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Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

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ABSTRACT

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BACKGROUND

The Placement of Aortic Transcatheter Valves (PARTNER) trial showed that among high-risk patients with aortic stenosis, the 1-year survival rates are similar with transcatheter aortic-valve replacement (TAVR) and surgical replacement. However, longer-term follow-up is necessary to determine whether TAVR has prolonged benefits.

METHODS

At 25 centers, we randomly assigned 699 high-risk patients with severe aortic stenosis to undergo either surgical aortic-valve replacement or TAVR. All patients were followed for at least 2 years, with assessment of clinical outcomes and echocardiographic evaluation.

RESULTS

The rates of death from any cause were similar in the TAVR and surgery groups (hazard ratio with TAVR, 0.90; 95% confidence interval [CI], 0.71 to 1.15; P=0.41) and at 2 years (Kaplan–Meier analysis) were 33.9% in the TAVR group and 35.0% in the surgery group (P=0.78). The frequency of all strokes during follow-up did not differ significantly between the two groups (hazard ratio, 1.22; 95% CI, 0.67 to 2.23; P=0.52). At 30 days, strokes were more frequent with TAVR than with surgical replacement (4.6% vs. 2.4%, P=0.12); subsequently, there were 8 additional strokes in the TAVR group and 12 in the surgery group. Improvement in valve areas was similar with TAVR and surgical replacement and was maintained for 2 years. Paravalvular regurgitation was more frequent after TAVR (P<0.001), and even mild paravalvular regurgitation was associated with increased late mortality (P<0.001).

CONCLUSIONS

A 2-year follow-up of patients in the PARTNER trial supports TAVR as an alternative to surgery in high-risk patients. The two treatments were similar with respect to mortality, reduction in symptoms, and improved valve hemodynamics, but paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality. (Funded by Edwards Lifesciences; ClinicalTrials.gov number, NCT00530894.)

AORTIC STENOSIS IS ASSOCIATED WITH high mortality after the appearance of cardiac symptoms.[1] Nevertheless, many patients do not undergo surgical aortic-valve replacement owing to real or perceived increased risks associated with surgery.[2-5] Transcatheter aortic-valve replacement (TAVR) has emerged as an alternative therapy in high-risk patients with aortic stenosis.[6-10] Observational registries from various countries have reported 1-month and 1-year outcomes after TAVR,[11-14] but there are limited long-term follow-up data.[15]

The Placement of Aortic Transcatheter Valves (PARTNER) trial was a randomized trial comparing TAVR with standard-of-care therapies in high-risk patients with aortic stenosis. One-year mortality outcomes from PARTNER showed that TAVR was superior to standard therapy in patients who could not undergo surgery[16] and was noninferior to surgical replacement in high-risk patients who could undergo surgery.[17] However, longer-term data are required to assess valve durability and to monitor late clinical complications, before TAVR is used more widely in clinical practice. This report describes the 2-year (and longer) clinical outcomes and echocardiographic findings after TAVR or surgical aortic-valve replacement in the high-risk patients in the PARTNER trial who could undergo surgery.

METHODS

PATIENTS

Patient selection for this cohort of the PARTNER trial has been described previously.[17] Inclusion criteria were severe symptomatic aortic stenosis (an aortic-valve area ≤0.8 cm² plus a peak velocity ≥4 m per second or a mean valve gradient ≥40 mm Hg) and high-risk status for surgical aortic-valve replacement, as determined by experienced surgeons. Patients were considered to be at high surgical risk if they had coexisting conditions that were associated with a risk of death of at least 15% by 30 days after the operation.

STUDY DEVICE AND PROCEDURE

The SAPIEN heart-valve system (Edwards Lifesciences) and the TAVR procedure have been described previously.[16,17] Most procedures were performed in a hybrid operating room with a fixed fluoroscopic imaging system, while the patient was under general anesthesia, and with transesophageal echocardiography. Transapical TAVR was per-formed through a small intercostal incision over the left ventricular apex with the use of a dedicated delivery catheter and the same SAPIEN valve.

Heparin was administered during the procedure, and dual antiplatelet therapy (aspirin and clopidogrel) was recommended for 6 months afterward. The outpatient regimen was frequently modified by the treating physicians because of increased bleeding risks.

STUDY DESIGN AND OVERSIGHT

The study design and data-management practices have been described previously.[16,17] A total of 699 patients from 25 sites were randomly assigned to TAVR or surgical replacement. Patients assigned to TAVR were treated by either the transfemoral or transapical approach on the basis of whether peripheral arteries could accommodate the large sheaths required (22 French for the 23-mm valve and 24 French for the 26-mm valve). Patients who were randomly assigned to surgical replacement were stratified according to whether a transfemoral or transapical approach would have been used.

The study was designed and monitored by the sponsor, Edwards Lifesciences, and the executive committee, which included four interventional cardiologists and four cardiac surgeons. The sponsor funded the study and participated in the selection and management of the sites, the collection of the data, and data monitoring. The first author and members of the executive committee had unrestricted access to the data after the database had been locked and prepared all drafts of the manuscript; they attest to the completeness and accuracy of the reported data and to the adherence of the study to the protocol (available with the full text of this article at NEJM.org). The trial was approved by the institutional review board at each site. Written informed consent was obtained from all patients.

STUDY END POINTS

The prespecified primary end point of the PARTNER trial was all-cause mortality at 1 year for the pooled cohort. Prespecified secondary end points included cardiovascular mortality, stroke, repeat hospitalization, acute kidney injury, vascular complications, bleeding events, and New York Heart Association (NYHA) functional class. All patients were followed for at least 2 years and had annual clinical visits and echocardiographic evaluations. Crossovers between the two treatment groups were not permitted. A clinical-events committee was

responsible for adjudicating all end points. Definitions of the end points are identical to those in the original trial and have been reported elsewhere.[16,17]

STATISTICAL ANALYSIS

For data analyses, the intention-to-treat analysis started at the time of randomization, and the as-treated analysis started at the time of induction of anesthesia in the procedure room. All clinical outcomes were primarily analyzed with the use of an intention-to-treat analysis, but the results of as-treated analyses are also presented for comparison. All echocardiographic analyses were performed with the use of the as-treated data. Categorical variables were compared with the use of Fisher's exact test. Continuous variables, presented as means ±SD, were compared with the use of Student's t-test. Survival curves for time-to-event variables were constructed with the use of Kaplan–Meier estimates based on all available data and were compared with the use of the log-rank test. To study the effect of risk factors on mortality, Cox proportional-hazards regression was performed. For the multivariable analyses, multiple imputations were used to accommodate missing baseline variables. The multivariable models included covariates with a P value of less than 0.20 in univariate analyses. An additional time-dependent covariate analysis was performed to test the association of complications during TAVR or surgical replacement with subsequent mortality. All statistical analyses were performed with the use of SAS software, version 9.2.

RESULTS

PATIENTS

In the randomized TAVR group, 244 patients had acceptable vascular access and were treated by means of the transfemoral approach, and the remaining 104 patients were treated by means of the transapical approach. Surgical replacement was performed in 351 patients. Figure 1 in the Supplementary Appendix, available at NEJM.org, shows the study-group assignments and follow-up. All patients were followed for at least 2 years (median, 727 days; maximum, 1490 days). The overall study population was elderly (mean age, 84.1±6.6 years), had severe cardiac symptoms (94.1% had NYHA class III or IV status), and had frequent coexisting conditions (75.5% had a his-

tory of coronary artery disease, 43.0% had a history of coronary-artery bypass surgery, 42.4% had peripheral vascular disease, 43.3% had pulmonary disease, and 41.3% had diabetes). The TAVR and surgery groups were generally well matched with regard to baseline characteristics (Table 1 in the Supplementary Appendix), except for a slightly higher incidence of renal dysfunction in the TAVR group (creatinine level >2 mg per deciliter [177 μmol per liter]: 10.8%, as compared with 6.4% in the surgery group; P=0.04). The mean Society of Thoracic Surgeons predicted risk of death at 30 days was 11.8±3.4%.

Of the 699 study patients, 42 did not receive the assigned therapy: 4 in the TAVR group and 38 in the surgery group.[17] The main reasons for nontreatment were withdrawal from the study and the patient's decision not to undergo surgery (28 patients).

MORTALITY AND STROKE

Outcomes at 30 days and 1 year have been described previously.[17] For the duration of the trial, there were no significant differences in survival between the TAVR and surgery groups in either the intention-to-treat analysis (hazard ratio with TAVR, 0.90; 95% confidence interval [CI], 0.71 to 1.15; P=0.41) or the as-treated analysis (hazard ratio, 0.98; 95% CI, 0.76 to 1.25; P=0.85) (Fig. 1). Between 1 and 2 years, there were 32 additional deaths in the TAVR group and 25 in the surgery group. At 2 years, there were no significant differences in mortality from any cause between the TAVR group (33.9%; 95% CI, 28.9 to 39.0) and the surgery group (35.0%; 95% CI, 29.8 to 40.2; P=0.78) (Table 1). Cardiovascular mortality at 2 years was also similar in the TAVR and surgery groups (21.4% [95% CI, 16.8 to 26.0] and 20.5% [95% CI, 15.8 to 25.3], respectively; P=0.80). Similarly, in the as-treated analysis, the TAVR and surgery groups did not differ significantly with respect to all-cause mortality (33.9% and 32.7%, respectively; P=0.75) or cardiovascular mortality (20.8% and 18.5%, respectively; P=0.50) (Table 2 in the Supplementary Appendix).

Between 1 and 2 years, eight strokes occurred (four in the TAVR group and four in the surgery group) and three transient ischemic attacks (two in the TAVR group and one in the surgery group). The frequency of all neurologic events (strokes and transient ischemic attacks) at 2 years was higher with TAVR than with surgical replacement (11.2%
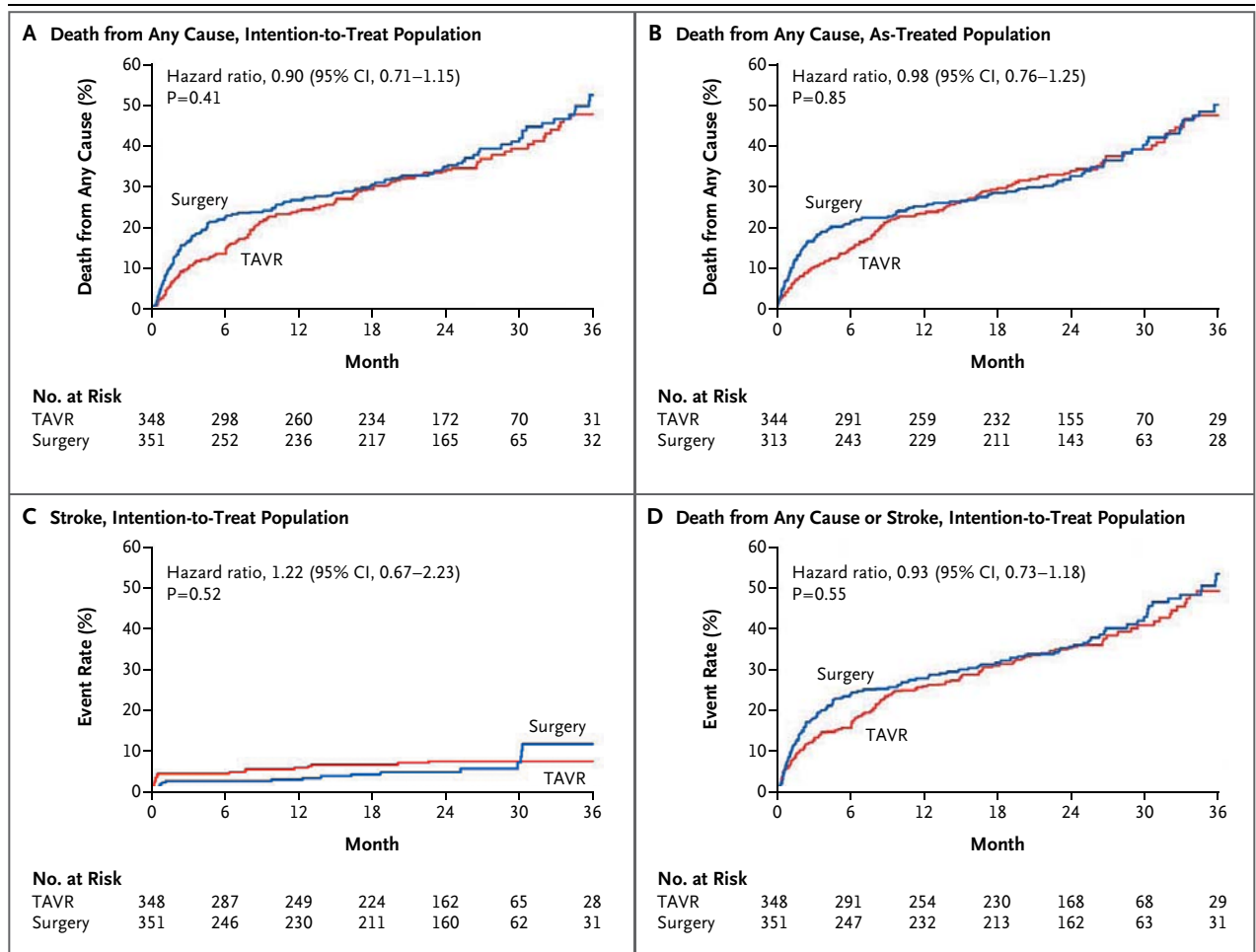
Figure 1. Time-to-Event Curves for the Primary and Other Selected End Points.

Events were calculated with the use of Kaplan–Meier methods and compared with the use of a log-rank test. TAVR denotes transcatheter aortic-valve replacement.

vs. 6.5%, P=0.05). However, there was no significant difference in the number of overall strokes between the TAVR and surgery groups (hazard ratio, 1.22; 95% CI, 0.67 to 2.23; P=0.52) (Fig. 1). After the early increased hazard of stroke in the first 30 days associated with TAVR (4.6% with TAVR vs. 2.4% with surgical replacement, P=0.12), there were 8 additional strokes in the TAVR group and 12 in the surgery group, such that the total number of strokes over the follow-up period (36 months) was 24 in the TAVR group and 20 in the surgery group. The composite of the rate of death from any cause or stroke did not differ significantly between the two treatment groups (hazard ratio, 0.93; 95% CI, 0.73 to 1.18; P=0.55) (Fig. 1); at 2 years, the rate was 37.1% in the TAVR group and 36.4% in the surgery group (P=0.85).

OTHER CLINICAL OUTCOMES

Other clinical events are summarized in Table 1. Major vascular complications and major bleeding events were frequent procedure-related complications in the TAVR and surgery groups, respectively, but after 1 year, these events were uncommon and did not differ significantly between the groups. No patients were treated with balloon aortic valvuloplasty or repeat TAVR between 1 and 2 years. Endocarditis was rare and occurred at a similar rate in the two groups (1.5% in the TAVR group and 1.0% in the surgery group, P=0.61). No patients in either group had structural valve deterioration requiring surgical replacement during follow-up.

At 2 years, there was no significant difference in the rate of repeat hospitalization between the

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Table 1. Clinical Outcomes at 1 Year and 2 Years with TAVR or Surgery (Intention-to-Treat Population).*

Outcome	1 Year			2 Years		
	Surgery (N=351)	TAVR (N=348)	P Value†	Surgery (N=351)	TAVR (N=348)	P Value†
	no. of patients (%)			*no. of patients (%)*		
Death						
From any cause	89 (26.8)	84 (24.3)	0.45	114 (35.0)	116 (33.9)	0.78
From cardiovascular causes	40 (13.0)	47 (14.3)	0.63	59 (20.5)	67 (21.4)	0.80
Repeat hospitalization‡	51 (17.7)	59 (18.6)	0.78	60 (21.7)	74 (24.7)	0.41
Death from any cause or repeat hospitalization‡	125 (37.7)	121 (34.9)	0.45	152 (46.5)	159 (46.6)	0.99
Stroke or TIA§						
All	13 (4.3)	28 (8.7)	0.03	18 (6.5)	34 (11.2)	0.05
Stroke	10 (3.2)	20 (6.0)	0.08	14 (4.9)	24 (7.7)	0.17
TIA	4 (1.5)	8 (2.6)	0.32	5 (2.0)	10 (3.6)	0.26
Death from any cause or stroke	95 (28.6)	95 (27.4)	0.74	119 (36.4)	127 (37.1)	0.85
Myocardial infarction	2 (0.6)	0	0.16	4 (1.5)	0	0.05
Major vascular complication¶	13 (3.8)	39 (11.3)	<0.001	13 (3.8)	40 (11.6)	<0.001
Major bleeding‖	88 (26.7)	52 (15.7)	<0.001	95 (29.5)	60 (19.0)	0.002
Endocarditis	3 (1.0)	2 (0.6)	0.63	3 (1.0)	4 (1.5)	0.61
Renal failure**	20 (6.5)	18 (5.4)	0.57	21 (6.9)	20 (6.2)	0.75
New pacemaker	16 (5.0)	21 (6.4)	0.44	19 (6.4)	23 (7.2)	0.69
SVD requiring surgical replacement	0	0		0	0	

* 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 in the study group. SVD denotes structural valve deterioration, TAVR transcatheter aortic-valve replacement, and TIA transient ischemic attack.

† P values are for between-group comparisons of the frequency of the event at each time point.

‡ Repeat hospitalizations were included in the analysis if they were for symptoms of heart failure, angina, or syncope due to aortic-valve disease that required aortic-valve intervention or intensified medical management.

§ Stroke was defined as a neurologic deficit lasting more than 24 hours or lasting less than 24 hours with a brain-imaging study showing infarction.

¶ Major vascular complications were defined as thoracic aortic dissection; access-site or access-related vascular injury leading to death, the need for substantial blood transfusion (>3 units), or percutaneous or surgical intervention; and distal embolization (noncerebral) from a vascular source requiring surgery or amputation or resulting in irreversible end-organ damage.

‖ Major bleeding was defined as any episode of major internal or external bleeding that caused death, hospitalization, or permanent injury or that necessitated the transfusion of at least 3 units of packed red cells or a pericardiocentesis procedure.

** Renal failure was defined as any condition requiring the initiation of any dialysis.

TAVR and surgery groups (24.7% and 21.7%, respectively; P=0.41). Among survivors at 2 years, the mean NYHA class was similar in the TAVR and surgery groups (1.72 and 1.70, P=0.87), and the majority of patients in both groups had NYHA class I or II status (83.9% in the TAVR group and 85.2% in the surgery group). Clinical outcomes in the subgroups of patients in whom a transfemoral or transapical approach was used are shown in Tables 3 through 6 in the Supplementary Appendix.

PREDICTORS OF MORTALITY

Predictors of mortality for the overall trial cohort as well as for each of the randomized groups are presented in Table 2. Treatment assignment was not a significant predictor of the risk of death.

The time-dependent effect of treatment complications on subsequent mortality was also evaluated. Strokes greatly increased the hazard of death in both groups (TAVR: hazard ratio, 2.47; 95% CI, 1.42 to 4.30; P<0.001; surgery: hazard ratio, 5.20; 95% CI, 3.07 to 8.80; P<0.001). Major

Table 2. Multivariable Predictors of Mortality.*

Variable	Hazard Ratio (95% CI)	P Value
Overall		
TAVR group	0.89 (0.70–1.13)	0.34
Body-mass index†	0.96 (0.94–0.98)	<0.001
Liver disease‡	2.24 (1.30–4.00)	0.006
Mean gradient per increase of 10 mm Hg	0.89 (0.81–0.98)	0.02
STS risk score§	1.04 (1.01–1.08)	0.02
Moderate or severe mitral regurgitation at baseline	1.36 (1.02–1.82)	0.04
TAVR		
Body-mass index†	0.93 (0.90–0.97)	<0.001
Mean gradient per increase of 10 mm Hg	0.82 (0.72–0.94)	0.003
Creatinine level at baseline¶	1.06 (1.00–1.13)	0.04
Prior vascular surgery or stent	1.85 (1.01–3.39)	0.05
Surgery		
CABG	0.57 (0.40–0.82)	0.002
STS risk score§	1.07 (1.02–1.12)	0.004
Liver disease‡	2.59 (1.16–5.43)	0.02
Moderate or severe mitral regurgitation at baseline	1.77 (1.17–2.68)	0.006

* Unless otherwise indicated, the hazard ratio reflects the presence or absence of the variable. CABG denotes coronary-artery bypass grafting.
† For body-mass index (the weight in kilograms divided by the square of the height in meters), the hazard ratio reflects an increase of 1.
‡ Liver disease indicates a history of any liver condition.
§ The Society of Thoracic Surgeons (STS) risk score predicts the 30-day risk of death (on a scale of 0% to 100%, with higher scores indicating higher predicted risk). The hazard ratio reflects an increase of 1%.
¶ For creatinine level at baseline, the hazard ratio reflects an increase of 1 mg per deciliter.

bleeding also increased the hazard of death in both groups (TAVR: hazard ratio, 2.11; 95% CI, 1.41 to 3.17; P<0.001; surgery: hazard ratio, 2.94; 95% CI, 2.08 to 4.15; P<0.001). Major vascular complications affected survival only in the TAVR group (hazard ratio, 1.71; 95% CI, 1.07 to 2.73; P=0.02).
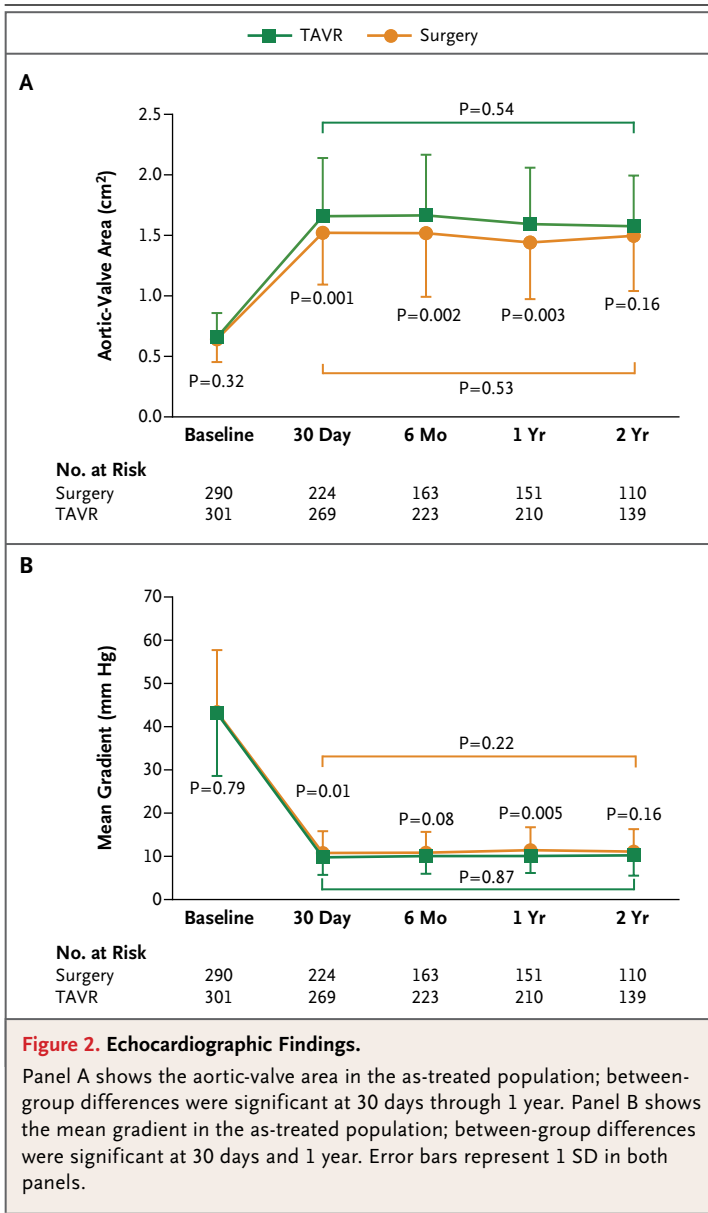
ECHOCARDIOGRAPHIC FINDINGS

The early hemodynamic improvements that were seen with both surgical replacement and TAVR were maintained at 2 years, with no significant changes in valve areas or mean gradients (Fig. 2). Moderate or severe paravalvular aortic regurgitation was more common after TAVR than after surgical replacement at both 1 and 2 years (7.0% vs. 1.9% at 1 year, and 6.9% vs. 0.9% at 2 years; P<0.001 for both comparisons). Among the 143 patients who underwent echocardiographic eval-

uation 2 years after TAVR, paravalvular aortic regurgitation remained unchanged in 46.2% of patients, was improved in 31.5%, and was worse in 22.4% (Table 7 in the Supplementary Appendix). The presence of paravalvular or total aortic regurgitation (mild, moderate, or severe vs. none or trace) after TAVR was associated with increased late mortality (hazard ratio, 2.11; 95% CI, 1.43 to 3.10; P<0.001) (Fig. 3). The effect of aortic regurgitation on mortality was proportional to the severity of the regurgitation (Fig. 3), but even mild aortic regurgitation was associated with an increased rate of late deaths.

DISCUSSION

The salient findings from this 2-year analysis of the randomized PARTNER trial are as follows: mortality after TAVR remained similar to that

niques, and device technologies.[12,14,16-18] However, 1- and 2-year mortality rates have remained above 20% and 30%, respectively,[11,15,19,20] raising a concern that TAVR may be associated with important late complications. The results from the PARTNER trial reveal similarly high mortality at 2 years with TAVR and with surgical replacement, indicating that coexisting conditions play a role in late mortality. The multivariable analysis from the combined TAVR and surgery groups affirms the importance of coexisting conditions, because the STS risk score was a significant predictor of mortality at 2 years. Although the STS score was designed to predict 30-day mortality after surgical replacement,[21] many of the baseline characteristics of the patients are also likely contributors to late mortality.

The 30-day and 1-year PARTNER results raised concern that TAVR was responsible for increased early and, possibly, late strokes.[16,17] The differences in stroke frequencies appeared in the first few days or weeks after TAVR, presumably owing to increased liberation of atherothrombotic debris (from the valve or aorta), causing embolic ischemic strokes. After this initial period, there is no evidence of higher stroke rates in either group, suggesting that the constant hazard of late strokes in these elderly high-risk patients is unrelated to the mode of valve-replacement therapy. The preferred anticoagulation regimen (early and late) for patients after TAVR has not been determined.[22] Early experiences with new cerebral filters[23] suggest the frequent appearance of captured atherothrombotic material after TAVR, but careful clinical studies with these new devices are just beginning.

The current study shows stable gradients and unchanged valve areas with the SAPIEN valve at 2 years. Nevertheless, structural valve deterioration is well known with surgical bioprostheses, and definitive assessments of valve durability will require much longer follow-up.[24-26]

A design limitation of transcatheter aortic valves has been paravalvular regurgitation, which results from incomplete circumferential apposition of the prosthesis with the annulus. Several reports have indicated a relation between paravalvular regurgitation and mortality, but the certainty of these findings has been limited by the lack of standardization of methods to assess aortic regurgitation.[11,12,27,28] In our study, semiquantitative measures of aortic-regurgitation severity were evaluated in an echocardiography core labo-

Figure 2. Echocardiographic Findings.

Panel A shows the aortic-valve area in the as-treated population; between-group differences were significant at 30 days through 1 year. Panel B shows the mean gradient in the as-treated population; between-group differences were significant at 30 days and 1 year. Error bars represent 1 SD in both panels.

after surgical replacement, stroke frequency was similar in the surgery and TAVR groups after 30 days, periprocedural complications (strokes, major bleeding, and major vascular events) affected mortality after TAVR or surgical replacement; aortic regurgitation (even mild) after TAVR was associated with increased long-term mortality, and valve performance in the TAVR group was maintained during follow-up and was similar to that in the surgery group.
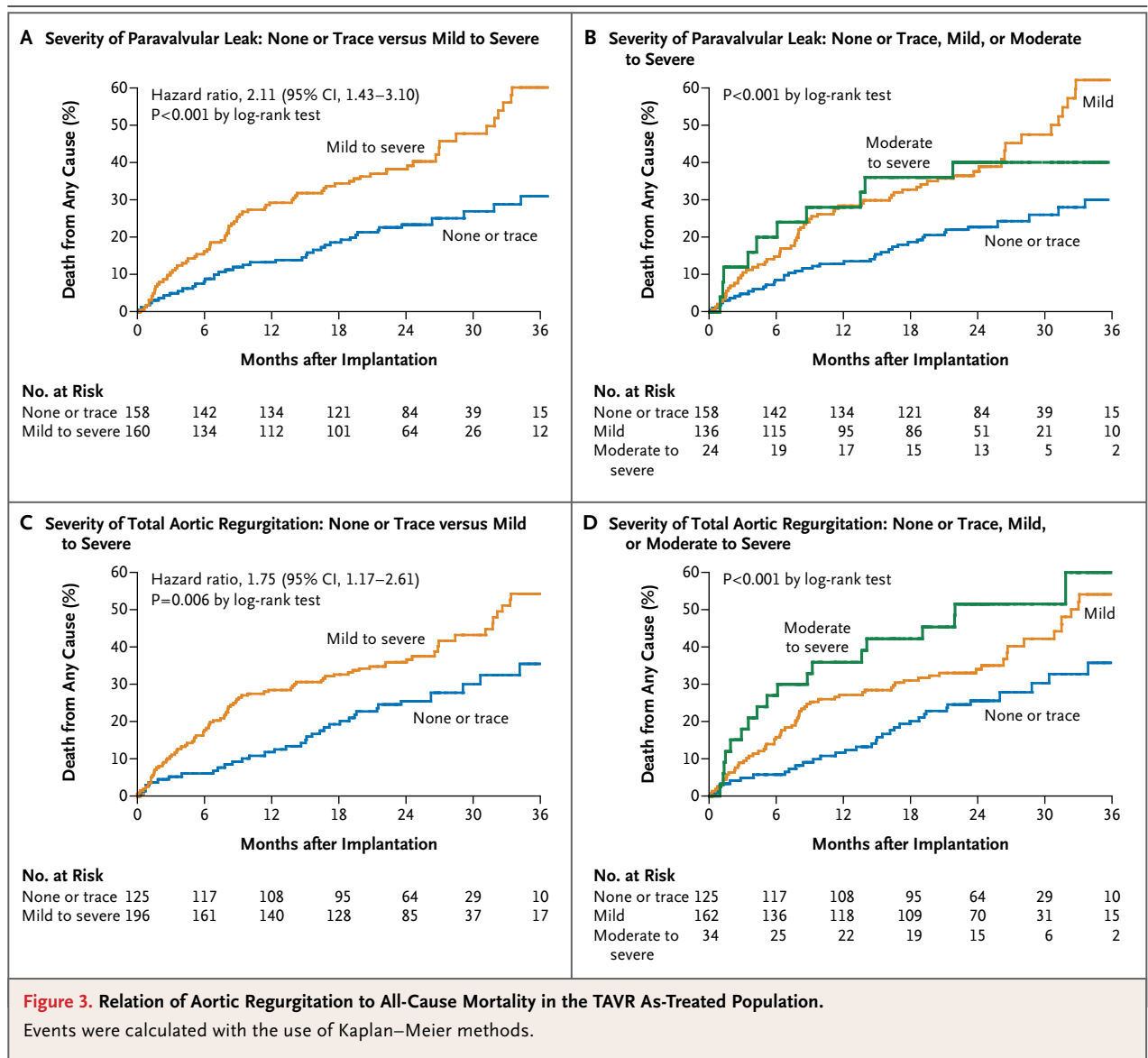
Early (30-day) mortality after TAVR has decreased to approximately 5% in several recent studies, probably because of a combination of improvements in patient selection, procedural tech-

A Severity of Paravalvular Leak: None or Trace versus Mild to Severe

Hazard ratio, 2.11 (95% CI, 1.43–3.10)
P<0.001 by log-rank test

Mild to severe

None or trace

No. at Risk

None or trace 158	142	134	121	84	39	15
Mild to severe 160	134	112	101	64	26	12

B Severity of Paravalvular Leak: None or Trace, Mild, or Moderate to Severe

P<0.001 by log-rank test

Mild

Moderate to severe

None or trace

No. at Risk

None or trace 158	142	134	121	84	39	15
Mild 136	115	95	86	51	21	10
Moderate to severe 24	19	17	15	13	5	2

C Severity of Total Aortic Regurgitation: None or Trace versus Mild to Severe

Hazard ratio, 1.75 (95% CI, 1.17–2.61)
P=0.006 by log-rank test

Mild to severe

None or trace

No. at Risk

None or trace 125	117	108	95	64	29	10
Mild to severe 196	161	140	128	85	37	17

D Severity of Total Aortic Regurgitation: None or Trace, Mild, or Moderate to Severe

P<0.001 by log-rank test

Moderate to severe

Mild

None or trace

No. at Risk

None or trace 125	117	108	95	64	29	10
Mild 162	136	118	109	70	31	15
Moderate to severe 34	25	22	19	15	6	2

Figure 3. Relation of Aortic Regurgitation to All-Cause Mortality in the TAVR As-Treated Population.
Events were calculated with the use of Kaplan–Meier methods.

ratory; these assessments indicated a low frequency of moderate or severe paravalvular aortic regurgitation (approximately 10%). Paravalvular aortic regurgitation remained stable without significant worsening during follow-up. Nevertheless, even mild paravalvular (or total) aortic regurgitation (occurring in approximately 40% of patients) was associated with increased late mortality (Fig. 3). Conversely, the absence of paravalvular aortic regurgitation or only trace regurgitation was associated with lower mortality in the TAVR group.

These findings provide an important target for improving outcomes after TAVR in the future. The factors that underlie paravalvular aortic re-gurgitation include the ratio of the transcatheter-valve size to the size of the annulus, the position of the prosthetic valve, and the pattern of calcification in the native valve.[29-32] In the PARTNER trial, the valve cover index,[32] defined as 100 × [(valve prosthesis diameter − annulus diameter) ÷ valve prosthesis diameter], was lower in patients with paravalvular aortic regurgitation, implicating systematic valve undersizing as an important causative factor. Recently, the routine use of three-dimensional imaging techniques has improved annulus sizing, resulting in better selection of properly sized valves.[33-37] In addition, the selective use of post-TAVR dilation of the transcatheter valve with slightly larger balloons may reduce im-

mediate paravalvular aortic regurgitation during TAVR, but the risks of aortic rupture, increased central aortic regurgitation, and increased embolic events must be considered. Future generations of TAVR devices with improved subannular fixation designs or external space-filling materials may also reduce incomplete apposition.

Several study limitations should be acknowledged. First, patients frequently declined surgery after random assignment to surgical replacement, resulting in a higher proportion of patients in the surgery group who did not receive the assigned treatment. Nonetheless, there were no significant differences in clinical outcomes between the intention-to-treat cohort and the as-treated cohort. Second, stroke assessments were limited, since neurologic assessments were not mandated, modified Rankin scores were not used to determine clinical disability, and documentation of atrial fibrillation episodes and anticoagulation regimens was not complete. Third, the small number of patients in whom the transapical approach was used and the differences in baseline characteristics make a comparison of the transfemoral and transapical subgroups unreliable. Finally, this study represented the initial experience with TAVR at most of the sites, with the use of a first-generation device. Multiple reports suggest that subsequent device generations and increased operator experience with TAVR may improve outcomes.[18,38-40]

In conclusion, this 2-year follow-up of patients in the PARTNER trial supports the use of TAVR as an alternative to surgery in selected high-risk patients with aortic stenosis. The two treatments were similar with respect to mortality, reduction in cardiac symptoms, and improved valve hemodynamics. The early increase in the risk of stroke with TAVR was attenuated over time. A new, important observation was the association of para-valvular regurgitation after TAVR with late mortality. Work now should be directed toward reducing paravalvular aortic regurgitation with improved device designs, techniques for more precise valve sizing and positioning, and judicious use of post-TAVR dilation.

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