ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

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ABSTRACT

BACKGROUND

We compared transcatheter aortic-valve replacement (TAVR), using a self-expanding transcatheter aortic-valve bioprosthesis, with surgical aortic-valve replacement in patients with severe aortic stenosis and an increased risk of death during surgery.

METHODS

We recruited patients with severe aortic stenosis who were at increased surgical risk as determined by the heart team at each study center. Risk assessment included the Society of Thoracic Surgeons Predictor Risk of Mortality estimate and consideration of other key risk factors. Eligible patients were randomly assigned in a 1:1 ratio to TAVR with the self-expanding transcatheter valve (TAVR group) or to surgical aortic-valve replacement (surgical group). The primary end point was the rate of death from any cause at 1 year, evaluated with the use of both noninferiority and superiority testing.

RESULTS

A total of 795 patients underwent randomization at 45 centers in the United States. In the as-treated analysis, the rate of death from any cause at 1 year was significantly lower in the TAVR group than in the surgical group (14.2% vs. 19.1%), with an absolute reduction in risk of 4.9 percentage points (upper boundary of the 95% confidence interval, −0.4; $P<0.001$ for noninferiority; $P = 0.04$ for superiority). The results were similar in the intention-to-treat analysis. In a hierarchical testing procedure, TAVR was noninferior with respect to echocardiographic indexes of valve stenosis, functional status, and quality of life. Exploratory analyses suggested a reduction in the rate of major adverse cardiovascular and cerebrovascular events and no increase in the risk of stroke.

CONCLUSIONS

In patients with severe aortic stenosis who are at increased surgical risk, TAVR with a self-expanding transcatheter aortic-valve bioprosthesis was associated with a significantly higher rate of survival at 1 year than surgical aortic-valve replacement. (Funded by Medtronic; U.S. CoreValve High Risk Study ClinicalTrials.gov number, NCT01240902.)

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*A complete list of the investigators, institutions, and research organizations participating in the U.S. CoreValve High Risk Study is provided in the Supplementary Appendix, available at NEJM.org.

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Aortic stenosis is a debilitating disease in elderly persons that carries a dismal prognosis after symptom onset.[1] Although surgical aortic-valve replacement remains the standard treatment for aortic stenosis,[2] many patients are not suitable candidates for surgical replacement owing to an increased risk of death during surgery.[3,4] Transcatheter aortic-valve replacement (TAVR) with a balloon-expandable device improves survival, as compared with medical therapy, in patients with severe aortic stenosis who cannot undergo surgery.[5] Balloon-expandable TAVR and surgical aortic-valve replacement are associated with similar survival rates at 1 year among patients considered to be at high surgical risk, although the frequency of neurologic events is higher among patients treated with balloon-expandable TAVR than among those treated surgically.[6,7]

An alternative transcatheter bioprosthesis comprising a self-expanding nitinol frame and trileaflet porcine pericardial valve (CoreValve, Medtronic) reduced the composite end point of death from any cause or major stroke at 1 year, as compared with an objective performance goal of medical management alone, in patients with severe aortic stenosis who were considered to be at extreme surgical risk.[8] The purpose of the present study was to assess the safety and effectiveness of TAVR with a self-expanding prosthesis as compared with surgical valve replacement in patients with severe aortic stenosis who were at increased surgical risk.

Methods

Study Design

This study was a multicenter, randomized, noninferiority trial performed at 45 clinical sites in the United States (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Medtronic funded the trial and developed the protocol (available at NEJM.org) in collaboration with the study steering committee (Table S2 in the Supplementary Appendix). The institutional review board at each site approved the study protocol. Medtronic was responsible for the selection of the clinical sites, monitoring of the data, and management of all source data and statistical analyses. The analyses for the primary and secondary end points were validated by the Harvard Clinical Research Institute (Boston). An independent clinical-events committee adjudicated all major clinical events. An independent data and safety monitoring board was responsible for study oversight.

The co-principal investigators (the first and second authors) wrote the first draft of the manuscript, and then all the authors critically reviewed it and made the decision to submit the manuscript for publication. All the authors vouch for the accuracy and completeness of the data and all analyses and confirm that the study was conducted according to the protocol.

Patient Selection

Patients with severe aortic stenosis and heart-failure symptoms of New York Heart Association (NYHA) class II or higher were eligible for inclusion in the study if they were considered to be at increased risk for undergoing surgical aortic-valve replacement. Aortic stenosis was defined as an aortic-valve area of 0.8 cm^2 or less or an aortic-valve index of 0.5 cm^2 per square meter or less and either a mean aortic-valve gradient of more than 40 mm Hg or a peak aortic-jet velocity of more than 4.0 m per second. Patients were considered to be at increased surgical risk if two cardiac surgeons and one interventional cardiologist at the investigative site estimated that the risk of death within 30 days after surgery was 15% or more and the risk of death or irreversible complications within 30 days after surgery was less than 50%. Surgical risk assessment included consideration of the Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) estimate[4] and other factors not included in the STS PROM assessment.[9] The STS PROM provides an estimate of the rate of death at 30 days among patients undergoing surgical aortic-valve replacement on the basis of a number of demographic and procedural variables. Details of the inclusion and exclusion criteria are provided in Table S3 in the Supplementary Appendix.

The investigative cardiac team at each study center presented a detailed portfolio, including the STS PROM estimate, other key surgical risk factors, and all cardiovascular imaging studies, to a national screening committee (Table S2 in the Supplementary Appendix). Trial eligibility was confirmed by consensus among at least two senior cardiac surgeons and one interventional cardiologist who were members of the screening committee. Patients were assigned to transcatheter aortic-valve replacement through the iliofemoral artery or an alternative access route (sub-

clavian artery or direct aortic approach) on the basis of computed tomographic (CT) studies. All the patients provided written informed consent.

STUDY PROCEDURES

The first three patients enrolled in the trial at each study site were considered to be "roll-in" participants. The roll-in participants did not undergo randomization but were assigned to TAVR in order to provide the participating investigators with experience with the CoreValve device. All subsequent patients were randomly assigned in a 1:1 ratio to treatment with TAVR or surgical valve replacement. Randomization was stratified according to investigational site and intended access site (iliofemoral or noniliofemoral) to ensure proportional assignment.

Patients assigned to surgical aortic-valve replacement were treated by means of conventional open-heart techniques with the use of cardiopulmonary bypass. The choice and size of the surgical prosthetic valve were left to the discretion of the surgeon. After the procedure, aspirin, at a dose of at least 81 mg daily, was given indefinitely in all the patients who underwent surgical valve replacement, including patients who continued to receive warfarin therapy.

Patients assigned to TAVR received the CoreValve self-expanding prosthesis (Fig. S1 in the Supplementary Appendix). Valve size was determined on the basis of a CT angiogram obtained before enrollment. Dual antiplatelet therapy with aspirin, at a dose of at least 81 mg daily, and clopidogrel, at a dose of 75 mg daily, was recommended before the procedure and for 3 months after the procedure, followed by aspirin or clopidogrel monotherapy at the same dose indefinitely. In the event that warfarin was indicated for other reasons, aspirin, at a dose of at least 81 mg daily, and warfarin were administered indefinitely without clopidogrel.

Follow-up assessments were performed at discharge and at 1 month, 6 months, and 1 year after the procedure. Follow-up assessments included a physical examination, NYHA classification, electrocardiography, echocardiography, quality-of-life questionnaires, and documentation of adverse events and study end points.

STUDY END POINTS

The primary end point was the rate of death from any cause at 1 year. Secondary clinical end points included the composite of major adverse cardiovascular and cerebrovascular events (defined as a composite of death from any cause, myocardial infarction, any stroke, or reintervention) at 30 days and 1 year, as well as the individual components of this composite. Definitions of these clinical end points, which are based on the definitions established by the Valve Academic Research Consortium,[10] are provided in Table S4 in the Supplementary Appendix. Improvement in symptoms was assessed with the use of the NYHA classification, and quality of life was assessed with the use of the Kansas City Cardiomyopathy Questionnaire and the Medical Outcomes Study 12-Item Short Form General Health Survey (SF-12).

In addition, echocardiographic outcomes were assessed, including the change in the mean aortic-valve gradient and the change in the effective orifice area from baseline to 1 year. An independent echocardiographic core laboratory (Mayo Clinic, Rochester, Minnesota) reviewed all echocardiograms. The Valve Academic Research Consortium definitions were used for the determination of valvular regurgitation.[10]

STATISTICAL ANALYSIS

The primary hypothesis was that the event rate at 1 year for death from any cause in the TAVR group would be noninferior to that in the surgical group, with a predefined noninferiority margin of 7.5 percentage points for the difference in risk between the two trial groups. Assuming a 1:1 ratio in the treatment assignments and an estimated rate of death at 1 year of 20% in each study group, we estimated that a total of 355 patients were required in each group for the study to have power of 80% at a one-sided alpha level of 0.05. Accounting for a 10% loss to follow-up, we calculated that we would need to enroll 790 patients.

The calculation of trial power also accounted for a secondary hypothesis, which was that the event rate at 30 days or discharge (whichever was later) for major adverse cardiovascular and cerebrovascular events in the TAVR group would be superior to that in the surgical group. The details of this power calculation are provided in the Supplementary Appendix.

The prespecified population for the primary analysis was the as-treated population, which included all the patients who underwent an attempted implantation (as defined in the Supplementary Appendix). The primary end point was also analyzed in the intention-to-treat popula-

tion, which included all the patients who had undergone randomization. Assuming that noninferiority was proved for the primary end point at a one-sided alpha level of 0.05, a subsequent test for superiority was planned at a one-sided alpha level of 0.05. Because this was a closed-test procedure, no adjustment for multiple comparisons was required.

For the secondary end points, a hierarchical testing procedure was prespecified to limit the overall type I error rate. In this procedure, each end point in the hierarchy was considered to be significant only if the P value for that end point and all prior end points indicated statistical significance. The hierarchical testing order and details of the test procedure are provided in the Supplementary Appendix. Additional end points not included in the hierarchical testing procedure were considered to be exploratory.

Categorical variables were compared with the use of Fisher's exact test or the chi-square test, as appropriate. Continuous variables were expressed as means ±SD and compared with the use of Student's t-test. Kaplan–Meier estimates were used to construct the survival curves on the basis of all available follow-up data for the time-to-event analyses. All echocardiographic measurements were evaluated with the use of a two-sample t-test or the Wilcoxon rank-sum test for continuous variables and the Mantel–Haenszel test for ordinal variables, as appropriate. All statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute).

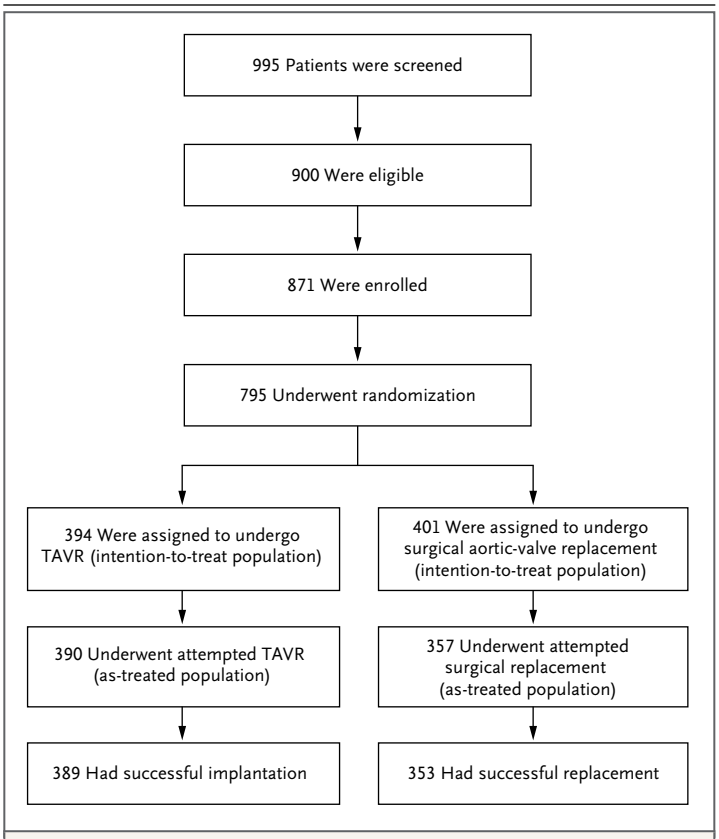

Figure 1. Randomization and Analysis Populations.
TAVR denotes transcatheter aortic-valve replacement.

RESULTS

PATIENTS

From February 2011 through September 2012, a total of 995 patients were screened for trial participation at 45 centers in the United States; of these patients, 795 underwent randomized treatment assignment (Fig. 1). The as-treated population included 747 patients, of whom 390 were treated with TAVR (performed with iliofemoral access in 323 patients and noniliofemoral access in 67), and 357 were treated with surgical aortic-valve replacement. The reasons for exclusion from enrollment and the reasons that patients did not undergo the assigned procedure are provided in the Supplementary Appendix.

The demographic and clinical characteristics of the patients at baseline according to treatment group are provided in Table 1; the characteristics of the patients who did not undergo surgery after randomization are provided in Tables S5 and S6 in the Supplementary Appendix. In the as-treated population, the mean age of the patients was 83.2 years, and 52.7% of the patients were men. On the basis of the STS PROM estimate, the average predicted mortality at 30 days was 7.4%. Diabetes mellitus was observed more often in the surgical group than in the TAVR group (45.4% vs. 34.9%, P=0.003), although there was no significant difference between the two groups with respect to diabetes controlled by insulin. A list of clinically significant coexisting conditions and indexes of frailty and disability are provided in Table S7 in the Supplementary Appendix. The majority of patients (55.8%) had a score of 5 or more on the Charlson comorbidity index (scores range from 0 to 33, with a score of ≥5 indicating a severe burden of illness).

Of the 747 patients in the as-treated population, 742 underwent successful valve implantation. The reasons for early termination of the

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Intention-to-Treat Population		As-Treated Population	
	TAVR Group (N=394)	Surgical Group (N=401)	TAVR Group (N=390)	Surgical Group (N=357)
Age — yr	83.2±7.1	83.5±6.3	83.1±7.1	83.2±6.4
Female sex — no. (%)	183 (46.4)	189 (47.1)	183 (46.9)	170 (47.6)
NYHA class — no. (%)				
Class II	56 (14.2)	53 (13.2)	56 (14.4)	47 (13.2)
Class III	258 (65.5)	277 (69.1)	255 (65.4)	248 (69.5)
Class IV	80 (20.3)	71 (17.7)	79 (20.3)	62 (17.4)
STS PROM estimate†				
Mean estimate — %	7.3±3.0	7.5±3.2	7.3±3.0	7.5±3.4
<4% — no. (%)	33 (8.4)	42 (10.5)	33 (8.5)	40 (11.2)
4–10% — no. (%)	308 (78.2)	288 (71.8)	304 (77.9)	251 (70.3)
>10% — no. (%)	53 (13.5)	71 (17.7)	53 (13.6)	66 (18.5)
Logistic EuroSCORE — %‡	17.6±13.0	18.4±12.8	17.7±13.1	18.6±13.0
Diabetes mellitus — no. (%)				
All	136 (34.5)	172 (42.9)	136 (34.9)	162 (45.4)
Controlled by insulin	43 (10.9)	49 (12.2)	43 (11.0)	47 (13.2)
Chronic kidney disease stage 4 or 5 — no./total no. (%)§	48/390 (12.3)	52/396 (13.1)	47/386 (12.2)	45/352 (12.8)
History of hypertension — no. (%)	375 (95.2)	386 (96.3)	371 (95.1)	343 (96.1)
Peripheral vascular disease — no./total no. (%)	163/391 (41.7)	169/398 (42.5)	159/387 (41.1)	148/355 (41.7)
Prior stroke — no./total no. (%)	51/394 (12.9)	53/400 (13.2)	49/390 (12.6)	50/356 (14.0)
Prior transient ischemic attack — no./total no. (%)	50/394 (12.7)	51/400 (12.8)	50/390 (12.8)	48/356 (13.5)
Cardiac risk factor — no./total no. (%)				
Coronary artery disease	297/394 (75.4)	306/401 (76.3)	294/390 (75.4)	271/357 (75.9)
Prior coronary-artery bypass surgery	117/394 (29.7)	121/401 (30.2)	115/390 (29.5)	111/357 (31.1)
Prior percutaneous coronary intervention	133/394 (33.8)	152/401 (37.9)	133/390 (34.1)	134/357 (37.5)
Preexisting pacemaker or defibrillator	92/394 (23.4)	83/401 (20.7)	91/390 (23.3)	76/357 (21.3)
Prior myocardial infarction	101/394 (25.6)	98/401 (24.4)	99/390 (25.4)	90/357 (25.2)
Congestive heart failure	376/394 (95.4)	387/401 (96.5)	372/390 (95.4)	345/357 (96.6)
Prior atrial fibrillation or atrial flutter	161/393 (41.0)	190/400 (47.5)	159/389 (40.9)	164/357 (45.9)

* Plus–minus values are means ±SD. There were no significant between-group differences in baseline characteristics, with the exception of status with respect to diabetes mellitus (P=0.02 in the intention-to-treat population, and P=0.003 in the as-treated population). NYHA denotes New York Heart Association, and TAVR transcatheter aortic-valve replacement.

† The Society of Thoracic Surgeons Predictor Risk of Mortality (STS PROM) provides an estimate of the rate of death at 30 days among patients undergoing surgical aortic-valve replacement on the basis of a number of demographic and procedural variables.

‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) is calculated by means of a logistic-regression equation, on a scale from 0 to 100%, with higher scores indicating greater surgical risk and a score of more than 20% indicating very high risk.

§ Chronic kidney disease of stage 4 is defined as an estimated glomerular filtration rate (GFR) of 15 to 29 ml per minute, and stage 5 (end-stage renal disease) as an estimated GFR of less than 15 ml per minute.

procedure in the other 5 patients, and the procedural outcomes in the patients who underwent implantation, are provided in the Supplementary Appendix. The average duration of follow-up was 14.1 months in the TAVR group and 12.8 months in the surgical group.

PRIMARY END POINT

In the as-treated analysis, the rate of death from any cause at 1 year, which was the primary end point, was lower in the TAVR group than in the surgical group (14.2% vs. 19.1%), representing an absolute risk reduction of 4.9 percentage points (upper boundary of the 95% confidence interval [CI], −0.4; P<0.001 for noninferiority; P=0.04 for superiority) (Fig. 2). The results were similar in the intention-to-treat analysis; the event rate was 13.9% in the TAVR group, as compared with 18.7% in the surgical group (absolute risk reduction, 4.8 percentage points; upper boundary of the 95% CI, −0.4; P<0.001 for noninferiority; P=0.04 for superiority). No significant interactions were observed between treatment and any of nine subgroups with respect to the primary end point (Fig. 3).

HIERARCHICAL TESTING OF SECONDARY END POINTS

The secondary end points assessed by means of hierarchical testing are shown in Table S8 in the Supplementary Appendix. Among patients who underwent successful implantation, the change in the mean aortic-valve gradient from baseline to 1 year in the TAVR group was noninferior to that in the surgical group (–39.04 mm Hg vs. –35.42 mm Hg, P<0.001 for noninferiority). The change in effective orifice area from baseline to 1 year in the TAVR group was also noninferior to that in the surgical group (1.20 cm² vs. 0.81 cm², P<0.001 for noninferiority).

The changes in the NYHA class (Fig. S2 in the Supplementary Appendix) and Kansas City Cardiomyopathy Questionnaire score were likewise noninferior in the TAVR group, as compared with the surgical group (P<0.01 for both comparisons). However, for the fifth test in the hierarchy (the rate of major adverse cardiovascular and cerebrovascular events at 30 days or discharge, whichever was later), which was also the secondary end point for which the trial was powered, the prespecified test goal of superiority was not met (8.2% in the TAVR group and 10.9% in the surgical group, P=0.10 for superiority).

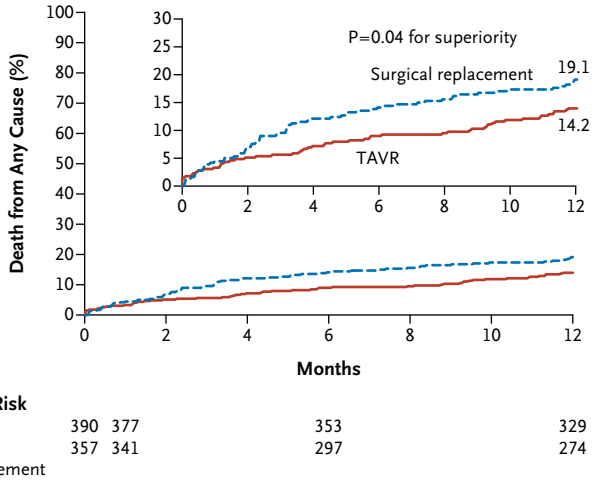

Figure 2. Kaplan–Meier Cumulative Frequency of Death from Any Cause.
The rate of death from any cause in the TAVR group was noninferior to that in the surgical group (P<0.001). A subsequent test for superiority at 1 year showed that TAVR was superior to surgical replacement (P=0.04). The inset shows the same data on an enlarged y axis.

OTHER OUTCOMES

Other clinical outcomes (Table S9 in the Supplementary Appendix) and echocardiographic outcomes (Table S10 in the Supplementary Appendix) were not included in the hierarchical testing procedure and were considered to be exploratory. The rate of major adverse cardiovascular and cerebrovascular events at 1 year was significantly lower in the TAVR group than in the surgical group (20.4% vs. 27.3%, P=0.03) (Fig. S3A in the Supplementary Appendix). The rates of any stroke were 4.9% in the TAVR group and 6.2% in the surgical group at 30 days (P=0.46) and 8.8% and 12.6%, respectively, at 1 year (P=0.10) (Fig. S3B in the Supplementary Appendix).

PROCEDURE-RELATED OUTCOMES

Procedure-related outcomes are shown in Table 2. Major vascular complications and permanent pacemaker implantations were significantly more frequent in the TAVR group than in the surgical group. Bleeding, acute kidney injury, and new-onset or worsening atrial fibrillation were significantly more common in the surgical group than in the TAVR group. There were five cases of cardiac perforation in the TAVR group and none in the surgical group. The rates of paravalvular regurgitation were significantly higher in the TAVR group than in the surgical group at all

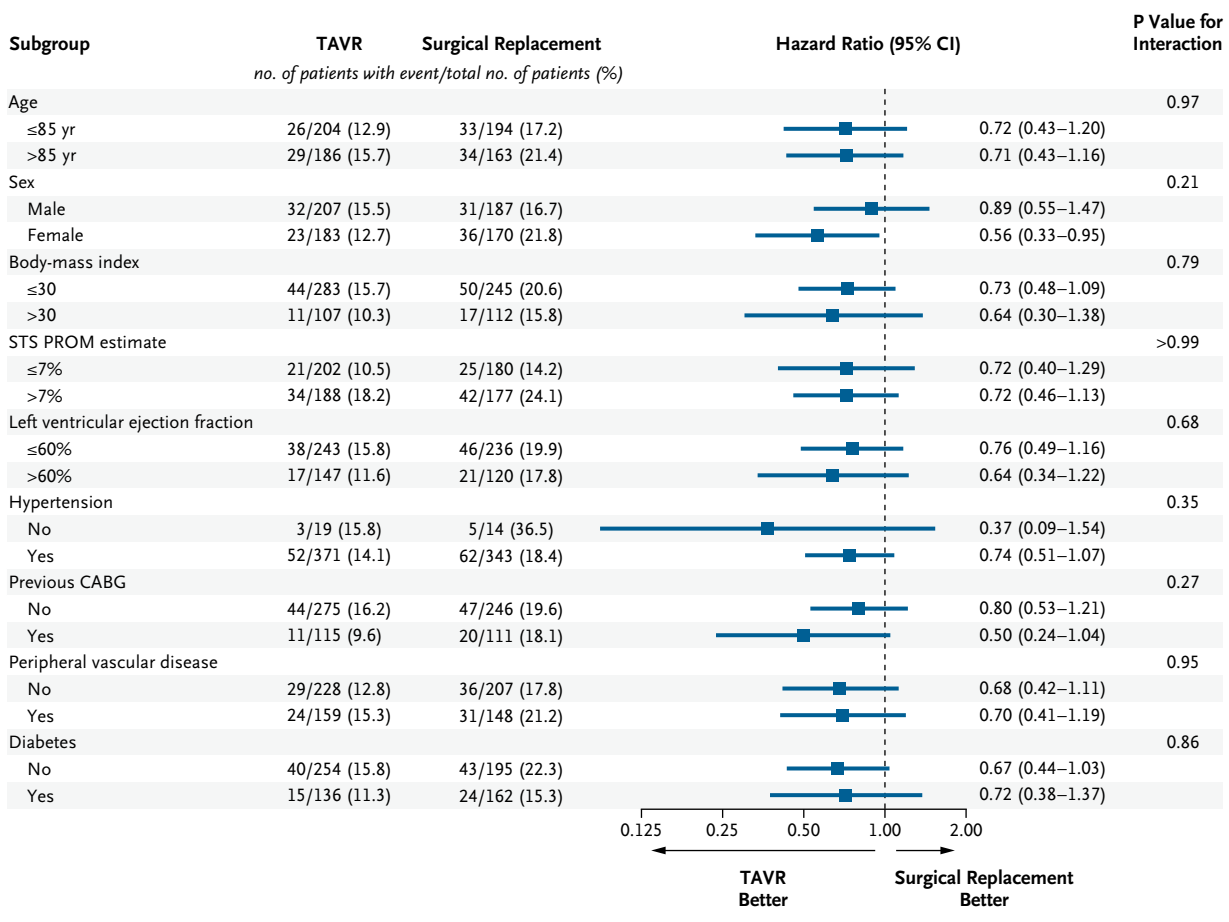

Figure 3. Subgroup Analysis for the Rate of Death from Any Cause at 1 Year.

The survival benefit with TAVR was consistent across nine clinical subgroups. The percentage of patients with an event represents the Kaplan–Meier event rate at 1 year. Horizontal lines indicate 95% confidence intervals. The body-mass index is the weight in kilograms divided by the square of the height in meters. The Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) provides an estimate of the rate of death at 30 days among patients undergoing surgical aortic-valve replacement on the basis of a number of demographic and procedural variables.[4] CABG denotes coronary-artery bypass grafting.

time points after the procedure (Table S10 in the Supplementary Appendix).

DISCUSSION

In our study, survival at 1 year after TAVR was superior to that after surgical aortic-valve replacement in symptomatic patients with severe aortic stenosis who were at increased surgical risk. The survival benefit with TAVR was consistent across nine clinical subgroups. Hierarchical testing of secondary end points showed that echocardiographic indexes of valve stenosis, functional status, and quality of life were noninferior with TAVR. Exploratory analyses also suggested that the occurrence of major adverse cardiovascular and cerebrovascular events was significantly lower through 1 year in the TAVR group than in the surgical group (P=0.03 by the log-rank test). The exploratory analyses did not show an increased risk of stroke with TAVR, as compared with surgery.

Our study relied on an interdisciplinary cardiac team that collectively determined the risk of death from aortic-valve surgery for each patient,[11,12] on the basis of assessments that incorporated both traditional surgical-risk assessment tools, such as the STS PROM,[4] and other risk factors that are not part of the STS PROM.[9] Our

Table 2. Procedural Outcomes at 30 Days and 1 Year in the As-Treated Population.*

Outcome	30 Days			1 Year		
	TAVR Group (N=390)	Surgical Group (N=357)	P Value	TAVR Group (N=390)	Surgical Group (N=357)	P Value
	number (percent)			*number (percent)*		
Major vascular complication	23 (5.9)	6 (1.7)	0.003	24 (6.2)	7 (2.0)	0.004
Bleeding event†						
Life-threatening or disabling bleeding	53 (13.6)	125 (35.0)	<0.001	64 (16.6)	136 (38.4)	<0.001
Major bleeding	109 (28.1)	123 (34.5)	0.05	114 (29.5)	130 (36.7)	0.03
Acute kidney injury	23 (6.0)	54 (15.1)	<0.001	23 (6.0)	54 (15.1)	<0.001
Cardiogenic shock	9 (2.3)	11 (3.1)	0.51	9 (2.3)	11 (3.1)	0.51
Cardiac perforation	5 (1.3)	0	0.03	5 (1.3)	0	0.03
Permanent pacemaker implantation	76 (19.8)	25 (7.1)	<0.001	85 (22.3)	38 (11.3)	<0.001
New-onset or worsening atrial fibrillation	45 (11.7)	108 (30.5)	<0.001	60 (15.9)	115 (32.7)	<0.001

* All data are reported as Kaplan–Meier estimates at the specific time point and do not equal the number of patients with events divided by the total number of patients in each treatment group. The corresponding P values were calculated by the log-rank test for all data through 30 days or 1 year.

† Life-threatening or disabling bleeding was defined as fatal bleeding; bleeding in a critical area or organ (e.g., intracranial, intraspinal, intraocular, or pericardial) necessitating pericardiocentesis, or intramuscular bleeding with the compartment syndrome; bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery; bleeding associated with a drop in the hemoglobin level of 5 g per deciliter or more; or bleeding necessitating a transfusion of 4 units or more of whole blood or packed red cells. Major bleeding was defined as bleeding associated with a drop in the hemoglobin level of at least 3.0 g per deciliter or bleeding requiring transfusion of 2 or 3 units of whole-blood red cells; in addition, major bleeding was bleeding that did not meet the criteria of life-threatening or disabling bleeding.

study differed from the Placement of Aortic Transcatheter Valves (PARTNER) A (PARTNER A) trial, which included patients who were considered to be candidates for surgery even though they were at high surgical risk and which used an STS PROM estimate of 10% or higher as a guideline for study inclusion.[6] The mean STS PROM estimate of the patients in our study was 7.4%, which is similar to the STS PROM estimate of 7% that has been reported with commercial use of the balloon-expandable transcatheter heart valve in the United States.[13] The actual mortality at 30 days among patients who underwent surgery was 4.5%, which was substantially lower than the predicted rate at enrollment.

We hypothesized that a number of factors may have contributed to the survival benefit observed with TAVR. These include the less-invasive nature of transcatheter replacement and more rapid mobilization and recovery with this approach, as compared with surgery, coupled with relatively low rates of strokes, paravalvular regurgitation, and vascular complications. Unlike the PARTNER A trial,[6] our study did not show an increased risk of neurologic events with the self-expanding TAVR prosthesis, as compared with surgery.

The rate of moderate or severe paravalvular regurgitation at 1 year was 6.1% in our study, as compared with rates of 7 to 16% in other multicenter series.[14-19] Although the rates of moderate or severe paravalvular regurgitation were higher at all time points after TAVR than after surgical valve replacement, they did not have an adverse effect on overall survival in our study. We found that the majority of patients (76.2%) with moderate or severe paravalvular regurgitation at discharge had mild or no regurgitation at 1 year. These outcomes may be attributable to the use of CT assessment of aortic annular diameter for valve-size selection before enrollment,[20,21] higher placement of the valve within the aortic annulus, and sustained expansion of the nitinol frame.

More patients declined surgical replacement after randomization than declined transcatheter replacement. We found no important differences between the risk profiles of patients who underwent surgical replacement and those who were assigned to the surgical group but withdrew consent. We also note that the rate of death within 30 days after surgery (4.5%) was lower than the estimated rate specified for inclusion in the study (≥15%), suggesting that the trial population may

have been at lower risk than was intended. Adverse events, including major vascular complications, conduction-system disturbances requiring permanent implantation of a pacemaker, and (rarely) cardiac perforation, were more frequent with TAVR than with surgical valve replacement.

In conclusion, we compared TAVR with the CoreValve self-expanding prosthesis with surgical aortic-valve replacement in patients with symptomatic, severe aortic stenosis who were at increased surgical risk. The rate of death from any cause at 1 year was significantly reduced with TAVR performed with the self-expanding prosthesis.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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