ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Low-Risk Patients at 7 Years

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ABSTRACT

BACKGROUND

Five-year data from the PARTNER 3 trial showed that among low-risk patients with severe, symptomatic aortic stenosis, outcomes were similar among patients who had undergone transcatheter aortic-valve replacement (TAVR) and those who had undergone surgical aortic-valve replacement. Longer-term assessments of clinical outcomes and valve durability are needed.

METHODS

Patients were randomly assigned in a 1:1 ratio to undergo transfemoral TAVR or surgery. The first primary end point was a nonhierarchical composite of death, stroke, or rehospitalization related to the procedure, the valve, or heart failure. The second primary end point was a hierarchical composite of death, disabling stroke, nondisabling stroke, and the number of rehospitalization days related to the procedure, the valve, or heart failure, analyzed with the use of a win ratio analysis. Clinical, echocardiographic, valve-durability, and health-status end points were assessed through 7 years.

RESULTS

A total of 1000 patients underwent randomization. In the analysis of the first primary end point, the Kaplan–Meier estimate of the incidence of an end-point event was 34.6% with TAVR and 37.2% with surgery (difference, –2.6 percentage points; 95% confidence interval [CI], –9.0 to 3.7). The win ratio for the second primary end point was 1.04 (95% CI, 0.84 to 1.30). In the TAVR and surgery groups, respectively, the Kaplan–Meier estimates for the incidence of components of the first primary end point were as follows: death, 19.5% and 16.8%; stroke, 8.5% and 8.1%; and rehospitalization, 20.6% and 23.5%. The mean (±SD) aortic-valve gradients assessed by echocardiography at 7 years were 13.1±8.5 mm Hg after TAVR and 12.1±6.3 mm Hg after surgery. The percentage of bioprosthetic valves that failed was 6.9% in the TAVR group and 7.5% in the surgery group. Patient-reported outcomes were similar in the two groups.

CONCLUSIONS

Among low-risk patients with severe, symptomatic aortic stenosis, no significant differences with respect to two primary composite end points involving death, stroke, and rehospitalization were observed at 7 years between those who had undergone TAVR and those who had undergone surgery. (Funded by Edwards Lifesciences; PARTNER 3 ClinicalTrials.gov number, NCT02675114.)

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Transcatheter aortic-valve replacement (TAVR) has been increasingly used as an alternative to surgery for treating patients with severe, symptomatic aortic stenosis.[1,2] Randomized trials have shown that in patients at low, intermediate, or high surgical risk, TAVR was superior or similar to surgical aortic-valve replacement through 5 years of follow-up.[3-19] As reported previously, the Placement of Aortic Transcatheter Valves (PARTNER) 3 trial showed that the incidence of death, stroke, or rehospitalization (the primary composite end point) at 1, 2, and 5 years after TAVR was lower than or was not different from that with surgery in younger, low-risk patients.[12-14] Late bioprosthesis failure after aortic-valve implantation remains an important consideration in lifelong patient-care decisions.[20,21] Here, we describe the 7-year clinical and echocardiographic results of the PARTNER 3 trial.

Methods

Trial Design and Oversight

In a prospective, multicenter, open-label, randomized trial, we assessed TAVR with the use of the balloon-expandable SAPIEN 3 valve (Edwards Lifesciences) as compared with surgery in patients with symptomatic, severe aortic stenosis at low surgical risk. Details of trial design and oversight and outcomes at 1, 2, and 5 years have been described previously.[12-14] The protocol (available with the full text of this article at NEJM.org) was developed by the trial sponsor (Edwards Lifesciences) and the steering committee and was approved by the institutional review board at each site. The sites and investigators are listed in Section A in the Supplementary Appendix (available at NEJM.org). The sponsor funded all trial-related activities and participated in site selection, data collection and monitoring, trial management, and statistical analysis. The trial leadership (authors who were not employees of the sponsor) had unrestricted access to the data, prepared all drafts of the manuscript (except for the first draft, which the first author wrote), participated in the decision to submit the manuscript for publication, and vouch for the accuracy and completeness of the data and for the adherence of the trial to the protocol.

Patients

Patients were eligible for inclusion if they had symptomatic, severe aortic stenosis and were considered to have low surgical risk on the basis of an evaluation by the heart team, including a score of less than 4% on the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM; scores range from 0 to 100%, with higher scores indicating a greater risk of death within 30 days after the procedure). Patients were excluded if they had anatomical features that made them unsuitable candidates for transfemoral TAVR (e.g., severe iliac or common femoral arterial disease). Patient eligibility was assessed and approved by a case review board. Eligibility criteria are provided in Section B, and trial representativeness is discussed in Section C, in the Supplementary Appendix. All the patients provided written informed consent.

Randomization, Procedures, and Follow-up

Patients were randomly assigned, in a 1:1 ratio, to undergo transfemoral TAVR with the use of a SAPIEN 3 valve or surgery with a commercially available bioprosthesis according to the operator's discretion. Patients with clinically meaningful concomitant coronary artery disease underwent revascularization procedures in accordance with the trial protocol. Details regarding the TAVR and surgical procedures have been published previously.[12] Clinical, echocardiographic, and health-status end points were assessed at baseline, at hospital discharge, and at serial time points during follow-up.

Clinical End Points

The two primary end points prespecified for this 7-year analysis were the same as those used for the 5-year analysis. The first was a nonhierarchical composite of death, stroke, or rehospitalization related to the procedure, the valve, or heart failure; this was also the original primary end point for the 1-year analysis. The second was a hierarchical composite of death, disabling stroke, nondisabling stroke, and the number of rehospitalization days related to the procedure, the valve, or heart failure. Details regarding these end points are outlined in Section D1 in the Supplementary Appendix, and secondary end points of

interest are described in Sections D2 and D3. Death from cardiovascular causes, stroke, rehospitalization, endocarditis, and valve thrombosis according to Valve Academic Research Consortium 3 (VARC-3) criteria[22] were adjudicated by a clinical events committee. A vital-status sweep (the use of telephone calls, medical records, or publicly available data to obtain information on vital status) was performed by the trial sites to include as much data as possible for the end point of death from any cause. Analyses of restricted mean event-free survival time[24] were performed to assess between-group differences for the primary end point, death from any cause, and death or disabling stroke. Patient-reported end points included the score on the Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS; scores range from 0 to 100, with higher scores indicating better health status).

ECHOCARDIOGRAPHIC ASSESSMENTS

All echocardiograms were evaluated at a central core laboratory with the use of standard hemodynamic measures and assessments of paravalvular aortic regurgitation.[22,23] Valve durability was assessed according to the VARC-3 definition of bioprosthetic valve failure, which defines failure as irreversible stage 3 (severe) hemodynamic valve deterioration, aortic-valve reintervention, or valve-related death.[22,23] If bioprosthetic valve failure was confirmed, the cause, type, and stage of hemodynamic valve deterioration were further adjudicated.

STATISTICAL ANALYSIS

The first primary end point was assessed with time-to-event curves and Kaplan–Meier estimates; the confidence interval for the between-group difference with respect to the primary end point at 7 years was estimated with the use of Greenwood's formula. The second primary end point was assessed with the win ratio method. Continuous variables are shown as means and standard deviations; categorical variables are shown as percentages and numbers of patients. Hazard ratios with 95% confidence intervals are provided for time-to-event analyses. The widths of the confidence intervals have not been adjusted for multiple comparisons and should not be used in place of hypothesis testing.

Clinical end points were analyzed in the as-treated population, which included the patients who underwent randomization and began to undergo the index procedure. Echocardiographic and valve durability findings were analyzed in the valve-implant population, which included the patients who received the intended valve. Data from patients who no longer had a functioning index valve (i.e., had a valve explant or valve-in-valve procedure) were censored for echocardiographic and valve durability analyses after the reintervention occurred (Section D5 in the Supplementary Appendix). In accordance with VARC-3 criteria,[22] the estimated percentage of bioprosthetic valve failure events was calculated with the cumulative incidence function, with death treated as a competing risk. The statistical methods that were used for additional analyses are provided in Section D6 in the Supplementary Appendix. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute).

RESULTS

PATIENTS, PROCEDURES, AND FOLLOW-UP

A total of 1000 patients underwent randomization at 71 clinical sites; 503 patients were assigned to undergo transfemoral TAVR and 497 to undergo surgery. The as-treated population included 496 patients in the TAVR group and 454 patients in the surgery group; 495 and 453 patients, respectively, received the intended valve. Information on implanted valve sizes and surgical valve types was published previously[14] (Fig. S1 and Table S1 in the Supplementary Appendix). The baseline characteristics of the patients are shown in Table S2. The mean age of the patients was 73 years, 69.3% were men, and the mean STS-PROM score was 1.9%. Randomization and follow-up through 7 years are shown in Figure S2. The primary end point could be evaluated at 7 years in 89.6% of the patients (92.7% of the patients in the TAVR group and 86.1% in the surgical group); a disproportionate number of withdrawals from the trial occurred in the surgery group in the first few years of follow-up. A vital-status sweep yielded a known status for 84 of 137 patients who were lost to follow-up or had withdrawn from the trial (28 patients in the TAVR group and 56 patients in the surgery group) (Table S3). Therefore, vital status was determined for 471 of 496 patients (95.0%) in the TAVR group and for 426 of 454 patients (93.8%) in the surgery group.

PRIMARY END POINTS

In the period from baseline to 7 years, death, stroke, or rehospitalization related to the procedure, the valve, or heart failure (the first primary end point) occurred in 165 of 496 patients (Kaplan–Meier estimate, 34.6%) in the TAVR group and in 156 of 454 patients (Kaplan–Meier estimate, 37.2%) in the surgery group (difference, –2.6 percentage points; 95% confidence interval [CI], –9.0 to 3.7; hazard ratio, 0.87; 95% CI, 0.70 to 1.08) (Fig. 1A and Table 1). The Kaplan–Meier estimates of the individual components of the first primary end point at 7 years in the TAVR and surgical groups, respectively, were as follows: death from

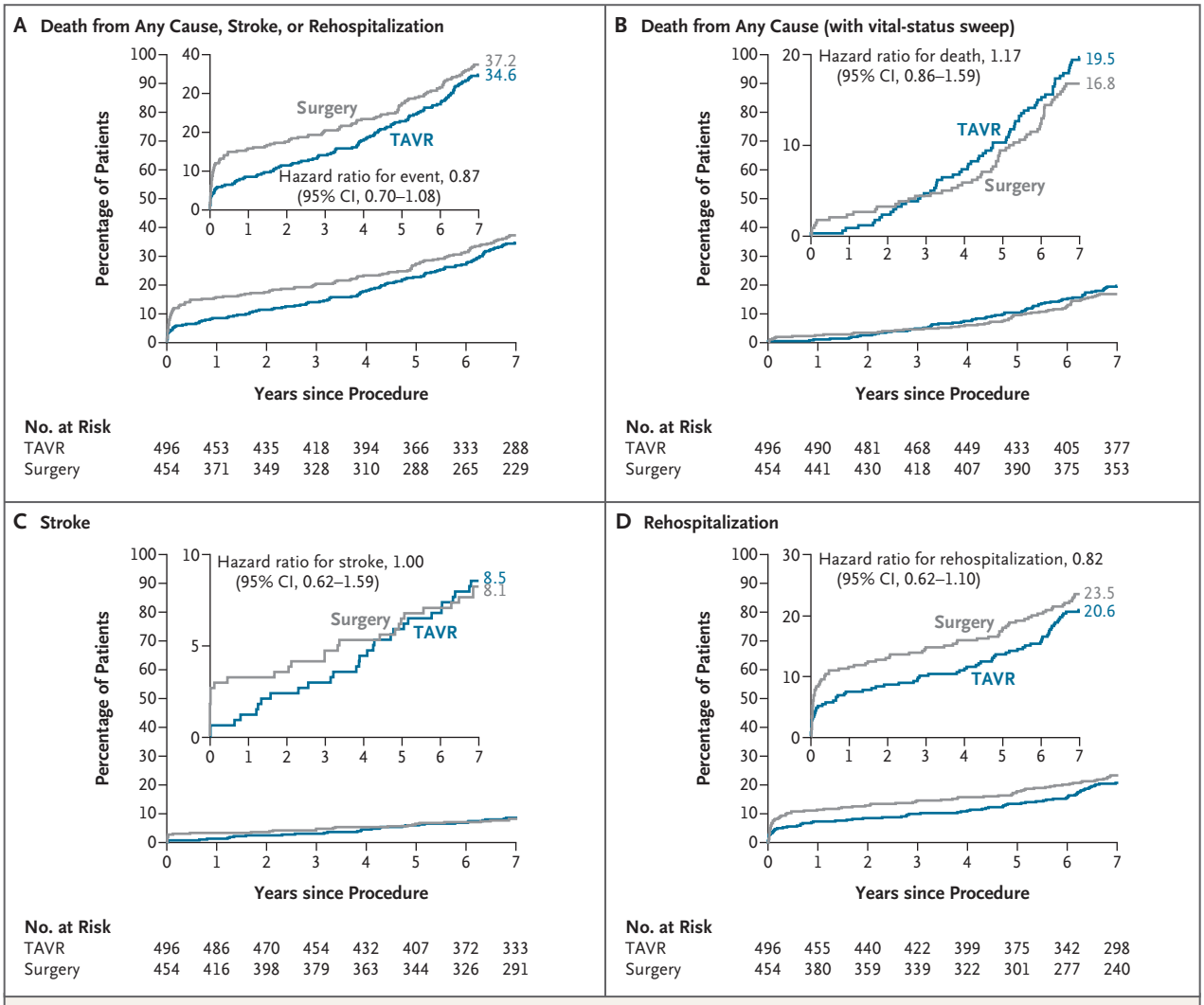

Figure 1. Kaplan–Meier Curves for the First Primary End Point and Its Components.

Panel A shows the Kaplan–Meier estimates for death from any cause, stroke, or rehospitalization related to the procedure, the valve, or heart failure (the first composite primary end point); these data do not include those obtained from the vital-status sweep. Panels B, C, and D show the estimates for the components of the end point. In accordance with the statistical analysis plan, the prespecified analysis of the composite primary end point involved the difference in the Kaplan–Meier estimates between transcatheter aortic-valve replacement (TAVR) and surgery, calculated with the Wald test (difference, –2.61%; 95% CI, –8.95% to 3.74%). To provide the most complete follow-up available, the analysis of death alone includes data obtained from the vital-status sweep. Additional details can be found in Table S3 in the Supplementary Appendix. Because some evidence was observed of nonproportionality of hazards over time for the component of death, the odds ratio was also assessed and was 1.20 (95% CI, 0.86 to 1.67). The inset in each panel shows the same data on an enlarged y axis. All analyses were performed in the as-treated population, which included the patients who underwent randomization and began to undergo the index procedure.

any cause including the data from the vital-status sweep, 19.5% and 16.8%; stroke, 8.5% and 8.1%; and rehospitalization, 20.6% and 23.5% (Fig. 1B, 1C, and 1D; Table 1; and Fig. S3). Table S4 and Figures S4A and S4B provide details regarding death from cardiovascular and noncardiovascular causes.

The results for the first primary end point appeared to be consistent across all major subgroups (Fig. S5). In a landmark analysis of the first primary end point for years 1 to 7 (calculated with the exclusion of data from the first year of follow-up), the Kaplan–Meier estimates were 28.5% in the TAVR group and 25.4% in the surgery group (hazard ratio for death, stroke, or rehospitalization, 1.15; 95% CI, 0.87 to 1.52) (Table 1 and Fig. S6). An analysis of the restricted mean event-free survival time and the restricted mean overall survival time for the first primary end point through 7 years indicated that TAVR resulted in 134 more event-free days (95% CI, 22 to 247) than surgery (Fig. 2A), and 15 fewer days of overall survival time (95% CI, −78 to 48) than surgery (Fig. 2B). The win ratio for the second primary end point was 1.04 (95% CI, 0.84 to 1.30) (Fig. S7). Additional data for death, stroke, death and disabling stroke, and rehospitalization are provided in Table 1, Tables S5 through S8, and Figures S8 through S11.

SECONDARY END POINTS

The Kaplan–Meier estimated percentages of patients with aortic-valve reintervention, endocarditis, myocardial infarction, serious bleeding, and revascularization events appeared to be similar in the TAVR and surgery groups from baseline through 7 years (Table 1 and Tables S8 through S10). New-onset atrial fibrillation occurred in 17.7% of the patients in the TAVR group and in 43.5% of the patients in the surgery group, and a new permanent pacemaker was implanted in 17.3% and 12.8% of the patients, respectively (Table 1). Clinically meaningful valve thrombosis occurred in 13 patients (2.8%) in the TAVR group and 2 patients (0.5%) in the surgery group (Table 1 and Table S11). Of the 13 patients with valve thrombosis in the TAVR group, 10 had stage 2 or 3 hemodynamic valve deterioration and 7 of the 13 cases resolved with anticoagulation (Table S11). None of the patients with valve thrombosis died. Tables S8 and S10 show the number of patients with death, stroke, myocardial infarction, revascularization, or new onset atrial fibrillation from 5 through 7 years.

ECHOCARDIOGRAPHIC FINDINGS

At 7 years, the mean (±SD) aortic-valve gradient was 13.1±8.5 mm Hg in the TAVR group and 12.1±6.3 mm Hg in the surgery group; the mean aortic-valve area was 1.9±0.6 cm^2 and 1.8±0.5 cm^2, respectively (Fig. 3A and 3B and Fig. S12A and S12B). Paired mean gradient and aortic-valve area analyses are shown in Figure S12C and S12D. Mild, moderate, or severe paravalvular aortic regurgitation was present in 17.7% of the patients in the TAVR group and in 2.0% of the patients in the surgery group (Fig. S13). In the TAVR group, 7-year mortality appeared to be similar among patients with no or trace paravalvular aortic regurgitation at 30 days after the procedure and among those with mild paravalvular regurgitation at 30 days after the procedure (18.7% and 20.7%, respectively; hazard ratio, 0.89; 95% CI, 0.57 to 1.38) (Fig. S14).

The cumulative incidence of bioprosthetic valve failure was 6.9% in the TAVR group and 7.5% in the surgery group (Fig. 3C). The results for the components of bioprosthetic valve failure in the TAVR and surgery groups, respectively, were as follows: irreversible stage 3 hemodynamic valve deterioration, 1.7% and 2.8%; valve reintervention, 4.7% and 4.3%; and valve-related death, 0.4% and 0.5% (Table 1 and Fig. S15). Overall, aortic-valve reintervention occurred in 6.0% of the patients in the surgery group and 6.7% of the patients in the TAVR group (hazard ratio, 1.11; 95% CI, 0.63 to 1.94) (Fig. 3D). The incidence of stage 2 or 3 structural valve deterioration appeared to be similar in the two groups (Fig. S16). At 7 years, 73.4% of the patients in the TAVR group and 74.8% of the patients in the surgery group were alive without bioprosthetic valve failure.

FUNCTIONAL AND HEALTH-STATUS END POINTS

The percentage of patients who were alive with New York Heart Association (NYHA) class I or II symptoms at 7 years was 72.9% in the TAVR group and 75.9% in the surgery group (Fig. S17). Disease-specific health status at 7 years appeared to be similar in the two groups, with a mean KCCQ-OS score of 84.9 in patients in the TAVR group and 86.2 in patients in the surgery group (Fig. S18A). At 7 years, 233 of 395 patients (59.0%) in the TAVR group and 210 of 332 patients (63.3%)

Table 1. Key Clinical End Points.*

End Point	Baseline to 1 Yr			1 Yr to 7 Yr			Baseline to 7 Yr		
	TAVR (N=496)	Surgery (N=454)	Hazard Ratio (95% CI)	TAVR (N=490)	Surgery (N=441)	Hazard Ratio (95% CI)	TAVR (N=496)	Surgery (N=454)	Hazard Ratio (95% CI)
	no. of patients with event (Kaplan–Meier %)			*no. of patients with event (Kaplan–Meier %)*			*no. of patients with event (Kaplan–Meier %)*		
Death, stroke, or rehospitalization related to procedure, valve, or heart failure†	42 (8.5)	71 (15.8)	0.51 (0.35–0.75)	123 (28.5)	85 (25.4)	1.15 (0.87–1.52)	165 (34.6)	156 (37.2)	0.87 (0.70–1.08)‡
Death from any cause with data from vital-status sweep	5 (1.0)	11 (2.4)	0.41 (0.14–1.19)	89 (18.7)	62 (14.7)	1.31 (0.94–1.81)	94 (19.5)	73 (16.8)	1.17 (0.86–1.59)§
Death from any cause without data from vital-status sweep	5 (1.0)	11 (2.5)	0.41 (0.14–1.17)	86 (18.6)	49 (12.8)	1.52 (1.07–2.16)	91 (19.4)	60 (14.9)	1.32 (0.95–1.83)§
Death from cardiovascular causes	4 (0.8)	9 (2.0)	0.40 (0.12–1.30)	42 (9.5)	22 (5.9)	1.65 (0.99–2.77)	46 (10.3)	31 (7.8)	1.29 (0.82–2.04)§
Death from noncardiovascular causes¶	1 (0.2)	2 (0.5)	0.44 (0.04–4.87)	44 (10.0)	27 (7.3)	1.41(0.88–2.28)	45 (10.2)	29 (7.7)	1.35 (0.85–2.15)§
Stroke	6 (1.2)	15 (3.3)	0.36 (0.14–0.92)	32 (7.3)	18 (5.0)	1.52 (0.85–2.70)	38 (8.5)	33 (8.1)	1.00 (0.62–1.59)
Disabling	1 (0.2)	5 (1.1)	0.18 (0.02–1.54)	21 (4.9)	9 (2.5)	2.02 (0.93–4.42)	22 (5.1)	14 (3.6)	1.37 (0.70–2.68)
Nondisabling	5 (1.0)	10 (2.2)	0.45 (0.15–1.32)	12 (2.7)	9 (2.4)	1.13 (0.48–2.68)	17 (3.7)	19 (4.6)	0.78 (0.40–1.50)
Death or disabling stroke†	5 (1.0)	14 (3.1)	0.32 (0.11–0.89)	97 (20.9)	54 (14.1)	1.56 (1.12–2.18)	102 (21.7)	68 (16.8)	1.31 (0.96–1.78)§
Rehospitalization related to procedure, valve, or heart failure	36 (7.3)	51 (11.5)	0.62 (0.41–0.95)	57 (14.4)	44 (13.5)	1.05 (0.71–1.56)	93 (20.6)	95 (23.5)	0.82 (0.62–1.10)
Aortic-valve reintervention¶	4 (0.8)	2 (0.5)	1.78 (0.33–9.71)	24 (5.9)	20 (5.5)	1.04 (0.58–1.89)	28 (6.7)	22 (6.0)	1.11 (0.63–1.94)
Endocarditis	1 (0.2)	2 (0.5)	0.44 (0.04–4.88)	11 (2.7)	9 (2.4)	1.05 (0.44–2.54)	12 (2.9)	11 (2.8)	0.94 (0.42–2.14)
Clinically significant valve thrombosis‖	2 (0.4)	0 (0.0)	NA	11 (2.4)	2 (0.5)	4.80 (1.06–21.64)	13 (2.8)	2 (0.5)	5.70 (1.29–25.25)
New left bundle-branch block¶	99 (20.0)	35 (7.7)	2.68 (1.83–3.95)	5 (1.4)	9 (2.4)	0.55 (0.18–1.64)	104 (21.1)	44 (9.9)	2.25 (1.58–3.20)
New onset atrial fibrillation¶	34 (8.2)	150 (40.9)	0.17 (0.12–0.24)	35 (10.4)	8 (4.3)	2.42 (1.12–5.21)	69 (17.7)	158 (43.5)	0.30 (0.23–0.41)
New permanent pacemaker¶	38 (7.9)	25 (5.8)	1.41 (0.85–2.33)	40 (10.3)	26 (7.4)	1.36 (0.83–2.23)	78 (17.3)	51 (12.8)	1.38 (0.97–1.97)
Serious bleeding¶**	24 (4.8)	46 (10.2)	0.45 (0.28–0.74)	47 (11.3)	31 (9.2)	1.27 (0.81–2.00)	71 (15.6)	77 (18.5)	0.79 (0.57–1.09)

Myocardial infarction¶	4 (0.8)	8 (1.8)	0.45 (0.14–1.49)	21 (5.2)	14 (3.8)	1.29 (0.65–2.53)	25 (6.0)	22 (5.6)	0.99 (0.56–1.75)
Revascularization¶	5 (1.0)	13 (2.9)	0.34 (0.12–0.96)	26 (6.4)	18 (5.0)	1.23 (0.68–2.25)	31 (7.3)	31 (7.7)	0.86 (0.53–1.42)
Percutaneous coronary intervention	5 (1.0)	8 (1.8)	0.56 (0.18–1.71)	23 (5.6)	18 (4.9)	1.10 (0.59–2.04)	28 (6.6)	26 (6.6)	0.94 (0.55–1.60)
Coronary-artery bypass grafting	1 (0.2)	5 (1.1)	0.18 (0.02–1.55)	3 (0.8)	1 (0.3)	2.60 (0.27–24.97)	4 (1.0)	6 (1.4)	0.59 (0.17–2.10)

* The total number of patients in each column header represents the number of patients at risk for death from any cause (including the data from the vital-status sweep) at the beginning of the interval. NA denotes not applicable, and TAVR transcatheter aortic-valve replacement.

† These data do not include those obtained from the vital-status sweep.

‡ The statistical analysis plan prespecified that the analysis of the first composite primary end point involved the difference in the Kaplan–Meier estimates between the TAVR group and the surgery group, calculated with the Wald test (difference, −2.6%; 95% CI, −9.0 to 3.7).

§ The following odds ratios with 95% confidence intervals were calculated for end points that showed evidence of nonproportionality of hazards from baseline to year 7: death from any cause with vital-status sweep, 1.20 (95% CI, 0.86 to 1.67); death from any cause without vital-status sweep, 1.37 (95% CI, 0.98 to 1.93); death from cardiovascular causes, 1.35 (95% CI, 0.86 to 2.11); death from noncardiovascular causes, 1.36 (95% CI, 0.86 to 2.13); and death or disabling stroke, 1.37 (95% CI, 0.99 to 1.90).

¶ The outcome was reported by the trial site through 7 years.

‖ Valve thrombosis was adjudicated according to Valve Academic Research Consortium 3 criteria.

** Serious bleeding included events that led to death or another serious event; resulted in life-threatening illness, injury, or permanent impairment; resulted in medical or surgical intervention; or resulted in hospitalization or prolongation of hospitalization.

in the surgery group were alive with a KCCQ-OS score of more than 75 (Fig. S18B); 65.5% and 66.6%, respectively, were alive with a KCCQ-OS score of more than 60 with a decline of 10 points or less from baseline.

DISCUSSION

After 7 years of follow-up in the PARTNER 3 trial, the incidence of death, stroke, or rehospitalization related to the procedure, the valve, or heart failure (the first composite primary end point, which was nonhierarchical) and the incidence of death, disabling stroke, nondisabling stroke, and the number of rehospitalization days (the second composite primary end point, which was hierarchical) were similar in the TAVR and surgery groups. The restricted mean event-free survival time over the course of 7 years in the analysis of the first composite end point was longer in the TAVR group, a finding that was possibly related to the between-group difference in rehospitalization. After the first year, differences in primary end-point events, which initially favored TAVR, were attenuated over time. Bioprosthetic valve durability at 7 years, including the incidence of aortic-valve reintervention, also appeared to be similar in the two groups. Among key secondary end points, new onset atrial fibrillation was less common in the TAVR group, whereas paravalvular aortic regurgitation, valve thrombosis, new left bundle-branch block, and pacemaker implantation were less common in the surgery group. Functional and health-status findings and the percentage of patients who were alive and well at 7 years appeared to be similar in the two groups.

TAVR is now accepted as an alternative therapy for eligible patients with severe, symptomatic aortic stenosis.[1,2] Recent randomized trials have also suggested that a change be made in the clinical management of severe, asymptomatic aortic stenosis, with an emphasis on the benefits of early referral and prompt aortic-valve replacement.[2,25-27] Since low-risk patients are generally younger, long-term follow-up to assess late clinical outcomes and valve durability are needed to inform lifetime patient-care decisions.[28] Five-year results of randomized trials comparing TAVR with surgery in low-risk patients showed similar clinical outcomes and valve durability.[14,15] This report of the 7-year outcomes from the PARTNER 3

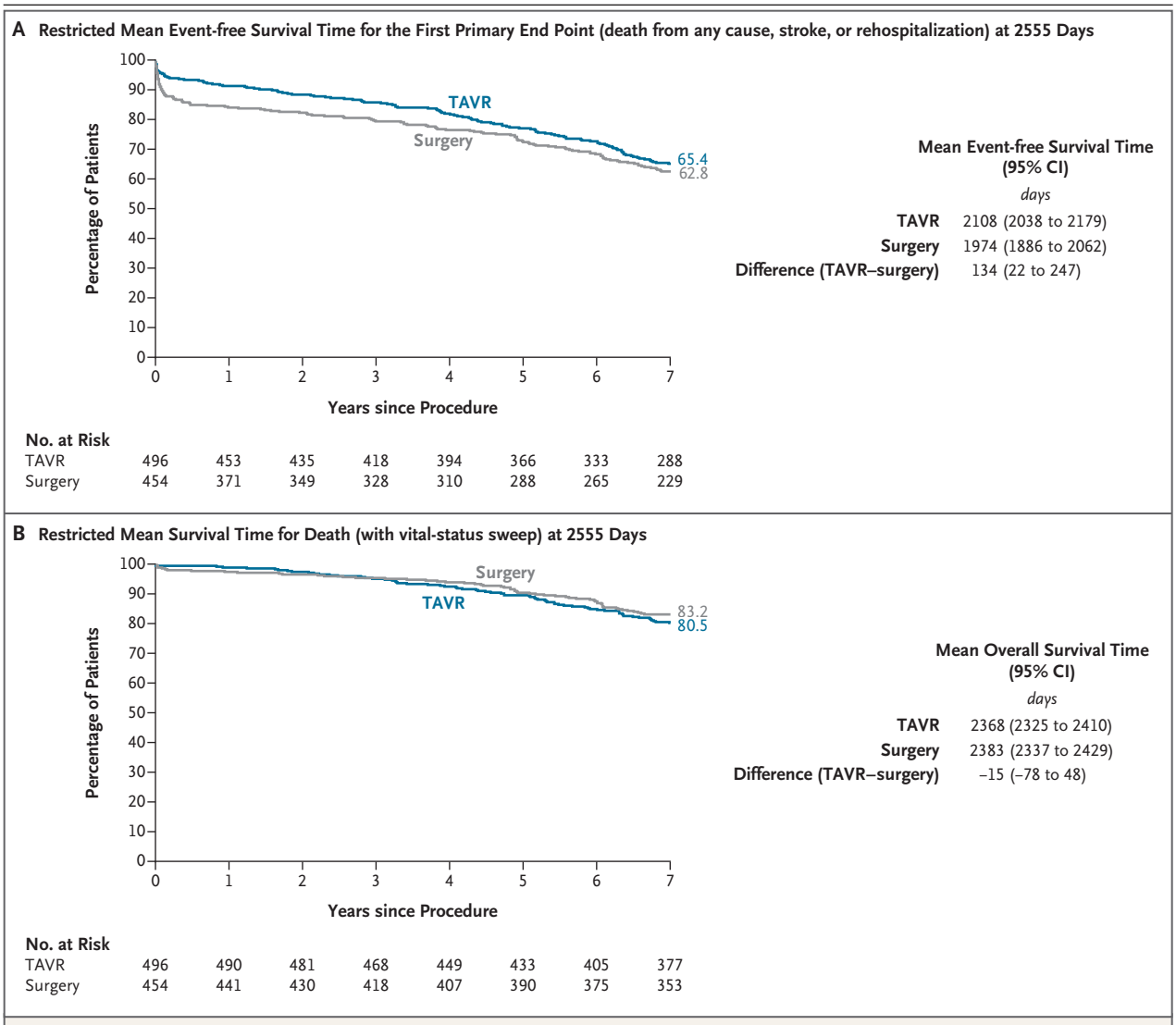

Figure 2. Restricted Mean Event-free Survival Time for the First Primary End Point and Death from Any Cause.

Panel A shows the restricted mean event-free survival time for the first primary end point, which is a composite of death from any cause, stroke, or rehospitalization related to the procedure, the valve, or heart failure; these data do not include those obtained from the vital-status sweep. Panel B shows the restricted mean survival time for death from any cause, including data obtained from the vital-status sweep. Additional details can be found in Table S3. In both analyses, event-free days are defined according to Gregson et al.[24] Additional details can be found in the Supplementary Appendix. All analyses were performed in the as-treated population.

trial extends these findings, showing no between-group differences in either of the composite primary end points or in their individual components. A consistent finding in PARTNER 3 follow-up analyses has been an attenuation of the between-group difference in primary end-point events, which favors TAVR over surgery in the first year with no between-group differences apparent during longer follow-up. A greater number of deaths, from both cardiovascular and noncardiovascular causes, occurred from year 1 to year 7 among patients who were assigned to TAVR than among those assigned to surgery. Greater numbers of strokes and rehospitalizations in the TAVR group than in the surgery group after the first year were also observed. Perhaps early benefits of a less-invasive TAVR treatment with reduced periprocedural complications were counterbalanced by an increased vulnerability to late adverse events in low-risk patients.

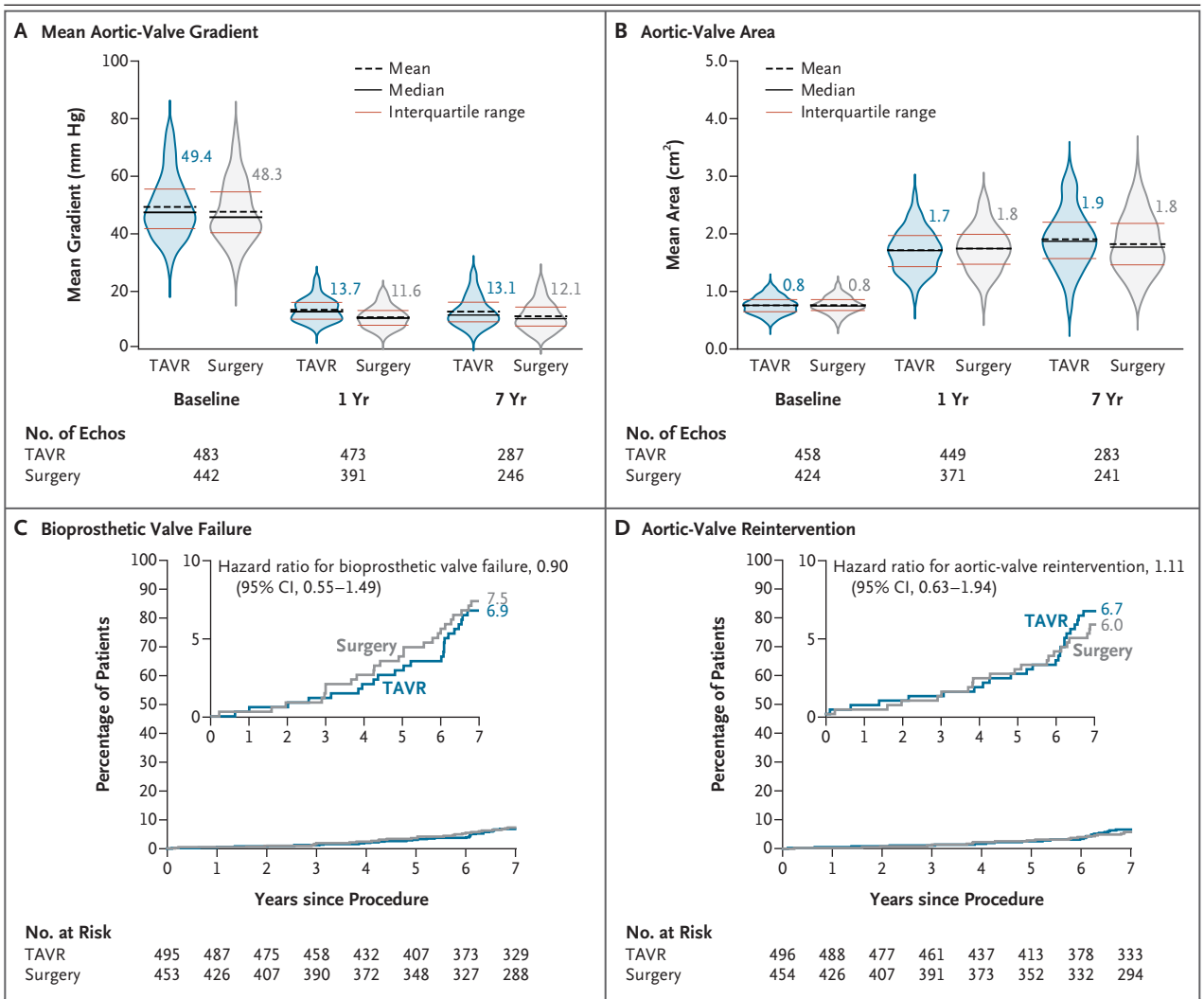

Figure 3. Valve Hemodynamics and Durability.

The mean aortic-valve gradients and mean aortic-valve areas as assessed by echocardiography at a core laboratory are shown in Panels A and B, respectively. Analyses were performed in the valve-implant population, which included the patients who received the intended valve. Data from patients who had their valve explanted or who received a valve-in-valve procedure were censored after reintervention. The cumulative incidence of bioprosthetic valve failure, adjudicated according to Valve Academic Research Consortium 3 criteria, is shown in Panel C; the hazard ratio for bioprosthetic valve failure was estimated with the Fine and Gray method, and the analysis was performed in the valve-implant population. Kaplan–Meier estimates for site-reported aortic-valve reintervention are shown in Panel D ; the analysis was performed in the as-treated population. The insets in Panels C and D show the same data on an enlarged y axis.

Most surgical bioprosthetic aortic valves are durable beyond 10 years,[20,21] but several showed early and accelerated (between 5 and 10 years) structural valve deterioration, which resulted in higher-than-expected rates of valve reintervention.[29,30] Although an increase in bioprosthetic valve failure and aortic-valve reintervention was observed between years 5 and 7 in the PARTNER 3 trial, the outcomes appeared to be similar in the TAVR and surgery groups, the rate of increase was consistent with expected findings for durable surgical bioprostheses,[20,21] and echocardiographic valve gradients remained stable in both treatment groups throughout follow-up. Mild, moderate, or severe paravalvular regurgitation, which occurred more frequently after TAVR than after surgery, was not associated with increased mortality or reduced valve durability. These favorable durability findings for balloon-expandable TAVR and surgery at 7 years were observed

in a large randomized trial cohort with serial echocardiographic assessments and adjudicated clinical outcomes.

Most of the results of the secondary end points in the PARTNER 3 trial at 7 years were consistent with earlier assessments at 5 years. New-onset atrial fibrillation was observed in fewer patients who had undergone TAVR than in patients who had undergone surgery, whereas conduction abnormalities, paravalvular regurgitation, and valve thrombosis were observed in fewer patients who had undergone surgery. Increases in valve thrombosis during the first few years in the TAVR group appear to have stabilized at later follow-up, with no late clinical consequences of previous valve thromboses. An unexpected late follow-up observation was a higher number of spontaneous myocardial infarctions between 5 and 7 years after the procedure among patients who had undergone TAVR than among those who had undergone surgery, which resulted in a higher incidence of late revascularizations. Possible explanations include a lower incidence of complete periprocedural revascularization with TAVR than with surgery in patients with concomitant coronary disease, changes in coronary flow dynamics with SAPIEN 3 valves that contributed to accelerated coronary stenoses, or simply a random chance finding. The higher incidence of late myocardial infarctions with TAVR was balanced by the higher incidence of early myocardial infarctions with surgery, such that overall the incidence of events was similar in the two groups.

Patient-reported outcomes continued to be favorable after 7 years, with similar and maintained KCCQ-OS scores in both groups. In both the TAVR and surgery groups, most patients were alive with NYHA class I or II symptoms and KCCQ-OS scores of more than 75.

The main limitations of this trial have been discussed previously.[12-14] This report helps address concerns of inadequate long-term follow-up; a final report at 10 years is planned. Other limitations include the constraints of a carefully defined trial population, which excluded patients with anatomical or clinical factors that precluded transfemoral access or increased the risk of complications associated with TAVR or surgery. As reported previously, the disproportionate percentage of patients in the surgery group who withdrew from the trial may have potentially biased findings. To help address missing data, a vital-status sweep was conducted, and data from this sweep reduced the apparent between-group difference in mortality. However, a vital-status sweep cannot correct for possible biases in underreporting of important nonfatal events. Predictive models to better explain the accumulation of excess events during late follow-up in the TAVR group are beyond the scope of this article. Finally, long-term follow-up assessments in older patients with multiple coexisting conditions are subject to the confounding and competing influences of events that are unrelated to TAVR or surgery.

Among patients with severe, symptomatic aortic stenosis at low surgical risk who underwent TAVR or surgery, the incidence at 7 years of follow-up of death, stroke, or rehospitalization related to the procedure, the valve, or heart failure (the first composite primary end point); the incidence of death, disabling stroke, nondisabling stroke, and the number of rehospitalization days (the second composite primary end point); and the durability of the bioprosthetic valve appeared to be similar in the two groups.

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