JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 74, NO. 23, 2019

PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATIONS

Health Status After Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients With Aortic Stenosis

Suzanne J. Baron, MD, MSc,[a,b] Elizabeth A. Magnuson, ScD,[b] Michael Lu, PhD,[c] Kaijun Wang, PhD,[b] Khaja Chinnakondepalli, MS,[b] Michael Mack, MD,[d] Vinod H. Thourani, MD,[e] Susheel Kodali, MD,[f] Raj Makkar, MD,[g] Howard C. Herrmann, MD,[h] Samir Kapadia, MD,[i] Vasilis Babaliaros, MD,[j] Mathew R. Williams, MD,[k] Dean Kereiakes, MD,[l] Alan Zajarias, MD,[m] Maria C. Alu, MS,[f] John G. Webb, MD,[n] Craig R. Smith, MD,[f] Martin B. Leon, MD,[f] David J. Cohen, MD, MSc,[o] on behalf of the PARTNER 3 Investigators

ABSTRACT

BACKGROUND In patients with severe aortic stenosis (AS) at low surgical risk, treatment with transcatheter aortic valve replacement (TAVR) results in lower rates of death, stroke, and rehospitalization at 1 year compared with surgical aortic valve replacement; however, the effect of treatment strategy on health status is unknown.

OBJECTIVES This study sought to compare health status outcomes of TAVR versus surgery in low-risk patients with severe AS.

METHODS Between March 2016 and October 2017, 1,000 low-risk patients with AS were randomized to transfemoral TAVR using a balloon-expandable valve or surgery in the PARTNER 3 (Placement of Aortic Transcatheter Valves) trial. Health status was assessed at baseline and 1, 6, and 12 months using the KCCQ (Kansas City Cardiomyopathy Questionnaire), SF-36 (Short Form-36 Health Survey), and EQ-5D (EuroQoL). The primary endpoint was change in KCCQ-OS (KCCQ Overall Summary) score over time. Longitudinal growth curve modeling was used to compare changes in health status between treatment groups over time.

RESULTS At 1 month, TAVR was associated with better health status than surgery (mean difference in KCCQ-OS 16.0 points; $p < 0.001$). At 6 and 12 months, health status remained better with TAVR, although the effect was reduced (mean difference in KCCQ-OS 2.6 and 1.8 points respectively; $p < 0.04$ for both). The proportion of patients with an excellent outcome (alive with KCCQ-OS ≥75 and no significant decline from baseline) was greater with TAVR than surgery at 6 months (90.3% vs. 85.3%; $p = 0.03$) and 12 months (87.3% vs. 82.8%; $p = 0.07$).

CONCLUSIONS Among low-risk patients with severe AS, TAVR was associated with meaningful early and late health status benefits compared with surgery. (J Am Coll Cardiol 2019;74:2833–42) © 2019 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]Lahey Hospital and Medical Center, Burlington, Massachusetts; [b]Saint Luke's Mid America Heart Institute, University of Missouri-Kansas City, Kansas City, Missouri; [c]Edwards LifeSciences, Irvine, California; [d]Baylor Scott and White Healthcare, Plano, Texas; [e]Marcus Heart and Vascular Center, Piedmont Heart Institute, Atlanta, Georgia; [f]Columbia University Medical Center, New York, New York; [g]Cedars-Sinai Medical Center, Los Angeles, California; [h]Hospital of University of Pennsylvania, Philadelphia, Pennsylvania; [i]Cleveland Clinic, Cleveland, Ohio; [j]Emory University School of Medicine, Atlanta, Georgia; [k]New York University Langone Medical Center, New York, New York; [l]Christ Hospital Heart and Vascular Center, Cincinnati, Ohio; [m]Washington University School of Medicine, Barnes-Jewish Hospital, St. Louis, Missouri; [n]St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; and the [o]University of Missouri-Kansas City, Kansas City, Missouri. The PARTNER 3 (Placement of Aortic Transcatheter Valves) clinical trial (NCT02675114) and quality of life sub-study was funded by a research

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2019.09.007

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

CI = confidence interval

EQ-5D = EuroQoL

KCCQ = Kansas City Cardiomyopathy Questionnaire

KCCQ-OS = Kansas City Cardiomyopathy Questionnaire–overall summary score

SAVR = surgical aortic valve replacement

SF-36 = Short Form-36 Health Survey

TAVR = transcatheter aortic valve replacement

Over the past decade, transcatheter aortic valve replacement (TAVR) has emerged as the preferred treatment strategy for patients with severe symptomatic aortic stenosis (AS) at high surgical risk (1,2) and an alternative treatment option for patients at intermediate surgical risk (3,4). With technical refinement of TAVR devices and increasing operator proficiency, TAVR has begun to expand to younger patients at lower surgical risk. Recently, 2 large randomized controlled trials demonstrated that transfemoral TAVR is both safe and effective compared with surgical aortic valve replacement (SAVR) in low-risk patients, although rates of periprocedural complications for the 2 treatments differed (5,6).

SEE PAGE 2843

Although improved long-term survival is an important consideration for patients with AS undergoing valve replacement, the impact of treatment on quality of life is critical as well. Although prior studies have demonstrated improved early health status with transfemoral TAVR compared with SAVR in intermediate- and high-risk patients, there is little evidence of any late health status benefit with TAVR (7–9), which could reflect the competing risk of mortality or a ceiling effect due to the multiple comorbidities seen in these higher-risk populations. Whether treatment of a lower-risk population might unmask late health status benefits of TAVR versus SAVR is unknown. Accordingly, we performed a prospective study alongside the PARTNER 3 (Placement of Aortic Transcatheter Valves) randomized trial to understand the impact of valve replacement strategy on early and late health status in patients with AS at low surgical risk.

METHODS

STUDY DESIGN AND POPULATION. The PARTNER 3 trial design has been described previously (6). In brief, patients with severe AS, who were considered to be low surgical risk based on a predicted 30-day surgical mortality of <4%, as determined by the Society of Thoracic Surgeons (STS) risk model and consensus of a multidisciplinary heart team, were enrolled at 71 sites. Key exclusion criteria included bicuspid aortic valve, severe untreated coronary artery disease, unfavorable anatomy for transfemoral TAVR, significant frailty, severe renal disease, and severe lung disease. Patients were randomized 1:1 to undergo either transfemoral TAVR using the SAPIEN 3 balloon-expandable valve (Edwards LifeSciences, Irvine, California) or SAVR. The trial was approved by the institutional review board at each site, and written informed consent was obtained from all patients.

MEASUREMENT OF HEALTH STATUS. Health status was evaluated at baseline and 1, 6, and 12 months.

grant from Edwards LifeSciences, Inc. Dr. Baron has served as a consultant for Edwards LifeSciences; and has served on the Advisory Board and received research funding from Boston Scientific Corporation. Dr. Magnuson has received research funding from Edwards LifeSciences, Abbott, Svelte Medical Systems, Cardiovascular Systems, and Corvia Medical. Dr. Lu is an employee of Edwards LifeSciences. Dr. Mack has received an institutional research grant and was co-principal investigator for Edwards LifeSciences; was co-principal investigator for Abbott; was study chair for Medtronic; and has served as a consultant for Gore Medical. Dr. Thourani has received research funding and served as a consultant for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and JenaValve. Dr. Kodali has received research funding from and served as a consultant for Abbott Vascular and JenaValve; has received research funding from Boston Scientific, Edwards LifeSciences, and Medtronic; has served as a consultant for Meril Life Sciences and Admedus; and has served on the Advisory Board of Thubrikar Aortic Valve Inc. and Dura Biotech. Dr. Makkar has received research funding from Edwards LifeSciences and Abbott. Dr. Herrmann has received research funding from Abbott Vascular and Boston Scientific Corp.; and has received research funding and served as a consultant for Edwards LifeSciences and Medtronic. Dr. Kapadia has received an institutional research grant and served on the steering committee of Edwards LifeSciences. Dr. Babaliaros has received an institutional research grant and served as a consultant and speaker for Edwards LifeSciences; and has served as a consultant and speaker for Abbott. Dr. Williams has received an institutional research grant from Edwards LifeSciences. Dr. Kereiakes has served as a consultant for HLT and JC Medical Inc.; and has served as a consultant and on the Advisory Board of Boston Scientific Corp. Dr. Zajarias has received research funding from and served as a consultant for Edwards LifeSciences, Abbott, and Boston Scientific; and has received research funding from Medtronic. Dr. Alu has received an institutional research grant from Edwards LifeSciences; and has served as a consultant for Claret Medical and Cardiac Dimensions. Dr. Webb has served as a consultant and proctor for Edwards LifeSciences. Dr. Smith has received an institutional research grant from Edwards LifeSciences. Dr. Leon has received an institutional research grant and served as co-principal investigator for Edwards LifeSciences; has received an institutional research grant from and served on the Advisory Board of Medtronic and Abbott; has received an institutional research grant from, served on the Advisory Board of, and received equity from Boston Scientific Corp; has served on the Advisory Board of Gore Medical; and has served as an advisor for Meril Life Sciences. Dr. Cohen has served as a consultant for and received research funding from Edwards LifeSciences, Medtronic, and Abbott; and has received research funding from Boston Scientific Corp. All other authors have reported that they have no relationships relevant to the content of this paper to disclose. Saif Anwaruddin, MD, served as Guest Associate Editor for this paper.

Manuscript received August 18, 2019; revised manuscript received September 11, 2019, accepted September 13, 2019.

Disease-specific health status was assessed using the KCCQ (Kansas City Cardiomyopathy Questionnaire). The KCCQ evaluates 5 domains of health status (physical function, social function, symptoms, quality of life, and self-efficacy/knowledge) in patients with heart failure and is scored from 0 to 100, with higher scores indicating better health status (10). The KCCQ has been shown to be a reliable and valid instrument in patients with AS (11) and has been used to assess patient-reported outcomes in multiple prior studies comparing TAVR and SAVR (7–9). The individual scales of the KCCQ may be converted into an overall summary score (KCCQ-OS). Changes of 5, 10, and 20 points on the KCCQ-OS have been shown to correlate with small, moderate, and large improvements in patient-level health status (12).

Generic health status was evaluated using the Medical Outcomes Study SF-36 (Short Form-36) questionnaire and the EQ-5D (EuroQoL). The SF-36 assesses 8 dimensions of health and includes physical and mental summary scales, which are scored such that the U.S. population mean is 50 ± 10 (13). Minimum clinically important differences for the SF-36 physical and mental summary scales are ~2 points (14), with higher scores representing better health status. The EQ-5D uses a 3-level scale to assess 5 dimensions of general health, and scores are transformed into preference-based utilities (range 0 to 1, with 0 representing death and 1 representing perfect health) using validated population sampling methods (15).

STATISTICAL ANALYSIS. The primary analytic cohort was composed of patients who underwent the assigned treatment (as-treated population) and had baseline health status data. The primary endpoint was the KCCQ-OS score over the 1-year follow-up period. Baseline characteristics were compared between treatment groups using Student's *t*-tests for continuous variables and Fisher exact tests for binary variables. Changes in health status at 1, 6, and 12 months were compared with baseline within each treatment group using paired Student's *t*-tests. Scores between treatment groups were compared at each follow-up time point using longitudinal random-effects growth curve models (16) with adjustment for age, sex, baseline health status, and treatment assignment. Linear and quadratic effects of time and interactions between treatment group and time also were considered. Variables were retained in the model if $p \leq 0.05$ using a backward elimination procedure, starting with the highest-order time-by-treatment interaction (7,8). Estimates of the differences in mean scores between treatment groups (with 95% confidence intervals) for each health status measure at 1, 6, and 12 months were obtained from the growth curve models.

Subgroup analyses were performed to evaluate for differential effects of treatment strategy on KCCQ-OS scores at 6 and 12 months, using analysis of covariance with adjustment for baseline health status, age, and sex. These pre-specified subgroups included sex, age (dichotomized at 75 years), STS risk score (dichotomized at 2), atrial fibrillation, ejection fraction (dichotomized at 50%), and New York Heart Association (NYHA) functional class (class I/II vs. III/IV).

Categorical analyses, using previously described endpoints incorporating both survival and health status (17,18), were performed to provide further perspective on the effect of treatment strategy at 6 and 12 months. Rates of favorable outcomes (defined as alive with a KCCQ-OS score >60 [corresponds to NYHA functional class II symptoms (12)] in the absence of a decrease of >10 points from baseline) and excellent outcomes (defined as alive with a KCCQ-OS score >75 [corresponds to NYHA functional class I symptoms (12)] in the absence of a decrease of >10 points from baseline) were compared between treatment groups using Fisher exact tests. To account for the competing risk of death, ordinal analyses also were performed based on established thresholds for clinically relevant changes in the KCCQ-OS (12): 1) dead; 2) worse (>5-point decrease from baseline); 3) no change (change between −5 and <5 points); 4) small improvement (increase between 5 and <10 points); 5) moderate improvement (increase between 10 and <20 points); and 6) large improvement (≥20 point increase). For these ordinal analyses, the impact of TAVR versus SAVR on health status was compared using ordinal logistic regression.

To investigate whether differences in periprocedural complication rates between the treatment groups might explain any observed differences in late health status, we performed exploratory analyses in which all serious complications within 30 days of the index procedure (stroke, life-threatening/disabling bleeding, major vascular complication, acute kidney injury stage 2 or 3, new atrial fibrillation, pacemaker implantation, moderate or severe paravalvular aortic regurgitation) were included in the original growth curve models. Mean differences in 1-year KCCQ-OS scores were then compared between treatment groups to assess whether the previously observed treatment effect was attenuated.

All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, North Carolina). A 2-sided p value of <0.05 was considered statistically significant with no correction for multiple comparisons.

TABLE 1 Baseline Characteristics of the Primary Analytic Cohort

	TAVR (n = 494)	SAVR (n = 449)	p Value
Age, yrs	73.3 ± 5.8	73.6 ± 6.1	0.467
Male	333 (67.4)	320 (71.3)	0.204
STS Risk Score	1.9 ± 0.7	1.9 ± 0.6	0.225
Diabetes mellitus	155 (31.4)	135 (30.1)	0.724
Coronary artery disease	136 (27.6)	124 (27.6)	0.999
Prior MI	28 (5.7)	26 (5.8)	0.999
Peripheral artery disease	34 (6.9)	33 (7.4)	0.801
Prior stroke	17 (3.4)	23 (5.1)	0.257
Atrial fibrillation	77 (15.6)	84 (18.8)	0.225
COPD	25 (5.1)	27 (6.0)	0.569
Creatinine >2 mg/dl	1 (0.2)	1 (0.2)	0.999
LV ejection fraction, %	65.7 ± 9.0	66.2 ± 8.6	0.431
Aortic valve area, cm^2	0.8 ± 0.2	0.8 ± 0.2	0.780
Mean aortic valve gradient, mm Hg	49.4 ± 12.7	48.4 ± 11.8	0.203
Baseline health status			
KCCQ Overall Summary	70.4 ± 19.4	70.1 ± 20.9	0.825
KCCQ Physical Limitations	76.6 ± 19.8	76.9 ± 20.6	0.814
KCCQ Total Symptoms	74.2 ± 18.9	73.0 ± 21.3	0.344
KCCQ Quality of Life	58.1 ± 24.4	58.2 ± 25.8	0.962
KCCQ Social Limitation	72.0 ± 25.9	71.7 ± 27.2	0.845
SF-36 Physical Summary	44.1 ± 9.2	44.1 ± 9.0	0.964
SF-36 Mental Summary	52.5 ± 9.1	51.3 ± 10.0	0.049
EQ-5D Utilities	0.83 ± 0.11	0.83 ± 0.13	0.591

Values are mean ± SD or n (%).

COPD = chronic obstructive pulmonary disease; EQ-5D = EuroQoL; KCCQ = Kansas City Cardiomyopathy Questionnaire; LV = left ventricular; MI = myocardial infarction; SAVR = surgical aortic valve replacement; SF-36 = Short Form 36 Health Survey; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

RESULTS

STUDY POPULATION. Between March 2016 and October 2017, 1,000 patients were enrolled in the PARTNER 3 trial, of whom 950 underwent the assigned treatment (496 TAVR; 454 SAVR). Baseline health status was available for 943 patients (494 TAVR; 449 SAVR), who formed the analytic cohort. **Table 1** summarizes the baseline characteristics of the analytic cohort. The mean age was 73, approximately two-thirds were male, and the mean STS risk score was 1.9. Baseline health status was mildly impaired with a mean KCCQ-OS score of 70 (corresponds to NYHA functional class II symptoms [12]).

WITHIN-GROUP COMPARISONS. Health status data were available for >93% of patients at all follow-up time points (Online Table 1). Patients with missing 1-year health status data (n = 47) had higher STS risk scores (2.1 vs. 1.9; p = 0.019) and higher rates of atrial fibrillation (34.0% vs. 16.4%; p = 0.005) compared with patients with available 1-year health status data (n = 880) (Online Table 2). There were no other significant differences in baseline characteristics between patients with and without 1-year health status data.

Compared with baseline, patients treated with TAVR demonstrated moderate to large improvements in all health status measures at 1 month (mean improvement of 18.5 points on the KCCQ-OS scale, 5.0 points on the SF-36 physical summary scale, 3.4 points on the SF-36 mental summary scale; p < 0.001 vs. baseline for all scales [**Table 2**]). Similar benefits were seen at 6- and 12-month follow-up. At 1 month, SAVR patients reported mixed effects with lower scores noted on scales assessing physical function (KCCQ-physical limitations; SF-36 physical summary) and modest benefits on other KCCQ scales (mean improvement of 2.5 points on KCCQ-OS scale; p = 0.016 vs. baseline); however, by 6 months, patients treated with SAVR demonstrated substantial improvement on all health status scales compared with baseline, and this benefit was sustained at 1 year (**Table 2**).

BETWEEN-GROUP COMPARISONS. Primary endpoint. When changes in health status were compared between treatment groups, patients undergoing TAVR demonstrated substantially greater improvement in 1-month KCCQ-OS scores compared with SAVR (mean adjusted difference 16.0 points; 95% confidence interval [CI]: 14.2 to 17.8; p < 0.001). The benefit of TAVR persisted at 6 and 12 months, although the magnitude was smaller (mean adjusted difference in KCCQ-OS 2.6 points [95% CI: 1.0 to 4.3; p = 0.002] at 6 months and 1.8 points [95% CI: 0.1 to 3.5; p = 0.033] at 12 months) (**Central Illustration**, Online Table 3).

Secondary endpoints. Results of the KCCQ subscales were similar to those for the KCCQ-OS with large differences in favor of TAVR at 1 month and modest differences at 6 and 12 months (**Central Illustration**, Online Table 3). Although there were significant benefits associated with TAVR at 1 month on all generic health status scales (mean adjusted difference in SF-36 physical summary 7.7 points [95% CI: 6.8 to 8.6]; mean adjusted difference in SF-36 mental summary 4.1 points [95% CI: 3.1 to 5.1]; mean adjusted difference in EQ-5D utilities 0.07 points [95% CI: 0.06 to 0.09]; p < 0.001 for all), there were no differences between TAVR and SAVR in generic health status measures at 6 or 12 months (**Figure 1**, Online Table 3).

Subgroup analyses. The health status benefits of TAVR versus SAVR were consistent across all prespecified subgroups at 6 months (Online Figure 1). At 12 months, however, patients reporting NYHA functional class III or IV symptoms at baseline derived

TABLE 2 Within-Group Changes in Health Status After TAVR or SAVR

	TAVR			SAVR		
	n	Paired Difference* (95% CI)	p Value	n	Paired Difference* (95% CI)	p Value
KCCQ Overall Summary						
1 month	490	18.5 (16.9 to 20.1)	<0.001	429	2.5 (0.5 to 4.6)	0.016
6 months	484	20.2 (18.5 to 21.9)	<0.001	402	17.4 (15.5 to 19.3)	<0.001
12 months	479	19.4 (17.7 to 21.1)	<0.001	400	17.4 (15.4 to 19.3)	<0.001
KCCQ Physical Limitations						
1 month	479	13.4 (11.8 to 15.1)	<0.001	423	−0.6 (−2.7 to 1.5)	0.589
6 months	470	14.0 (12.3 to 15.8)	<0.001	398	10.6 (8.7 to 12.6)	<0.001
12 months	466	12.7 (10.9 to 14.5)	<0.001	395	11.1 (9.2 to 13.1)	<0.001
KCCQ Total Symptoms						
1 month	490	13.4 (11.7 to 15.2)	<0.001	428	4.4 (2.3 to 6.5)	<0.001
6 months	483	13.4 (11.7 to 15.2)	<0.001	401	12.1 (10.1 to 14.0)	<0.001
12 months	479	12.6 (10.8 to 14.4)	<0.001	399	12.3 (10.2 to 14.3)	<0.001
KCCQ Quality of Life						
1 month	489	29.8 (27.7 to 32.0)	<0.001	427	11.7 (9.1 to 14.4)	<0.001
6 months	484	33.7 (31.5 to 35.9)	<0.001	400	29.3 (26.8 to 31.9)	<0.001
12 months	477	33.2 (30.9 to 35.4)	<0.001	398	29.7 (27.1 to 32.3)	<0.001
KCCQ Social Limitation						
1 month	436	17.9 (15.4 to 20.4)	<0.001	380	−6.5 (−9.8 to −3.2)	<0.001
6 months	435	19.8 (17.2 to 22.3)	<0.001	362	17.8 (15.2 to 20.4)	<0.001
12 months	424	19.4 (16.8 to 22.0)	<0.001	348	16.8 (14.0 to 19.6)	<0.001
SF-36 Physical Summary						
1 month	479	5.0 (4.3 to 5.7)	<0.001	416	−2.7 (−3.6 to −1.9)	<0.001
6 months	474	5.9 (5.2 to 6.7)	<0.001	393	5.1 (4.3 to 5.9)	<0.001
12 months	469	5.2 (4.4 to 6.0)	<0.001	389	5.0 (4.2 to 5.9)	<0.001
SF-36 Mental Summary						
1 month	483	3.4 (2.6 to 4.2)	<0.001	417	0.1 (−1.0 to 1.1)	0.921
6 months	476	3.5 (2.8 to 4.3)	<0.001	394	4.5 (3.5 to 5.4)	<0.001
12 months	473	3.5 (2.7 to 4.3)	<0.001	391	4.0 (3.1 to 4.9)	<0.001
EQ-5D Utilities						
1 month	484	0.06 (0.05 to 0.07)	<0.001	419	−0.01 (−0.03 to 0.00)	0.062
6 months	477	0.05 (0.04 to 0.06)	<0.001	390	0.05 (0.04 to 0.07)	<0.001
12 months	475	0.04 (0.03 to 0.05)	<0.001	391	0.04 (0.03 to 0.06)	<0.001

*Paired differences reflect changes with baseline.
CI = confidence interval; other abbreviations as in Table 1.

greater benefit from TAVR (p value for interaction = 0.020) (Online Figure 2).

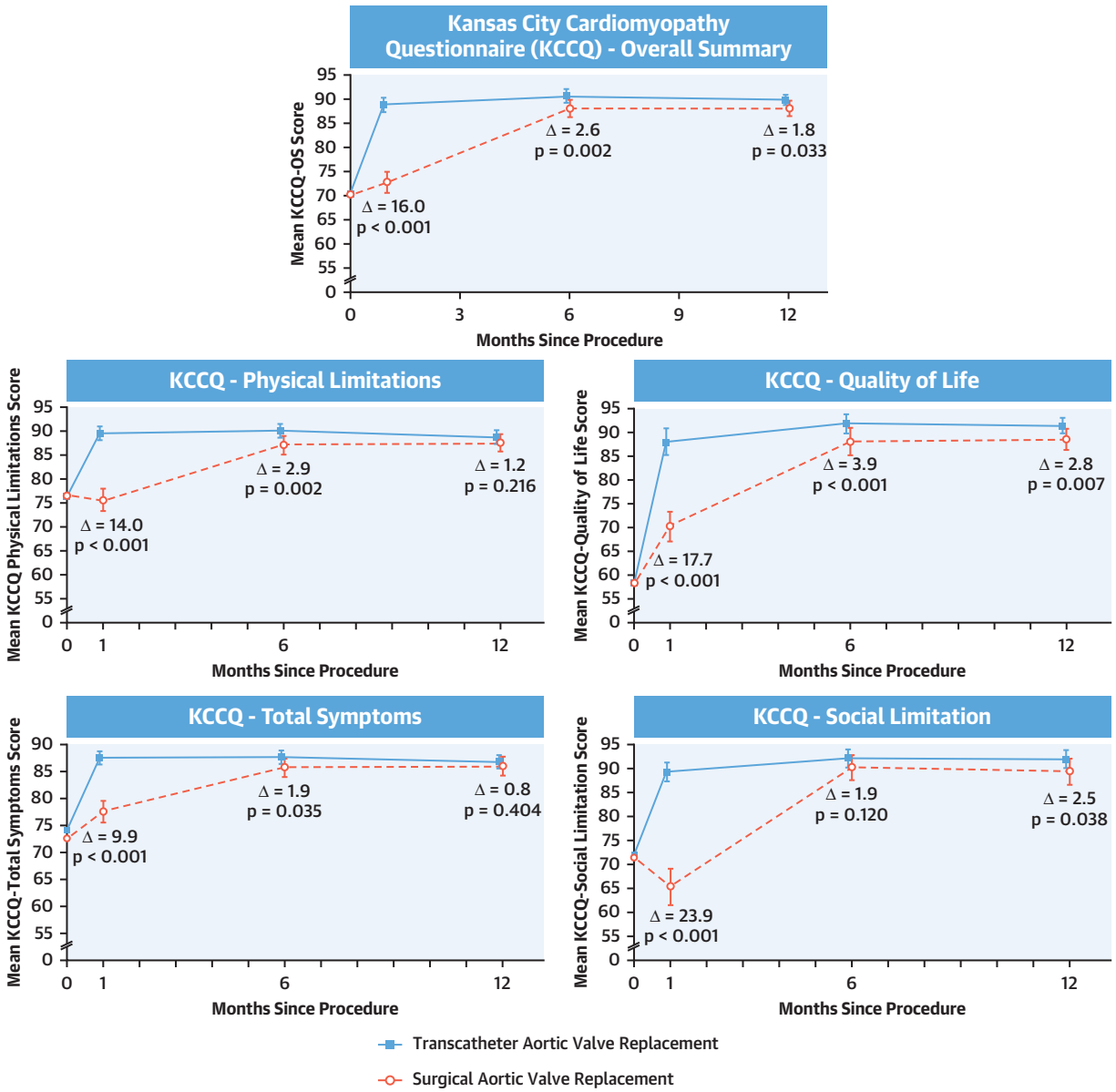
CATEGORICAL ANALYSES. At 6 months, the proportion of patients who achieved either a favorable or excellent outcome was significantly higher with TAVR compared with SAVR (favorable: 95.2% vs. 91.5%, p = 0.028; excellent: 90.3% vs. 85.3%, p = 0.029) (Online Table 4). Although rates of favorable and excellent outcomes remained numerically higher with TAVR at 12 months, the differences were no longer significant. When change in health status was analyzed as an ordinal variable with death as the worst outcome, TAVR demonstrated a significant benefit compared with SAVR at all time points (p < 0.05) (**Figure 2**, Online Table 5). Cumulative response curves showing the distribution of change in the KCCQ-OS by treatment group suggested that the late benefits of TAVR were driven by differences in the proportion of patients who experienced a large improvement in the KCCQ-OS (Online Figures 3 and 4).

EXPLANATORY ANALYSES. Exploratory analyses were performed to assess the extent to which differential rates of postprocedural complications contributed to our findings of a late health status benefit with TAVR. When 30-day complications were added to the growth curve model, the predicted difference between TAVR and SAVR on the KCCQ-OS at 12 months was reduced to 1.3 points (95% CI: −0.6 to 3.1; p = 0.175).

DISCUSSION

This is the first study to evaluate the effects of TAVR and SAVR on health-related quality of life in patients with severe AS at low surgical risk. Over the 1-year

CENTRAL ILLUSTRATION **Disease-Specific Health Status After Transcatheter Aortic Valve Replacement or Surgical Aortic Valve Replacement: Between-Group Comparisons**

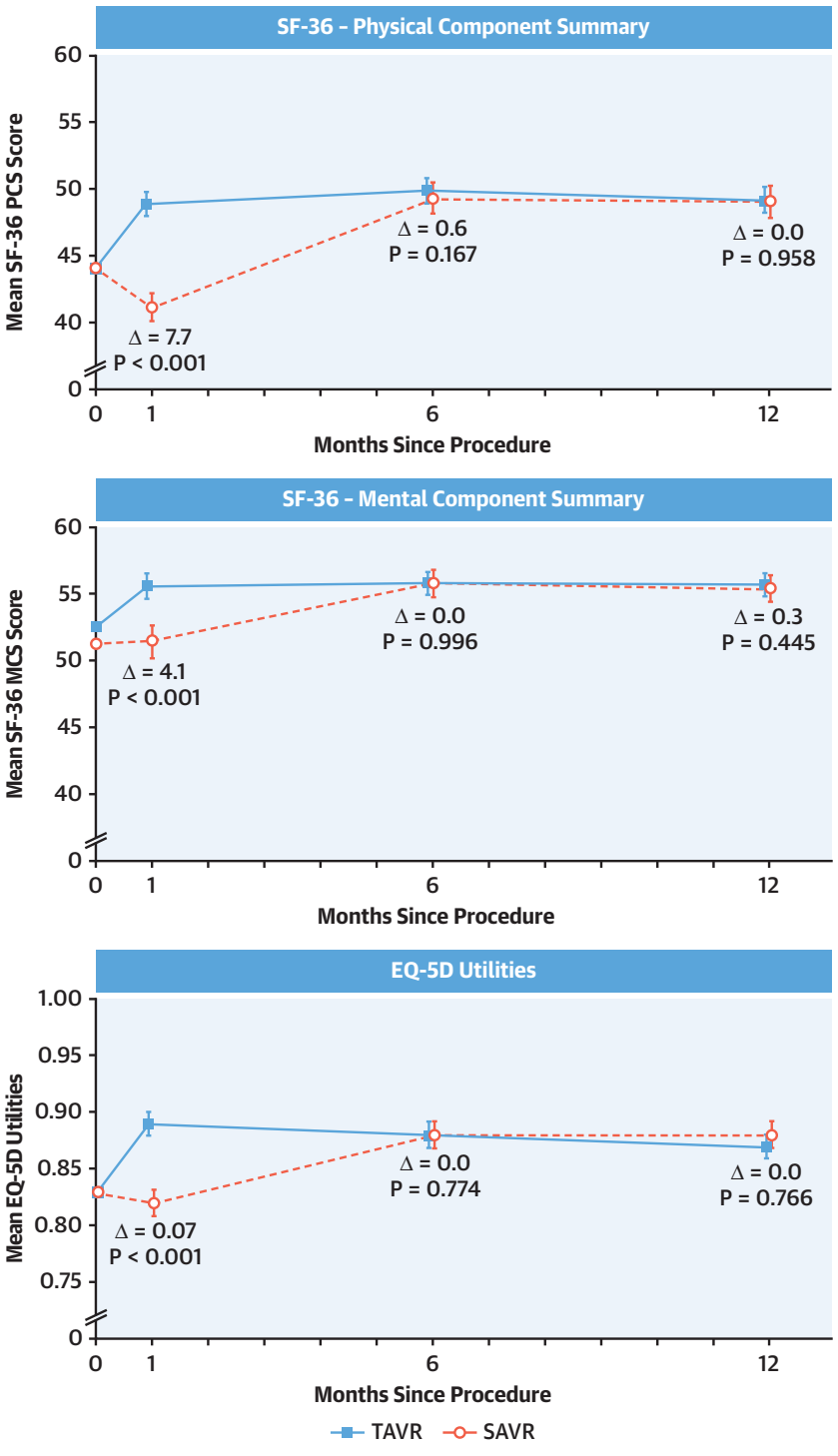


Baron, S.J. et al. J Am Coll Cardiol. 2019;74(23):2833–42.

Predicted mean values of disease-specific health status according to the KCCQ (Kansas City Cardiomyopathy Questionnaire) Overall Summary Scale and selected subscales of the KCCQ at 1, 6, and 12 months after transcatheter aortic valve replacement **(blue squares)** and surgical aortic valve replacement **(red circles)**. Mean values and p values were derived from longitudinal growth curve models. **Error bars** represent 95% confidence intervals.

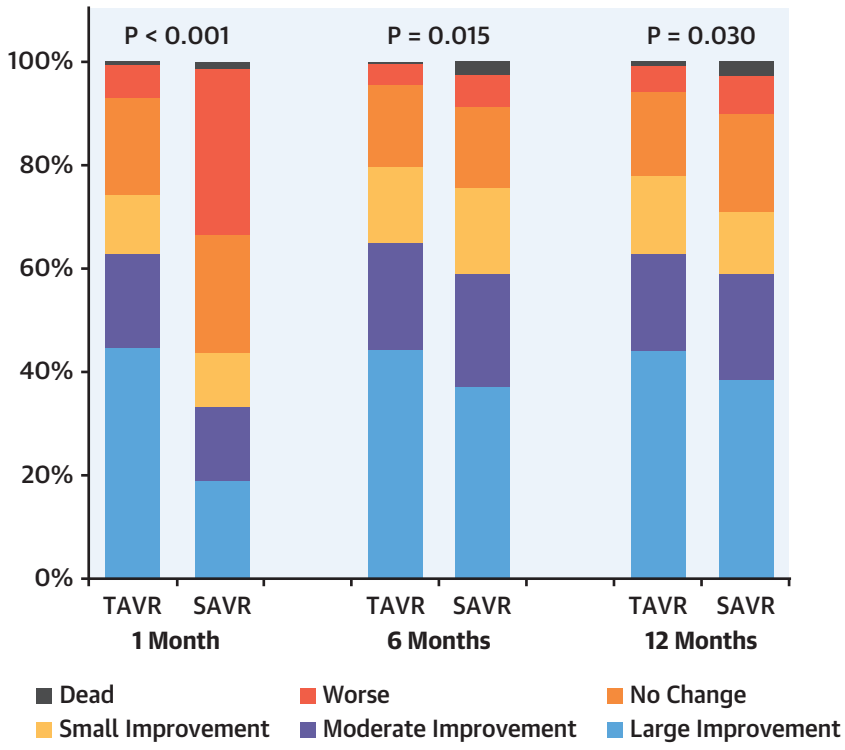
follow-up period, treatment with either TAVR or SAVR resulted in substantial improvement in both disease-specific and generic health status compared with baseline. Consistent with previous studies of transfemoral TAVR, TAVR was associated with significantly better health status than SAVR at 1 month on all scales; however, in contrast to prior analyses, we observed a persistent (albeit modest) benefit of TAVR over SAVR in disease-specific health status at 6 and 12 months.

FIGURE 1 **Between-Group Comparisons of Generic Health Status After TAVR or SAVR**



Predicted mean values of generic health status measures according to the SF-36 (Short Form-36 Health Survey) and EQ-5D (EuroQoL) at 1, 6, and 12 months after transcatheter aortic valve replacement (TAVR) **(blue squares)** and surgical aortic valve replacement (SAVR) **(red circles)**. Mean values and p values were derived from longitudinal growth curve models. **Error bars** represent 95% confidence intervals.

FIGURE 2 Proportion of Patients Achieving Specific Levels of Change in the KCCQ-OS After TAVR or SAVR



Changes in health status from baseline at 1 month, 6 months, and 12 months as defined in the Methods section. The p values were derived from ordinal logistic regression models. KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-Overall Summary; other abbreviations as in Figure 1.

Similar to prior studies of patients at higher surgical risk (7–9), we found that both TAVR and SAVR resulted in substantial improvement (~17 to 20 points on the KCCQ-OS) in the health status of low-risk patients with AS at 6 and 12 months compared with baseline. Not only were these health status changes statistically significant, the improvement was also clinically relevant because prior studies have demonstrated that changes of even 5 points on the KCCQ-OS scale are meaningful at the patient level (12). Although the magnitude of 1-year health status improvement was slightly less than in prior studies of patients with high- and intermediate-risk AS (mean 1-year changes in KCCQ-OS of 20 to 28 points) (7–9), it is noteworthy that substantial improvement was still observed in low-risk patients, despite most patients having only NYHA functional class I or II symptoms at baseline. Thus, these findings demonstrate that patients with low-risk AS with even minimal symptoms can still derive important health status benefits from valve replacement.

Although multiple studies have demonstrated an early health status benefit with TAVR versus SAVR (7–9), this is the first randomized trial to demonstrate a persistent, albeit modest, health status advantage with TAVR at 6 and 12 months—timepoints at which patients are assumed to have recovered fully from surgery. Although the observed difference in mean 1-year KCCQ-OS scores between TAVR and SAVR was numerically small, a 2-point population difference is nonetheless important, as it likely represents a larger, meaningful improvement for a subset of individual patients. For example, if 20% of patients saw a 10-point improvement in their KCCQ-OS score with a specific intervention and 80% of patients saw no improvement, this would result in only a 2-point mean difference for the overall study population, but would still be considered a clinically meaningful improvement for 20% of the individuals in the study. Indeed, the theory that the persistent 1-year health status benefit with TAVR is driven by the greater proportion of TAVR patients who demonstrated a large improvement in the KCCQ-OS is corroborated by

both the cumulative response curves (absolute risk difference of 5.2%—corresponds to a number-needed-to-treat of 19 to achieve a ≥20-point difference in the KCCQ-OS at 1 year) and the categorical analyses (absolute risk difference of 4.5%—corresponds to a number-needed-to-treat of 22 to achieve an excellent outcome).

There are several possible mechanisms for the late health status benefit of TAVR in the low-risk population. First, higher rates of certain SAVR-related complications (e.g., bleeding, acute kidney injury, postoperative atrial fibrillation) (6) in conjunction with a relative decrease in the rates of some TAVR-associated complications (e.g., vascular injury, paravalvular leak) (19) may have contributed to the greater health status benefit seen after TAVR. Prior studies have demonstrated that postoperative atrial fibrillation, major bleeding, and stroke are all associated with worse quality of life after either TAVR or SAVR (20–22). Indeed, our exploratory analyses, which demonstrated that the 1-year health status benefit of TAVR versus SAVR was mildly reduced after adjustment for postprocedural complications, suggests that differential complication rates may have contributed to our findings. Second, as indicated by the categorical and cumulative response analyses, there may be a subset of patients who derive better health status outcomes with TAVR than SAVR in the low-risk population, even in the absence of major complications. Stratified analyses suggest that one such subgroup may be patients with worse functional impairment at baseline (i.e., NYHA functional class III/IV symptoms). Last, it is possible that any late health status benefits of TAVR have been previously masked by the high burden of comorbid conditions and age-related disability present in the higher-risk populations studied in prior trials.

STUDY LIMITATIONS. Our findings should be interpreted in light of the following limitations. Because the study population was restricted to patients who were treated with a balloon-expandable valve via transfemoral access, our results may not be generalizable to other types of TAVR prostheses, to alternative access routes, or to other patients who were excluded from the PARTNER 3 trial population. In addition, because treatment assignment was unblinded, it is possible that provider or subject bias regarding the expectations of treatment outcome could have been introduced, although it is unlikely that this would explain the persistent health status differences seen at 1 year. Finally, because health status assessments were available through only 1 year, the durability of these results beyond 1 year is unknown.

CONCLUSIONS

Among patients with severe AS at low surgical risk, both TAVR and SAVR were associated with substantial improvements in disease-specific and generic health status through 1 year compared with baseline. In addition to TAVR being associated with an early benefit over SAVR on all health status measures, TAVR also was associated with persistent benefits in disease-specific health status at 1 year compared with SAVR. Longer-term follow-up is necessary (and ongoing) to determine whether these findings are durable beyond 1 year in this low-risk patient population.

ADDRESS FOR CORRESPONDENCE: Dr. Suzanne J. Baron, Lahey Hospital and Medical Center, 41 Mall Road, Burlington Massachusetts 01805. E-mail: suzanne.j.baron@lahey.org. Twitter: @suzannejbaron.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with severe AS at low surgical risk, treatment with either TAVR or SAVR results in substantial improvement in both disease-specific and general health status over 1 year. Not only is TAVR associated with better health status than SAVR 1 month after the procedure, a modest advantage of TAVR over SAVR in disease-specific health status persists at 6 and 12 months.

TRANSLATIONAL OUTLOOK: Further studies are needed to evaluate the durability of health status benefits with TAVR compared with SAVR beyond 1 year in patients with severe AS at low surgical risk.

REFERENCES

1. Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;371:967–8.

2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

3. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016;374:1609–20.

4. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med 2017; 376:1321–31.

5. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med 2019;380:1706–15.

6. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695–705.

7. Arnold SV, Reynolds MR, Wang K, et al. Health status after transcatheter or surgical aortic valve replacement in patients with severe aortic stenosis at increased surgical risk: results from the CoreValve US Pivotal Trial. J Am Coll Cardiol Intv 2015;8:1207–17.

8. Reynolds MR, Magnuson EA, Wang K, et al. Health-related quality of life after transcatheter or surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results from the PARTNER (Placement of AoRTic TraNscathetER Valve) Trial (Cohort A). J Am Coll Cardiol 2012;60:548–58.

9. Baron SJ, Arnold SV, Wang K, et al. Health status benefits of transcatheter vs surgical aortic valve replacement in patients with severe aortic stenosis at intermediate surgical risk: results from the PARTNER 2 Randomized Clinical Trial. JAMA Cardiol 2017;2:837–45.

10. Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. J Am Coll Cardiol 2000;35:1245–55.

11. Arnold SV, Spertus JA, Lei Y, et al. Use of the Kansas City Cardiomyopathy Questionnaire for monitoring health status in patients with aortic stenosis. Circ Heart Fail 2013;6:61–7.

12. Spertus J, Peterson E, Conard MW, et al. Monitoring clinical changes in patients with heart failure: a comparison of methods. Am Heart J 2005;150:707–15.

13. Ware JE Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30: 473–83.

14. Ware JE Jr., Kosinski M, Bjorner JB, Turner-Bowkes DM, Gandek B, Maruish ME. Determining important differences in scores (Chapter 10). In: User's Manual for the SF-36v2 Health Survey. Lincoln, RI: QualityMetric Incorporated, 2007: 125–33.

15. Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Med Care 2005; 43:203–20.

16. Jennrich RI, Schluchter MD. Unbalanced repeated-measures models with structured covariance matrices. Biometrics 1986;42:805–20.

17. Arnold SV, Spertus JA, Lei Y, et al. How to define a poor outcome after transcatheter aortic valve replacement: conceptual framework and empirical observations from the placement of aortic transcatheter valve (PARTNER) trial. Circ Cardiovasc Qual Outcomes 2013;6:591–7.

18. Arnold SV, Reynolds MR, Lei Y, et al. Predictors of poor outcomes after transcatheter aortic valve replacement: results from the PARTNER (Placement of Aortic Transcatheter Valve) trial. Circulation 2014;129:2682–90.

19. Grover FL, Vemulapalli S, Carroll JD, et al. 2016 Annual Report of The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. J Am Coll Cardiol 2017;69:1215–30.

20. Arnold SV, Zhang Y, Baron SJ, et al. Impact of short-term complications on mortality and quality of life after transcatheter aortic valve replacement. J Am Coll Cardiol Cardiovasc Interv 2019;12: 362–9.

21. Kapadia SR, Huded CP, Kodali SK, et al. Stroke after surgical versus transfemoral transcatheter aortic valve replacement in the PARTNER Trial. J Am Coll Cardiol 2018;72:2415–26.

22. Bramer S, ter Woorst FJ, van Geldorp MW, et al. Does new-onset postoperative atrial fibrillation after coronary artery bypass grafting affect postoperative quality of life? J Thorac Cardiovasc Surg 2013;146:114–8.

KEY WORDS low surgical risk, quality of life, transcatheter aortic valve replacement

APPENDIX For supplemental tables and figures, please see the online version of this paper.