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Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement

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ABSTRACT

BACKGROUND

There are scant data on long-term clinical outcomes and bioprosthetic-valve function after transcatheter aortic-valve replacement (TAVR) as compared with surgical aortic-valve replacement in patients with severe aortic stenosis and intermediate surgical risk.

METHODS

We enrolled 2032 intermediate-risk patients with severe, symptomatic aortic stenosis at 57 centers. Patients were stratified according to intended transfemoral or transthoracic access (76.3% and 23.7%, respectively) and were randomly assigned to undergo either TAVR or surgical replacement. Clinical, echocardiographic, and health-status outcomes were followed for 5 years. The primary end point was death from any cause or disabling stroke.

RESULTS

At 5 years, there was no significant difference in the incidence of death from any cause or disabling stroke between the TAVR group and the surgery group (47.9% and 43.4%, respectively; hazard ratio, 1.09; 95% confidence interval [CI], 0.95 to 1.25; P=0.21). Results were similar for the transfemoral-access cohort (44.5% and 42.0%, respectively; hazard ratio, 1.02; 95% CI, 0.87 to 1.20), but the incidence of death or disabling stroke was higher after TAVR than after surgery in the transthoracic-access cohort (59.3% vs. 48.3%; hazard ratio, 1.32; 95% CI, 1.02 to 1.71). At 5 years, more patients in the TAVR group than in the surgery group had at least mild paravalvular aortic regurgitation (33.3% vs. 6.3%). Repeat hospitalizations were more frequent after TAVR than after surgery (33.3% vs. 25.2%), as were aortic-valve reinterventions (3.2% vs. 0.8%). Improvement in health status at 5 years was similar for TAVR and surgery.

CONCLUSIONS

Among patients with aortic stenosis who were at intermediate surgical risk, there was no significant difference in the incidence of death or disabling stroke at 5 years after TAVR as compared with surgical aortic-valve replacement. (Funded by Edwards Lifesciences; PARTNER 2 ClinicalTrials.gov number, NCT01314313.)

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*A complete list of the PARTNER 2 Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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A Quick Take is available at NEJM.org

Transcatheter aortic-valve replacement (TAVR) is an alternative to surgery in patients with symptomatic aortic stenosis, on the basis of clinical evidence from multiple randomized trials.[1-12] However, there are limited data on long-term clinical outcomes and bioprosthetic-valve function after TAVR as compared with surgical aortic-valve replacement.[13-16] The Placement of Aortic Transcatheter Valves (PARTNER) 2 cohort A trial is a randomized trial comparing the outcomes of TAVR and surgery in more than 2000 patients with severe aortic stenosis at intermediate risk for surgery. This report from the PARTNER 2 cohort A trial is a 5-year follow-up analysis of clinical outcomes, valve function, and quality-of-life measures in patients undergoing TAVR or surgery.

Methods

Patients and Trial Design

Details of the trial design have been published previously.[6] From December 2011 through November 2013, a total of 2032 patients with severe, symptomatic aortic stenosis at intermediate surgical risk were enrolled at 57 centers in the United States and Canada. Intermediate-risk status was determined by a multidisciplinary heart team and included a predicted 30-day surgical mortality of 4% to 8%, as calculated with a risk model developed by the Society of Thoracic Surgeons (STS).[17] Complete inclusion and exclusion criteria are provided in the Supplementary Appendix, available with the full text of this article at NEJM.org. Written informed consent was obtained from all the patients.

Patients were stratified according to the intended access route if assigned to TAVR (transfemoral or transthoracic) on the basis of imaging studies, including computed tomography (CT), and were then randomly assigned (in a 1:1 ratio) to undergo either TAVR or surgery. Patients and their treating physicians were aware of the treatment assignments.

Device and Procedures

The second-generation balloon-expandable SAPIEN XT heart-valve system (Edwards Lifesciences) and the TAVR procedure have been described previously.[18] In patients assigned to TAVR, transfemoral access was preferred; in those requiring transthoracic access, either transapical or direct aortic access was used. Patients who were assigned to surgery were required to be good candidates for aortic-valve replacement with the use of a bioprosthetic valve. An Edwards Lifesciences surgical bioprosthesis was recommended; mechanical valve prostheses were not allowed. Standard surgical techniques were applied by experienced valve surgeons who had fulfilled qualification standards; limited thoracotomy approaches were allowed, according to surgeon preference. The use of concomitant procedures during surgery was also at the discretion of the surgeon. Patients with concomitant noncomplex coronary artery disease undergoing revascularization could be treated with percutaneous coronary intervention (PCI) in the TAVR group or coronary-artery bypass grafting (CABG) in the surgery group at the discretion of the heart team.

Recommended pharmacotherapy in the TAVR group before the procedure included aspirin (81 mg daily) and clopidogrel (75 mg daily) and after the procedure included aspirin indefinitely and clopidogrel for at least 1 month. For patients in the surgery group, the same postprocedure drug regimen was recommended. In patients receiving long-term oral anticoagulation, clopidogrel was added at the physician's discretion (see the Supplementary Appendix).

Trial Oversight

The trial was designed and monitored by the sponsor (Edwards Lifesciences) and the physician executive committee. The trial protocol, which is available at NEJM.org, was approved by the institutional review board at each site. All the patients were reviewed before randomization by a multidisciplinary case-review committee. Data collection and storage were conducted by the sponsor with the use of an electronic data-capture system. All echocardiograms were interpreted at a central core laboratory. All adverse events occurring during the first 2 years of the trial were adjudicated by an independent clinical-events committee. The committee continued to adjudicate all deaths, strokes, and rehospitalizations occurring between 2 and 5 years after the procedure, whereas other clinical events were site-reported. Statistical analysis for the 5-year manuscript was performed by the sponsor. The first author and last two authors had unrestricted access to the data after the database was locked, wrote the first draft of the manuscript (with assistance from other authors), made the decision to submit the manuscript for publication,

and vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol.

END POINTS

The primary end point of the trial was a nonhierarchical composite of death from any cause or disabling stroke at 2 years in the intention-to-treat population. Disabling stroke was defined as a score on the modified Rankin scale of 2 or more (with scores ranging from 0 [no symptoms] to 6 [death]) and an increase of at least 1 point from baseline to 30 or 90 days after the stroke. The key end points reported in this analysis are 5-year incidences of death from any cause, disabling stroke, repeat hospitalization (procedure-, valve-, or heart failure–related), and aortic-valve reintervention, as well as New York Heart Association (NYHA) functional class, quality-of-life measures, and echocardiographic assessments of aortic-valve area, aortic-valve gradients, and paravalvular regurgitation. Patients were followed yearly for clinical end points. Echocardiographic results were reported from core laboratory assessments. Details of end-point definitions and clinical follow-up are provided in the Supplementary Appendix, including Table S1.

STATISTICAL ANALYSIS

All clinical outcomes were analyzed in the intention-to-treat population (i.e., all the patients who underwent randomization, regardless of the treatment received). The as-treated population (patients in whom the intended procedure was initiated) was used for sensitivity analyses. Echocardiographic analyses were performed in patients who received the intended valve therapy. The transfemoral-access cohort and the transthoracic-access cohort were prespecified analysis subgroups for the primary end point. Because the statistical analysis plan did not include corrections for multiple comparisons with respect to tests for secondary or other outcomes in the 5-year follow-up data, results are reported as point estimates and 95% confidence intervals. Because the margins of the confidence intervals were not adjusted for multiple comparisons, the intervals should not be used to infer definitive treatment effects for secondary outcomes.

The chi-square test or Fisher's exact test was used to compare categorical variables. Continuous variables, which are presented as means with standard deviations, were compared with the use of Student's t-test. Analysis of the primary end point and other time-to-event end points used Kaplan–Meier estimates; comparisons were made with the log-rank test. Interaction analyses were performed in the same subgroups as prespecified for the 2-year analysis.[6] To account for the possibility of nonproportional hazards, restricted mean survival time (restricted to 5 years) and restricted mean event-free time for the end point of death or disabling stroke were calculated.

Ordinal categories that were based on previously established thresholds for clinically relevant changes in the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score were defined as death, worsened (decrease from baseline of >5 points), no change (change of −5 to <5 points), mildly improved (increase of 5 to <10 points), moderately improved (increase of 10 to <20 points), and substantially improved (increase of ≥20 points).[19,20] The relative effect of TAVR as compared with surgery on health status was then compared with the use of ordinal logistic regression. Absolute mean changes in the KCCQ-OS score from baseline to 5 years are also presented. Statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

RESULTS

PARTICIPANTS, PROCEDURES, AND FOLLOW-UP

Among 2032 patients who were enrolled, 1550 (76.3%) were suitable candidates for transfemoral access, and the remaining 482 (23.7%) were included in the transthoracic-access cohort. Patient characteristics at baseline are shown in Table 1. The mean age was 81.6 years, and the mean STS risk score 5.8%; 45.5% of the patients were female. A total of 700 patients (69.2%) in the TAVR group and 679 (66.5%) in the surgery group had coronary artery disease, with similar incidences in the two groups of previous CABG (23.6% and 25.6%, respectively) and previous PCI (27.1% and 27.6%).

A total of 994 of 1011 patients in the TAVR group and 944 of 1021 in the surgery group underwent the assigned procedure (Fig. S1 in the Supplementary Appendix). Concomitant planned or unplanned procedures during surgery were performed in 86 of 944 patients in the surgery group, including aortic endarterectomy, aortic-root enlargement or replacement, and mitral-valve or tricuspid-valve repair or replacement.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	TAVR (N=1011)	Surgery (N=1021)
Age — yr	81.5±6.7	81.7±6.7
Male sex — no. (%)	548 (54.2)	560 (54.8)
Body-mass index†	28.6±6.2	28.3±6.2
STS risk score‡	5.8±2.1	5.8±1.9
NYHA class III or IV — no./total no. (%)	782/1011 (77.3)	776/1020 (76.1)
Coronary artery disease — no. (%)	700 (69.2)	679 (66.5)
Previous myocardial infarction — no. (%)	185 (18.3)	179 (17.5)
Previous CABG — no. (%)	239 (23.6)	261 (25.6)
Previous PCI — no. (%)	274 (27.1)	282 (27.6)
Previous balloon aortic valvuloplasty — no. (%)	51 (5.0)	50 (4.9)
Cerebral vascular disease — no. (%)	325 (32.1)	317 (31.0)
Peripheral vascular disease — no. (%)	282 (27.9)	336 (32.9)
Diabetes mellitus — no. (%)	381 (37.7)	349 (34.2)
COPD — no. (%)		
Any	321 (31.8)	306 (30.0)
Oxygen-dependent	34 (3.4)	32 (3.1)
Renal insufficiency — no. (%)§	51 (5.0)	53 (5.2)
Atrial fibrillation — no. (%)	313 (31.0)	359 (35.2)
Permanent pacemaker — no. (%)	118 (11.7)	123 (12.0)
Frail condition — no./total no. (%)		
5-Meter walk-test time >7 sec	416/936 (44.4)	418/901 (46.4)
Serum albumin <3.5 g/dl	150/988 (15.2)	140/951 (14.7)
Liver disease — no. (%)	19 (1.9)	26 (2.5)
Aortic-valve area — cm^2	0.7±0.2	0.7±0.2
Aortic-valve gradient — mm Hg	44.9±13.4	44.6±12.5
Left ventricular ejection fraction — %	56.2±10.8	55.3±11.9
Left ventricular mass index — g/m^2	119.8±31.5	120.6±32.6
Moderate or severe mitral regurgitation — no./total no. (%)	151/899 (16.8)	171/894 (19.1)

* Plus–minus values are means ±SD. Data on left ventricular ejection fraction were missing for 348 patients assigned to transcatheter aortic-valve replacement (TAVR) and for 347 assigned to surgical aortic-valve replacement. CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, NYHA New York Heart Association, and PCI percutaneous coronary intervention.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Scoring on the risk model of the Society of Thoracic Surgeons (STS) uses an algorithm that is based on the presence of coexisting illnesses in order to predict 30-day operative mortality. The STS score equals the predicted mortality expressed as a percentage.
§ Renal insufficiency was defined as a serum creatinine level of more than 2 mg per deciliter (177 μmol per liter).

Coronary revascularization was performed in 39 of 994 patients in the TAVR group (who underwent PCI) and in 137 of 944 patients in the surgery group (who underwent CABG).

Data were available at 5 years for 920 patients (91.0%) in the TAVR group and for 831 (81.4%) in the surgery group. Baseline characteristics of patients with missing 5-year follow-up as compared with those with complete follow-up are presented in Table S2. Patients with complete follow-up were more likely than those with missing follow-up to be male, to be in NYHA class III or IV, and to have diabetes and were less likely to have moderate or severe mitral regurgitation. To account for varying percentages of patients with missing 5-year data for specific

Table 2. Clinical End Points at 2 and 5 Years (Intention-to-Treat Population).*

End Point	At 2 Years			At 5 Years		
	TAVR (N = 1011)	Surgery (N = 1021)	Hazard Ratio (95% CI)	TAVR (N = 1011)	Surgery (N = 1021)	Hazard Ratio (95% CI)
	no. of patients (%)			*no. of patients (%)*		
Death from any cause or disabling stroke	192 (19.3)	202 (21.1)	0.89 (0.73–1.09)	456 (47.9)	388 (43.4)	1.09 (0.95–1.25)
Death						
From any cause	166 (16.7)	170 (18.0)	0.92 (0.74–1.13)	436 (46.0)	370 (42.1)	1.09 (0.95–1.25)
From cardiac causes	97 (10.1)	105 (11.4)	0.87 (0.66–1.15)	245 (29.4)	223 (27.8)	1.02 (0.85–1.23)
Not from cardiac causes	69 (7.4)	65 (7.4)	0.99 (0.70–1.38)	191 (23.6)	147 (19.8)	1.20 (0.97–1.49)
Neurologic event						
Any event	121 (12.7)	104 (11.1)	1.13 (0.87–1.47)	166 (19.5)	134 (16.0)	1.20 (0.95–1.50)
Transient ischemic attack	34 (3.7)	21 (2.5)	1.54 (0.89–2.65)	45 (5.3)	32 (4.3)	1.33 (0.84–2.09)
Any stroke	91 (9.5)	85 (8.9)	1.04 (0.78–1.40)	128 (15.3)	107 (12.5)	1.15 (0.89–1.49)
Disabling stroke	59 (6.2)	61 (6.4)	0.93 (0.65–1.33)	83 (9.8)	75 (8.6)	1.05 (0.77–1.44)
Nondisabling stroke	33 (3.4)	27 (2.9)	1.20 (0.72–2.00)	43 (5.1)	33 (3.9)	1.27 (0.81–2.00)
Rehospitalization	186 (19.9)	158 (17.5)	1.12 (0.91–1.39)	281 (33.3)	209 (25.2)	1.28 (1.07–1.53)
Death from any cause or rehospitalization	306 (30.7)	283 (29.8)	1.03 (0.87–1.21)	559 (58.1)	460 (51.0)	1.16 (1.02–1.31)
Death from any cause or any stroke	223 (22.4)	225 (23.4)	0.94 (0.78–1.13)	488 (51.1)	406 (45.2)	1.13 (0.99–1.29)
Death from any cause, any stroke, or rehospitalization	346 (34.7)	328 (34.1)	1.00 (0.86–1.17)	597 (61.8)	490 (53.5)	1.16 (1.03–1.31)
Myocardial infarction	43 (4.7)	37 (4.3)	1.10 (0.71–1.70)	84 (11.1)	62 (8.2)	1.26 (0.91–1.75)
New atrial fibrillation	112 (11.5)	275 (27.5)	0.37 (0.30–0.46)	141 (15.8)	291 (30.4)	0.43 (0.35–0.53)
New permanent pacemaker implantation	114 (11.8)	97 (10.3)	1.17 (0.89–1.53)	138 (15.5)	113 (13.0)	1.20 (0.94–1.54)
Endocarditis	15 (1.7)	13 (1.5)	1.07 (0.51–2.25)	30 (3.9)	19 (2.5)	1.46 (0.82–2.60)
Aortic-valve reintervention	6 (0.7)	4 (0.5)	1.40 (0.40–4.98)	21 (3.2)	6 (0.8)	3.28 (1.32–8.13)
Surgical aortic-valve replacement	2 (0.2)	4 (0.5)	0.47 (0.09–2.59)	3 (0.3)	5 (0.6)	0.56 (0.13–2.35)
Balloon aortic valvuloplasty	1 (0.1)	0	NA	1 (0.1)	0	NA
Valve-in-valve	3 (0.3)	0	NA	17 (2.7)	1 (0.2)	15.88 (2.12–119.27)

* All percentages are Kaplan–Meier estimates at the specific time point and thus do not equal the number of patients divided by the total number of patients in the treatment group. NA denotes not applicable.

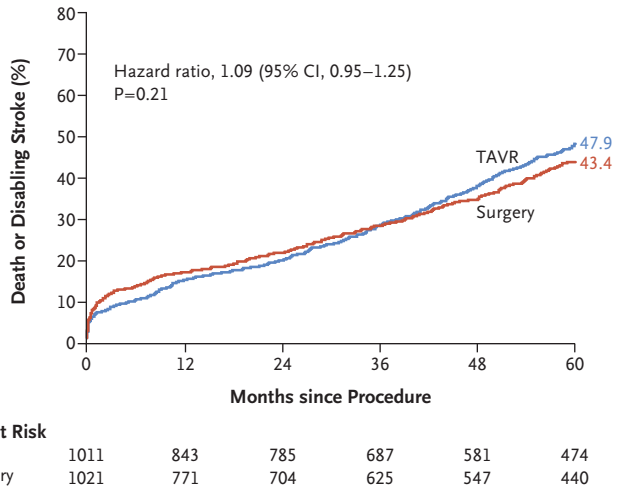


Figure 1. Time-to-Event Curves for Death from Any Cause or Disabling Stroke to 5 Years.

Shown is the incidence of death from any cause or disabling stroke among patients assigned to transcatheter aortic-valve replacement (TAVR) and those assigned to surgical aortic-valve replacement. Values for incidence were calculated with the use of Kaplan–Meier methods and were compared with the use of the log-rank test. The number of patients at risk at 60 months includes patients with early visits ahead of the follow-up window.

Figure 2 (facing page). Echocardiographic (Echo) Findings.

Panels A and B show the mean aortic-valve area and the mean aortic-valve gradient, respectively, from baseline to 5 years for surviving patients with available data. Panel C shows the percentages of surviving patients with available data with paravalvular aortic regurgitation from 30 days to 5 years after the procedure. Percentages may not total 100 because of rounding. Panel D shows time-to-event curves for death from any cause according to the severity of paravalvular aortic regurgitation at 30 days (or discharge if 30-day data were not available) for the TAVR cohort (post hoc analysis).

end points in the TAVR and surgery groups (NYHA class, 15.7% vs. 23.4%; KCCQ-OS score, 19.6% vs. 23.7%; and echocardiographic findings, 30.4% vs. 35.7%), sensitivity analyses to account for missing data were performed with the use of multiple imputation or linear mixed-effects models and paired analyses (see the Supplementary Appendix).

DEATH AND STROKE

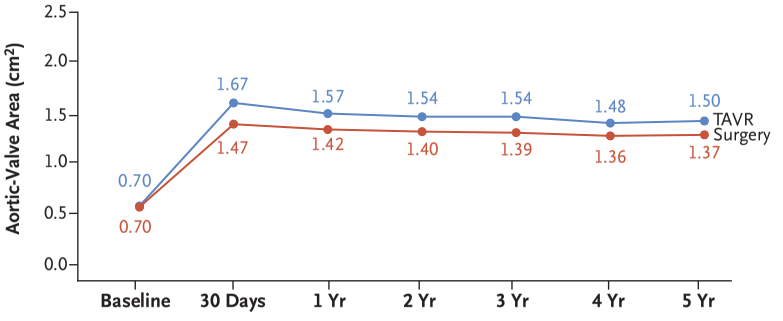
At 5 years, there was no evidence of a significant difference in the incidence of the composite end point of death from any cause or disabling stroke between the TAVR group and the surgery group (47.9% and 43.4%, respectively; hazard ratio, 1.09; 95% confidence interval [CI], 0.95 to 1.25; P=0.21) (Table 2 and Fig. 1). Results of a sensitivity analysis performed with the use of multiple imputation were consistent with these findings (Table S3). In the transfemoral-access cohort, the incidence of death or disabling stroke was similar in the TAVR group and the surgery group (44.5% and 42.0%, respectively; hazard ratio, 1.02; 95% CI, 0.87 to 1.20) (Fig. S2A). However, the incidence of death or disabling stroke was higher after TAVR than after surgery in the transthoracic-access cohort (59.3% vs. 48.3%; hazard ratio, 1.32; 95% CI, 1.02 to 1.71) (Fig. S2B). Apart from access route, there was no heterogeneity of treatment effect for death or disabling stroke for any subgroup tested (Fig. S3).

The incidences of death from any cause in the TAVR and surgery groups were 46.0% and 42.1%, respectively, in the overall population, 42.7% and 40.5% in the transfemoral-access cohort, and 56.9% and 47.3% in the transthoracic-access cohort (Table 2 and Table S4). Adjudicated causes of death are presented in Table S5. The incidence of disabling stroke was similar in the TAVR group and the surgery group, regardless of cohort. Results of a sensitivity analysis that were restricted to the as-treated population were consistent with the intention-to-treat results (Table S6). Post hoc landmark analyses of events occurring between 2 and 5 years after the procedure are presented in Figure S4 and Table S7. The 5-year restricted mean survival time was similar for TAVR and surgery (46.3 months and 46.6 months, respectively), as was the restricted mean event-free time for the end point of death or disabling stroke (45.0 months and 44.8 months) (Table S8).

OTHER CLINICAL OUTCOMES

Rehospitalization occurred more frequently after TAVR than after surgery at 5 years (33.3% vs. 25.2%; hazard ratio, 1.28; 95% CI, 1.07 to 1.53) (Table 2 and Fig. S5); reasons for rehospitalization are shown in Table S9. Aortic-valve reintervention was uncommon in both groups but was more frequent among patients in the TAVR group than among those in the surgery group (3.2% vs. 0.8%; hazard ratio, 3.28; 95% CI, 1.32 to 8.13) (Table 2 and Table S10). Reinterventions after TAVR were due to progressive stenosis (10 of 21 cases) or aortic regurgitation (11 of 21

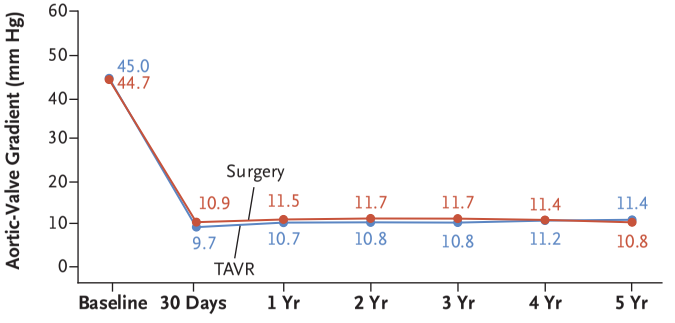
A Aortic-Valve Area



No. of Patients with Echo Findings and Patients Alive

TAVR							
Echo findings	899	827	695	572	468	365	289
Alive	974	945	854	800	697	595	475
Surgery							
Echo findings	861	726	590	490	413	349	259
Alive	936	896	796	727	649	568	459

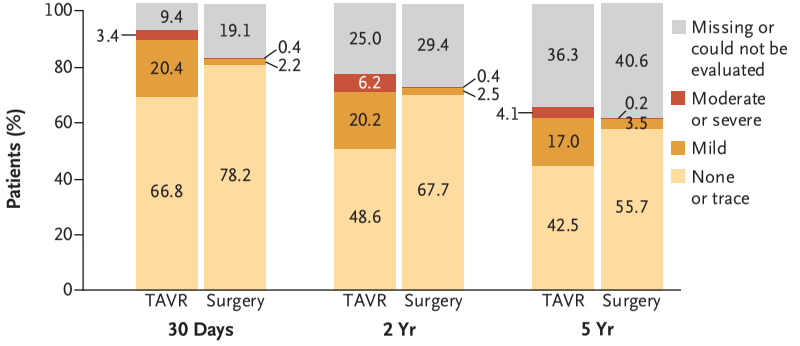
B Aortic-Valve Gradient



No. of Patients with Echo Findings and Patients Alive

TAVR							
Echo findings	959	890	751	633	522	405	323
Alive	974	945	854	800	697	595	475
Surgery							
Echo findings	916	788	633	538	453	377	288
Alive	936	896	796	727	649	568	459

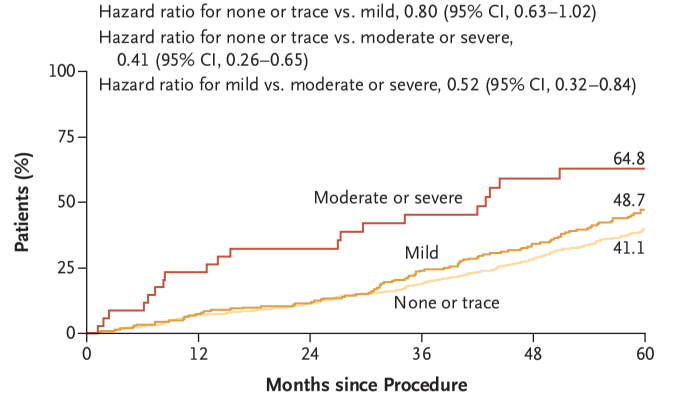
C Paravalvular Aortic Regurgitation



No. of Patients with Echo Findings and Patients Alive

TAVR			
Echo findings	872	609	310
Alive	945	800	475
Surgery			
Echo findings	757	516	272
Alive	896	727	459

D Death from Any Cause, According to Severity of Paravalvular Aortic Regurgitation



No. at Risk

Moderate or severe	33	25	20	16	11	5
Mild	196	178	170	143	120	63
None or trace	643	592	557	495	427	225

cases), and most patients (18 of 21) were treated with either repeat TAVR or balloon valvuloplasty. Endocarditis was the main cause of the reintervention in patients in the surgery group (4 of 6 cases), most of whom were treated with repeat surgery. In-hospital mortality from valve reintervention was 5% (1 of 21 patients) in the TAVR group and 50% (3 of 6 patients) in the surgery group.

ECHOCARDIOGRAPHIC FINDINGS

In both treatment groups, initial gains in aortic-valve areas and reductions in mean gradients were sustained for 5 years (Fig. 2A and 2B). Among surviving patients with echocardiograms, mild or greater paravalvular aortic regurgitation was observed in 33.3% of the patients in the TAVR group and in 6.3% of those in the surgery group (Fig. 2C and Fig. S6). Results of sensitivity analyses of the echocardiographic findings to account for missing data with the use of multiple imputation are presented in Table S11. Moderate or severe paravalvular aortic regurgitation after TAVR was associated with an increased risk of death at 5 years in the overall population (Fig. 2D) and in the transfemoral-access cohort (Fig. S7). Changes in left ventricular dimensions and ejection fraction are presented in Table S12 and Figures S8 and S9.

FUNCTIONAL AND HEALTH STATUS

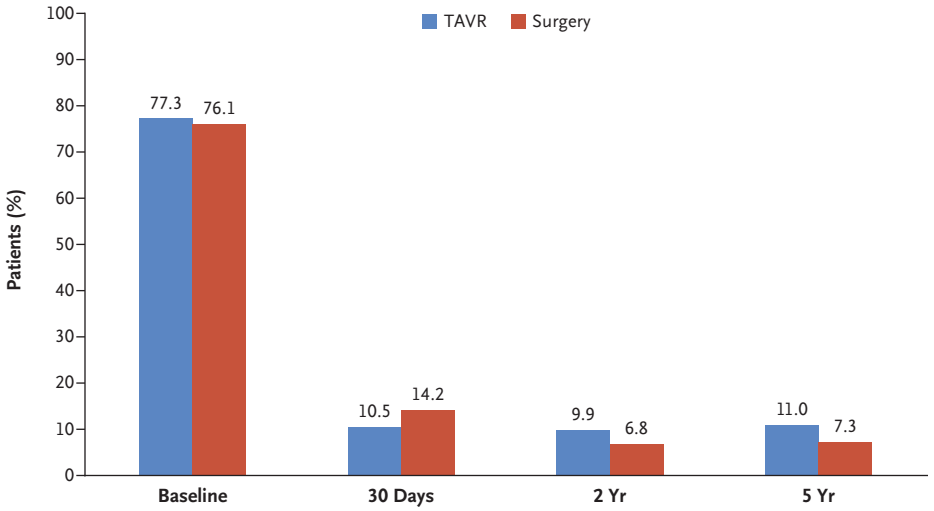
Among surviving patients with available data, both TAVR and surgery led to improvements in health status at 5 years (NYHA functional class I or II, 89.0% and 92.7%, respectively; average increase from baseline in the KCCQ-OS score, 19.6 points and 20.5 points) (Fig. 3A and 3B). When patients were stratified according to established thresholds for clinically relevant changes in the KCCQ-OS score, there was no evidence of a substantial difference between the TAVR group and the surgery group at 5 years (Fig. S10). Results of sensitivity analyses to account for missing data with the use of multiple imputation (for data on the NYHA class) and linear mixed-effects models (for data on the KCCQ-OS score) are shown in Tables S13 and S14.

DISCUSSION

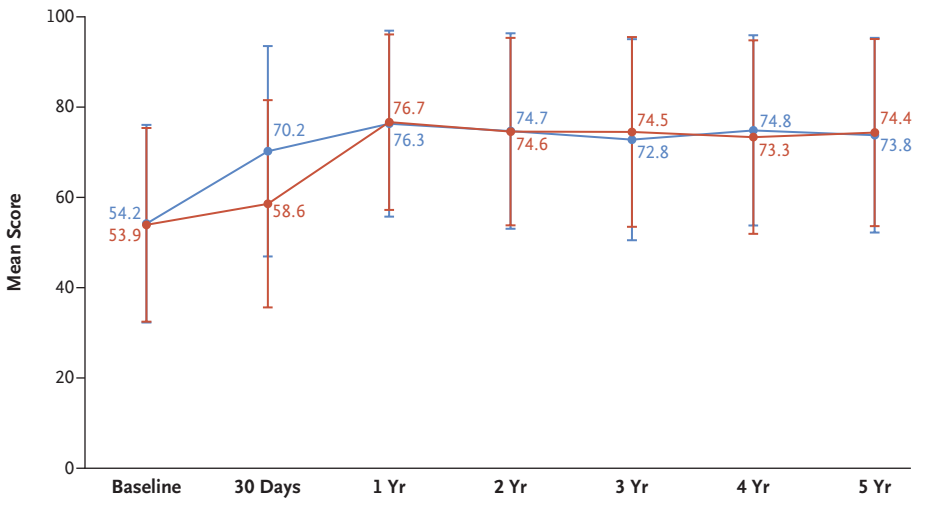
The PARTNER 2 cohort A trial compared TAVR with surgical aortic-valve replacement in patients with severe, symptomatic aortic stenosis at intermediate surgical risk. The main findings from the 5-year follow-up of the trial can be summarized as follows. First, there was no significant difference between the two groups in the primary end point of death from any cause or disabling stroke up to 5 years. Second, valve hemodynamics after TAVR were similar to those after surgery (with larger valve areas and similar valve gradients), but TAVR was associated with higher incidences of mild and moderate or severe paravalvular aortic regurgitation. Third, TAVR and surgery resulted in similar improvements in functional status and disease-specific quality-of-life measures through 5 years. Fourth, valve-related reintervention and rehospitalization were more frequent among patients undergoing TAVR than among those undergoing surgery.

A key subgroup analysis showed that the outcomes of TAVR through transthoracic access, but not through transfemoral access, were inferior to those of open-heart surgery. The progressive divergence of time-to-event curves for death or disabling stroke in the transthoracic-access cohort suggests that considerations beyond procedural factors, including a delayed effect of paravalvular regurgitation on left ventricular function, may play a role. In contemporary practice with smaller-diameter TAVR systems, transfemoral access is used in more than 95% of patients undergoing TAVR. In addition, other transvascular-access routes (axillary, carotid, and caval) are being used preferentially instead of transthoracic access in many centers.[21-23]

In landmark analyses from 2 to 5 years after the procedure, we observed a higher incidence of death from any cause or disabling stroke and a higher incidence of death from any cause with TAVR than with surgery. Possible explanations for the higher mortality during this time period among patients in the TAVR group than among those in the surgery group may be the negative effect of increased moderate or severe paravalvular regurgitation after TAVR or the higher prevalence of untreated clinically significant coronary disease in the TAVR cohort than in the surgery cohort. Several previous studies have shown an association between moderate or severe paravalvular regurgitation and mortality after TAVR,[24,25] which has led to device refinements and improved valve-sizing techniques with the use of CT imaging.[26-28] The currently used SAPIEN 3



No. of Observations	1011	1020	940	857	738	650	391	343
No. of Patients Alive	1011	1021	963	933	810	730	484	461



No. of Patients							
TAVR							
Observed	950	913	797	717	580	470	373
Alive	1011	963	865	810	707	605	484
Surgery							
Observed	883	792	686	618	505	446	342
Alive	1021	933	802	730	651	570	461

Figure 3. Functional Status and Quality of Life.

The percentages of surviving patients with available data in New York Heart Association (NYHA) class III or IV are shown from baseline to 5 years (Panel A). Quality-of-life metrics according to Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) scores are shown for surviving patients with available data from baseline to 5 years (Panel B). Scores range from 1 to 100, with higher scores indicating better quality of life. The I bars indicate standard deviations.

valve, which incorporates an external sealing skirt and is implanted with the use of CT sizing, is associated with markedly lower incidences of postprocedural and 1-year moderate or severe paravalvular aortic regurgitation than were seen with previous-generation devices.[8,24,29-31]

Although aortic-valve reintervention was uncommon, it was more frequent after TAVR than after surgery, and the causes of reintervention were distinctly different. Reintervention after TAVR usually occurred after 2 years and was due to progressive aortic-valve stenosis or regurgitation. Most of these patients were treated with repeat TAVR (valve-in-valve), with favorable early outcomes. In contrast, reintervention after surgery was most commonly due to endocarditis and was managed with repeat open-heart surgery, which resulted in a high surgical mortality.

This analysis has several limitations. The device used (SAPIEN XT) is no longer in clinical use, which reduces the clinical applicability of the current trial. Bioprosthetic-valve failure increases with time, and 5-year comparative data may not reflect the true durability of transcatheter or surgical valves at later time points. The mean age of the patients in this trial was 81 years, and it would be inappropriate to extrapolate these findings to younger patients or patients with lower surgical risk who have higher activity expectations and longer life spans. Missing 5-year data for some of the important secondary end points, such as the echocardiography results, may have biased our findings regarding valve hemodynamics.

Among patients with severe, symptomatic aortic stenosis at intermediate surgical risk, the incidence of the composite end point of death from any cause or disabling stroke at 5 years was similar with TAVR and surgical aortic-valve replacement.

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APPENDIX

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