and echocardiographic data at baseline, 30 days, and 1 year follow-up by AS subtype

	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
KCCQ-12: baseline	46.1 ± 25.2	45.3 ± 26.1	39.5 ± 20.1[a]	49.2 ± 25.1	.02
KCCQ-12: 30 d	72.8 ± 21.1	73.2 ± 20.4	68.9 ± 20.6	73.4 ± 22.0	.39
KCCQ-12: 1 year	77.9 ± 19.3	79.4 ± 18.7	74.9 ± 17.5	76.9 ± 20.3	.40
AV peak velocity	4.01 ± 0.74	4.43 ± 0.62[b,c]	3.33 ± 0.67[a]	3.64 ± 0.53	<.001
AVA	0.73 ± 0.16	0.70 ± 0.17[c]	0.71 ± 0.15[a]	0.77 ± 0.15	<.001
LVEF: baseline	57.3 ± 12.7	58.5 ± 11.7[b,c]	36.1 ± 9.4[a]	62.6 ± 6.6	<.001
LVEF: 30 d	59.3 ± 10.8	60.3 ± 9.2[b,c]	43.5 ± 12.9[a]	62.3 ± 8.2	<.001
LVEF: 1 y	59.0 ± 11.4	60.1 ± 10.9[b]	46.2 ± 12.9[a]	60.5 ± 9.7	<.001
AV mean gradient: baseline	40.2 ± 14.3	50.5 ± 11.4[b,c]	26.7 ± 7.5[a]	30.1 ± 6.8	<.001
AV mean gradient: 30 d	24.7 ± 16.7	28.7 ± 18.5[b,c]	15.9 ± 11.4[a]	21.6 ± 13.0	<.001
AV mean gradient: 1 y	12.6 ± 7.4	13.1 ± 6.5	11.1 ± 6.0	12.5 ± 8.6	.47
AVA baseline	0.73 ± 0.16	0.70 ± 0.17[c]	0.71 ± 0.15	0.77 ± 0.15	<.001
SVI: baseline	38.0 ± 11.1	40.7 ± 11.6[b,c]	31.1 ± 10.2[a]	37.2 ± 9.7	<.001
SVI: 30 d	49.6 ± 153.1	42.1 ± 13.8	42.2 ± 13.8	42.3 ± 13.7	.07
SVI: 1 y	39.2 ± 15.5	39.7 ± 17.0	37.4 ± 17.7	38.9 ± 13.6	.87
AV V_{max}: baseline	3.90 ± 0.69	4.36 ± 0.56[b,c]	3.36 ± 0.53	3.54 ± 0.52	<.001
AV V_{max}: 30 d	2.86 ± 0.91	3.00 ± 1.00[b,c]	2.56 ± 0.79	2.76 ± 0.77	<.001
AV V_{max}: 1 y	2.36 ± 0.59	2.43 ± 0.52	2.16 ± 0.50	2.33 ± 0.67	.08
AV VTI: baseline	0.82 ± 0.24	0.77 ± 0.23[c]	0.83 ± 0.33	0.87 ± 0.21	<.001
AV VTI: 30 d	1.80 ± 0.78	1.75 ± 0.79	1.88 ± 0.67	1.85 ± 0.80	.37
AV VTI: 1 y	1.62 ± 0.64	1.66 ± 0.69	1.67 ± 0.80	1.57 ± 0.57	.68

Values are mean ± SD.

[a] D2 vs D3, $P < .05$.

[b] D1 vs D2, $P < .05$.

[c] D1 vs D3, $P < .05$.

All analyses performed using Sidak multiple-comparison post hoc tests.

Table 3.

Postprocedural outcomes by AS subtype in hospital, at 30 days, and 1 year

Outcome	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
Death					
In-hospital	8 (1.3)	7 (2.1)	0 (0)	1 (0.4)	.18
30-d FU (does not include hospital death)	8 (1.3)	8 (2.5)	0 (0)	0 (0)	.03
1-y FU (does not include hospital or 30-d death)	78 (12.6)	37 (11.8)	14 (18.4)	27 (11.8)	.27
All death by 30 d	15 (2.4)	14 (4.3)	0 (0)	1 (0.4)	.005
All death by 1 y	94 (14.8)	52 (15.9)	14 (18.4)	28 (12.2)	.30
Ischemic stroke					
In-hospital	15 (2.4)	11 (3.4)	1 (1.3)	3 (1.3)	.29
30-d FU	4 (0.64)	2 (0.6)	0 (0)	2 (0.9)	>.99
1-y FU	2 (0.32)	2 (0.6)	0 (0)	0 (0)	.62
Hemorrhagic stroke					
In-hospital	0 (0)	0 (0)	0 (0)	0 (0)	—
30-d FU	0 (0)	0 (0)	0 (0)	0 (0)	—
1-y FU	2 (0.3)	0 (0)	1 (1.3)	1 (0.4)	.11
Dialysis					
In-hospital	8 (1.3)	4 (1.3)	0 (0)	4 (1.7)	.68
30-d FU	0 (0)	0 (0)	0 (0)	0 (0)	—
1-y FU	1 (0.2)	1 (0.3)	0 (0)	0 (0)	>.99
New pacemaker					
In-hospital	56 (8.8)	29 (8.8)	9 (11.8)	18 (7.8)	.52
30-d FU	3 (0.5)	2 (0.6)	0 (0)	1 (0.4)	>.99
1-y FU	1 (0.2)	1 (0.3)	0 (0)	0 (0)	>.99
New ICD					
In-hospital	4 (0.6)	3 (0.9)	1 (1.3)	0 (0)	.18
30-d FU	0 (0)	0 (0)	0 (0)	0 (0)	—
1-y FU	4 (0.7)	1 (0.3)	1 (1.3)	2 (0.9)	.45
Life-threatening bleed					
30-d FU	2 (0.3)	1 (0.3)	0 (0)	1 (0.4)	>.99

Outcome	Total (N = 634)	D1 (n = 328)	D2 (n = 76)	D3 (n = 230)	*P* value
1-y FU	1 (0.2)	0 (0)	0 (0)	1 (0.4)	.49
Major bleed					
30-d FU	5 (0.8)	3 (0.9)	0 (0)	2 (0.9)	>.99
1-y FU	6 (1.0)	3 (1.0)	0 (0)	3 (1.3)	.73
Valve-related readmission					
30-d FU	6 (1.0)	2 (0.6)	0 (0)	4 (1.8)	.33
1-y FU	8 (1.3)	4 (1.3)	0 (0)	4 (1.8)	.69
Non–valve-related readmission					
30-d FU	51 (8.2)	24 (7.5)	2 (2.6)	25 (10.9)	.06
1-y FU	69 (11.2)	29 (9.3)	6 (7.9)	34 (14.9)	.09

Values are n (%).

FU, follow-up; ICD, implantable cardioverter defibrillator.